Mauro Filipe da Silva Pinto

Evaluation and Prediction of Multiple Sclerosis Disease Progression

Thesis submitted to the Faculty of Sciences and Technology of the University of Coimbra for the degree of Master in Biomedical Engineering with specialisation in Bioinformatics, supervised by Prof. Dr. César Teixeira and Professor Dr. Pedro José Mendes Martins.

February 2018

Universidade de Coimbra

• U C •

FCTUC FACULDADE DE CIÊNCIAS
E TECNOLOGIA
UNIVERSIDADE DE COIMBRA

Mauro Filipe da Silva Pinto

Evaluation and Prediction of Multiple Sclerosis Disease Progression

Dissertion presented to the University of Coimbra
in order to complete the necessary requirements to
obtain the Master's degree in Biomedical Engineering.

Supervisors:
Prof. Dr. César Alexandre Domingues Teixeira (Orientator)
Prof. Dr. Pedro José Mendes Martins (Co-Orientator)

Coimbra, 2018

This work was developped in collaboration with:

Centre for Informatics and Systems of the University of Coimbra

Serviço de Neurologia dos Hospitais da Universidade de Coimbra

Acknowledgments

É mesmo hora, meu amor, de me ir embora. Coimbra, a cidade que Italo Calvino se esqueceu de descrever.

Em primeiro lugar, gostaria de agradecer aos Professores César Teixeira e Pedro Martins, não apenas por toda a orientação e disponibilidade mas também por todo o clima de à vontade que se proporcionou. Pelas conversas paralelas que, de Engenharia Biomédica, muito pouco tinham. E que bem que sabiam. Foi um prazer.

À Doutora Sónia Batista, um obrigado muito especial também pela orientação e por toda a paciência necessária para se conseguir fazer a ponte entre o modo de pensar médico e o modo de pensar informático. Neste tipo de trabalhos, sem esta recta final, perde-se a aplicabilidade toda do trabalho.

Ao Professor Alexandre Pinto, obrigado pela experiência das RAN's. Foi pena não poder ter entrado para este trabalho. Ficou, no entanto, a memória de um processo muito creativo acima de tudo, com grande liberdade e vontade de experimentar.

Aos Neurorradiologistas Luís Rito Cruz e Mafalda Mendes Pinto, o meu muito obrigado por toda a paciência e por todo o tempo e todo trabalho que vos foi pedido, não só a recolher as ressonâncias mas também a fazer a marcação das lesões. Tenho a certeza que esta base de dados servirá de ponto de partida para muitos trabalhos vindouros relacionados com esta área.

Ao Departamento de Física, para sempre DF, aos Professores que me inspiraram nesta aventura de 5 anos, quer pela paixão, quer pela sua maneira singular de ver esta coisa em que vivemos, ao Núcleo de Estudantes do Departamento de Física, o NEDF, à Rádio Universidade de Coimbra, a RUC dos 107.9fm, o meu mais que sincero obrigado. Deram-me mais do que eu alguma vez vos poderei dar.

À Engenharia Biomédica e aos meus colegas de curso, que com vocês todos os dias aprendi algo.

Ao meu grupo de amigos da universidade, ao meu grupo de amigos de Estremoz, um muito obrigado. Vemo-nos por cá, por aí.

Se Coimbra é uma lição de sonho e tradição, se Coimbra é uma canção, se Coimbra é um livro, se Coimbra ainda é capital, se Coimbra é dos amores, se Coimbra é dos doutores, do Choupal e da Lapa e se aprende a dizer saudade, então Coimbra não foi Coimbra. Coimbra foi simplesmente alguém chamada Francisca Pereira que viveu em Celas. Coimbra foi tudo. Tão pequena que coube na palma da minha mão e tão grande que nunca me pude afastar o suficiente para deixar de a ver. Um obrigado especial a ti, Francisca.

Aos meus pais. Acabou uma luta, mas muitas mais virão. Cá estaremos os três na luta, cá estaremos.

Ao André. Serás sempre a pessoa modelo.

"É hora, meu amor, de me ir embora"

Balada da Despedida 2017, Grupo de Fado "Insígnia"

Abstract

Evaluating and predicting Multiple sclerosis disease progression can be a complicated task. With an original database from Centro Hospitalar e Universitário de Coimbra curated by the author, this progression was studied. This database is constituted by clinical history data and by MRI brain scans. The raw database was handled in order to be possible to create different databases with different progression perspectives. As a consequence, a deeper study was achieved.

For each created database, the predictors with higher discriminatory power were chosen regarding several labels, like MS course and others directly related to EDSS (the global scale used for quantifying the neurological condition of an MS patient and, as consequence, the disease progression). At the data processing level, an alternative MRI brain scan processing method was developed, as well as an extensive feature extraction from several brain structures/regions and tissues, such as white matter, grey matter and cerebrospinal fluid. This was possible due to the use of the MRI brain SRI-24 atlas.

For each database in each situation, machine learning algorithms were applied with different partition methods and with or without dimensionality reduction techniques. With the obtained results in the form of confusion matrix and area under the ROC curve, all databases were handled with not only a unification goal but also with a complementarity objective regarding the disease progression.

Thus, it was possible to build an evaluation performance system in order to choose the best-ranked labels in terms of prediction in a general term for every case scenario. At the clinical data level, the predictors' selection was significantly interesting. Not only the expected predictors were chosen, such as EDSS-related variables, gender, MS course, number of years with MS but also other non-expected but interesting factors. These were the ratio of pyramidal tract clinical manifestations in the first 2 years after MS onset and MS initial manifestations related to spinal cord and optic pathways.

At imaging level, the performed study had an intensive feature extraction, not only in the brain as a complete structure but also in several smaller specific structures

and tissues. In a similar process when compared to the one of finding the most important features in clinical data, two regions with a significant discriminatory power were found: superior frontal gyrus and orbitofrontal gyrus.

Keywords: Multiple sclerosis; Machine Learning; Disease Progression Tracking; MRI.

Resumo

Avaliar e prever a progressão de Esclerose Múltipla num doente pode ser uma tarefa complicada. Com uma base de dados tratada pelo autor, originária do Centro Hospitalar e Universitário de Coimbra, esta progressão foi estudada. A base de dados é constituída por dados clínicos e ressonâncias magnéticas ao cérebro. Devido ao número reduzido de doentes, esta foi tratada de modo a ser possível a criação de várias bases de dados com diferentes perspectivas da progressão de modo a abranger um estudo com a maior amplitude possível.

Para cada base de dados, foram escolhidos os predictores com maior poder discriminatório para determinados acontecimentos, tais como o subtipo de Esclerose Múltipla e outros relacionados com o EDSS (a escala global utilizada para quantificar a condição neurológica de um doente e, por consequência, da progressão da doença). Ao nível de tratamento de dados, este projeto conta ainda com um método alternativo de pré-processamento de ressonâncias magnéticas, bem como a extracção de estruturas cerebrais e de tecidos como matéria cinzenta, branca e líquido cefalorraquidiano, com a utilização do atlas cerebral SRI-24.

Para conjunto de predictores de cada base de dados e para cada acontecimento desejável de ser previsto, foram aplicados algoritmos de machine learning com diferentes métodos de partição e com ou não técnicas de redução de dimensionalidade. Com os resultados em forma de matriz confusão e em área debaixo da curva ROC, todas as bases de dados foram compreendidas com um objetivo de unificação e complementaridade relativamente à progressão da doença.

Assim, foi possível construir um sistema de avaliação de performance e escolher os acontecimentos com maior capacidade de serem previstos pelos modelos criados. Ao nível dos dados clínicos encontraram-se os predictores com maior poder, estando não só aqueles que já eram esperados, como variáveis relacionadas com o valor de EDSS, subtipo de Esclerose Múltipla, género, número de anos de doença mas também outros factores não esperados mas interessantes. Estes foram o rácio de manifestações de Esclerose Múltipla encontradas ao nível das vias piramidais nos primeiros dois anos da doença e manifestações iniciais da mesma ao nível da espinal

medula e das vias ópticas.

A nível imagiológico, o estudo teve uma extracção de predictores intensa, não só na totalidade do cérebro como também em inúmeras estruturas cerebrais específicas e tecidos. Num processo semelhante de encontrar as regiões com maior poder de discriminação nas bases de dados clínicas, foram encontradas duas regiões: córtex frontal superior e córtex orbitofrontal.

Palavras-chave: Esclerose Múltipla; Machine Learning; Rastreamento da progressão da doença; Ressonância Magnética.

List of Figures

List of Tables

Acronyms

ANIFC Associação Nacional de Imagiologia Funcional Cerebral
AUC Area Under the Curve
CGMM Constrained Gaussian Mixture Model
CHUC Coimbra Hospital and University Centre
CIS Clinically Isolated Syndrome
CNN Convolutional Neural Network
CNS Central Nervous System
CSF Cerebrospinal Fluid
CT Computed Tomography
DIS Dissemination in Space
DIT Dissemination in Time
EDSS Expanded Disability Status
EM Expectation-Maximization
FCM Fuzzy C-Means
FFT Fast Fourier Transform
FLAIR T_2-weighted-Fluid_Attenuated Inversion Recovery
FS Functional System
GA Glatiramer Acetate
GLCM Gray Level Co-Ocurrence Matrix
GLM Generalized Linear Model
GM Grey Matter
HUC Hospitais da Universidade de Coimbra
ICBM International Consortium for Brain Mapping
ICNAS Instituto de Ciências Nucleares Aplicadas à Saúde
IIH Intensity Inhomogeneity
IIT Illinois Institute of Tecnhology
IM Intramuscular

IMI unidade de Ressonância Magnética in Centro Hospitalar de Leiria
IV Intravenous
KNN K-Nearest Neighbors
LDA Linear Discriminant Analysis
LONI Laboratory of Neuro Imaging
LOO Leave One Out
LPBA40 LONI Probabilistic Brain Atlas
MICCAI Medical Image Computing and Computer Assisted Intervention
MP Methylprednisolone
MRI Magnetic Resonance Imaging
mRMR minimum Redundancy Maximum Relevance
MS Multiple Sclerosis
NMO Neuromyelitis Optica
NPV Negative Predictive Value
PCA Principal Component Analysis
PD Proton Density-Weight MRI
PP Primary Progressive
PPV Predictive Positive Value
PR Progressive Relapsing
QDA Quadratic Discriminant Analysis
RAD HUC'S Radiology Service
RBF Radial Basis Function
ROC Receiver Operating Characteristic
RR Relapsing Remitting
SP Secondary Progressive
SPM Statistical Parametric Mapping
SVM Support Vector Machine
T1 T_1 weighted MRI
T2 T_2 weighted MRI
TOADS Topology preserving Anatomical Segmentation
VEP Visual Evoked Potential
WM White Matter

Index

Chapter 1

Introduction

1.1 Context

Multiple Sclerosis (MS) is a disabling neurological condition with a tremendous variability concerning clinical manifestations. It is considered to be an autoimmune disease of the Nervous Central System (CNS), characterized by its attacks directed against myelin, causing its loss. Myelin is a substance that surrounds the axon of neurons by forming an electrically insulating layer. It is very important for the CNS since it ables a faster communication between neurons. This condition is believed to be triggered by environmental agents acting in genetically susceptible people.

Currently, brain and spinal cord magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) analysis and evoked potential tests are used as main diagnostic tools. However, it would be desirable to reduce the number of diagnostic tests. The MRI technique has as goal the visualization of brain and spinal cord lesions. The CSF liquid is obtained through a lumbar puncture, which is a very effective method in terms of diagnosis but very invasive and painful. Besides, it is tested for the presence of oligoclonal bands which are not specific for MS. Evoked potential tests are relatively easy to perform and a good complement. However, the most important diagnostic tools are clearly MRI and CSF [2, 6, 18].

Although disease impact varies between patients, it is possible to list several probable symptoms due to lesions caused by the already mentioned myelin loss and axonal injury: optic lesions and sensitivity decrease, pain, weakness and sensory loss in the arms/legs, fatigue, memory problems and depression, among others.

Since these lesions are a pathological hallmark of MS, commonly seen in the

spinal cord, optic nerves, brainstem/cerebellum and periventricular white matter, imaging techniques are a very interesting approach when it comes to diagnosis and predicting prognosis. Actually, studies reveal a correlation between lesion dissemination in space and time on MRI and MS. This factor is one of the most important in the McDonald Criteria, which is the gold standard diagnosis method used by physicians [16].

This thesis aims to evaluate and predict the MS progression via pattern recognition techniques in the patient's medical and treatment history and in the patient's MRI history. In order to do this, image processing and segmentation tools for lesion detection and region examination will also be an interesting focus in this project. Another interesting focus is related to the source of the used database since it belongs to Coimbra Hospital and University Centre (CHUC) and since it was curated by the author for this dissertation.

1.2 Motivation

Evaluating and predicting the progression is not an easy task, due to its influence in the entire CNS and to the heterogeneous clinical manifestations. This can be comproved by the lack of efficient computational algorithms based on clinical and lesion information regarding this condition. Besides, there is not a gold standard method for segmentation and lesion detection for MS in brain MRI yet, despite the large quantity of investigation done in this area [6].

In order to gain effectiveness and to reduce time, the development of a standard acquisition protocol with an automatic trustful procedure would be an important key to assist a physician in the moment of a diagnosis and/or prognosis. Besides, some MS manifestations can take more time to be diagnosed or to develop into more severe scenarios, which makes interesting the possibility to predict sooner these cases.

The possibility to analyze and ensemble data from different sources, such as MRI image segmentation, temporal analysis and pattern recognition techniques via clinical and treatment history, also constitutes a very strong reason for the development of this work, since the last two have not been explored as much as the first one. Since lumbar puncture is an evasive and a very painful method but effective in the diagnosis, it is desirable to build an equally efficient algorithm mainly based on minimally invasive procedures.

1.3 Main goals

In order to fully evaluate and predict this disease progression, some goals must be accomplished:

1. Construction of a robust algorithm against different metrics, enabling a quantification of the disease progress through time and space lesion dissemination and several clinical events.
2. Application of several heuristics, biologic and clinical rules into a mathematical complex model, providing a total MS context and clear interpretation in order to get an automatic and assisted diagnosis and prognosis.
3. A clinical view with a clear interpretation of the obtained results in order to open new investigation scenarios regarding new variables and other factors.

Summing up, there is the need to provide an effective procedure for all case scenarios, standardizing a valid, efficient and trustful framework, able to ensemble different natures of data.

1.4 Structure

This dissertation is divided into nine chapters. **Chapter 1** presents a brief discussion and context of MS, explaining the complexity and current situation regarding diagnosis and progression algorithms. The motivation of working in this condition is also addressed according to the previously mentioned situation. The main goals desirable to be achieved are also presented. At last, the thesis structure is presented.

Chapter 2 provides the basic and necessary knowledge of MS from a medical point of view in order to address this dissertation. It is explained its complexity, exploring several aspects like the existing subtypes of clinical manifestations, diagnosis and treatment. The historical context is also approached throughout the chapter in order to understand its medical evolution.

Chapter 3 provides the fundamentals of the MRI techniques.

Chapter 4 summarizes the current situation regarding computational algorithms using MRI lesions and clinical information. MS lesion detection and segmentation is also deepened since it is an area of development. Some other natures of work like different information ensemble or different pattern recognition approaches are also mentioned.

Chapter 5 presents a full description on CHUC's database, describing the way

the data was collected and also the way some related problems were addressed.

Chapter 6 describes all the experimental work performed on the database, moreover how feature engineering and data manipulation was used to construct more specific databases. Feature selection and machine learning techniques procedures are presented. The MRI images processing is also described.

Chapter 7 presents not only the obtained results of the machine learning algorithms,

Chapter 8 provides a detailed discussion about all thesis aspects and about the obtained results. A deeper data exploration regarding the results output is also performed.

Chapter 9 highlights the critical points found in chapter 8, along with a reflection about all the dissertation work and with future perspectives.

Chapter 2

Multiple Sclerosis

MS is the most common disabling neurological condition that affects young adults (from 20 to 45 years of age). Having a high social burden, its course is highly heterogeneous and unpredictable [2]. It is characterized by initial episodes of reversible neurological problems often followed by progressive neurological deterioration over time [19]. Like some other autoimmune diseases, it is more common in females.

2.1 Brief historical context

Jean Martin Charcot, a French neurologist, was the first to describe MS, in 1868. The observation of an unusual accumulation of inflammatory cells in a perivascular distribution within the brain and spinal cord white matter in patients suffering from episodes of neurologic dysfunction led to the term *sclerose en plaques disseminées*. Some years after, in 1948, it was observed an abnormal increase in the quantity of oligoclonal immunoglobulin in the Cerebrospinal Fluid (CSF) of patients with MS, evidencing its inflammatory character.

Currently, this condition is known to be associated with not only multiple sharply demarcated plaques in the CNS white matter, especially in periventricular regions, brain stem and spinal cord but also with substantial axonal injury and myelin loss [20]. Although its cause is unknown, a combination of genetic susceptibility and non-genetic events seem to be involved, resulting in a recurrent series of self-sustaining attacks against the CNS [19].

2.2 Epidemiology

There are temporal and geographic variations when it comes to MS risk, where the migrating activity is an influent factor. Despite the considerable number of potential causal factors studied, no single one was successfully identified as related to this condition [1].

MS is a rarer condition in tropical areas when compared to temperate ones. Regions where it is visible a higher prevalence include northern Europe, northern USA, Canada, southern Australia and New Zealand, while medium prevalence includes regions like southern Europe, northern Australia and the southern USA. Asia and South America seem to be low prevalence regions. Due to some high variations over very small geographic distances, it seems that ethnicity (and therefore genetics) and socioeconomic structure of a country constitute also an interesting demographic factor, as visible in Figure 2.1 [1, 21].

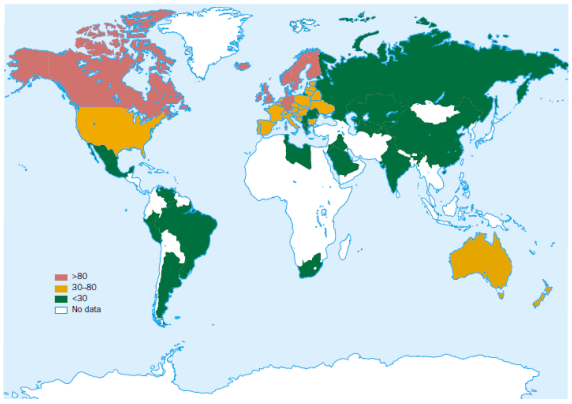

Figure 2.1: Worldwide prevalence of MS per 100 000 population, 2004 [1].

The prevalence seems to increase with repeated surveys in the same areas over time. These results can be a consequence of better access to medical facilities, advances taken in this condition (eg: MRI techniques and the revised McDonald criteria) and an increase in life expectancy time [21]. As previously mentioned, migration activity seems to be an influent factor, where differences between migrants and their offspring reflect an early timing of environmental exposure or an inevitable phenotypical selection process. In fact, early studies claim that a critical age for migration activity regarding MS seems to be around 15 years [22].

The family relationship was also studied, providing some useful epidemiological insights. It seems to exist a relationship between family and MS. Monozygotic twins have higher concordance than dizygotic. In fact, some studies reveal a certain proportionality between the degree of kinship and the influence of this condition

[22, 21].

2.3 Diagnosis

There is important to denote the nonexistence of a single diagnostic test. The diagnosis must be based on a series of evidence, like the existence of lesion dissemination in time and space. The lesion dissemination can be seen in time and space through MRI [16, 19].

The gold standard criteria for this disease is the McDonald Criteria, which is directed for an early diagnosis with a high degree of both specificity and sensitivity. With this, it is expected a better counseling and an earlier treatment. Better results are achieved with a typical Caucasian adult as these criteria were built paying attention to higher prevalence regions.

In order to understand the diagnosis, it remains very important to do a correct interpretation of the symptoms and signs of a patient, like an attack/relapse, defined as an acute inflammatory demyelinating event in the CNS, current or historical, lasting at least 24 hours with an absence of fever or infection [16].

Regarding the criteria for the Dissemination in Space (DIS), it can be claimed its occurrence when a patient has at least one T2 Lesion in at least two of the following CNS areas: periventricular, juxtacortical, infratentorial and spinal cord. With respect to Dissemination in Time (DIT), its occurrence can be proved by the presence of a new T2 and/or gadolinium-enhancing lesion on a follow-up scan. However, it is possible to identify a dissemination without a follow-up MRI, if a simultaneous presence of gadolinium-enhancing and nonenhancing lesions can be identified [16].

Clinical findings in the CSF, such as an abnormal increase in the immunoglobulin G or other oligoclonal bands, strongly suggest inflammatory demyelinating lesions [16].

In order to understand the full diagnosis mechanism, it is presented in Table 2.1 from the 2010 McDonald Diagnostic Criteria [16].

As a result, if these criteria are satisfied and any other possible diagnoses are excluded, the patient is diagnosed with MS. If the criteria are not fully satisfied but there is suspicious of this disease, the diagnosis is "possible MS". The final result can also deny this condition if another diagnosis arises during the evaluation, resulting in a better explanation according to the clinical findings [16, 19].

Since the 2010 McDonald Criteria focused on differential diagnosis in order to avoid a treatment misguidance, special attention must be paid to Neuromyelitis

Table 2.1: The 2010 McDonald Criteria for Diagnosis of MS [16].

Clinical Presentation	Additional Criteria Needed for MS diagnosis
At least 2 attacks; objective clinical evidence of at least 2 lesions or objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack	None
At least 2 attacks; objective clinical evidence of 1 lesion	DIS; Await a further clinical attack implicating a different CNS site
1 attack; objective clinical evidence of at least 2 lesions	DIT; Await a second clinical attack
1 attack; objective clinical evidence of 1 lesion (CIS)	DIS and DIT; Await a second clinical attack
Insidious neurological progression suggestive of MS (PP)	1 year of disease progression plus 2 of the following: 1. Evidence for DIS in the brain base on >1 T2 lesions in a MS characteristic region 2. Evidence for DIS in the spinal cord based on >2 T2 lesions in the cord

Optica (NMO) and related disorders. This phenotype was agreed to be separated from typical MS due to the shown poor response against therapy [16].

2.4 Types

Since the course of this condition can have a high variability, several patterns of clinical manifestation were grouped. Thus, in 1996, the first standardized definitions were discussed and implemented, as shown below [23, 19, 2, 24]:

1. **Relapsing-remitting (RR):** the most common form, affecting 85% of MS patients, is characterized by a series of relapses followed by periods of neurological improvement and/or symptoms absence, known as remission periods.
2. **Secondary progressive (SP):** may be gradually developed in patients who suffer from relapsing-remitting type. With secondary progressive type, the patient's neurological condition continues to worsen with or without remission periods.
3. **Primary progressive (PP):** a less common form, affecting 10% of MS patients, associated with a gradual decrease in the patient's neurological condition without the occurrence of relapses or remission periods. It's also characterized by its higher resistance against treatment.
4. **Progressive-relapsing (PR) :** A rarer form, affecting this way less than 5% of the patients. It is progressive from the start accompanied by relapses and worsening symptoms, without any remission periods [2, 24].

In Figure 2.2, these clinical definitions are shown according to the respective

patient's Expanded Disability Status Scale (EDSS) score over time, it is possible to have a clearer vision about the existing differences between each MS course. The EDSS scale is described at the end of the present chapter.

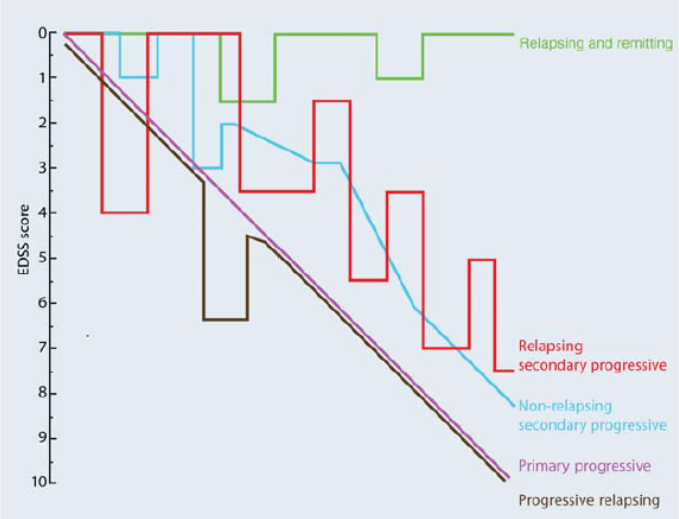

Figure 2.2: Types of MS courses (from the top to the bottom): Relapsing and remitting (green), Relapsing secondary progressive (red), Non-relapsing secondary progressive (blue), Primary progressive (purple) and Progressive-relapsing (black), according to the 1996 MS clinical course descriptions [2]. Greater the EDSS, worser is the patient's neurological capacity.

In 2011, a Committee constituted by the European Committee for Treatment and Research in MS, the National Multiple Sclerosis Society and other experts like the MS Phenotype Group, started to review the 1996 clinical course descriptions, whose main goal was to improve the phenotype description by including an updated clinical terminology, MRI and other techniques [24].

It was decided that the basic features of 1996 would be maintained with some improvements and clarifications. Clinically Isolated Syndrome (CIS) was one of the terms included, which means the first clinical presentation of a disease with characteristics of an inflammatory demyelination. However, as it can be seen in Figure 2.3, a CIS may not correspond afterward to MS. In order to do so, the criteria of dissemination in time must also be accomplished.

Since it is possible to observe dissemination in time and in space with a single MRI scan, the problem of having a high number of patients categorized with CIS is diminished.

Activity was also introduced in this revision, where it is recommended to assess the disease activity by clinical and brain imaging criteria in an annual way. For progressive subtypes this is recommended, however, there was no consensus about the optimal assessment frequency in terms of imaging. Thus, as an example, a patient is

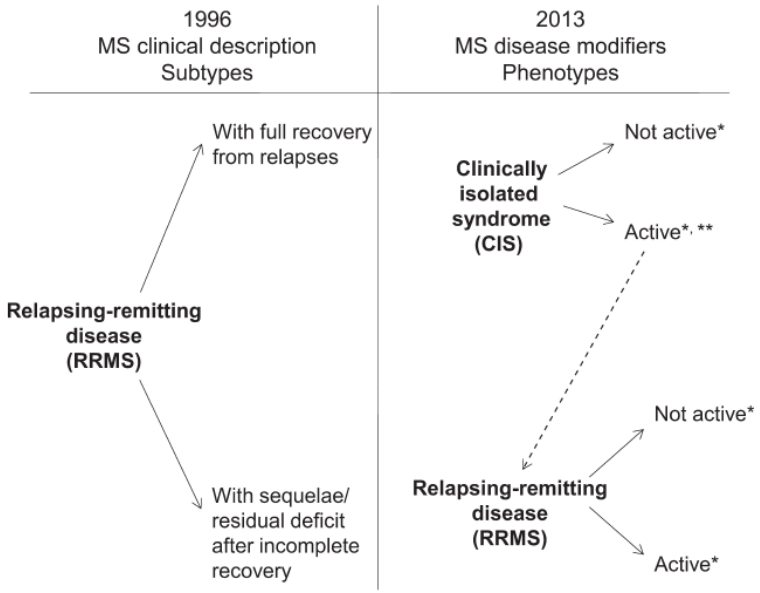

Figure 2.3: The differences observed between the 1996 and the 2013 MS phenotype descriptions in the Relapsing remitting course [3].

considered to have an RR active phenotype when a new gadolinium-enhancing lesion is present in a current MRI. If no signs of relapses, gadolinium-enhancing activity or newly enlarging T2 lesions during assessment period are present, the clinical course is considered as a non-active one.

Progression is another factor needing to be addressed, determining whether or not there is clinical evidence of this phenomenon. This progression is independent of relapses. It is characteristic of patients suffering from a progressive disease course. It was suggested that this should be determined with an annual period as progression is considered to have a non-uniform course. As a consequence, a disease course is considered to have progression if significant changes are observed over a period of a year. This way, as an example, a patient with SP course with a gradual worsening of its neurological condition and with gadolinium-enhancing lesions present on MRI is classified as an active SP with progression. In Figure 2.4, it is possible to see the different MS course phenotypes according to progression and an active or not form.

This way, in 2013 the new revision of the MS clinical courses was published, concluding the studies started in 2011. An MS course of a new patient starts with an active or a non-active CIS, where this factor is determined by clinical relapses and/or MRI activity, specifically by the existence of contrast-enhancing lesions or enlarging T2 lesions over an annual period. If there is a subsequent series of events that fulfill the current MS diagnostic criteria, the disease course becomes an RR one (this course can also be active or non-active).

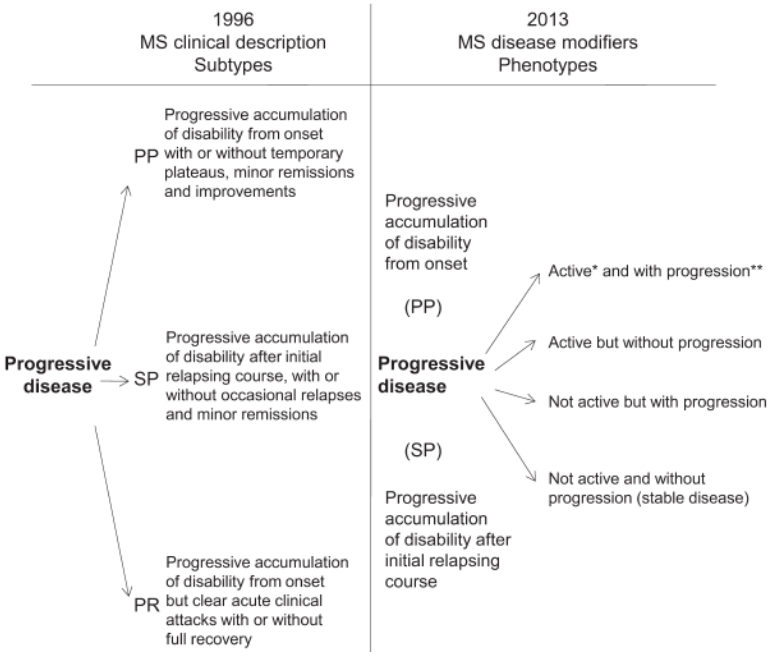

Figure 2.4: The differences observed between the 1996 and the 2013 MS phenotype descriptions in the courses with progression symptoms [3].

If a progressive accumulation of disability is observed from the onset, the PP arises while SP is characterized by a progressive accumulation of disability after an initial relapsing course instead [24].

There are also the terms benign and malignant, which are not a standard pattern of MS clinical manifestation, but rather indicators of the severity over time. As a result, benign is not a common form, known by few attacks and little or no disability after 20 years, while malignant is known for frequent disabling attacks along with an incomplete recovery, resulting in a fast progressive development. Their criteria are not precise, since different experts tend to use varying the EDSS rating to define these indicators [2, 24, 25].

2.5 Therapy

The underlying pathologic mechanism of this condition as an inflammatory CNS disease was critical for the existing classes of immunomodulating options responsible for the course of MS. Studies with each drug separately showed common findings, such as a reduced number of relapses and a lower severity associated, a reduced development of new inflammation areas as shown in MRI and a clear delay in the short-term disease progression. In contrast to the variability of therapies for MS, a curing agent yet remains to be found [19, 20, 23].

Normally, either an induction or an escalation approach is taken as the first step for a patient's treatment. An escalation approach consists of a first-line medication followed by a second line if an unsatisfactory response is shown to the first drug. The first line consists of a drug with high safety and a moderate efficacy, while the second is more effective and less safe. An induction approach starts immediately with a second-line treatment, which is intended for patients with frequent and severe relapses. Normally, the decision of which approach to take is made taking special attention to the first symptoms. The commonest one is the escalation form [26, 25].

Regarding acute relapses (Table 2.2), they are treated with a short course, from 3 to 5 days with a corticosteroid, typically intravenous (IV) methylprednisolone (MP) or dexamethasone due to its rapid onset of action and to its low adverse effects. Besides MP or dexamethasone, there is also the possibility to use oral prednisolone over a period of 2 to 3 weeks. In a presence of a patient whose acute exacerbations do not react to steroid treatment, plasma exchange may be an effective alternative. Long-term use of these drugs is not recommended since is unclear its improvement in the long-term course of MS [23, 25].

Table 2.2: Most common treatments regarding acute relapses.

Name	Duration	Administration
Methylprednisolone	3-5 Days	IV
Dexamethasone	3-5 Days	IV
Prednisolone	2-3 Weeks	Oral
Plasma Exchange	NA	IV

Avonex, Rebif (Interferon beta-1a), Betaseron and Extavia (Interferon beta-1b), are Beta Interferon drugs, produced naturally by the human body through the secretion of immune cells whose function is the regulation of the immune system. This class of drugs, used in first-line treatments, has been shown to reduce the relapse frequency, reducing the appearance of inflammatory brain MRI lesions by 50% to 80%. Side effects such as flu-like symptoms, liver, thyroid function abnormalities and depression are recurrent within patients having this drug. While Betaseron and Rebif are administered subcutaneously, Avonex is taken via intramuscular (IM) injection [2, 19, 23, 26].

Known as Copaxone, Glatiramer Acetate (GA) is a first-line treatment drug. Side effects differ from the ones found with Beta Interferon treatment, where transient skin reactions and tightness of the chest and facial flushing are the most common. Unlike Beta Interferon, GA is not associated with liver and thyroid abnormalities. Its administration occurs subcutaneously [2, 19, 23, 26].

Tysabri (Natalizumab) when used, is administered via IV once a month, reducing the relapse frequency. Its major adverse effect is the progressive multifocal leukoencephalopathy, known as a viral brain infection leading to death or to a severe disability condition. Longer the administration period, greater the risk of this adverse effect. Natalizumab is considered a second line treatment drug.

In the past, Novantrone (Mitoxantrone) was used to treat some forms of cancer, since it has the ability to suppress the activity of certain parts of the immune system, like T cells, B cells and macrophages. As MS is an autoimmune disease, these were responsible for leading attack against myelin. This drug should be used in patients whose episodes of relapses and remission are very frequent or whose MS course takes the secondary progressive form, which makes it a second or third line treatment. Posterior side effects of Mitoxantrone include cardiotoxicity, myelosuppression and leukemia, where the last one a rare situation. It is administered via IV infusion [2, 19, 26].

As seen, there is a great variety of drugs with the objective of MS treatment. The most common are mentioned and summarized above in Table 2.3, adapted from [19].

Table 2.3: Most common drugs used in MS therapy.

Name	**Line of Treatment**	**Administration**
Avonex	First line	IM
Rebif (Interferon beta-1a)	First line	Subcutaneously
Betaseron	First line	Subcutaneously
Extavia (Interferon beta-1b)	First line	Subcutaneously
Copaxone (Glatiramer acetate)	First Line	Subcutaneously
Tecfidera (Dimethyl fumarate)	First Line	Oral
Aubagio (Teriflunomide)	First Line	Oral
Gilenya (Fingolimod)	Second or Third Line	Oral
Tysabri (Natalizumab)	Second or Third Line	IV
Novantrone (Mitoxantrone)	Second or Third Line	IV

All mentioned drugs so far have been approved by FDA. However, the use of others for MS treatment is not a rare event, like the case of Azathioprine (Imuran),

Methotrexate or Mycophenolate Mofetil (CellCept) [19].

It is possible to verify a certain difficulty when it comes to choosing an appropriate treatment for the primary progressive form as it carries the worst prognosis. Thus, there is not a consensual treatment in these situations. Thus, it is often the use of off-label treatment drugs [26].

2.6 Expanded Disability Status Scale (EDSS)

EDSS is a proposed method by Kurtzke [17] to evaluate the neurological condition of an MS patient through time. With this scale, a grade is given according to the state of eight Functional Systems (FS): Pyramidal, Cerebellar, Brain Stem, Sensory, Bowel & Bladder, Visual, Cerebral or Mental and Other or Miscellaneous. Higher the EDSS scale value, worst is the neurological condition of the patient. Figure 2.5 brings an intuitive and quick idea about its meaning. Basically, the EDSS will provide a scale ranging from 0 (normal) to 10 (death by MS). Levels from 1.0 to 4.5 correspond to patients still having a high degree of ambulatory ability. Patients with levels from 5.0 to 9.5 have a severe loss of ambulatory ability [17, 4].

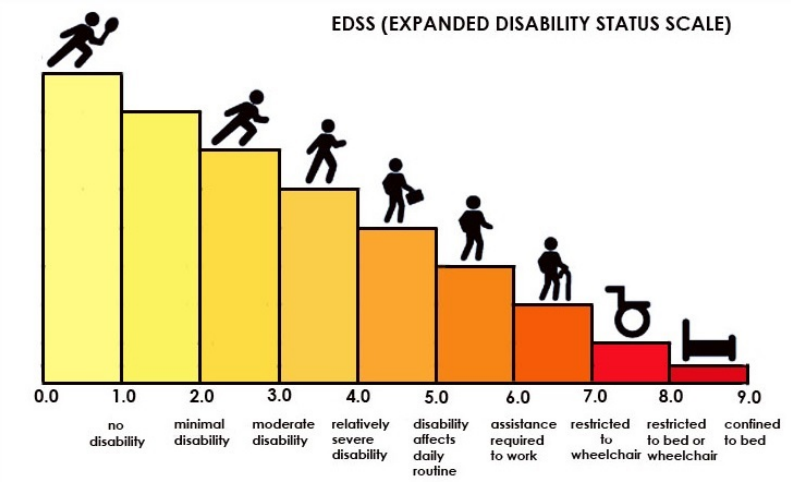

Figure 2.5: An intuitive graphical view on the EDSS scale [4].

All FS except the Miscellaneous one are graded on a scale from 0 (normal condition) to 5 or 6, corresponding to the worst system condition. The Other or Miscellaneous system is binary, where grade 0 corresponds to normal and 1 to some abnormality present. The FS Scale tables are present in section A.

Thus, the EDSS scale [17] is briefly enumerated below:

1. **EDSS 0**. Normal neurologic exam; Cerebral grade 1 acceptable.
2. **EDSS 1.0**. No disability, minimal signs in one FS; Cerebral grade 1 excluded.

3. **EDSS 1.5**. No disability, minimal signs in more than one FS; Cerebral grade 1 excluded.
4. **EDSS 2.0**. Minimal disability in one FS; one FS grade 2, others 0 or 1.
5. **EDSS 2.5**. Minimal disability in two FS; two FS grade 2, other 0 or 1.
6. **EDSS 3.0**. Moderate disability in one FS; one FS grade 2, others 0 or 1.
7. **EDSS 3.5**. Fully ambulatory but with moderate disability in one FS or mild disability in three or four FS though fully ambulatory; one FS grade 3 and others 0 or 1 or three/four FS grade 2, others 0 or 1.
8. **EDSS 4.0**. Fully ambulatory without aid, self-sufficient. Able to walk 500 meters without aid or rest; one FS grade 4, others 0 or 1 or other combinations exceeding the previous limits.
9. **EDSS 4.5**. Fully ambulatory without aid, self-sufficient much of the day. Able to walk 300 meters without aid or rest; one FS grade 4, others 0 or 1 or other combinations exceeding the previous limits.
10. **EDSS 5.0**. Ambulatory without aid or rest for about 200 meters. Disability severe enough to impair full daily activities; one FS grade 5 and others 0 or 1 or other combinations exceeding the previous limits for EDSS 4.0.
11. **EDSS 5.5**. Ambulatory without aid or rest for about 100 meters. Disability severe enough to preclude full daily activities; one FS grade 5 and others 0 or 1 or other combinations exceeding step 4.0.
12. **EDSS 6.0**. Intermittent or unilateral constant assistance required to walk about 100 meters with or without resting; usually combinations with two FS having grade 3+.
13. **EDSS 6.5**. Constant bilateral assistance required to walk about 20 meters without resting; usually combinations with more than two FS having more grade 3+.
14. **EDSS 7.0**. Unable to walk beyond about 5 meters even with aid, essentially restricted to wheelchair; combinations with more than one FS with grade 4+, very rarely pyramidal grade 5 alone.
15. **EDSS 7.5**. Unable to take more than a few steps, restricted to wheelchair may need aid in transfer and may require a motorized wheelchair; combinations with more than one FS grade 4+.
16. **EDSS 8.0**. Essentially restricted to bed much of the day but may be out of bed itself much of the day. Retains many self-care functions; usually FS grade 4+ in several systems.
17. **EDSS 8.5**. Essentially restricted to bed much of the day, has some effective

use of arms and retains some self-care functions; usually FS grade 4+ in several systems.

18. **EDSS 9.0**. Helpless bed patient; can communicate and eat; usually combinations where most systems have grade 4+.
19. **EDSS 9.5**. Totally helpless bed patient; almost all systems have grade 4+.
20. **EDSS 10**. Death to MS.

As it can be seen, the EDSS scale can be very helpful in evaluating neurologically a patient, since it was specifically designed for the MS disease progression. However, one must not forget that although its specific criteria, there is present some subjectivity. Sometimes it is hard to distinguish some criteria between the steps, happening the same in each FS scale. Nevertheless, it is the most used system for neurological condition evaluation in MS patients.

Chapter 3

Magnetic Resonance Imaging

MRI is a non-ionizing technique, with a good spatial resolution and excellent soft tissue contrast used to obtain anatomical images of human body parts containing hydrogen. In general, its temporal resolution is slower when compared with ultrasound techniques or with a CT, having scans lasting from three to ten minutes. As a result, an MRI exam is more susceptible to the patient's motion. In essence, it measures the magnetic properties of tissues by studying the behavior of atomic nuclei with spin and magnetic moment different than zero, through the application of external magnetic fields [27, 3].

3.1 Physical principles

MRI principles can be explained according to Quantum Mechanics, due to the intrinsic property of quantization: the measurement of a physical variable will result in a multiple of a unitary amount named quantum. Thus, when measuring an electron energy, its possible values are restricted to:

$$E = -m\gamma\hbar B_0, \text{ with } m = -j, -j+1, ..., j-1, 1,$$

The quantum is $\gamma\hbar B_0$, where B_0 is the magnetic field intensity, γ the gyromagnetic ratio (ratio of its magnetic moment to its angular moment) and $\hbar$ the Planck constant. The constant j is the spin quantum number, where a given nucleus is characterized by a unique spin value. This value will depend on the number of protons and neutrons present in the nucleus.

Focusing now on the proton (nucleus of $^1_1$H) example for being the simplest case (j=1/2): logically, the spin value of the nuclei must be non-null, existing a

special preference for the proton, not only for having j=1/2 but also because of its abundance in the human body. In the absence of an external magnetic field, the total magnetization is null due to the random precessing direction. When applied an external magnetic field, the precession takes a parallel direction, as visible in Figure 3.1.

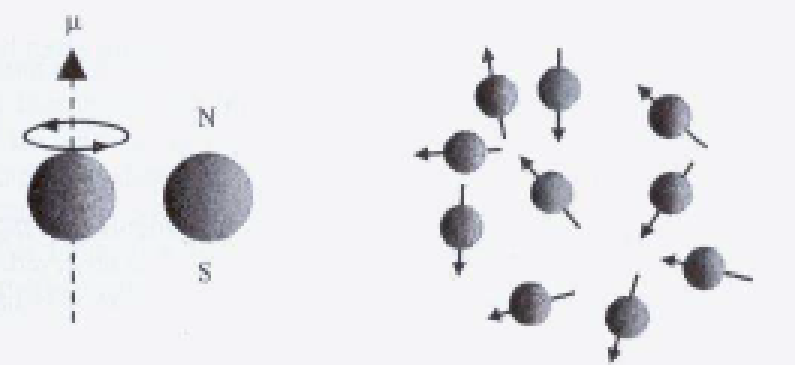

Figure 3.1: The differences between the precessing direction in the presence (left) and absence (right) of an external magnetic field [3].

This way, there are two possible quantized energy levels:

$$E(spin - up) = -\tfrac{1}{2}\gamma\hbar B_0,$$
$$E(spin - down) = +\tfrac{1}{2}\gamma\hbar B_0.$$

This phenomenon is known as the Zeeman effect, where the "spin-up" level has the lowest energy, being this way preferentially occupied. As a consequence, the total magnetization is no longer null. Since there is a random distribution of a large number of spins with transverse components in all directions of the x-y plane, its sum will be zero, making the total magnetization parallel to the external magnetic field direction (3.2). The net magnetization vector $\vec{M}$ in equilibrium will be:

$$\vec{M} = (0,0,M_0).$$

The net magnetization $\vec{M}_0$ in a volume element (voxel) is proportional to its spin quantity. Since direct measurement of the magnitude M_0 is not possible, there is the need to disturb this equilibrium in order to measure the transverse component of the magnetization (x-y component). To do this by interacting with the nuclei magnetic fields, the resonance condition through the transmission of photons with the frequency obtained by the Larmor equation must be achieved:

$$\omega_0 = \gamma B_0, \text{ for a photon with energy } E = \hbar\omega_0.$$

According to this, if $B_0 = 1T$ (Tesla), for example, the Larmor frequency is approximately 42.6 MHz for the proton case, since $\gamma\hbar B_0$ is the needed energy for a spin on the "spin-up" (lowest energy) state transit to the "spin-down" (highest energy) one [27, 3].

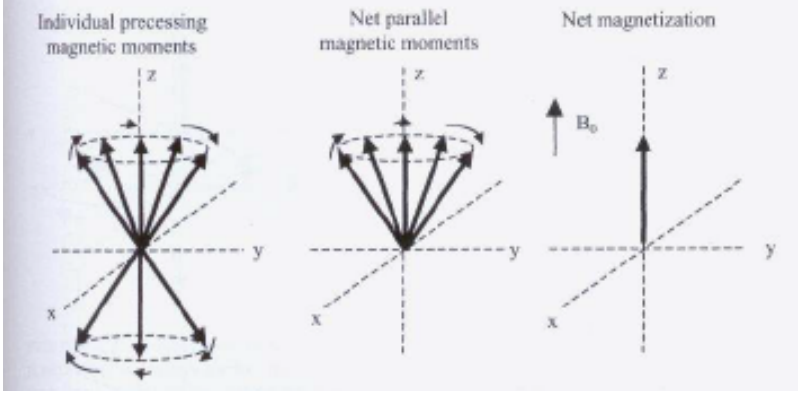

Figure 3.2: Since there is a random distribution of a large number of spins with transverse components in all directions of the x-y plane, its sum will be zero, making the total magnetization parallel to the external magnetic field direction [3].

3.2 Interaction with tissue

As mentioned, the dynamic equilibrium can be disturbed via transmission of photons with the appropriate energy, as described by the Larmor Equation. Taking the proton case and the previous example: in the case of a magnetic field of 1 T, this can be realized with an electromagnetic wave at a frequency of 42.6 MHz, as calculated.

This electromagnetic wave is named as RF wave. It is generated by sending alternate currents in two coils (Figure 3.3) along the x and y-axis of the coordinate system. Since its energy is equal to the energy difference between the two proton possible states, spins can change its occupancy level, resulting in a disturbance leading to the appearance of a longitudinal component of the net magnetization vector $\vec{M}$. This field forces all individual spins to rotate in phase. This phenomenon is known as phase coherence. [27].

The application of this RF field is not enough to produce the MRI image: it is necessary to apply flip angles. Two of the most important flips are the 90ª pulse, bringing the $\vec{M}$ along the y-axis and the 180º pulse, rotating $\vec{M}$ to the negative z-axis.

With the 90º pulse, both energy levels will have the same occupancy of spins, having no longitudinal magnetization, that is:

$$\vec{M} = (0,M_0,0).$$

With the 180º pulse, also named as inversion pulse, the majority of spins occupy the highest energy level:

$$\vec{M} = (0,0,-M_0).$$

When the RF magnetic field is turned off, the system will return to its dynamic

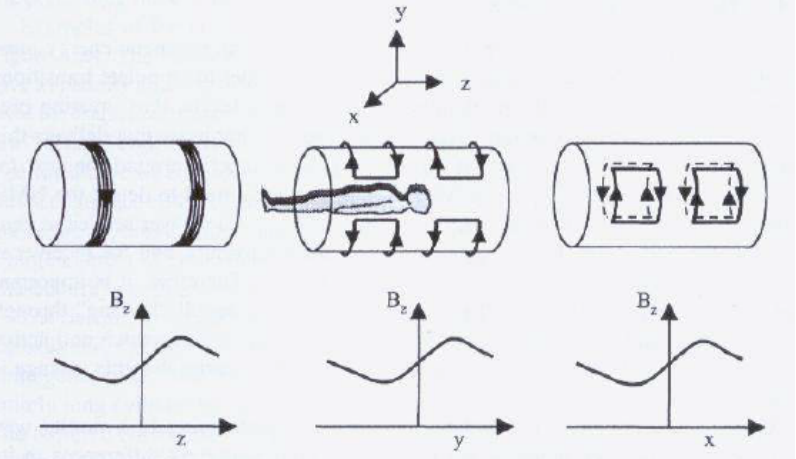

Figure 3.3: The basic design of the magnetic field gradient coils used. The arrows indicate the direction of the current flow, where each coil is constituted by multiple turns of wire and responsible for the production of external magnetic fields [3].

equilibrium, making the transverse component return to zero (Spin-Spin Relaxation) and the longitudinal component to return to M_0 (Spin-Lattice Relaxation) [27, 28].

Physically, each spin vector has a different magnetic influence due to the surrounding molecules and atoms and its structures. A proton from a H_2O will have a different influence from a proton belonging to a Methyl group. The spin-rotation will be influenced by this factor, resulting in a loss of phase coherence and, as a consequence, a decrease in the transverse component. This phase coherence can be conceptualized as the maintenance of a constant phase relationship between all the magnetic moments. Thus, even if the magnetic field B_0 was homogeneous, the spin precession would be different due to the magnetic fields of the surrounding environment. This process can be modeled as a first-order model, where the time constant of the exponential decay is called the spin-spin relaxation time (T_2) :

$$\vec{M}_{tr}(t) = \vec{M}_{tr}(0)e^{-\frac{t}{T_2}}$$

In fact, the loss of coherence does not only arise from the surroundings, but also from spatial variations in the magnetic field within the body. These variations have two different origin sources: the impossibility to design a perfectly uniform magnetic field over the entire body and the local variations in the magnetic field due to the different tissues. The last one is more pronounced at boundaries, especially air/tissue and bone/tissue [27, 3].

T_2 is the time needed for the transverse component to reach 37% of its maximum value [28].

Spin-lattice relaxation is the energy phenomenon responsible for the return of the longitudinal component of the net magnetization vector to M_0. Its physical

basis involves the loss of proton energy to the surrounding lattice, leading to an increase of molecule vibrations that will be transformed into heat. This process can be modeled as a first-order model, where the time constant of the exponential growth is called the spin-lattice relaxation time (T_1). It is the time needed for the transverse magnetization to recover 63% of its maximum :

$$\vec{M}_z(t) = \vec{M}_0(1 - e^{\frac{-t}{T_1}}).$$

Thus, both T_1 and T_2 are properties that depend intrinsically on the tissue type. On every tissue, the first one is always larger when compared to the second [27, 3, 28].

3.3 Imaging

Most clinical studies acquire a series of slices of the anatomical region of interest. where each slice is characterized by a defined orientation and thickness. As a consequence, the slice selection is realized through the adequate choice of the RF field frequency and through the adequate magnetic field gradient.

To construct an image it is necessary a mechanism able to distinguish several points from a certain tissue. This problem was handled through the application of a magnetic field gradient. By applying a gradient and not a static field, the magnetic intensity will change evenly according to the propagation direction. As a consequence, spins from different slices (perpendicular regions to the propagation direction) will precess at different frequencies. This is the reason why slice selection is made by requiring the adequate choice of the RF field frequency and magnetic field gradient, existing this way a certain freedom for the possibility to capture images of the human body by different angles (Figure 3.4). By changing the axis of the magnetic fields and changing the axis of the magnetic fields gradients it is possible the existence of different slice orientations.

The thickness (T) of each slice can be determined with:

$$T = \frac{2\triangle\omega_s}{\gamma G_{slice}}.$$

The slice thickness can be increased by the decrease of the magnetic field gradient or by the increase of the RF bandwidth. The ideal pulse shape for the RF is the rectangular one, having the same incidence angle applied to all protons. Besides this, its Fourier transform is a sinc function, having more frequency precision since the frequency spectrum is narrower.

Another magnetic field is applied, transversal to the other two (in the x-axis). Through the application of two perpendicular gradients, there is an encoding phase and a frequency phase. This way, it is possible to choose automatically a point to

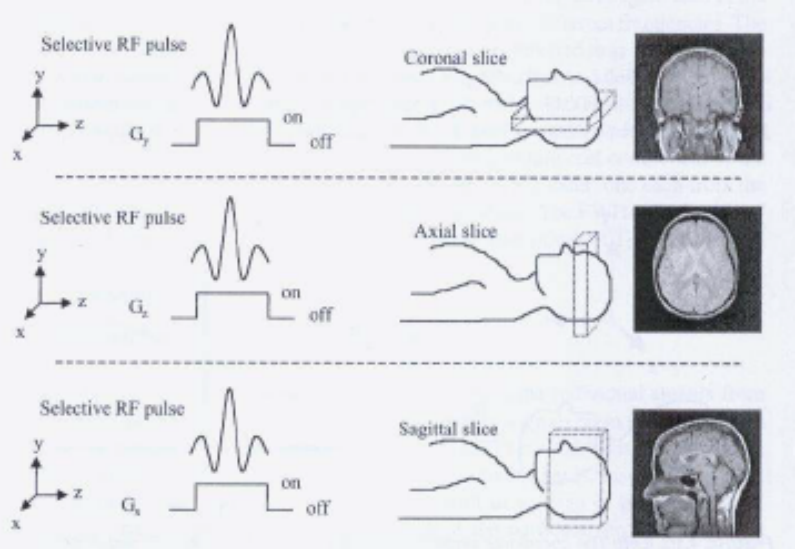

Figure 3.4: By selecting an adequate RF pulse and the respective magnetic gradient fields, it is possible to capture images from different angles, having therefore coronal, axial and sagital slice orientations [3].

represent a certain volume (voxel) [3, 28].

3.3.1 Spin echo pulse Sequence

The two-dimensional Fourier transform Spin Echo imaging is the most used technique in MRI due to the existing pulse sequence flexibility and to the existing freedom when it comes to choosing the weight influence of either T_1 or T_2 relaxation times.

The 2D Spin Echo pulse sequence is constituted by the following steps:

1. Application of a slice selection gradient G_z with a 90º and a 180º RF pulse. The first pulse is responsible for the creation of the precess transverse magnetization, while the second one is responsible for removing most of the already mentioned artifacts present in T_2 (non-magnetic homogeneities). Each pulse will be applied simultaneously with G_z.
2. Application of the phase-encoding gradient G_y.
3. Application of the frequency-encoding gradient G_x and signal measuring.

The acquired raw data constitutes a 256×256 matrix since 256 rows are measured by applying 256 phase-encoding gradients and 256 samples per row are taken during a measurement [27, 3].

3.3.2 Weighted imaging

The intensity of an axial image acquired through the spin-echo sequence is given by:

$$I(x,y) \propto \rho(x,y)(1 - e^{\frac{-TR}{T_1}}))e^{\frac{-TE}{T_2}},$$

where $I(x,y)$ is the pixel intensity at each point (x,y) and $\rho(x,y)$ the number of points at each point, known as proton density. As it can be seen, the first order models of spin-spin relaxation and spin-lattice relaxation are present, representing T_2 and T_1 weighting: $1 - e^{\frac{-TR}{T_1}}$ represents the extent to which the image intensity is influenced by the different T_1 tissue values and $e^{\frac{-TE}{T_2}}$ the extent to which the image intensity is influenced by the different T_2 tissue values.

TR and TE values are also chosen according to the target tissues, with the goal of providing the biggest contrast possible (Figure 3.5). For example, if TR is similar to the tissue T_1 values, the image has a bigger $T_1 - weight$. If the chosen TR is much greater than any T_1 value, it will not be possible to distinguish any tissue with this term. A similar relationship is applied to TE and T_2-weighting [3].

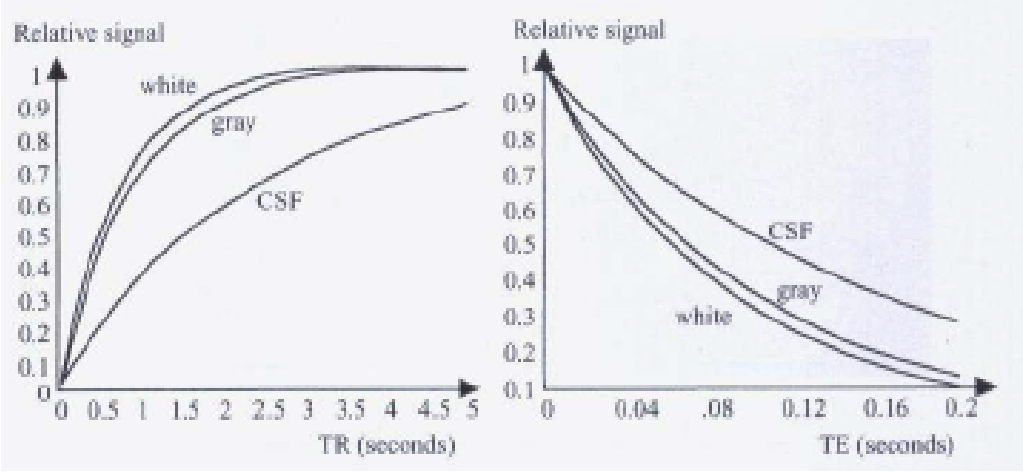

Figure 3.5: The effect of the TR (left) and TE (right) time parameters on the relative signal intensity from CSF, white and gray matter in the brain [3].

This way, images can be acquired with proton density-weight, with T_1 weight or T_2 weight. To achieve a proton density-weight, one must choose a TR much longer than tissue T_1 and a TE much smaller than the tissue T_2, producing this way contrast mainly based on the number of protons. To acquire a T_1 weighted image, one must choose short TE and TR values, while to acquire a T_2 weighted image one must use long TE and TR values [3, 28]. T_1 weighted images are often called only T1, just like T_1 weighted images (T2) and Proton Density-Weight (PDw or PD).

There is also a common weighted image named T2-weighted-Fluid_Attenuated

Inversion Recovery (FLAIR). Basically, the sequences use very long TR and TE values, removing the CSF from the resulting images. Figure 3.6 is illustrative of the image differences while using different TR and TE ponderations.

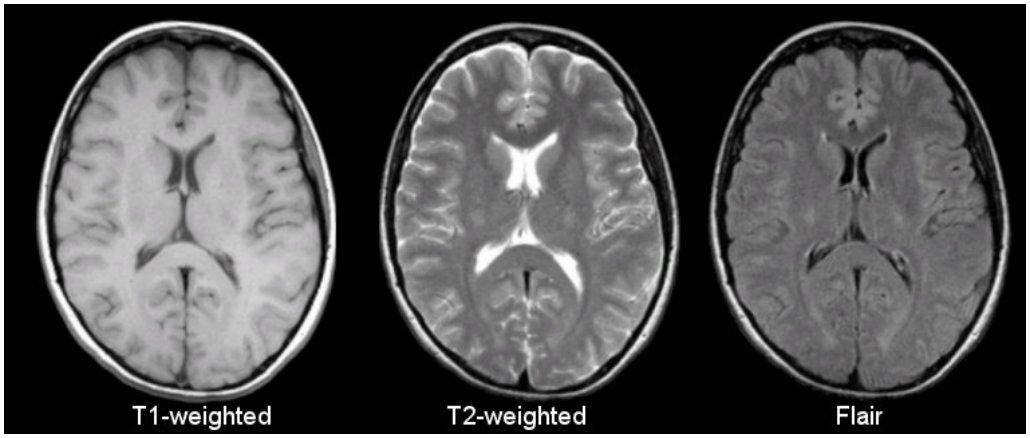

Figure 3.6: Different weighted images, from left to right: T1, T2 and FLAIR [5].

3.3.3 Contrast agents

In most of the clinical diagnoses, there is a contrast/noise ratio high enough on the acquired images to distinguish healthy tissue from pathological one. However, in some situations such as the detection of very small lesions, MRI contrast agents can be used to increase the contrast. There are two classes of MRI contrast agents: paramagnetic agents and superparamagnetic, also named as ferromagnetic agents.

Paramagnetic contrast agents are based on metal ions due to a large number of unpaired electrons, shortening the tissue T_1 relaxation time. Since the magnetic moment of an electron is up to 660 times as big as the magnetic moment of the proton, these unpaired electrons will result in a big contrast due to the significant increase in the magnetic moment. Gadolinium is especially used due to its seven unpaired electrons (Gd^{3+}).

Since metal ions are toxic to the human body, there is the need to bind it to a chelate, working as a chemical cage. The detected signal does not have a direct source of the contrast agent, but rather its biodistribution through the effect on the relaxation times of the neighboring water molecules.

The most commonly used paramagnetic contrast agent is gadolinium diethylen-etriaminepentaacetic acid (Gd-DTPA).

Superparamagnetic MRI contrast agents consist of small magnetic particles containing iron, having high magnetic moments due to the cooperative alignment of the electron spins. These work by causing inhomogeneities in the local magnetic

field, causing a reduction in signal intensity in the tissues, shortening its T_2 [3].

3.4 Multiple Sclerosis findings on MRI

A patient suffering from MS will present characteristic abnormalities in the brain: T1-hypointense and T2-hyperintense lesions. These abnormalities are often found in a periventricular distribution. However, it's not uncommon to find these white matter lesions in other locations, such as the subcortical white matter, optic nerves, corpus callosum, internal capsule, cerebellar peduncles, brainstem and spinal cord.

With the administration of a contrast agent, some MS lesions are enhanced, depending on its age and activity. After 2 months of its activity period, the contrast will no longer exist on these. Therefore, contrast agents are useful for evaluating DIT.

When comparing T2 with T1 scans (Figure 3.7), it is visible a discrepancy between the size of the same lesion, reflecting different properties/components related to edema, inflammation and demyelination. Despite the fact that seems to exist a causal relation between lesions and symptoms, there is a poor correlation between MRI findings and clinical events, since it is common to find frequent enhancing lesions in clinically stable patients.

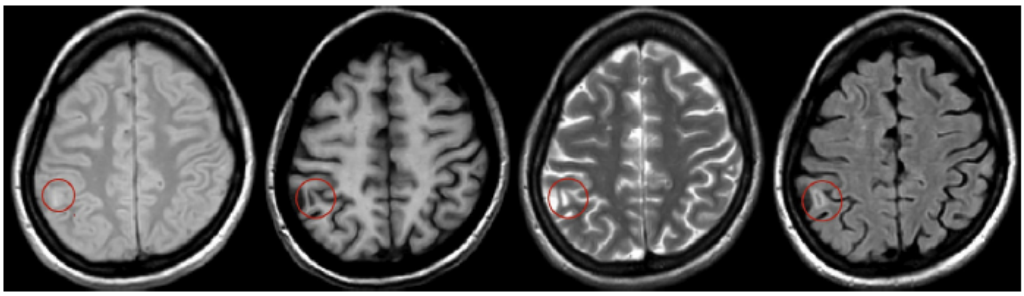

Figure 3.7: Example of a juxtacortical lesion (red). From left to right: PD, T1, T2, and FLAIR images of an MS patient [6].

For a proper detection of demyelinating lesions in the white matter, the MRI images must provide a high tissue/lesion and a high CSF/lesion ratios, permitting an immediate detection [29].

Chapter 4

State of the Art

There is already a considerable quantity of research work regarding segmentation of MS lesions in MRI scans. In fact, it is arguably the most common approach for computer-aided diagnosis of MS despite the possibility to ensemble different sources of data or despite the possibility to explore the disease progression via pattern recognition using several metrics, such as EDSS or MS type.

Lesion detection can be performed in three different ways: manually, semi-automatically and automatically. While a manual detection is time-consuming and very susceptible to variability as it depends on the evaluator's experience (usually a physician), automatic methods tend to be completely reproducible, enabling the efficient use and processing of a large quantity of data. A semi-automatic method is a compromise between these two methods, where an algorithm helps the expert by reducing lesion segmentation time and the associated variability. Most of the proposed semiautomatic methods allow the manual detection of existing lesions, whereas the rest of the process is conducted automatically, through region growing algorithms, either intensity gradients or even fuzzy connectivity. Despite the fact that several automatic algorithms have been proposed through time, none has been employed at a wide scale, since satisfactory results have not been accomplished yet [7, 30].

As a consequence of not existing a good validation framework and because only a limited number of methods are freely available to the community, there is a lack of comparative studies of different methods. To the best of our knowledge, the MS Lesion Segmentation Challenge at the Medical Image Computing and Computer Assisted Intervention (MICCAI) in 2008 [31] is the exception to this scenario.

Both physicians and existing methods concentrate their efforts in detecting White Matter (WM) Lesions. However, it is currently known that a demyelination process occurs in parallel in the Grey Matter (GM) with MS patients, where these lesions are not easily detected as they do not alter the tissue properties of T2 and T1 in a sufficient way to be displayed in the respective MRI scans [7, 30].

The core lesion detection ideas are based on the physical properties demonstrated in Chapter 3: possible lesions as brighter regions when compared to the surrounding WM in T2 and FLAIR scans, and as darker regions in the T1 scans. These commonly have an ovoid or round shape, occurring in most cases in the periventricular WM, juxtacortical and infratentorial regions. Lesions can also be described into several groups, regarding the contrast enhancement, T2 hyperintensity and T1 hypointensity, since their appearance in different modalities has a considerable heterogeneity as well (Figure 4.1).

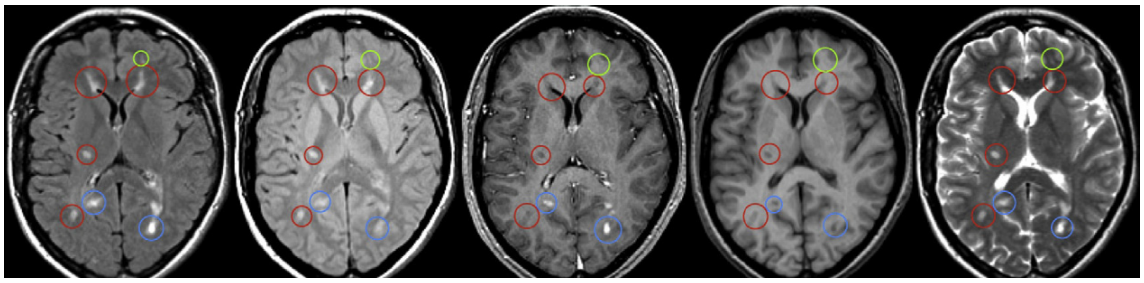

Figure 4.1: Example of the existing variability when it comes to MS Lesions. From left to right: FLAIR, PD, T1 Gd-enhanced, T1 and T2. Blue: enhancing lesions, green: T2 lesions, red: black holes. Best viewed in color. [7].

Inflammation and atrophy are translated into diffuse regions in MRI, named as visible-abnormal (WM or GM) as these processes can appear outside of lesions whose borders are clearly defined (focal lesions). Thus, lesions can also be described according to its focalization and contrast, existing diffuse regions with visible-abnormal WM and clearly focal lesions (Figure 4.2)[7].

4.1 General aspects of MRI in MS

Since the intensity is the main key for detecting regions as lesions, there is a certain absence of precise criteria. Defining an ad hoc threshold can be an almost impossible task due to the MRI acquisitions variability. Even on the same exam, the same threshold would not be effective as the lesion intensity depends on the modality and quantity of partial volume. Usually, when looking at different scans, the neuroradiologist has the need for abstracting his/her mind in order to combine

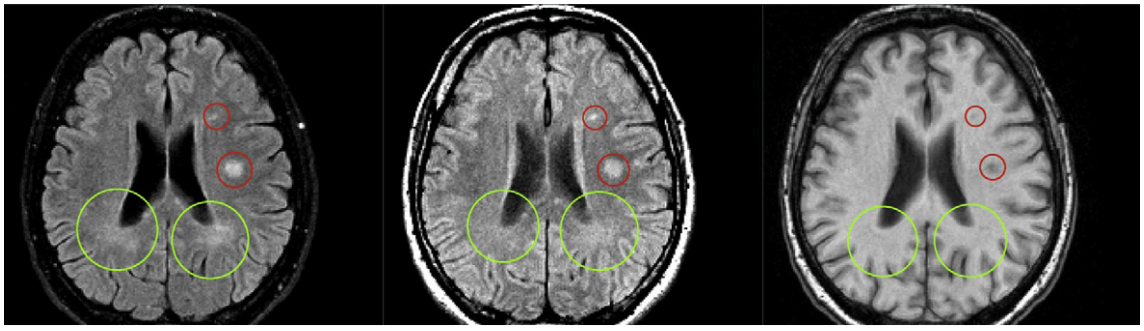

Figure 4.2: Difference between focal lesions (red) and diffuse regions of visible-abnormal WM (green). From left to right: FLAIR, PD and T1. [7].

the different 2D sequences (coronal, sagittal or transversal) for reproducing a 3D structure of the brain.

Another problem that may arise is the occurrence of non-MS lesions related to other pathologies such as vascular ones or progressive multifocal leukoencephalopathy lesions, for example. The slice thickness and the magnet strength are both factors that will also influence directly the number of detected lesions [7, 32].

In MS lesion segmentation, detection is not the only challenge: once a lesion is identified, its boundaries must be determined, even on unclear boundary cases, such as fuzzy borders due to inflammation and atrophy processes. This delineation is not a straightforward task since the partial volume can have a distortion effect, by permitting that several tissue types contribute to the image intensity in the border voxels.

In manual segmentation, this is also a harder task for diffuse lesions than its detection, since the human visual system works better with local contrast than with absolute intensities [7].

4.2 Preprocessing steps

In the majority of automatic methods, there are a lot of processing steps which are applied before the segmentation procedure. These might be a fundamental key to the outcome.

Nonetheless, a great effort has been made to unravel these problems through the use of open source software specially developed for MRI brain processing. One of the most common is FreeSurfer: an open source suite of tools that aims for the analysis of neuroimaging data in order to quantify the functional, connectional and structural properties of the human brain. This tool is being constantly improved and extended, resulting in a very wide use for brain MRI analysis in MS patients.

SPM (Statistical Parametric Mapping), which was designed to work with MATLAB, is also a very common software regarding MRI analysis and processing.

Currently, these two software, among others, provide a series of possibilities for an easy and fast preprocessing, like skull stripping, bias field correction, gray and white matter segmentation, labeling of regions on the cortical surface and subcortical brain structures, motion correction among other functionalities [33].

4.2.1 Registration

Registration can be defined as the process of transforming different sets of data into the same coordinate system. Since MRI is susceptible to the patient's motion, it is desirable to correct this motion in the different scans for a better tissue position correlation.

Despite the existence of different methods and techniques, most of them work in an iterative way. Figure 4.3 presents an accurate scheme regarding the main idea behind the overall process of registration. An initial set of transformation parameters is applied to the floating image (the image about to be registered in a referenced one). The output of the transformed floating image is compared to the referenced by assessing the similarity between them, using a metric. If the similarity is high enough (defined through a series of conditions or through a defined threshold), the registration will be concluded. Otherwise, the transformation parameters will be iteratively updated and applied again to the floating image, and so on until the stoppage criteria are satisfied [34, 8].

In this procedure, it also might be interesting to make an alignment with an atlas, in order to provide an estimation probability map of the brain tissues. As some atlases are widely distributed, it offers the possibility to build reproducible methods more easily [7].

Given two image data sets, registration will require the determination of a transformation matrix T applied afterward to the floating image. Thus, the moving image will be aligned with the reference one. This transformation is achieved through maximizing similarity criteria. The two basic types of transformations are rigid body, where only translations and/or rotations are performed and non-rigid body, which includes more complex transformations, such as severe deformations. Figure 4.4 shows an example of a non-rigid body transformation, which was implemented by a series of rigid registrations performed in local neighborhoods (as the ones shown in the box on the left). By moving the box to different locations, a rigid body transformation is applied [8].

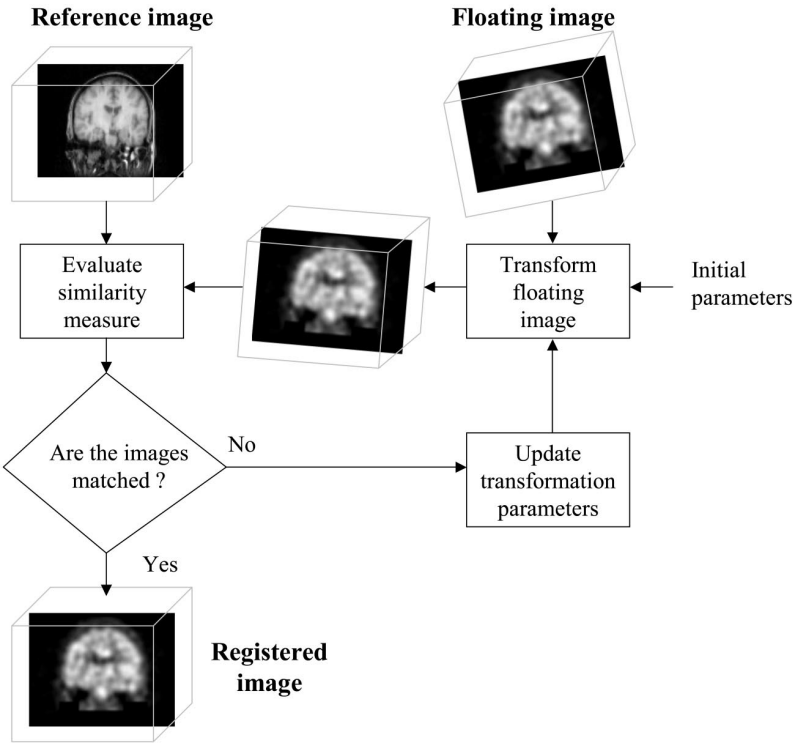

Figure 4.3: Scheme of a general image registration algorithm [8].

Some of the similarity measures can be through the surface and edge measures, minimizing the average distance between the correspondent ones in the given images, or through voxel intensity measures. Principal axes, the center of mass and orientation can also be determined in order to align the floating image. Variance can also play an important role, where the goal is to minimize it or to use cross-correlation for similarity measures. Another popular technique is the maximization of mutual information through the use of the joint intensity histogram [8].

Most MRI registration methods use conventional optimization techniques with a multiresolution strategy in order to avoid unnecessary computational-heavy processing. Usually, these optimization techniques are based on a local search with a use of a smooth cost function in order to limit the searching region. As seen in [35], Jenkinson et al. showed that even the commonly used multiresolution local optimization methods can be substantially affected by local minima. However, there are also strategies using global optimization [34].

Sajja et al. [36] used a technique that combines a genetic algorithm in continuous space with a dividing rectangle [34]. The method was based on the combination of the GACS (Genetic Algorithm in Continuous Space) algorithm and with the DIRECT (DIviding RECTangle) optimization.

Klein et al. [37] performed the largest evaluation of nonlinear deformation

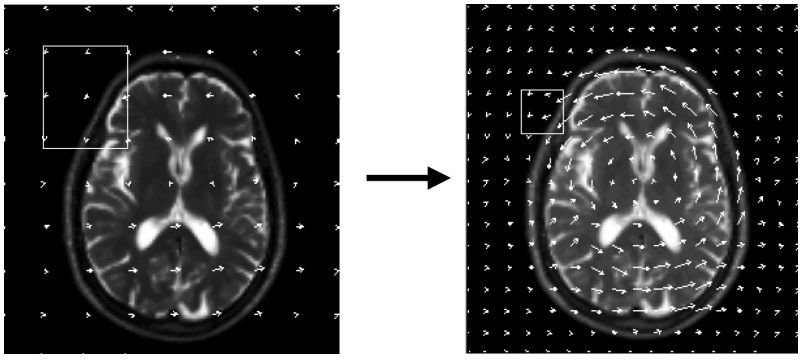

Figure 4.4: An example of a non-rigid transformation, which was implemented by a series of rigid registrations performed in local neighborhoods (as the ones shown in the box on the left) [8].

algorithms applied to brain MRI registration in 2008. One of the most significant findings was the fact that the relative performances of the compared registration methods do not have a significant difference when a different labeling protocol or a different patient is chosen. This way, it is possible to generalize a registration method to a new population with a different protocol without affecting performance.

4.2.2 Brain extraction

Brain extraction can be defined as the selection process of the slices corresponding to the brain, confining the segmentation activity to these ones. This can be done since MS lesions in MRI brain scans can only be found in the brain itself [7].

Klein et al. [37] extracted each brain from its whole-head image through the construction of a mask from the corresponding manually labeled image.

Inside brain extraction, it is possible to go deeper by applying skull stripping (Figure 4.5). This process eliminates fat, skull, skin and other non-brain tissues that may cause misclassification and whose presence is not necessary for the clinical context. Brain Extraction Tool (BET), Brain Surface Extractor (BSE), Minneapolis Consensus Strip (McStrip) and Statistical Parametric Mapping (SPM2) are examples of this process [38]. Boesen et al [9] made a quantitative comparison of these which revealed that McStrip consistently outperformed the others.

4.2.3 Intensity inhomogeneity (IIH) correction and noise reduction

IIH correction and noise reduction have as goal the simplification of the segmentation procedure by smoothly reducing variations of intensity of the existing

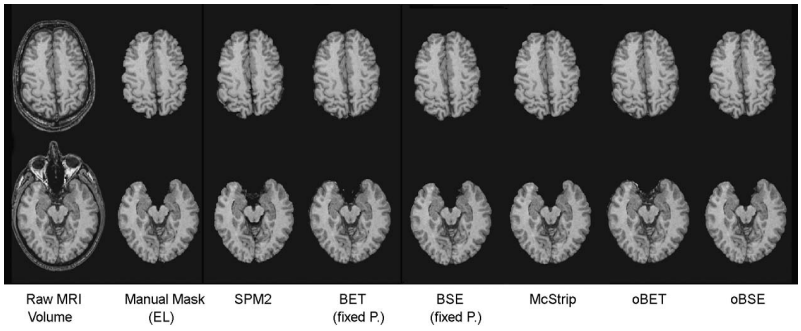

Figure 4.5: An example of brain extraction activity with skull stripping. A quantitative study of brain extraction by Boesen et al [9], example with subject B, dataset 3.

tissues. This can be useful to eliminate the inhomogeneities of the applied magnetic fields applied during the MRI exams, which are responsible for assigning different intensities to the same tissues [7].

From the point of view of the independence of these artifacts regarding the real image, it is common to simplify the situation by defining the intensity of each Voxel Y as:

$$Y = \alpha X + \beta$$

where X is the real intensity, α a constant bias factor causing intensity inhomogeneities and β additive noise, which is usually assumed to follow a Gaussian distribution [38].

Another path is through the use of atlases. By using statistical atlases, a prior probability of each voxel belonging to a certain tissue is obtained. By looking at the strategies based on atlas information, it is possible to distinguish between the use of both statistical and topological atlases. Thus, according to the situation, it is possible to identify inhomogeneities and noise cases by having deeper knowledge about the tissues [38].

Shiee et al. [12] took advantage of an atlas application by introducing modifications to Topology preserving Anatomical Segmentation (TOADS) algorithm in order to generalize the model for brain images with MS since this was meant for healthy brain images. By using a statistical and a topological atlas, a fuzzy segmentation was performed based on a model including inhomogeneities and noise artifacts.

According to Hou [39], the most popular models to describe the IIH field are the low frequency, the hypersurface and the statistical one. Some of the most appealing methods are the filter-based due to its speed and easy implementation. These can have a great variability as there is the possibility to be adaptative, surface fitting and to conjugate with other methods/techniques, like segmentation, registration,

feature extraction or clustering activity.

4.2.4 Intensity normalization

Intensity normalization is the step where all voxels are transformed into the same intensity range which allows a fair comparison between different acquisitions. Contrast, signal, contrast-to-noise ratios are non-uniform factors that can have a wide range of values even when using similar sequences with similar parameters. Thus, it is important to note that MRI imaging is not a quantitative imaging technique: it enhances the property differences between the existing tissues. Since these are not related to any medical or clinical factor, intensity normalization will not result in an information loss [7].

For instance, Sajja et al. [36] and Datta et al. [40] performed histogram normalization. Authors that use atlas approaches already have intensity normalization built-in in their methods, like Leemput et al. [41]. Wu et al. [42] took advantage of the Expectation-Maximization (EM) algorithm by using a component responsible for compensating intra-scan and inter-scan intensity variations. The EM segmenter has a component that compensates for intra and inter-scan intensity inhomogeneities and normalizes the observed scan intensities.

4.3 MRI segmentation

As already mentioned, MRI segmentation algorithms constitute the majority of investigation work regarding MS assisted diagnosis. However, these can have different functions and ideas behind their common goal: lesion detection. Some try to segment all the brain into different tissues, like bone, GM, WM, CSF. Other approaches consist in directly finding lesions while others consist in using machine learning mechanisms. More complex techniques ensemble all these ideas.

4.3.1 Feature extraction

Feature extraction consists in the extraction of characteristics that are discriminant to a given situation, making possible to distinguish types of lesions, to distinguish lesion from a non-lesion or to distinguish several tissues. For logical reasons (as it is the main feature physicians intuitively use), the voxel intensity in the different sequences constitutes a group of classical features.

However, voxel intensity may not be sufficient to solve this problem, as there is a considerable need to integrate more information from different natures, like

spatial and anatomical derived from previously studied atlas. Coordinate systems and distance metrics for the lesion locations are also often used. These features may not be raw, that is, directly extracted but actually an output of an operation [7].

4.3.2 Tissue segmentation

One common approach is a global tissue segmentation (Figure 4.6), where an algorithm has a wide sense of the existing structures in the brain.

Freifeld et al. [10] proposed the use of the Constrained Gaussian Mixture Model (CGMM) [43] to capture the brain structures spacial layout. This model was used as a probabilistic one based on a mixture of multiple spatially oriented Gaussians per tissue. The intensity of a certain tissue was considered a global parameter, constrained to be the same value for the entire set of Gaussians related to the same type. Like many other mentioned approaches, MS lesions were identified as outlier Gaussian components and grouped to form a new class. With a probability-based curve evolution technique, lesion boundary is redefined.

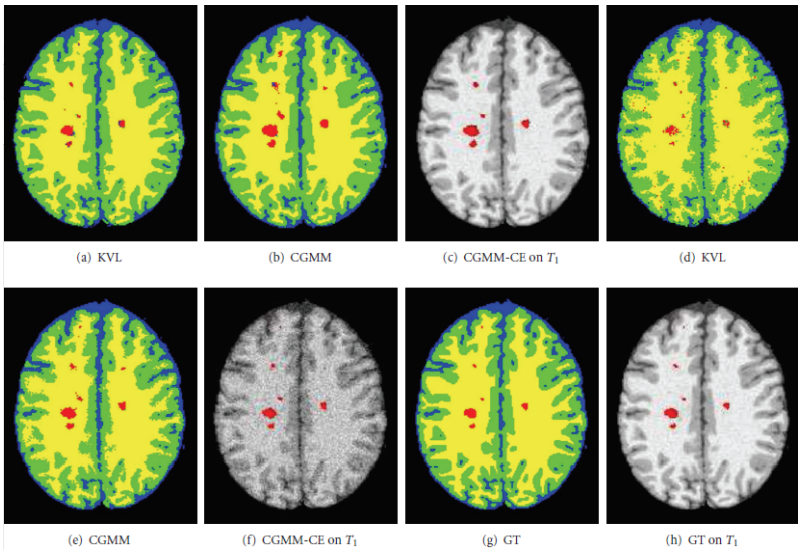

Figure 4.6: An example of tissue segmentation into CSF, GM, WM, and Lesions. Segmentation results of different algorithms on BrainWeb data, slice 105 from [10]. Blue: CSF; Green: GM; Yellow: WM; Red: Lesions. (a)–(c) 3% noise, (d)–(f) 9% noise, (g) and (h) ground truth. Best viewwed in color.

Garcia-Lorenzo et al. [44] proposed a combination of two different segmentation methods for an improved performance. Through the Mean Shift technique, a local segmentation is performed and through a variant of the Expectation-Maximization algorithm, this segmentation is refined by classifying these previously regions into normal appearing brain tissues or into lesions [38].

Another approach is texture analysis, which seems to be an underdeveloped field in MS lesion segmentation when compared to other techniques. As brain structures have patterns, Zhang et al. [45] evaluated these interpixel relationships using first and second-order statistical and spectral approaches. Techniques like Fourier and wavelet transforms are already common in lesion segmentation of other neurodegenerative diseases, such as Alzheimer or Parkinson.

4.3.3 Lesion-only segmentation

Lesion-only segmentation can be seen as a segmentation with more specific criteria, in a way that only lesions fulfill them (Figure 4.7). For instance, Bedell et al. [46] did a post-processing technique based on automatic image segmentation which identified successfully all lesions larger than a certain dimension (5 mm^3), producing no false-positives or false-negatives above the mentioned volume.

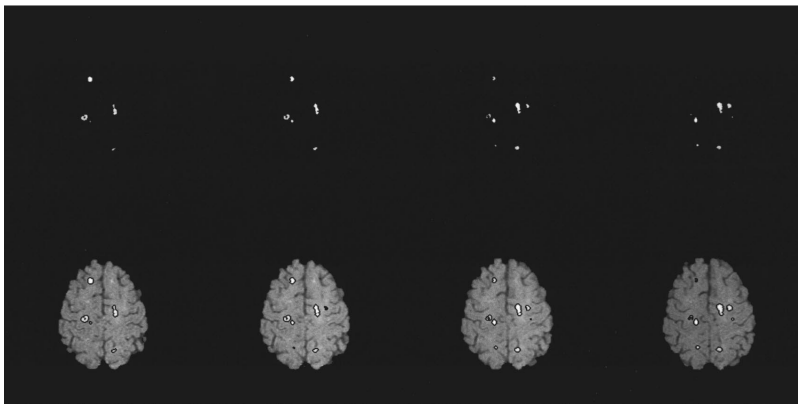

Figure 4.7: An example of lesion-only segmentation, in this case a segmentation of contrast-enhanced lesions performed by He et al [11]. The identified lesions are shown in the upper row.

Since contrast-enhanced lesions are clearly visible, it is possible to build stricter criteria for its identification regarding other structures. Likewise, He et al [11] proposed a segmentation of contrast-enhanced MS lesions. Its procedure relied on an adaptive local segmentation based on morphological operators. These worked in both lesion and non-lesions enhancements. Datta et al. [40] also took this approach by using morphological operators as well.

Lesion-only segmentation can also be seen as an after-step on tissue segmentation, when another condition is required for a certain structure to be considered a lesion, like Boudraa et al. [47] proposal. An initial segmentation with Fuzzy C-Means algorithm was performed to extract an external CSF/lesions mask preceded by a local image contrast enhancement. The created mask was afterward

superimposed on the corresponding data set containing only CSF structures and lesions. The clustering algorithm was applied a second time in order to remove false negatives under the base of a deeper anatomical knowledge due to the previous superimposition.

Saha et al. [48] proposed an alternative clustering technique for lesion segmentation, through the use of a fuzzy genetic clustering where a point symmetry base distance constitutes the membership value.

4.3.4 Learning based on atlas

Like previously mentioned, topological (Figure 4.8) and statistical atlases constitute a very common approach since they provide a trustful source of spatial information. Atlas consists in a detailed mapping of the brain, through the study of brain MRI of different patients.

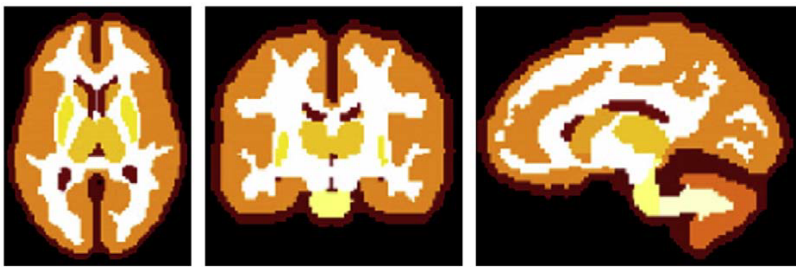

Figure 4.8: An example of a topological atlas in axial, coronal and saggital views, present in [12].

A statistical one provides the prior probability of each voxel belonging to a certain tissue, previously built from a set of manual segmentations. Besides, in a creation of an atlas, the structure boundaries take into account not only anatomical variations but also smooth probability deviations. This way, besides classification, an atlas can also be very helpful when dealing with noise or inhomogeneities.

The greatest disadvantage with approaches based on atlas is the alignment with the dataset, existing the need for a good registration process [38].

These methods are particularly common in providing a healthy model to contrast with non-healthy ones, like Leemput et al. [49] by proposing and intensity-based tissue classification based on a normal brain model which detects MS lesions as outliers that were not well explained by the created model. Due to the atlas properties, inhomogeneities, noise and other artifacts were taken into account providing this way a built-in preprocessing by incorporating its contextual information by conjugating it with a Markov Random Field. The brain model was created by extracting information from the atlas with an EM algorithm [42].

Some authors applied classic classification algorithms like Wu et al. [50] by using k-Nearest Neighbour (kNN). This classifier was combined with an atlas segmentation in order to create masks that only extracted white matter, discarding this way lesions outside the masks. Besides classification methods, other authors like Shiee et al. [12] decided to apply clustering algorithms by conjugating a statistical and a topological atlas with the fuzzy C-means (FCM) algorithm.

The principle applied by Leemput et al. [49] was also reproduced by many authors. For instance, Bricq et al. [50] performed tissue classification with base on the Trimmed Likelihood Estimation of a mixture model with neighborhood information encoded by a hidden Markov chain while lesions were also detected as outliers. Prastawa and Gerig [51] segmented lesions as spatially coherent objects and avoid spurious lesion detected, making the algorithm more robust to noise. Thus, classification was performed on regions (connected groups of voxels) where each vocal location is assigned to a region according to criteria. In this case, the objective is to maximize the relative entropy or the Kullback-Leibler divergence between neighboring regions. Tomas and Warfield [52] used a similar principle by creating a distance based map and applied afterward a Bayes classification.

Besides clustering, other unsupervised methods were also applied on intermediate steps, like Kroon et al. [53] by using Principal Component Analysis (PCA). The proposed method was based on a local feature vector containing neighborhood voxel intensities and histogram information working as a filter and probabilistic atlas information to exclude false lesions in unlikely areas. PCA technique was applied with a log-likelihood ratio to classify each voxel. The atlas information also worked as a preprocessing tool.

As seen, atlas-based methods can be used to segment both tissues and lesions and to create structure models. The most significant drawback of these approaches is the adaptation of the atlas to the clinical images, requiring a very precise registration, which can be a very hard task when dealing with patients suffering severe atrophy, large number of lesions, among other factors [38].

4.3.5 Supervised learning

There is a certain freedom in this part, regarding the level of granularity desired to be achieved. It can be a case of a binary labeling (lesion or not lesion) or a multiclass problem regarding different types of lesions, contrast agents enhancement, activity or other factors.

With a supervised learning procedure, there is an inherent learning process

regarding the definition of lesions, using previously labeled examples. The most common labeled examples are performed by experts, providing a better reliability. These constitute a training database, where its info is used aftwerward to classify other data. Special attention needs to be paid to the database since variability is a very import factor due to the heterogeneity of this condition.

A standard pipeline for these methods consists of the following steps: normalizing the data, preprocessing, feature generation, learning or classifier training and post processing [7].

4.3.5.1 Learning based on manual segmentation

These approaches are mainly characterized by feature extraction and training in order to do the segmentation task. Likewise, Goldberg-Zimring et al. [54] proposed an automatic detection system constituted by three main stages: detection and contouring of all hyperintense signal regions, partial elimination of false positive segments using properties like size, shape index and anatomical location and Artificial Neuronal Network training in order to perform segmentation. Anbeek et al. [55] performed a kNN classification by using voxel location and signal intensity information, determining this way the probability of existing a lesion in a certain voxel. By applying a threshold on these probabilities, lesion segmentation was obtained.

Although this may be a classic approach from image processing/machine learning point of view, there are several possibilities. Sajja et al. [36] decided to use segmentation through the use of a Parzen windows classifier for CSF and lesions and to use contextual information through hidden Markov random field expectation-maximization algorithm to reduce misguided classifications by segmenting gray and white matter. A Parzen window classifier can be very interesting, as it is a nonparametric method. Thus, it assumes that lesions and CSF do not follow any known distribution.

Another alternative approach was the one taken by Morra et al. [56], by proposing an automatic subcortical segmentation using an auto-context model with a series of AdaBoost weak learners and with a probabilistic boosting tree. Each weak learner consisted of a feature, a threshold and a boolean stating the feature value regarding the threshold.

Decision trees are also a common technique among supervised learning methods since a random decision forest achieves a better generalization by growing an ensemble of many independent decision trees, resembling the existing variability in MS. Likewise, Geremia et al. [57] presented a discriminative random decision forest framework which provided a voxel-wise probabilistic classification of the volume

using spatial context and symmetry concepts.

Cerasa et al [58] presented a genetic algorithm evolving a Cellular Neural Network capable of segmenting lesions directly from 2-dimensional images as in these techniques (Cellular Neural Networks) it is possible to provide local spatial information since neighboring cells interact with each other.

Convolutional Neural Networks (CNN) is a technique whose interest has renewed in last few years in computer vision. Problems in brain imaging, especially in tissue segmentation and brain tumor segmentation have gained special interest but MS lesion segmentation is an exception since only a few number of CNN methods have been introduced so far. Besides, MS MRI databases tend to be small, constituted by a reduced number of patients which can be a significant drawback since CNN require a significant volume of data due to overfitting issues. In order to overcome this problem, authors like Valverde et al. [59] propose a simple architecture constituted by a cascade of two 3D patch-wise convolutional CNN. The first network was trained to be more sensitive regarding lesion detection while the second is specialized in detecting false detections from the first.

Brosh et al. [60] proposed a CNN encoder with shortcut connections. The architecture consists of two interconnected pathways, a convolutional one to learn increasingly more abstract and higher-level features, and a deconvolutional for predicting the final result at the voxel level.

Thus, supervised learning methods from manual segmentation make possible the integration of expert knowledge into the process. By proceeding to an initial segmentation, it is possible to have a significant variety of classifiers since a classical machine learning approach can be taken. One of the most significant disadvantages of these methods is the dependability of the acquisition protocol as features and properties extracted are based on the raw image characteristics. Thus, if one decides to apply supervised learning in lesion segmentation, a robust preprocessing is desirable for a good performance [38].

4.3.6 Unsupervised learning

Unsupervised learning methods work in an independent way of labels, where most procedures consist of clustering techniques by discriminating clusters of voxels into certain groups (clusters). These groups, according to the used features and to the existing tissues, usually represent either white matter, gray matter, CSF or lesions.

The information basis is the same as the one from the supervised learning. It

is also very often the use of atlas to reduce acquisition variability and to correlate with spatial and anatomical information.

The main advantage of using unsupervised learning is the possibility of using simultaneously the information of the whole brain, and not only chosen voxels (lesions) like in supervised learning. This way, data related to volume and properties of normal appearing healthy tissues can be used with a deeper meaning.

With unsupervised learning, especially clustering methods, it is easy to create a system able to identify not only clusters but also outliers. This was also an interesting approach: the creation of an unsupervised learning model of a healthy human brain, whereas consequence, lesions would be considered outliers [7].

4.4 Synthetic images

BrainWeb [13, 61] is a wildly known online database of synthetic MRI images. Originally, a healthy subject was scanned 20 times to obtain an image with a very high signal to noise ratio in order to create a healthy anatomical phantom. In this anatomical image, each voxel belongs to a specific tissue class, constituting an advantage when it comes to discrimination goals as there is less freedom to uncertainty. There are also available MS patients scans, through the implementation of real manually segmented lesions from patients with a different lesion load level. Currently, 20 more healthy subjects are available.

With these models, it is possible to create T1w, T2w and PDw (Figure 4.9) imaging sequences with the pretended MR parameters and with artifact parameters as well.

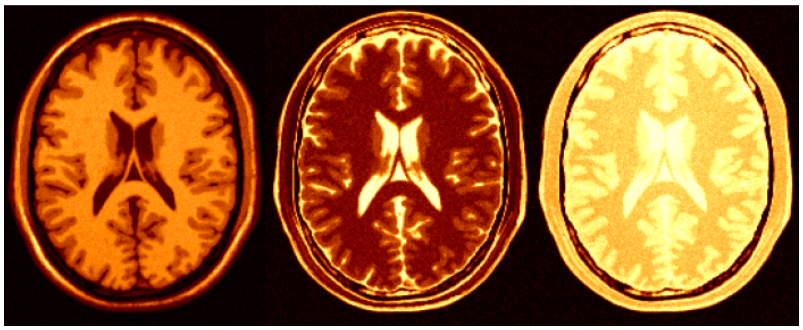

Figure 4.9: An example of MRI sequences generated by BrainWeb [13], from left to right: T1,T2, PD.

This online database, due to its small quantity of information, can be useful not to create new algorithms but to test new ones created with different datasets. Its significant advantage is the existing availability since it is free for the community,

transforming it into a comparison and evaluation reference in MS lesion segmentation as a validation database.

However, 21 brain models constitute a reduced number to represent a database with significant variability, having also the disadvantage of not covering all the lesion load levels. Its limitation to T1w, T2w and PDw also constitutes a serious limitation, since most MRI protocols also perform FLAIR and Gd-enhanced T1 sequences. As the MS patient model was constructed by mixing a healthy brain along with manually segmented lesions from real patients, the final output is still far from the existing reality [7].

4.5 Clinical images

Since the main objective of MS lesion segmentation is the application to the clinical context, its use and validation with real clinical images is an absolute necessity. As already mentioned, variability is one of the properties that any database must possess, especially in problems with this level of heterogeneity.

As there is not a large availability of MS databases and since it is very unlikely to have a reasonable quantity of equal features with the same procedures, there is a significant lack of comparative studies and a lack of cross information.

Another considerable limitation to comparison activity is the differences between the employed MR protocols since most authors do not often provide a detailed description of the used ones in MRI acquisitions. As a consequence, there is a certain isotropy when it comes to creating a standard pipeline for MRI acquisitions.

4.5.1 The ground truth

This can be a significant limitation to the segmentation task in the validation level. Although a ground truth is not necessary for reproducibility, it is strictly necessary for measuring the performance of the algorithms.

Even though manual segmentation is the gold standard, its outputs will still have a considerable variability from expert to expert. With this case, a good alternative is the comparison of segmentations performed by different experts. There is always the possibility to use a semiautomatic method for this scenario.

The STAPLE method [62] is also used to define a ground truth, which is a very interesting approach. It is considered an EM algorithm for simultaneous truth and performance by considering a collection of segmentations and computing a probabilistic estimate of the true segmentation. It also computes a measure of the perfor-

mance level represented by each segmentation. This procedure was the one used in the MICCAI Challenge 2008 [31].

4.6 MICCAI 2008 Segmentation Workshop

The MICCAI 2008 Segmentation Workshop is one of the references in MS lesion segmentation. It is the most relevant and the largest comparative study. Several authors compared different algorithms on the same dataset. It represents the first public database available to the community for white matter lesion segmentation in MS. Besides that, using this database is the fairest way to compare new algorithms to the ones applied to this workshop, having a trustful comparison [7, 31].

Likewise, it was clearly noted that the initials steps of Bosc et al. [63], up to change detection, were considered since then the standard preprocessing steps for time-series data despite a recent relative death of work in automated segmentation time-series [31]. The proposed method uses an association of a nonlinear intensity normalization method with statistical hypothesis test methods to provide reliable change detection. In order to reduce the false rate detection, multimodal data is optionally exploited. A receiver operating characteristics (ROC) analysis was used.

4.6.1 The data

The validation dataset was constituted by MRI T1w, T2w, FLAIR and diffusion-weighted scans from two different sites where the acquisition protocol was not provided. There was no other clinical information about the patients. This dataset was divided into a training set, off-site test set, and on-site test set.

All data suffered the same preprocessing: the baseline (first time-point) MPRAGE was inhomogeneity-corrected using N4, skull-stripped, dura stripped followed by a second N4 inhomogeneity correction and suffered a rigid body registration to a 1mm isotropic MNI template [31]. Thus, teams preprocessing methods were less effective, especially the denoising ones. As noise is characterized by an independence from voxel to voxel, denoising methods are based on that principle. With the application of previous preprocessing methods, this assumption is no longer valid.This way, this decision had positive and negative aspects.

The training set had as the goal the adaptation/creation of each algorithm to the given sequences, consisting of 20 images along with a manual segmentation. The off-site test data set consisting of 25 images without a manual segmentation. Authors had to process the given data and send afterward the segmentation results.

The on-site test was provided during the workshop in order to test the performance within a time window, testing other factors besides results performance [7].

4.6.2 Performance evaluation

The performance of the authors' algorithms was measured by different metrics, such as the difference of total volumes divided by the reference volume, the distance between borders of the reference volume and the segmentation, true positives ratio, dice overlap, volume correlation, average symmetric surface distance, false positives ratio, among others. These metrics were all normalized ranging from 0 to 100, where 100 was the maximum score and 90 the typical score of an expert in MS. This way, it is possible to verify if there are theoretically automatic algorithms performing better than an expert.

Two experts performed manual segmentation on the given datasets, obtaining a significative variability when it came to the final output. The two only agreed on 68% of the lesions, limiting the maximum accuracy, since the procedures will not agree with both segmentations simultaneously [7, 31].

4.6.3 Teams performance

Team IIT Madras won the contest while Team PVG One and Team IMI ranked second and third, respectively. The final score difference between these three was minimal, existing an equal interest in these three algorithms. Despite they are all based on machine learning principles and in supervised learning, their steps are significantly different. Team IIT Madras modeled a voxel-wise classifier with multichannel 3D patches of MRI volumes as input by training a CNN and segmented lesions by combined the probabilities obtained through the created CNN. Team PVG One built a hierarchical framework for segmenting not lesions but also healthy tissues through the use of MRF combined with multi-atlas, using a random forest classifier for a region level refinement. Team IMI also used random forest methods, however, the procedure is different than the one from PVG One as it is given a lot more emphasis on decision trees.

Carass et al.[31], when looking back at the performances and rankings, had some surprises regarding some techniques and algorithms, such as a low performance of CNN in some teams and a low performance of Lesion-TOADS. Nonetheless, the authors attributed an uncertainty about the reasons that might explain the low performance, pointing out that it could be due, in part, to the differences in the training data and choices about how much and which portion of the available data

was used to train the method. However, it may simply reflect a basic instability in machine learning based approaches.

4.7 Patient's clinical history

There is some investigation work regarding other patient aspects of MS. However, it is worth denoting that there is a large difference between the existing volume of work between MRI lesion segmentation and other MS fields. Most of the existing studies are related with correlations and statistical tests, which makes rare its direct machine learning application. This particular reason may have to do with the difficulty in reaching a trustful and large enough database, whose variability reaches all case scenarios.

Another motive is directly connected to the fact that MRI is the most used tool by the physician to perform the diagnosis along with the general concept of relapse, as it can be demonstrated by the McDonald diagnosis criteria [16] and by the 2013 revisions of MS clinical course [24].

Treatment can be a difficult decision for the physician to take as there are several options with different characteristics regarding the condition, especially in the early stages where MS subtype is unknown and there is no information about how the severity is going to evolve. These two problems were addressed by Rodrígues et al [64] by proposing multidimensional Bayesian network classifiers to model and exploit the existing relations. However, this study recurred not only to clinical information but also to DNA.

Feinstein et al. [65] performed a longitudinal study taking into account MRI, psychometric and psychiatric abnormalities, showing an emphasized lack of close correlation between psychiatric morbidity and extent of measurable brain pathology. Boiko et al. [66] enhanced a significant correlation between the number of relapses during the first year of disease and its course. This way, a high frequency of relapses is proportionally correlated with disability.

A. Brex et al. [67] developed a longitudinal study of abnormalities on MRI conjugating them with the disability, more precisely with the EDSS scale. The reached conclusions pointed out a moderated correlation, retrieving an inadequacy for choosing the disease-modifying treatment based only in the brain lesion volume. Sastre-Garriga et al. [68] studied the relation between grey and white matter volume in the early phases of patients with PP by examining brain volume changes due to MRI scans, with the EDSS scale and Multiple Sclerosis Functional Composite. The developed study retrieved some interesting conclusions, like significant volume

changes over 1 year due to mainly changes in grey matter in PP patients.

Tedeschi et al. [69] showed similar findings regarding reduced white matter and grey matter volume fraction and fatigue. These findings are coherent with the ones showed by Zivadinov et al. [70] where the main pathological substrate of brain atrophy in the early stage of the disease is an early axonal loss (demonstrated by grey and white matter volume reduction), causing the progression of neurological deficits and the development of cognitive impairment.

Crimi et al. [71] proposed a totally different approach from the previous literature by characterizing CIS patients according to lesion pattern, capable of identifying three major different lesion patterns. Moreover, patients were classified according to the nature of the inflammatory lesion patterns recurring to a two-tire classification discovering spatiotemporal lesions that would characterize groups of patients. Minneboo et al. [72] performed a study within some similar guidelines by retrieving specific lesion characteristics in order to predict a severe long-term disability, by emphasizing in lesion location within the different MRI scans. Thus, it was noted that several MRI criteria derived from baseline T2w images were strongly related to progression to an EDSS score of 3 at follow-up, where the presence of at least 2 infratentorial lesions was the strongest predictor. However, it was not found any criteria derived from T1w or gadolinium-enhancing lesions for an EDSS prediction progression.

More recently, Zhao et al. [73] performed an exploratory work of machine learning techniques in predicting MS disease course using only clinical observations. Race, family history of MS and brain parenchymal fraction were the best-ranked predictors of the non-worsening group while brain T2 lesion volume ranked high as a predictor for the worsening group.

4.8 Point of situation

The interest in investigation work related to MS lesion segmentation and disease prediction is far from finished. Despite the quantity of work, literature, and advances, a suitable automated method is still not available.

Besides, the retrieved conclusions from a investigation still remain limited due to the employed methods. Regarding supervised learning, the procedure can be roughly described as a black box system, since it is only constituted by the set of features and a classification algorithm, which may not have in concern the clinical contextualization. With supervised learning, there is the problem of not being possible to discriminate the participation of each feature and each classification algorithm

individually, difficulting its adaptation to a logical and universal series of steps.

Regarding lesion segmentation, algorithms must not focus only on one nature of information but in different ones. The use of multimodal information is necessary, as it ables a confirmation of lesions through different scans, avoiding false positives. Thus, image intensity is necessary but not sufficient. Spatial and anatomical information provides a significant noise reduction and an improved coherence of results.

On MS image segmentation, there is not a clear vision about the best type of learning, unsupervised or supervised. While supervised has the advantage of requiring a ground truth, making it simpler for a future adaptation to a different acquisition protocol, there is the need to have a full variability integrated and is not possible to evaluate non-detected lesions. On the other hand, unsupervised learning algorithms act on the entire part of the image, making use of spatial and anatomical information more significantly, while taking advantage of outliers.

Besides the volume of literature in MS prediction and detection through the use of MRI lesion segmentation, there is an existing gap on integrating other medical information, such as the patient's clinical history, relapses, treatments, among other factors. It can be found some literature regarding clinical history in prediction and detection, where is shown a lack of correlation between MS progression and different aspects. No paper was found that integrated in a meaningful way these two natures of information.

Besides, most work that integrates clinical and observation data are based only on statistical inferences and parameterization, pointing out an existing gap in machine learning application.

Chapter 5

Dataset description

The database from CHUC is constituted by clinical and MRI data. Although the clinical database contains information of 1135 patients, many were not valid for this study since there was a lot of missing data in important fields, such as visits made to the hospital, onset and diagnosis dates and clinical exam history. Besides, some suffer from Neuromyelitis Optica (NMO) which is a different situation. The PP cases were also excluded due to being a different course and its proportion was considerably reduced when compared with RR and SP. Besides, in the database the number of PP patients was minimal.

As one of the goals of this thesis was to integrate different sources of information, the first step consisted in selecting an adequate number of patients to retrieve its clinical history and respective MRI scans. Since retrieving the MRI scans was a very complex and time-consuming issue regarding CHUC's database (due to the hospital servers and its changes, where it took about 30 to 45 minutes to retrieve an exam of one patient), there was the need for a compromise between an adequate quantity of data and time consumed by the Doctors Luís Rito Cruz and Mafalda Mendes Pinto.

Thus, a selection of 47 patients was performed. In order to obtain a representative database regarding MS course (RR or SP), 32 RR patients and 17 SP patients were chosen. The choosing process was made by guaranteeing the accomplishment of several criteria. The group of RR patients guaranteed the following criteria:

1. all patients have made at least 5 MRI exams with brain scans,
2. all patients have the MS onset age (the age when MS condition starts to manifest) between 20 and 40 years old.

As the SP course is a rarer form, there was a considerable reduction of the

number of patients regarding this condition. As a consequence, the group of the selected SP patients had less restricted criteria:

1. all patients have made at least 2 MRI exams with brain scans,
2. all patients have the MS onset age (the age when MS condition starts to manifest) between 20 and 40 years old.

However, due to problems related to the MRI scans extraction from the hospital servers, this list had to be shortened to 36 patients. Thus, the RR group consisted of 25 patients and the SP group consisted of 11 patients, as it was not possible to retrieve any MRI exam from any of the other 11 excluded patients due to time and server issues. This also affected the quantity of MRI scans of the 36 patients, since not all exams could be retrieved. This way, in the thesis database there are patients with only one MRI exam. From the 36 selected patients, 20 were women, which is a representative factor of MS gender reality, as mentioned in Chapter 2.

5.1 Clinical database

The raw database of clinical data consisted of an .xls file automatically exported from the hospital's Neurology Department database. This file is very extense which includes several sheets. Some were considered and others were not, as indicated below:

1. **Identification** (used): general information regarding patients, such as age, onset date, diagnosis date, initial MS manifestations.
2. **Concomitant Diseases** (not used): contains information of a reduced quantity of patients.
3. **Family History** (not used): contains information of a reduced quantity of patients.
4. **Visits** (used): information regarding the visits a patient made to the hospital, such as the momentaneous EDSS and the score of the functional systems of EDSS scale (mentioned in Chapter 2).
5. **MRI** (used): only for patient selection regarding the number of brain MRI scans performed. Contains a considerable volume of missing data.
6. **CSF** (not used): despite the fact it contains considerably interesting and pertinent information regarding the patient status, there was a considerable volume of missing data and a reduced number of patients.
7. **Evoked Potential** (not used): despite the fact it contains considerably interesting and pertinent information regarding the patient status, there was a

considerable volume of missing data and a reduced number of patients.

8. **Laboratory Test** (not used): despite the fact it contains considerably interesting and pertinent information regarding the patient status, there was a considerable volume of missing data and a reduced number of patients.
9. **Relapses** (used): contains information about the functional systems of EDSS, treatment and its duration and corticosteroids use or not.
10. **Adverse Event** (not used): contains a reduced number of patients as samples.
11. **Pregnancy** (not used): contains a reduced number of patients as samples.
12. **Treatments** (not used): contains information regarding the treatments of each patient and relapses treatment as well. It also contains MS non-related treatment. Despite the quality of information, the decision of prescribing a treatment or drug is directly related to the rest of other clinical factors. This way, if data from this sheet would be used, a bias would certainly happen, as explained and advised by Doctor Sónia Batista.
13. **Flexifields Paraclinical Test** (not used): a case of complete missing data and a minimal number of samples.
14. **Flexifields Medical Event** (not used): a case of complete missing data and a minimal number of samples.

In order to get a quick but deep insight of the features, each used sheet will be explored in order to describe each raw feature extracted.

5.1.1 Identification

In this section, the used raw features present in the Identification sheet are presented with a brief explanation of them or their use:

1. **Patient ID**: the identification number of each patient. As it is entirely dependent on the Neurology Department database, it is independent of the health's patient code.
2. **Birth date**: this date will be used along with the onset date, diagnosis date and with the secondary progressive diagnosis date, in order to calculate the patient's age at these events.
3. **Gender**.
4. **Date of onset**: the moment when MS is believed to have started in the patients. To use along with birth date, diagnosis date and with the secondary progressive diagnosis date in order to calculate these time intervals.
5. **Supratentorial**: binary field, if there were initial manifestations of MS related to the supratentorial region.

6. **Optic Pathways**: binary field, if there were initial manifestations of MS related to the optic pathways.
7. **Brainstem-Cerebellum**: binary field, if there were initial manifestations of MS related to the brainstem and/or cerebellum.
8. **Spinal Cord**: binary field, if there were initial manifestations of MS related to the spinal cord.
9. **Date of diagnosis**: the moment MS was diagnosed. To use along with birth date and secondary progressive diagnosis date.
10. **Clinical findings**: binary field, if there were pieces of clinical evidence in the MS initial manifestations.
11. **MRI**: binary field, if there were initial MS manifestations visualized in MRI scans (lesions).
12. **Evoked Potentials**: binary field, if there were initial MS manifestations in the evoked potentials test.
13. **CSF**: binary field, if there were MS initial manifestations presents in the lumbar puncture exam.
14. **Date SP**: the moment when secondary progressive course was diagnosed. To use along with birth date and diagnosis date.
15. **MS Course/McDonald Classification**: binary field, the actual MS course a patient is believed to have (RR or SP).
16. **Active**: binary field, if the disease progression is active or not, as explained in Chapter 2.

5.1.2 Visits

In this section, the used raw features present in the Visits sheet are presented with a brief explanation of them or their use:

1. **Patient ID**: the identification number of each patient. As it is entirely dependent on the Neurology Department database, it is independent of the health's patient code.
2. **Visit date**: the moment when the visit to the hospital was made. To use along with the birth date.
3. **Routine**: binary field, if a visit it is a routine or an emergency one.
4. **Suspected relapse**: binary field, if a relapse is expected or not.
5. **EDSS**: 0-10, the EDSS value of the patient at the visit moment.
6. **Score Pyramidal**: 0-6, the momentaneous score for the Pyramidal FS.
7. **Score Cerebellar**: 0-5, the momentaneous score for the Cerebellar FS.

8. **Cerebellar Weakness**: yes or no, if there are manifestations of cerebellar weakness.
9. **Score BrainStem**: 0-5, the momentaneous score for the Brain Stem FS.
10. **Score Sensory**: 0-6, the momentaneous score for the Sensory FS.
11. **Score Bowel**: 0-6, the momentaneous score for the Bowel and Bladder FS.
12. **Score Visual**: 0-6, the momentaneous score for the Visual FS.
13. **Visual Symptom**: yes or no, if there are visual symptoms.
14. **Score Mental**: 0-6, the momentaneous score for the Cerebral FS.

5.1.3 Relapses

In this section, the used raw features present in the Visits sheet are presented with a brief explanation of them or their use:

1. **Patient ID**: the identification number of each patient. As it is entirely dependent on the Neurology Department database, it is independent of the health's patient code.
2. **Relapse date**: the moment when the relapse occurred. To use along with the birth date.
3. **CNS Pyramidal Tract**: binary field, if there were MS manifestations related to the Pyramidal tract.
4. **CNS Brain Stem**: binary field, if there were MS manifestations related to the brain stem.
5. **CNS Bowel Bladder**: binary field, if there were MS manifestations related to the bowel and bladder.
6. **CNS Neuropsycho Functions**: binary field, if there were MS manifestations related to neuropsycho functions.
7. **CNS Cerebellum**: binary field, if there were MS manifestations related to the cerebellum.
8. **CNS Visual Functions**: binary field, if there were MS manifestations related to visual functions.
9. **CNS Sensory Functions**: binary field, if there were MS manifestations related to sensory functions.
10. **Hospital**: binary field, if the relapse required hospital admission.
11. **Ambulatory**: binary field, if the relapse did not required hospital admission.
12. **Corticosteroids**: if it was used a drug for relapse treatment. If positive, it presents the drug name.

13. **Treatment start**: the moment when treatment regarding the relapse starts. To use along with treatment ending date.
14. **Treatment end**: the moment when treatment regarding the relapse starts. To use along with treatment starting date.

5.2 Image database

The retrieval of MRI brain scans from CHUC's database was not a simple task, as mentioned. Despite this difficulty, more obstacles appeared. As not all MRI scans were performed in the same machine/location, the heterogeneity of these was large in several aspects, such as brightness, contrast, number of slices and magnetic field intensity. In 98 MRI exams, 75 were considered to be normal (group A). In other words, they were performed with a similar procedure resulting in scans with similar brightness, contrast and noise levels. From these 75, 13 were considered to have smooth perturbations from what was considered a normal scan (group B). However, these changes were minimal when examining the total heterogeneity of the image database. The other 24 were considered to have some considerable obstacles (group C), not only considerable differences in brightness and contrast levels but also parts of the human head not included in the scan, such as the lateral part of the skull and nose. The lack of head parts may have led to problems during the registration process. From these 24, 11 were considered to be really problematic (group D), since the brightness, contrast levels and noise levels had a large difference leading to very bad quality scans.

The MRI scans were acquired in 5 different places: HUC'S Radiology Service (RAD), Instituto de Ciências Nucleares Aplicadas à Saúde (ICNAS), Hospitais da Universidade de Coimbra (HUC), unidade de Ressonância Magnética in Centro Hospitalar de Leiria (IMI Leiria) and Associação Nacional de Imagiologia Funcional Cerebral (ANIFC), which is also in ICNAS. The scans performed in RAD, HUC and IMI Leiria have a magnetic field intensity of 1.5T, while the ones performed in ICNAS and ANIFC have a magnetic field intensity of 3T. This magnetic field difference increases contrast in scans, generally improving the scan quality. However, most of MRI belonging to group D have a magnetic field intensity of group D and the majority of group A have a magnetic field intensity of 1.5 T. Despite brightness, color and noise, scans with magnetic field intensity of 3T have a higher number of slices. The most common protocol with 3T magnetic field intensity scans was 3mm of slice thickness, 3.9 mm of space between slices and a variable number of slices, from 35 to 140. The most common protocol with 1.5T magnetic field intensity scans

was 5mm of slice thickness, 6mm of space between slices, and a more homogenous number of slices, from 20 to 24. This information can be seen in Tables 5.1, 5.2 and 5.3.

Table 5.1: Image database scheme for MRI scans performed in IMI, RAD and ANIFC.

Patient ID	Patient Code	Study	Exam Place	Magnetic Field Intensity (T)	Slice thickness (mm)	Number of slices	Space between slices (mm)	Group
349	19460100198	2014	RAD	1.5	5	24	6	A
142	19640800325	27.11.2007	RAD	1.5	3	16	3	A
142	19640800325	2014	RAD	1.5	5	24	6	A
212	19670100799	2008	RAD	1.5	5	20	6	B
310	19700500561	2015	RAD	1.5	5	24	6	A
788	19721001493	2014	RAD	1.5	5	22	6	C
627	19741201396	2014	RAD	1.5	5	24	6	A
894	19751001167	2014	RAD	1.5	5	24	6	A
49	19760600961	2014	RAD	1.5	5	24	6	A
287	19780700241	2014	RAD	1.5	5	22	6	A
662	19890500969	2015	RAD	1.5	5	25	6.5	A
252	19790501183	2011	ANIFC	3	3	60	NA	A
1077	19830601318	2013	IMI LEIRIA	1.5	5	24	6.5	B
1077	19830601318	2014	IMI LEIRIA	1.5	5	24	6.5	B

In order to understand the scan quality between groups (A, B, C, D), some examples will be shown. From group A, a MRI scan from patient 349 in 2014 was selected (Figures 5.1 and 5.2). As seen, the majority of MRI scans classified as A were acquired with a 1.5T magnetic intensity field. However, there were also several 3.T MRI scans classified as A. Regarding group B, it was selected as an example an MRI exam from patient 93 in 2015 (Figures 5.3 and 5.4). These scans, although similar, have a significantly increased contrast, which is normal since the majority of MRI B scans have a magnetic intensity field of 3T. As these are in a minor quantity regarding the other similar ones, the letter B was assigned to them.

Regarding MRI scan groups considered to have more obstacles at processing level, for group C was selected an exam from patient 79 in 2016 (Figures 5.5 and 5.6) and for D was selected an exam from patient 894 in 2016 (Figures 5.7 and 5.8). In patient 79, it is visible that parts of the head are not displayed (lateral and anterior parts). In patient 894 it is visible a considerable difference in brightness levels. Due to the present darkness in the mentioned scan, there are some structures not shown in the MRI, especially at the bottom of the brain.

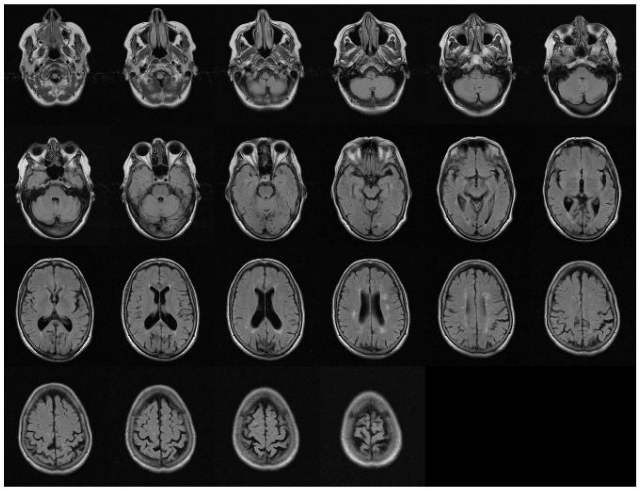

Figure 5.1: MRI FLAIR scan from patient 349 in 2014, 22 slices displayed. Exam performed at RAD, classified as A.

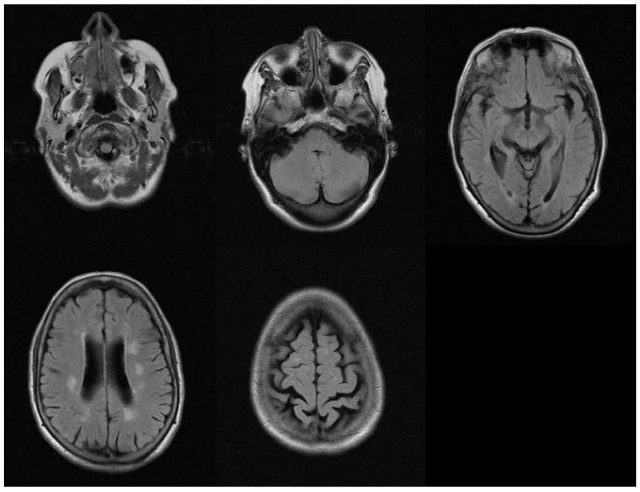

Figure 5.2: MRI FLAIR scan from patient 349 in 2014, 5 slices displayed. Exam performed at RAD, classified as A.

Table 5.2: Image database scheme for MRI scans performed in ICNAS.

Patient ID	Study	Exam Place	Magnetic Field Intensity (T)	Slice thickness (mm)	Number of slices	Space between slices (mm)	Group
79	2016	ICNAS	3	2	70	NA	C
645	2015	ICNAS	3	3	35	3.9	D
645	2016	ICNAS	3	3	35	3.9	D
93	2015	ICNAS	3	3	35	3.9	B
142	2013	ICNAS	3	3	40	3.9	B
142	2015	ICNAS	3	3	36	3.9	B
4	2013	ICNAS	3	3	35	3.9	B
275	2016	ICNAS	3	3	35	3.9	D
90	2014	ICNAS	3	3	40	3.9	B
90	2016	ICNAS	3	2	65	NA	C
90	2017	ICNAS	3	3	35	3.9	C
756	2015	ICNAS	3	3	37	3.9	B
756	2016	ICNAS	3	3	35	3.9	B
750	2016	ICNAS	3	2	140	NA	C
777	2016	ICNAS	3	3	35	3.9	B
376	2016	ICNAS	3	3	70	NA	A
788	2015	ICNAS	3	3	37	3.9	C
788	2016	ICNAS	3	1	70	NA	D
788	2017	ICNAS	3	3	35	3.9	A
627	2016	ICNAS	3	2	65	NA	B
894	2016	ICNAS	3	3	35	3.9	D
760	2017	ICNAS	3	3	37	3.9	C
49	2016	ICNAS	3	3	45	NA	C
287	2016	ICNAS	3	3	35	3.9	A
734	2014	ICNAS	3	3	37	3.9	A
734	2016	ICNAS	3	2	70	NA	B
252	2015	ICNAS	3	3	37	3.9	A
903	2013	ICNAS	3	3	35	3.9	A
903	2015	ICNAS	3	3	35	3.9	A
903	2017	ICNAS	3	3	35	3.9	D
708	2016	ICNAS	3	3	35	3.9	C
970	2016	ICNAS	3	1	65	NA	A
317	2016	ICNAS	3	2	65	NA	A
785	2017	ICNAS	3	3	35	3.9	A
22	2015	ICNAS	3	3	35	3.9	A
22	2017	ICNAS	3	3	35	3.9	D
1077	2016	ICNAS	3	1	70	NA	D
1077	2017	ICNAS	3	3	35	3.9	D
795	2016	ICNAS	3	3	35	3.9	A
764	2016	ICNAS	3	1	65	NA	D
673	2017	ICNAS	3	3	35	3.9	A
662	2014	ICNAS	3	3	35	3.9	A
662	2016	ICNAS	3	3	35	3.9	B

Table 5.3: Image database scheme for MRI scans performed in HUC.

Patient ID	Study	Exam Place	Magnetic Field Intensity (T)	Slice thickness (mm)	Number of slices	Space between slices (mm)	Group
93	2009	HUC	1.5	5	20	6	A
93	2012	HUC	1.5	5	22	6	A
142	16.01.2007	HUC	1.5	5	20	6	A
142	2009	HUC	1.5	5	20	6	A
142	2010	HUC	1.5	5	22	6	A
142	2011	HUC	1.5	5	22	6	A
212	2013	HUC	1.5	5	24	6	B
212	2015	HUC	1.5	5	24	6	A
275	2008	HUC	1.5	5	20	6	A
275	2009	HUC	1.5	5	22	6	A
275	2013	HUC	1.5	5	24	6	A
90	2010	HUC	1.5	5	22	6	A
310	2008	HUC	1.5	5	22	6	A
310	2009	HUC	1.5	5	22	6	A
750	2014	HUC	1.5	5	22	6	A
777	2015	HUC	1.5	5	24	6	A
376	23.4.2008	HUC	1.5	5	20	6.5	A
376	4.6.2008	HUC	1.5	5	20	6.5	A
376	25.3.2011	HUC	1.5	5	24	6	A
376	14.10.2011	HUC	1.5	5	24	6	A
376	2012	HUC	1.5	5	24	6	A
376	2013	HUC	1.5	5	24	6	A
894	2008	HUC	1.5	5	20	6	C
894	2009	HUC	1.5	5	22	6	C
894	2012	HUC	1.5	5	22	6	A
49	2007	HUC	1.5	5	20	6	A
654	2014	HUC	1.5	5	22	6	A
654	2015	HUC	1.5	5	24	6	A
287	2009	HUC	1.5	5	20	6	A
287	2011	HUC	1.5	5	22	6	A
287	2012	HUC	1.5	5	20	6	A
252	2010	HUC	1.5	5	24	6	A
528	2010	HUC	1.5	5	22	6	D
708	2015	HUC	1.5	5	22	6	A
317	2008	HUC	1.5	5	20	6	A
317	2009	HUC	1.5	5	22	6	A
317	2010	HUC	1.5	5	22	6	A
317	2014	HUC	1.5	5	24	6	A
774	2014	HUC	1.5	5	25	6	A
22	2009	HUC	1.5	5	22	6	A
22	2011	HUC	1.5	5	22	6	A
22	2013	HUC	1.5	5	22	6	A

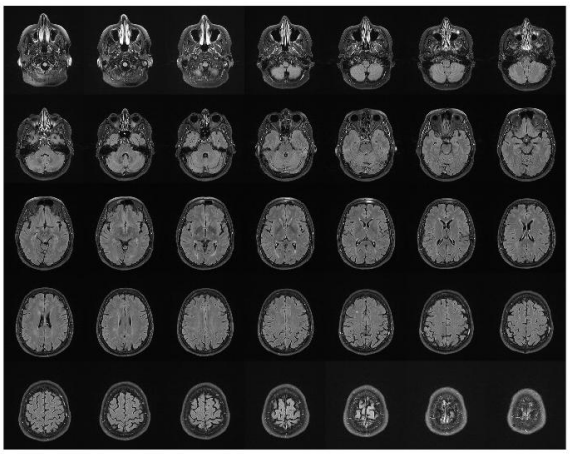

Figure 5.3: MRI FLAIR scan from patient 93 in 2015, 35 slices displayed. Exam performed at ICNAS, classified as B.

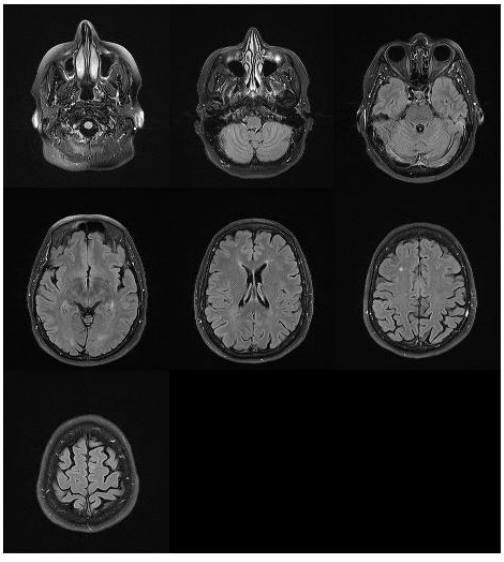

Figure 5.4: MRI FLAIR scan from patient 93 in 2015, 7 slices displayed. Exam performed at ICNAS, classified as B.

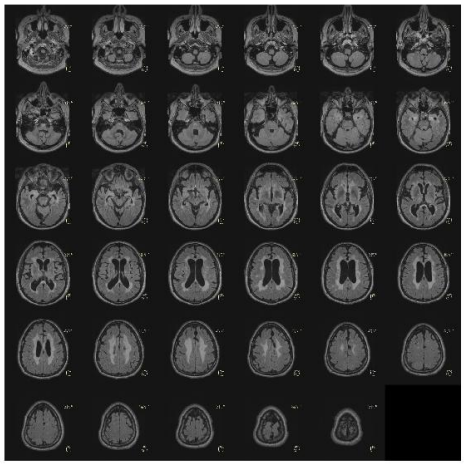

Figure 5.5: MRI FLAIR scan from patient 79 in 2016, 35 slices displayed. Exam performed at ICNAS, classified as C.

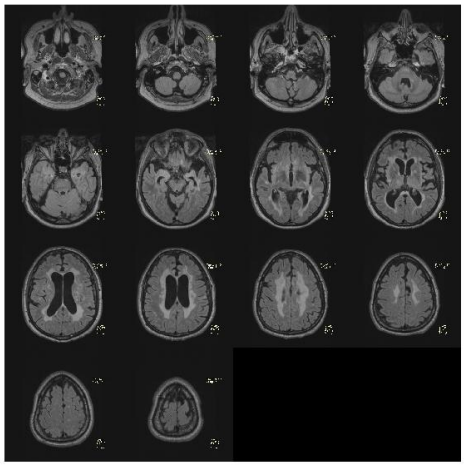

Figure 5.6: MRI FLAIR scan from patient 79 in 2016, 14 slices displayed. Exam performed at ICNAS, classified as C.

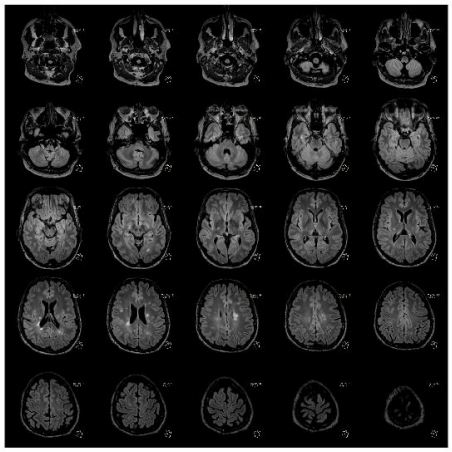

Figure 5.7: MRI FLAIR scan from patient 894 in 2016, 25 slices displayed. Exam performed at ICNAS, classified as D.

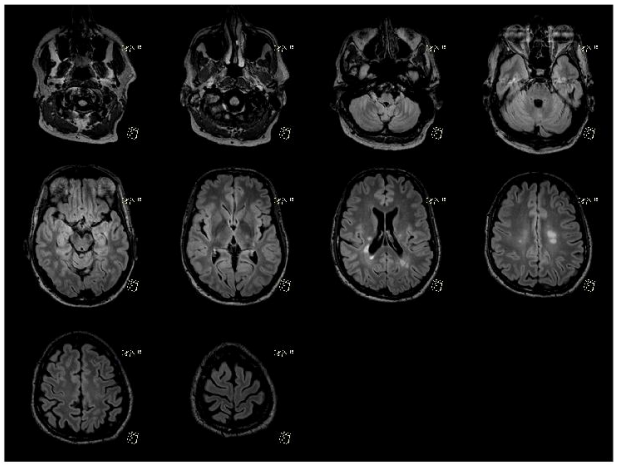

Figure 5.8: MRI FLAIR scan from patient 894 in 2016, 10 slices displayed. Exam performed at ICNAS, classified as D.

Chapter 6

Experimental procedure

The experimental procedure will be described in two parts due to the origins of data: clinical and image. As its origin it is completely different, the methods used for handling the information were different. Nevertheless, the processing pipeline used for both was the same: feature extraction, data normalization, feature selection according to label and machine learning prediction algorithms.

6.1 Clinical database

In the clinical database procedure (Figure 6.1), the first step consisted of feature extraction by using the present raw features. As there was data regarding several moments of the same patient (dynamic data) and intemporal data (static data), it was possible to extract features with different purposes. As a consequence, in order to explore the clinical database in a meaningful way, it was possible to create 4 different datasets: 1 static, where features were obtained by using all moment information as static and where time is no longer a changing factor, and 3 dynamics, regarding specific moments in time.

In the static database, one sample is one patient, in other words: a sample is constituted by the information regarding all clinic history of a patient. In the dynamic databases, one sample is a patient appointment, in other words: a sample is constituted by the information regarding all clinic history from the beginning until a defined moment or only the information regarding the mentioned defined moment. The 3 dynamic databases are intuitively named *Groundzero*, *Momentaneous* and *Momentaneous* with past. *Groundzero* is constituted only by information about the

entry at the clinic of each patient, *Momentaneous* by the momentaneous information regarding a defined moment of a patient when visited the clinic and *Momentaneous with past* has the same information of *Momentaneous* with the addition of data regarding previous moments.

After building the 4 raw databases, there is the need to apply feature normalization. This is extremely important, not only due to the use of machine learning algorithms but also to compensate the database flaws. As known, a patient goes to the clinic on routine appointments with a 3 or 6-month frequency. However, the database does not possess the same number of appointments for all patients, i.e., the amount of data varies from patient to patient without a logical reason. This way, by normalizing the information through the use of ratios, for example, it is possible to balance missing information in some cases.

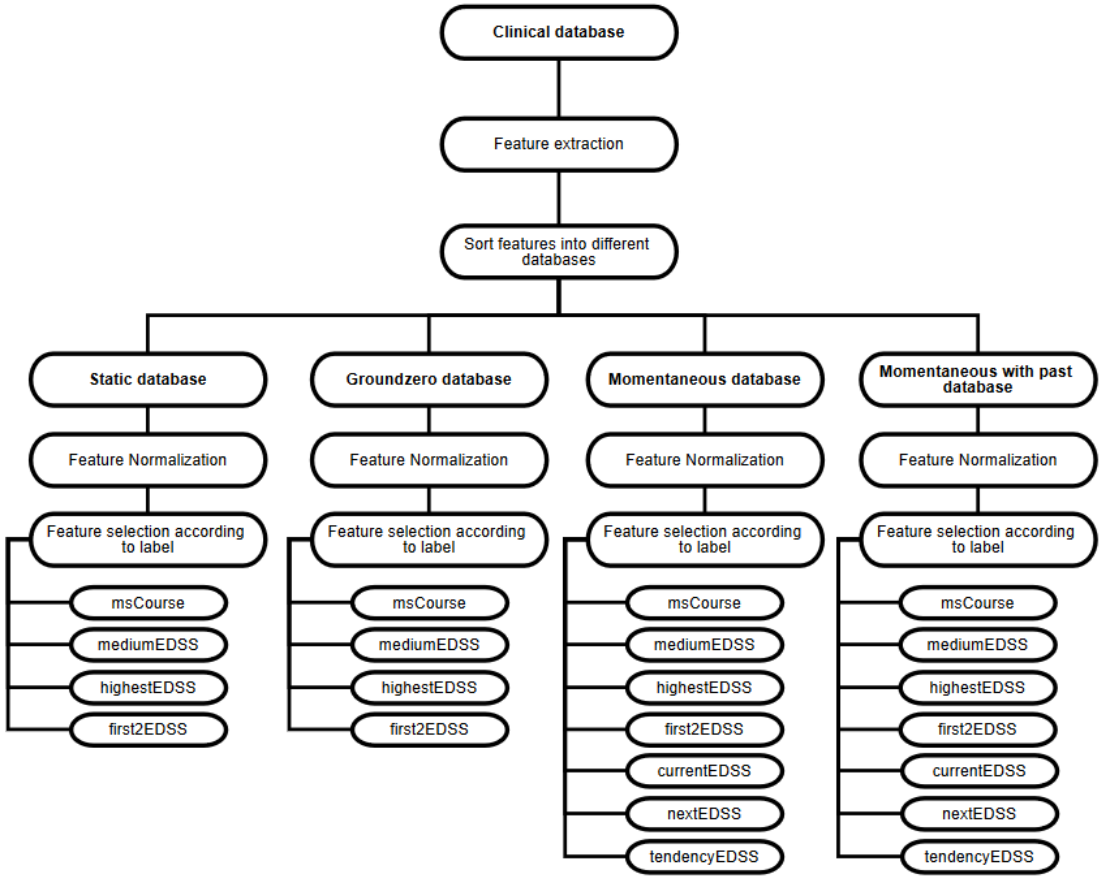

Figure 6.1: Clinical data procedure scheme.

Afterwards, feature selection according to different labels was performed. As a consequence, each database had a different set of features for different labels.

The chosen labels are related to MS course (PP or SP) and to EDSS, since it is the worldwide neurological scale used to evaluate the patient's condition and the disease progression. The procedures were always made with binary labels. This way, the EDSS-related labels were transformed from scales of 0-10 to binary ones. For each EDSS-related label, two different labels were created: EDSS-related value higher than 3 (> 3) and EDSS-related value higher than 5 (> 5). Using 5 as threshold was a natural decision, since not only is the medium value of the scale but also represents the beginning of a severe loss of ambulatory ability. 3 was also used as a threshold since Doctor Sónia Batista claimed it would be interesting as well, since physicians are also interested in this threshold. The first feature selection was performed entirely with the value 5 as it makes a clear separation of ambulatory ability in a considerable way.

The *mediumEDSS* label is the average value per year of a patient. When the patient has visited the clinic more than once in a year, the EDSS value of a defined year is the average of that time period. The *highestEDSS* label is the highest EDSS value that a patient might present during all appointments. *CurrentEDSS* label it is the EDSS value of a patient during a defined appointment. *NextEDSS* label is the EDSS of that patient next time he goes to the clinic. *First2EDSS* is the average EDSS value per year during the first 2 years in which the patient has visited the clinic. *TendencyEDSS* represents the fact that the EDSS will increase or not for a patient on the next visit to the clinic.

Due to the nature of the features, it was not possible to choose a set of features for each label in all databases. Thus, in *Static* and *Groundzero* databases it was only possible to do this for labels msCourse, *mediumEDSS*, *highestEDSS* and *first2EDSS*. After having the primary set of features for each possible label, a division for each set occurred (Figures 6.2 and 6.3): investigation procedure and standard procedure. Standard procedure works like a bypass, where nothing happens in this step. However, during the development of investigation procedure, clinically obvious features for the used label were deleted, as it is one of the thesis goals to discover some hidden feature influence.

Afterwards, a stricter feature selection was performed according to the pretended label, where only a reduced number of features was taken into account. There was the need for a small number of features due to overfitting since all databases have a small number of samples. *Groundzero* and *Static* databases have 37 samples each while *Momentaneous* and *Momentaneous with past* databases have 87 samples each. In Tables 6.1 and 6.2, it is possible to see the class distribution of each label for each database.

Table 6.1: Class distribution of the labels *msCourse*, *mediumEDSS*, *highestEDSS*, *highestEDSS* and *first2EDSS* for the *Static* and *Groundzero* databases.

Label	Samples of class 1 (number)	Samples of class 1 (%)
msCourse	11	29.73
mediumEDSS>3	15	40.54
mediumEDSS>5	6	16.22
highestEDSS>3	17	45.95
highestEDSS>5	7	18.92
first2EDSS>3	10	27.03
first2EDSS>5	1	2.70

Table 6.2: Class distribution of the labels *msCourse*, *mediumEDSS*, *highestEDSS*, *highestEDSS*, *first2EDSS*, *currentEDSS*, *nextEDSS* and *tendencyEDSS* for the *Momentaneous* and *Momentaneous with past* databases.

Label	Samples of class 1 (number)	Samples of class 1 (%)
msCourse	25	28.74
mediumEDSS>3	35	40.23
mediumEDSS>5	10	11.49
highestEDSS>3	45	51.72
highestEDSS>5	24	27.59
first2EDSS>3	22	25.29
first2EDSS>5	5	5.75
currentEDSS>3	35	40.23
currentEDSS>5	16	18.39
nextEDSS>3	34	39.08
nextEDSS>5	19	21.84
tendencyEDSS	11	12.64

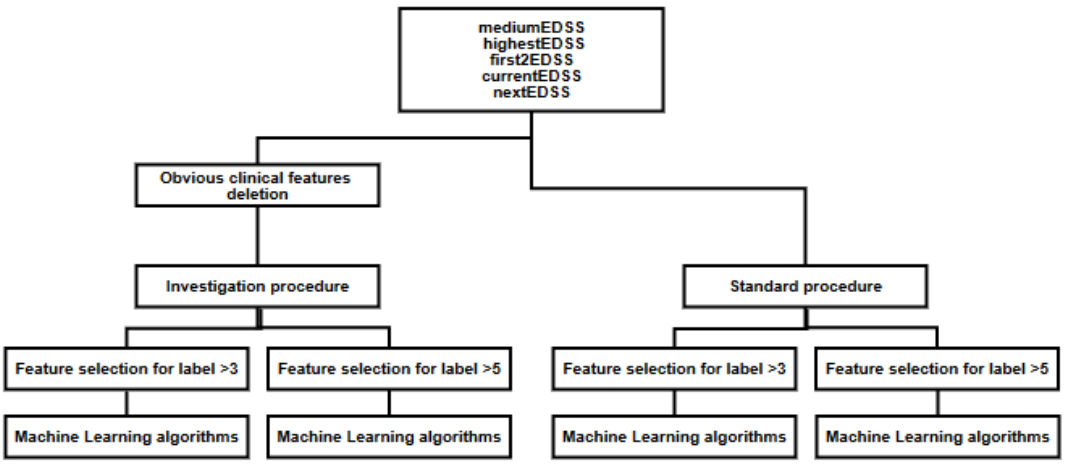

Figure 6.2: Clinical data procedure after first feature selection for EDSS-related features.

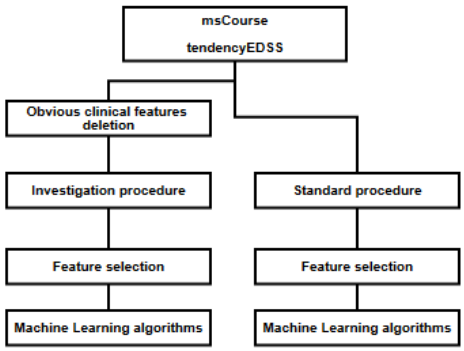

Figure 6.3: Clinical data procedure after first feature selection for non EDSS-related features.

6.1.1 Databases construction

Tables 6.3, 6.4 and 6.5 present a scheme of all features and all databases along with the normalization value (every feature is divided by this value in order to be normalized into a range of 0-1). The full explanation regarding every feature and its normalization process according to each database can be found in Appendix II (Clinical databases description).

Table 6.3: Scheme of all clinical features and databases regarding the Identification sheet.

Feature Name	Static	Groundzero	Momentaneous	Momentaneous with past	Normalization Value
Gender	X	X	X	X	1
Age of onset	X	X	X	X	50
Supratentorial	X	X	X	X	1
Optic Pathways	X	X	X	X	1
Brainstem-Cerebellum	X	X	X	X	1
Spinal Cord	X	X	X	X	1
Age of diagnosis	X	X	X	X	50
Years from onset to diagnosis	X	X	X	X	20
Clinical Findings	X	X	X	X	1
MRI	X	X	X	X	1
Evoked potentials	X	X	X	X	1
CSF	X	X	X	X	1
Age at SP diagnosis	X	X	X	X	60
Years from onset to diagnosis SP	X	X	X	X	25
MS Course	X		X	X	1
Active:	X		X	X	1
Age Visit			X	X	70
Years since onset			X	X	35

Table 6.4: Scheme of all clinical features and databases regarding the Visits sheet.

Feature Name	Static	Groundzero	Momentaneous	Momentaneous with past	Normalization Value
Nb of visits per year	X			X	3
Nb of visits 1st year	X			X	3
Nb of visits first 2 years	X			X	5
Suspected Relapses ratio per year	X			X	3
Suspected relapses ratio 1st year	X			X	3
Suspected relapses ratio first 2 years	X			X	5
EDSS medium value/year	X			X	10
EDSS 1st year	X			X	10
EDSS first 2 years	X			X	10
EDSS std/year	X			X	3
EDSS 1st year std	X			X	3
EDSS first 2 years std	X			X	3
EDSS medium variation/year	X			X	2
EDSS medium variation 1st year	X			X	3
EDSS medium variation first 2 years	X			X	3
EDSS std of variation/year	X			X	2
EDSS std of variation 1st year	X			X	3
EDSS std of variation first 2 years	X			X	3
EDSS increase 1st year	X			X	1
EDSS increase first 2 years	X			X	1
Ratio nb EDSS increase	X			X	1
Ratio nb EDSS decrease	X			X	1
Ratio nb EDSS decrease 1st year	X			X	1
Ratio nb EDSS decrease first 2 years	X			X	1
Routine visits ratio	X			X	1
Routine visits ratio 1st year	X			X	1
Routine visits first 2 years	X			X	1
No years	X			X	32
EDSS (momentaneous)		X	X		10
Routine (momentaneous)		X	X		1
Suspected Relapse (momentaneous)		X	X		1
Weakness (momentaneous)			X		1
Sympton (momentaneous)			X		1
Visit Age		X			60

Table 6.5: Scheme of all clinical features and databases regarding the Relapses sheet.

Feature Name	Static	Groundzero	Momentaneous	Momentaneous with past	Normalization Value
Relapses per year	X			X	4
Relapses 1st year	X			X	4
Relapses First 2 years	X			X	6
Pyramidal Ratio	X			X	1
Pyramidal 1st year	X			X	1
Pyramidal first 2 years	X			X	1
Brain Stem ratio	X			X	1
Brain Stem 1st year	X			X	1
Brain Stem first 2 years	X			X	1
Bowel ratio	X			X	1
Bowel 1st year	X			X	1
Bowel first 2 years	X			X	1
Neuropsycho ratio	X			X	1
Neuropsycho 1st year	X			X	1
Neuropsycho first 2 years	X			X	1
Cerebellum ratio	X			X	1
Cerebellum 1st year	X			X	1
Cerebellum 2 years	X			X	1
Visual ratio	X			X	1
Visual 1st year	X			X	1
Visual first 2 years:	X			X	1
Sensory ratio	X			X	1
Sensory 1st year	X			X	1
Sensory first 2 years	X			X	1
Corticosteroids ratio	X			X	1
Corticosteroids/year	X			X	1
Corticosteroids 1st year	X			X	1
Corticosteroids first 2 years	X			X	1
Average treatment intensity	X			X	3
Average treatment 1st year	X			X	3
Average treatment first 2 years	X			X	3
Average duration	X			X	10
Average duration 1st year	X			X	10
Average duration first 2 years	X			X	10
Relapse age		X			60
Time since onset		X			20
Pyramidal Tract (momentaneous)		X	X	X	1
Brain Stem (momentaneous)		X	X	X	1
Bowel Bladder (momentaneous)		X	X	X	1
Neuropsycho functions (momentaneous)		X	X	X	1
Cerebellum (momentaneous)		X	X	X	1
Visual functions (momentaneous)		X	X	X	1
Sensory functions (momentaneous)		X	X	X	1
Hospital (momentaneous)		X	X	X	1
Ambulatory (momentaneous)		X	X	X	1
Corticosteroids (momentaneous)		X	X	X	1
Treatment name (momentaneous)		X	X	X	3
Duration days (momentaneous)		X	X	X	10

6.2 Image database

For the MRI database (Figure 6.4), the first step consisted of processing the MRI scans in order to reduce the heterogeneity and to overcome the natural obstacles implied in this exam. Regarding the objective, this processing procedure has

different endings, although its structure is the same.

From this database, four databases were created. One is called *MRI Total Head* database as it is comprised of features extracted directly from the scans by ignoring the existence of lesions. In this database, a sample corresponds to features extracted from an MRI scan from a patient. The remaining databases are created by extracting features exclusively from regions manually marked as lesions. This procedure was performed by the Neuroradiologists Luís Rito Cruz and Mafalda Mendes Pinto. From the marked lesion regions, it was possible to extract different features and to sort them into different databases like it was performed with the clinical data. By corresponding one sample to one lesion, one sample to one study and one sample to one study, three databases are created regarding different levels of data:*One sample-One lesion*, *One sample-One study*, *One sample-One patient*. Intuitively, one can understand that *One sample one lesion* has only features extracted from a marked lesion, *One sample one study* has features extracted from all marked lesions regarding one MRI scan and *One sample one patient* has features extracted from all marked lesions from a patient.

Due to the structure of feature extraction for each database, the sample number was different. *One sample one lesion* is the largest as it is comprised of 6030 samples. *MRI total head* and *One sample one study* have the same number of samples, since the extracted features have an MRI study as a source of data (99 samples each). Finally, *One sample one patient* contains 36 samples, as it is the number of patients in the database. In Tables 6.6- 6.8, it is possible to see the class distribution of each label for every database.

Table 6.6: Class distribution of the labels *msCourse*, *mediumEDSS*, *highestEDSS*, *highestEDSS*, *first2EDSS*, *currentEDSS*, *nextEDSS* and *tendencyEDSS* for the *MRI total head* database and for *One sample one study* database.

Label	Samples with value 1 (number)	Samples with value 1 (%)
msCourse	20	20.20
mediumEDSS>3	41	41.41
mediumEDSS>5	15	15.15
highestEDSS>3	51	51.52
highestEDSS>5	21	21.21
first2EDSS>3	19	19.19
first2EDSS>5	8	8.08
currentEDSS>3	37	37.37
currentEDSS>5	21	21.21
nextEDSS>3	39	39.39
nextEDSS>5	22	22.22
tendencyEDSS	26	26.26

Table 6.7: Class distribution of the labels *msCourse*, *mediumEDSS*, *highestEDSS*, *highestEDSS*, *first2EDSS*, *currentEDSS* and *nextEDSS* for the *One sample one lesion* database.

Label	Samples with value 1 (number)	Samples with value 1 (%)
msCourse	1840	30.51
mediumEDSS>3	2864	47.50
mediumEDSS>5	902	14.96
highestEDSS>3	3492	57.91
highestEDSS>5	1501	24.89
first2EDSS>3	1094	18.14
first2EDSS>5	172	2.85
currentEDSS>3	2872	47.63
currentEDSS>5	1753	29.07
nextEDSS>3	2843	47.15
nextEDSS>5	1810	30.02

Table 6.8: Class distribution of the labels *msCourse*, *mediumEDSS*, *highestEDSS*, *highestEDSS* and *first2EDSS* for the *One sample one patient* database.

Label	Samples with value 1 (number)	Samples with value 1 (%)
msCourse	10	27.78
mediumEDSS>3	14	38.89
mediumEDSS>5	5	13.89
highestEDSS>3	16	44.44
highestEDSS>5	7	19.44
first2EDSS>3	7	19.44
first2EDSS>5	2	5.56

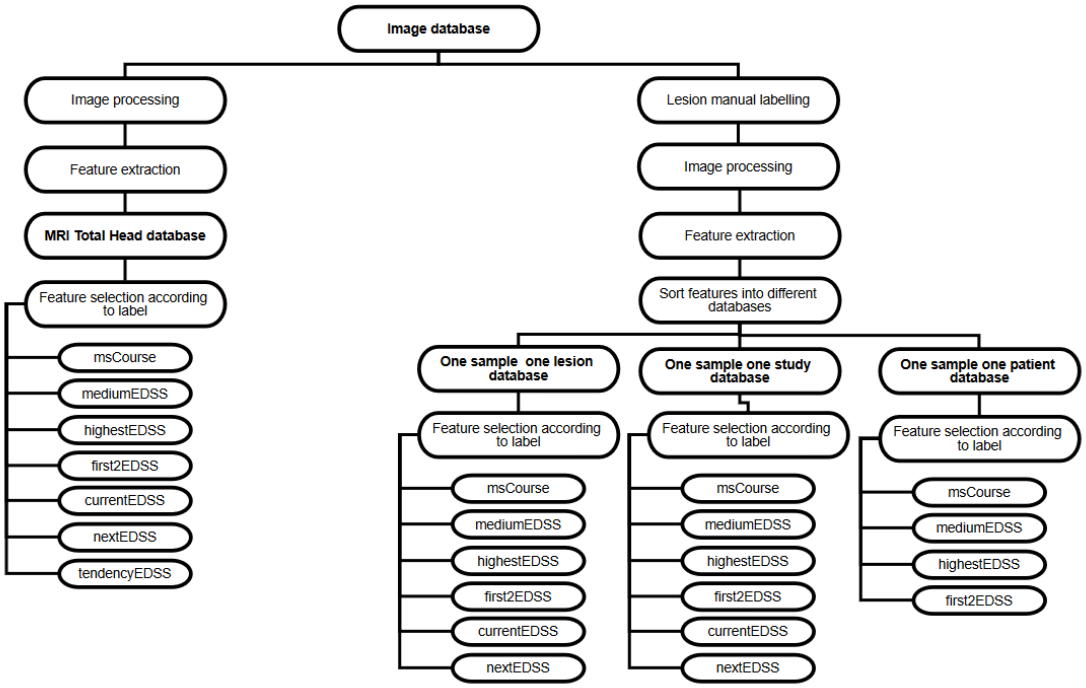

Figure 6.4: Image data procedure scheme.

As with the other (clinical) databases, each database suffered a feature selection process regarding specific labels: *msCourse*, *mediumEDSS*, *highestEDSS*, *first2EDSS*, *currentEDSS*, *nextEDSS*, *tendencyEDSS*, the same used with the clinical databases. However, the procedure from this step on was different (Figures 6.5 and 6.6) : there was not an investigation and a standard procedure since all features were image related. Thus, the risk of having obvious predictors was non existential. After the first feature selection, there was an immediate stricter selection regarding each label. If the label was EDSS-related, two different feature selections were performed, regarding the value 3 and 5 as binary labeling thresholds. If the label was

not EDSS-related, in other words, if it was already binary, the stricter selection is performed immediately. Afterwards, machine learning algorithms were applied.

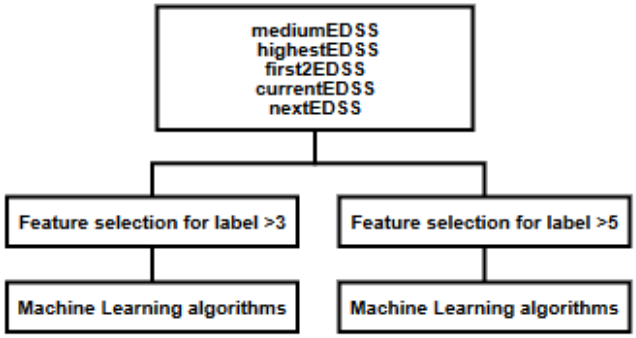

Figure 6.5: Image data procedure after first feature selection for EDSS-related features.

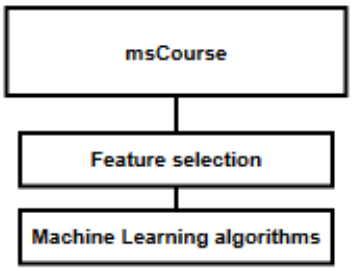

Figure 6.6: Image data procedure after first feature selection for non EDSS-related features.

6.2.1 Image processing

MRI brain scans analysis require a rigorous processing due to the existing heterogeneity of its procedure. Factors like the MRI machine, magnetic field intensity, slice thickness, spacing between slices and even body patient movement have a considerable influence on the final outcome.

6.2.1.1 SRI24 Atlas

Due to the research work described in Chapter 4, the use of an atlas seemed very adequate, not only due to the idea of using a statistical brain constructed by several different brains but also due to the variability of the MRI scans of CHUC's database.

Thus, a reference MRI scan was needed. As no atlas with MRI longitudinal scans was found, this study only comprised of transversal scans.

Several atlases were found, with the Illinois Institute of Technology (IIT) Human Brain Atlas (v4.1), the Laboratory of Neuro Imaging (LONI) Probabilistic Brain Atlas (LPBA40) [74], SRI24 [75], International Consortium for Brain Mapping (ICBM) 452 [76] and SPM12 atlas being the most interesting ones.

The chosen one was the SRI24, as it was the most complete in terms of information regarding the MRI scans. Besides having the T1, T2 and PD scans, it also contained brain-only sequences of the mentioned modalities, tissue probability density maps for CSF, GM, WM, tissue segmentation map and two anatomical maps of the brain. In Table 6.9, a comparison between atlases is made where it is possible to confirm that SRI24 is the atlas with more study tools.

Table 6.9: Comparison between the existing tools in the IIT Human Brain Atlas, LPBA40, SRI24, ICB452 and SPM12 atlases.

Atlas	**IIT Human Brain Atlas**	**LPBA40**	**SRI24**	**ICBM 452**	**SPM12**
T1	X	X	X		X
T2	X		X		X
PD scan			X		X
T1 (brain only)			X		
T2 (brain only)			X		
PD (brain only)			X		
CSF probability map	X	X	X	X	
GM probability map	X	X	X	X	
WM probability map	X	X	X	X	
Background, CSF, GM and WM full tissue map			X		
Anatomical Map		X	X	X	X

The SRI24 atlas is an MRI-based atlas of normal adults through the use of template-free non-rigid registration from images of 24 normal subjects. Its image resolution is 1mm and the magnetic field intensity is 3T. Additionally, it has been proved that this atlas allows equally accurate spatial normalization of MRI scans when compared to atlases acquired at 1.5T. As CHUC's database consists largely of by 1.5T scans, this factor constitutes a primary key to the image processing procedure. This atlas comprises 155 slices where each slice has a dimension of 240×240. Thus, all sequences and maps have dimensions of 240×240×155. Figures 6.7-6.18 provide a full insight of the SRI atlas, showing all study tools that will be necessary for the image processing procedure and feature extraction.

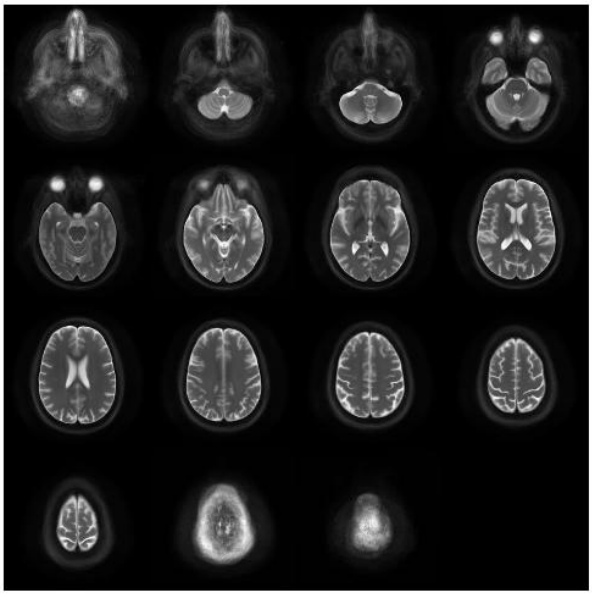

Figure 6.7: The SRI24 T2 sequence. Slices displayed (left to right, top to bottom): 10,20,30,40,50,60,70,80,90,100,110,120,130,140 and 150.

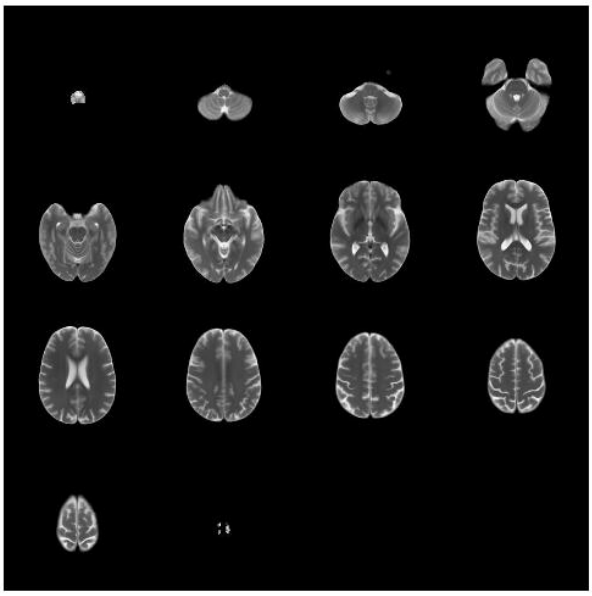

Figure 6.8: The SRI24 T2-brain sequence. Slices displayed (left to right, top to bottom): 10,20,30,40,50,60,70,80,90,100,110,120,130,140 and 150.

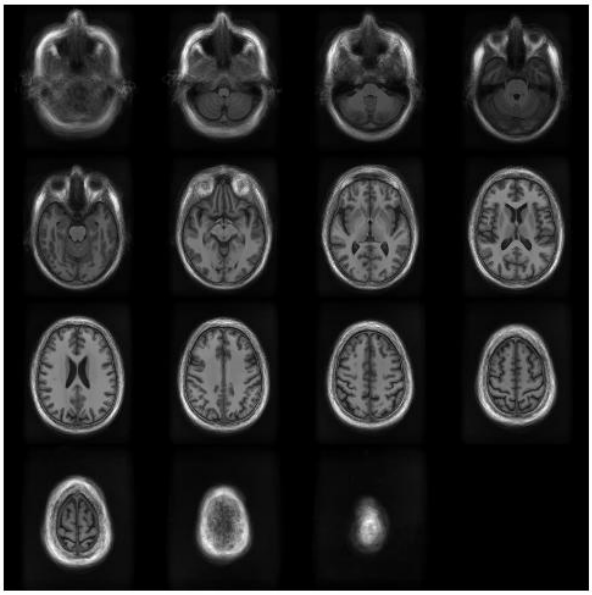

Figure 6.9: The SRI24 T1 sequence. Slices displayed (left to right, top to bottom): 10,20,30,40,50,60,70,80,90,100,110,120,130,140 and 150.

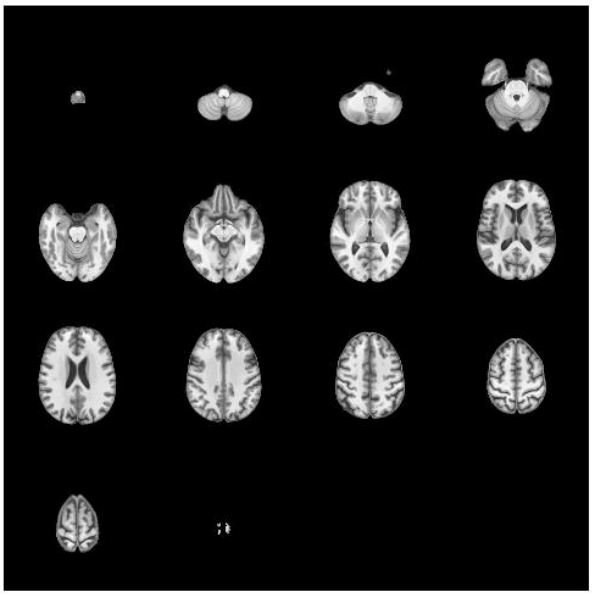

Figure 6.10: The SRI24 T1-brain sequence. Slices displayed (left to right, top to bottom): 10,20,30,40,50,60,70,80,90,100,110,120,130,140 and 150.

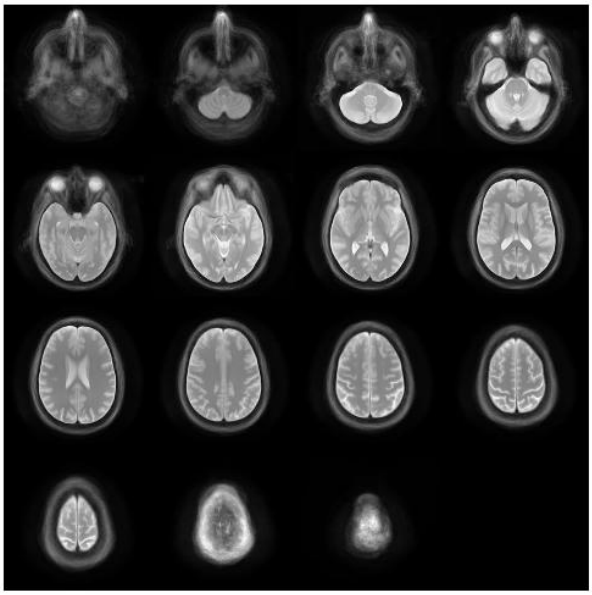

Figure 6.11: The SRI24 PD sequence. Slices displayed (left to right, top to bottom): 10,20,30,40,50,60,70,80,90,100,110,120,130,140 and 150.

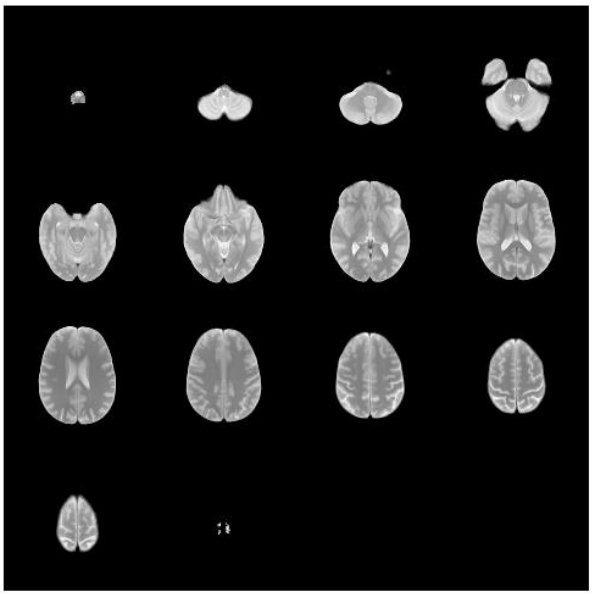

Figure 6.12: The SRI24 PD-brain sequence. Slices displayed (left to right, top to bottom): 10,20,30,40,50,60,70,80,90,100,110,120,130,140 and 150.

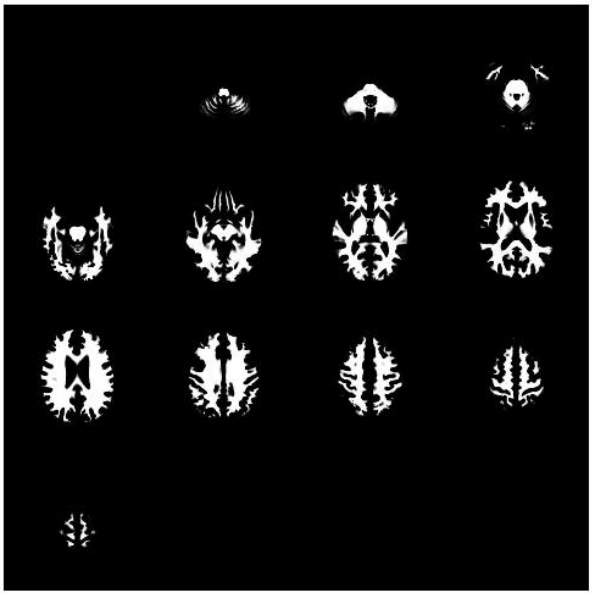

Figure 6.13: The SRI24 WM probability map. Slices displayed (left to right, top to bottom): 10,20,30,40,50,60,70,80,90,100,110,120,130,140 and 150.

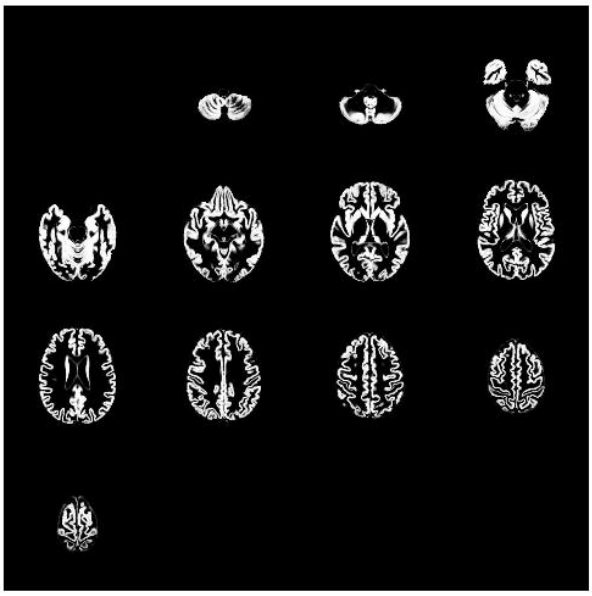

Figure 6.14: The SRI24 GM probability map. Slices displayed (left to right, top to bottom): 10,20,30,40,50,60,70,80,90,100,110,120,130,140 and 150.

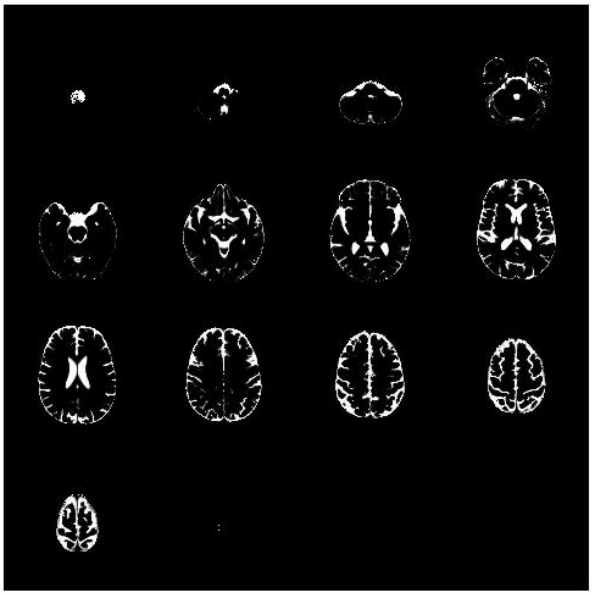

Figure 6.15: The SRI24 CSF probability map. Slices displayed (left to right, top to bottom): 10,20,30,40,50,60,70,80,90,100,110,120,130,140 and 150.

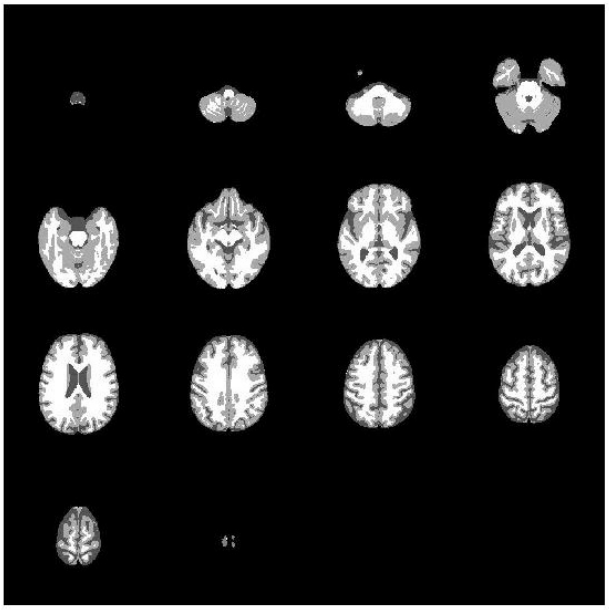

Figure 6.16: The SRI24 tissues map. Black corresponds to background, white to WM, light gray to GM and dark gray to CSF. Slices displayed: 10,20,30,40,50,60,70,80,90,100,110,120,130,140 and 150.

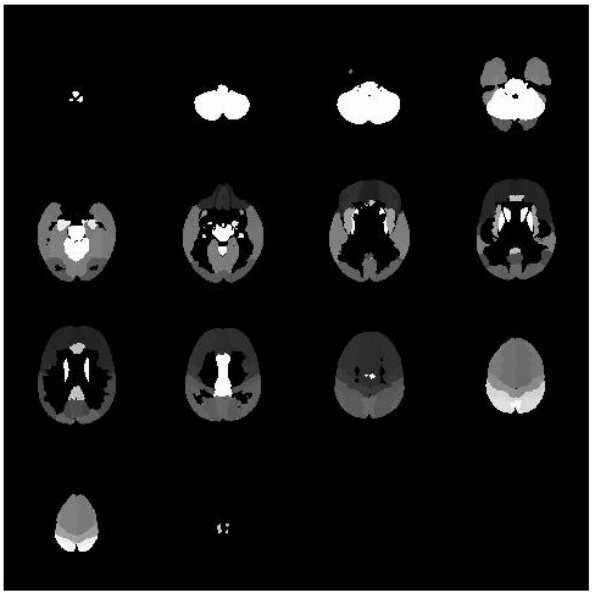

Figure 6.17: The SRI Anatomical Map I. This map divides the brain into 56 regions. Each different level of gray represents a different region.

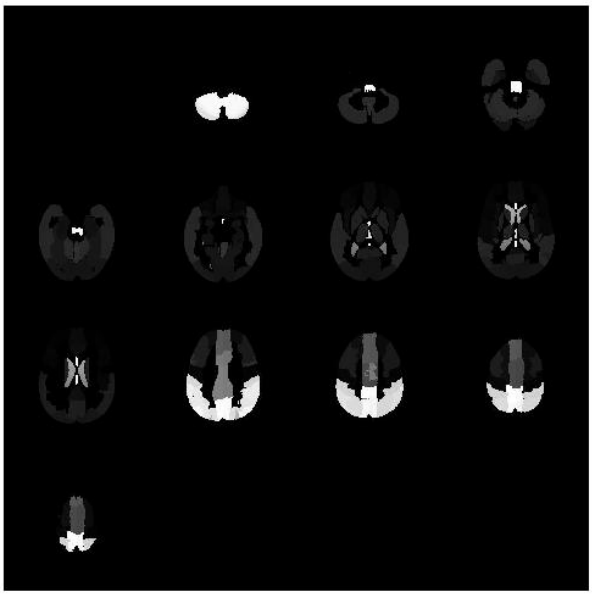

Figure 6.18: The SRI Anatomical Map II. This map divides the brain into 404 regions. Each different level of gray represents a different region.

6.2.1.2 Sequence selection and image resizing

The sequence selection and image resizing procedure is summed up in Figure 6.19. The first step consisted of checking the modality of the scan. An MRI study of the image database comprises a T1, T1-Gde, T2, FLAIR and PD sequences. Each sequence had this image processing procedure separately since patient movement and image characteristics were influencing factors.

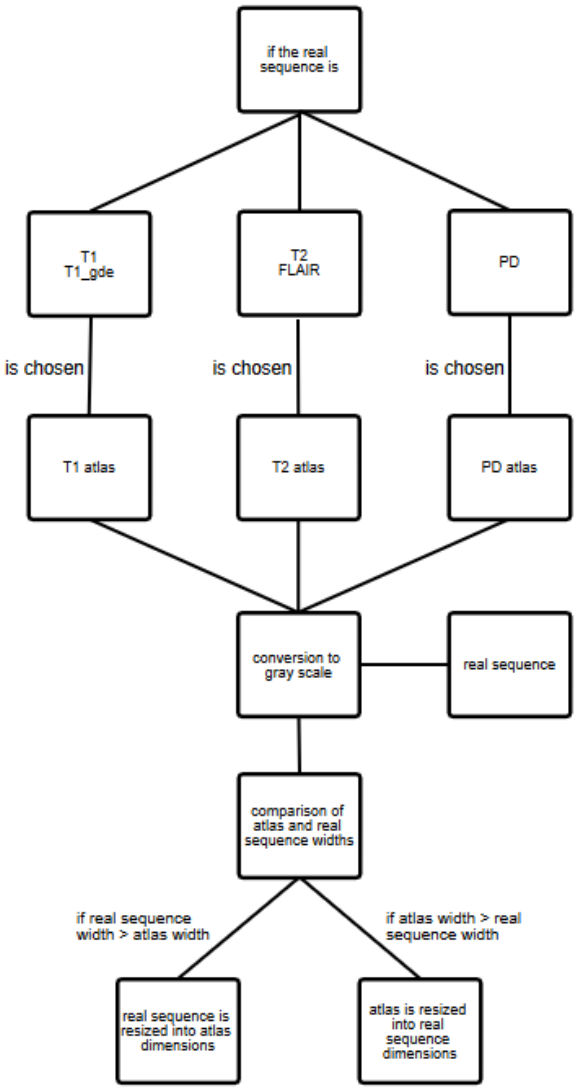

Figure 6.19: Sequence selection and image resizing procedure scheme.

The procedure for every sequence was similar, where the only modification was regarding the atlas sequence to be used. If the sequence to be analyzed was a T1 or a T1-Gde, the chosen atlas sequence would be a T1. If it was a T2 or FLAIR, the

chosen sequence would be a T2. At last, if it was a PD, the chosen atlas sequence would be the PD one. The chosen atlas sequence was converted into a grayscale image. The same operation was performed to the real sequence. Besides, reducing the differences between both was useful in the next steps.

As known, CHUC's database has different sources of MRI scans. Thus, the dimensions of all scans were not equal. Besides, the atlas dimensions also needed to be taken into account. As there was the need to work with the same dimensions regarding the real MRI scan and the atlas, the dimensions of both images were compared. If the atlas width was larger than the one from the real sequence, the atlas would be resized to the sequence dimension. Otherwise, the real sequence would be resized to the atlas dimensions. It was chosen to always reduce the dimension instead of increasing it, since the last one would create artifacts. By reducing the dimension, some information is lost, but theoretically the created artifacts would be less than the ones created by an increase process. The resizing process was performed with a bicubic interpolation.

6.2.1.3 Top and bottom head delimitation

The top and bottom head delimitation procedure is summed up in Figure 6.21. Not all MRI scans started and ended at the exact same slice number. As a consequence, a process that chooses the slices delimiting the volume of the brain had to be performed. As the atlas is not mutable, it seemed appropriate to first choose the starting and ending slices in the atlas. The chosen bottom head slice was the seventh one and the top slice was the 130th one (Figure 6.20).

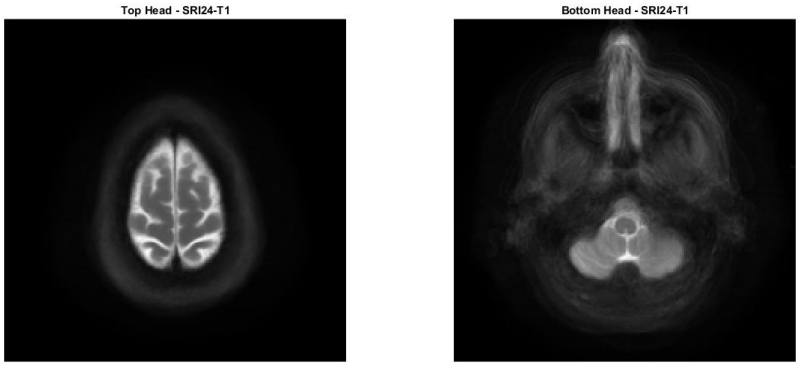

Figure 6.20: Atlas slices 130 and 7, top head slice (on the left) and the atlas bottom head (on the right).

The methods for choosing the adequate slice were different regarding top and bottom slices. As seen in Figure 6.20, the evolving complexity regarding the top and bottom head was quite different. While at the top there will be always a great homogeneity regarding the slice, at the bottom, there are many structures, such as the ending and beginning of the brain, spinal cord ending, bones, eyes, among other tissues. Thus, the top head slice search was relatively straightforward: the sequence slice with the highest 2D correlation with atlas 130th slice was defined as the head ending.

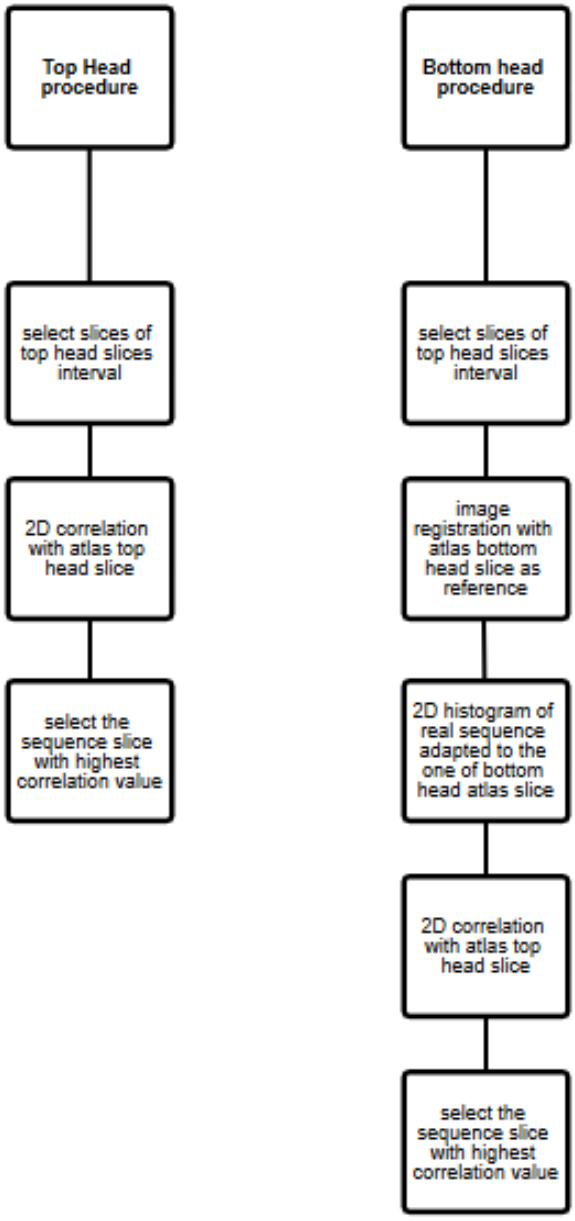

Figure 6.21: Top and bottom head limitation on real sequence procedure scheme.

This method was attempted for the bottom head but it was not successful.

A deeper approach was taken despite the decisive metric being the same: 2D correlation value with the bottom head atlas slice. This way, before calculating the correlation between the two images, an intermediate two-step process was driven in order to reduce the variability between both. Firstly, for each slice, it was performed an intensity-based image registration, where the fixed image was the reference (atlas slice). The geometric transformation applied was an affine one, which is a combination of translation, rotation, scale and shear operations. As MATLAB was the used software, it was possible to use function *imregister* along with function *imregconfig* where multimodal mode was chosen due to differences in brightness and/or contrast. Normally, when comparing two MRI images, the monomodal mode is the chosen one. However, the results with this modality mode were not satisfactory. After the slice is registered into the atlas slice, a histogram 2D adjustment was applied to the atlas image to match the histogram of the registered image. Afterwards, the 2D correlation was calculated between the two, where the highest slice value determined the slice to be used as the bottom of the brain.

Since this process required a certain computational power due do to the registration process, some conditions were applied to speed up the process. As all MRI scans direction is from the bottom to the top, the top image slice will never be found in the first slices. The same applies to the last slices and the bottom of the head. Thus, a manual study regarding all MRI scans was made in order to explore a safety search interval for both slices (see Table C.1 in Appendix III). In this study, all top and bottom slices were chosen manually. Afterwards, the standard deviation from MRI ending and start was calculated regarding the number of slices for each scan, in order to have the deviation results as a proportion value. With the normalized deviation values, an average and standard deviation values for top and bottom slices were calculated (Table 6.10).

With these calculated values and since the study comprised approximately 500 MRI sequences, it was assumed it followed a Gaussian distribution. By the law of large numbers, theoretically, there is a 99.7% probability of finding the correct slice in the chosen secure interval since it was used a distance of $\mu + 3\sigma$, where μ represents the mean value and σ the standard deviation. Thus:

1. **Top slice search interval:** from $slicesNumber$ to ($slicesNumber$ - ($\mu TopSlice$+ $3\sigma TopSlice$) $\times$ $slicesNumber$).
2. **Bottom slice search interval:**: from $First_Slice$ to ($\mu BottomSlice$+$3\sigma TopSlice$)$\times$ $slicesNumber$)

Table 6.10: The study performed with Table C.1 in order to calculate its medium and standard deviation values to speed up the brain limits selection process

Bottom Slice	**Top Slice**
μ **(Bottom - first)**	μ **(Last - top)**
0.11	0.15
σ **(Bottom - first)**	σ **(End - top)**
0.48	0.29

6.2.1.4 Slice atlas/sequence assignment

The slice atlas/sequence slice assignment procedure is summed up in Figure 6.22. With the existence of starting and ending slices for the MRI scans to be examined, the ones outside the starting-ending interval were removed. As the atlas and the MRI scans had a different number of slices, a slice matching between both was performed. A simple method would be to make the atlas slice assignment by choosing the one with the highest correlation value for each real sequence slice since the number of slices is always higher than in the real sequence.

However, the results were not successful since significant differences in brightness and contrast made some assignments without any anatomical logic. Thus, a more complex method was followed, where the order of each slice and its relative position were significant for the slice assignment process.

The first step consisted of creating two vectors of relative spatial positions, one for the atlas and another for the sequence. Both started at 0 and ende at 1 where values increased according to a regular scale determined by the length of the vectors. From the number of slices of each source, a search factor (N) was defined:

$$N = round(\frac{AtlasNumberOfSlices}{SequenceNumberOfSlices}).$$

N denotes the number of possible atlas slices that can be assigned to a real sequence. Thus, for every real sequence slice, it was computed the theoretical N closest atlas slices through the use of the two relative spatial position vectors. As a result, there was not a repetition of atlas slices assigned and the slices order was always respected.

From the N slices assigned to the sequence, there can only be a chosen one. A procedure similar to the one used for the bottom head slice followed up: for all the possible slices, an intensity-based image registration process (also affine and in multimodal mode) followed by a histogram adjustment was performed. However, in this case, the adapted histogram was the one from the atlas to the sequence one and not the inverse as in the previous case. The slice that presented the highest 2D

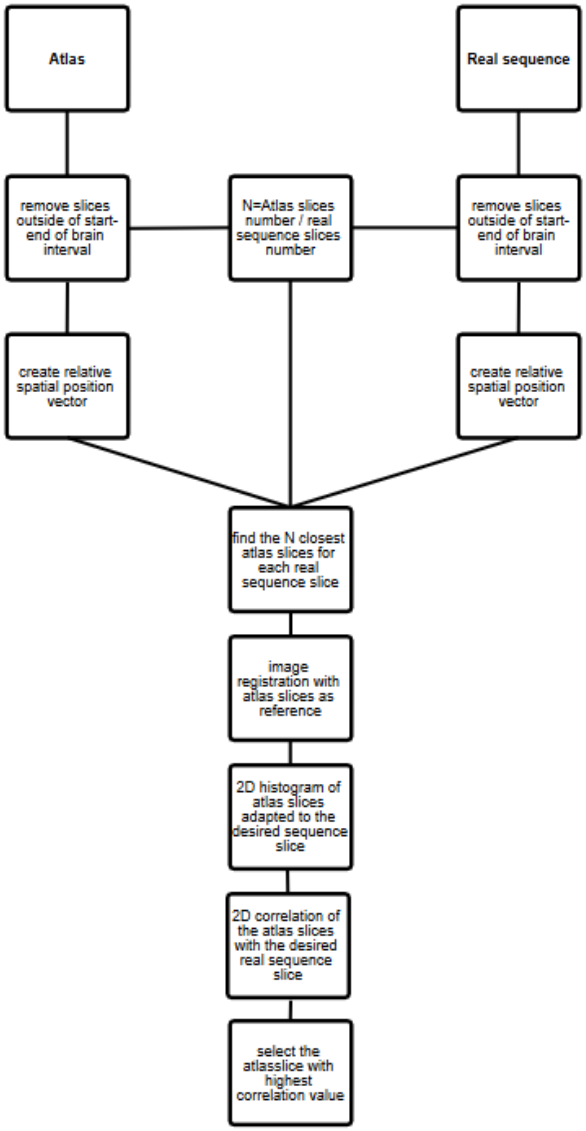

Figure 6.22: Slice atlas/sequence slice assignment procedure scheme.

correlation with the real sequence slice was is the assigned one.

However, this method had its flaws. Atlases are statistical studies of several patients and it is known that each brain is different. Thus, it was possible to encounter patients with brains having different structure size proportions. Despite this, this method seemed to be an interesting one since it took into account the relative positions and eliminated an incorrect order assignment while it still offered some freedom since there was a choice between N (if $N > 1$) atlas slices.

6.2.1.5 Image registration

The registration procedure is summed up in Figure 6.23. As each sequence slice had assigned an atlas slice, there was the need for transforming one of them in order to reduce as maximum possible their differences. Although a registration process had been used two times, it was only to improve the reliability of the 2D correlation results in the previous steps.

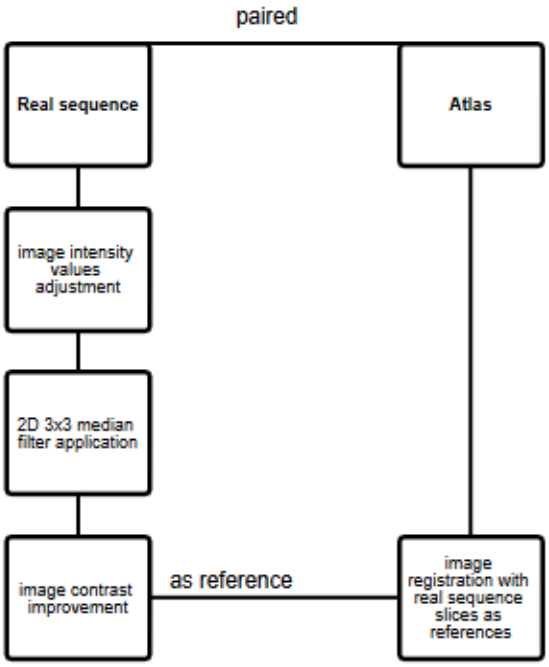

Figure 6.23: Registration procedure scheme.

The first step consisted in adjusting the real sequence intensity values followed by the application of a 2D median filter. In the used median filter, each output pixel contained the median value in a 3-by-3 neighborhood around the corresponding pixel. This filter eliminated some singularities and transformed each slice into a smoother and more uniform one. To improve contrast, the image was sharpened by using an unsharp masking method. In this method, an image is sharpened by subtracting a blurred (unsharp) version of the image from itself.

After this, an intensity-based image registration was performed. However, with a different form: the reference image was the real sequence slice and not the atlas slice. This change was decisive for the next steps regarding feature extraction. As properties like area, diameter, length, among others, were used, registering the real image into the atlas would leave to distortions and artifact creation. So, theoretically, it was more reasonable to adapt the atlas to the real sequence and not the

other way around.

6.2.1.6 MRI total head database

In order to proceed to the feature extraction regarding the *MRI total head* database, there was still an extra step. As features were extracted from different structures and used as ratios and differences against others, a skull stripping action was performed. Thus, it was possible to select only the brain in each MRI scan and it was also possible to select the non-brain structures, as seen in Figures 6.24 and 6.25.

Both sequences were constructed by using the brain-only atlas sequence and the head atlas sequence. To perform the skull stripping, the brain-only atlas sequence was turned into a binary mask and applied to the sequence. To perform the non-brain structures extraction, both total head and brain-only atlas sequences were turned into binary masks and applied to the sequence. Then the brain-only sequence was subtracted from the total head sequence.

MRI noise outside the head from the total scan was also eliminated, by applying the total head sequence as a mask. Therefore, every pixel positioned outside the registered head atlas was turned into value 0. To smooth the surfaces of the obtained scans by applying masks, a closing operation was performed with a disk of 12 pixels of diameter.

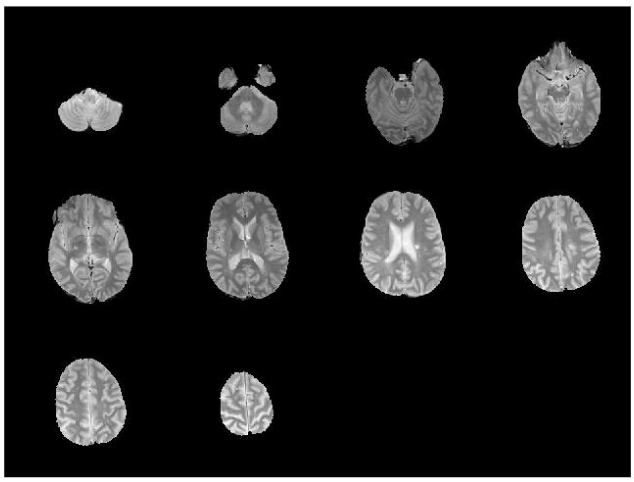

Figure 6.24: Skull stripped sequence of the patient 894, PD scan.

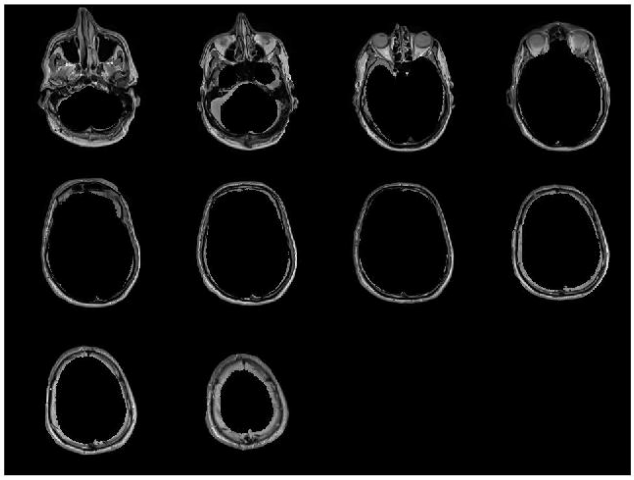

Figure 6.25: Non brain structures sequence of the patient 894, PD scan.

6.2.1.7 Manual lesion labeling

The first step of this process was performed by two neuroradiologists: Luís Rito Cruz and Mafalda Mendes Pinto. Their task was to label lesions by marking the existing lesions in FLAIR scans. The ones that presented contrast in T1-Gde sequences were also labeled. This labeling job was done through a DICOM reader software where it was possible to mark regions with green ellipses. Thus, a detection algorithm was performed by extracting the color green from the images followed by an automated circle detection function. This was applied to all FLAIR and T1-Gde contrasting lesions. An example can be seen in Figures 6.26, 6.27 and 6.28.

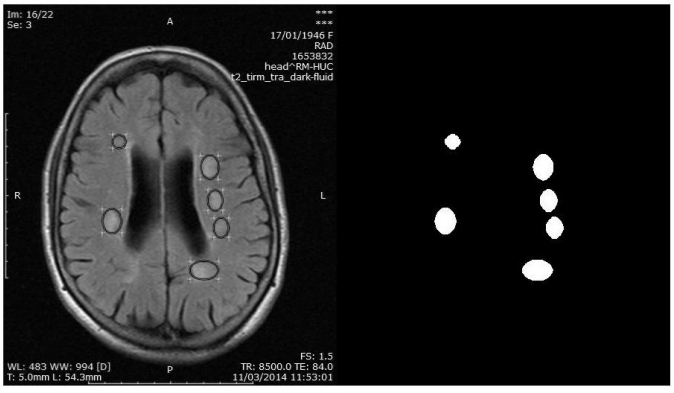

Figure 6.26: Lesion labeling example and its output as lesion mask. Patient 349, FLAIR scan, slice number 16.

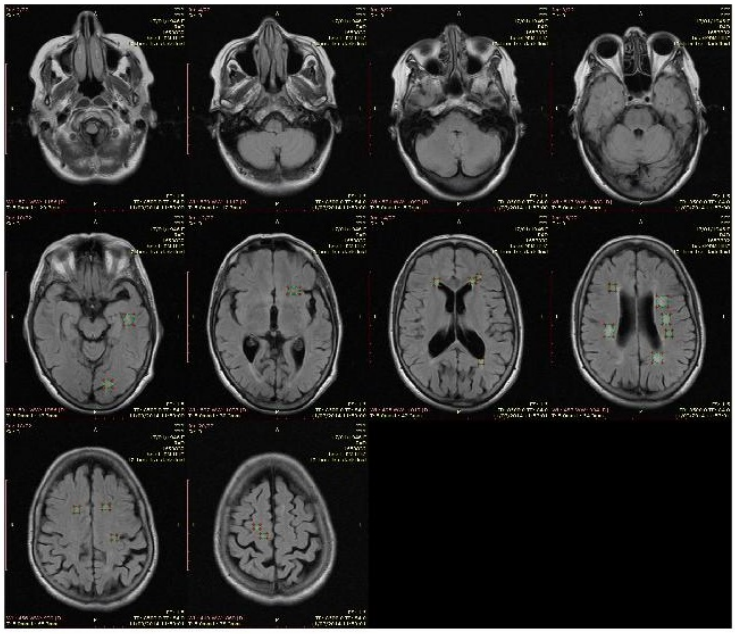

Figure 6.27: Lesion labeling example output. Patient 349, FLAIR scan. Pair slices only.

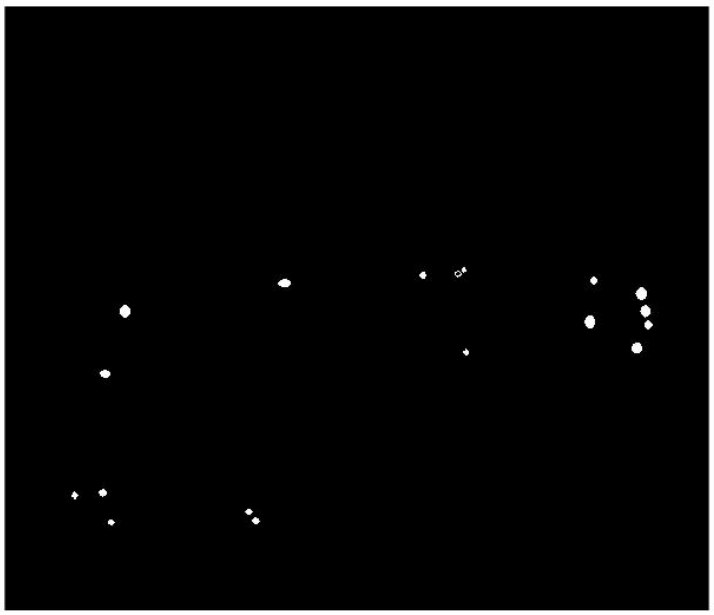

Figure 6.28: Lesion labeling output as lesion mask. Patient 349, FLAIR scan. Pair slices only

This process was also one of the reasons why the registration procedure was

performed with the atlas as moving image and not as reference. If it would have been the other way around, the lesion masks would have to suffer a registration process as well, modifying directly its shape, among other properties.

As these masks were made with FLAIR and not with the other sequences as well, these masks constituted an approximation for other modalities besides FLAIR. However, since all the modalities were acquired in a short period of time and it is known to the patient that is not allowed movement, the differences must not be significant. A process that could overcome this obstacle would be the registration of the lesion mask into the used sequence using the FLAIR sequence. However, that procedure was not as effective as the one when an atlas is used. An alternative strategy would be to label manually the other scans as well, which was a considerable hard task due to the time it consumes.

As a consequence, in order to minimize the computational complexity and to avoid hard time-consuming tasks, the one-modality lesion masks (FLAIR and T1-Gde) were used as approximations to the other modalities sequences, since the sequences were necessarily almost identical in terms of the number of slices and positioning. However, not all modalities had the exact same number of slices, as confirmed manually. So, a way of overcoming this obstacle was through the relative spatial position vector used in the registration process, in order to attribute lesion positioning in different locations. Each region marked in each slice was be considered a lesion since the existing differences between slices spacing and slice thickness would make a significant difference when calculating lesion volume.

In this process, the regions identified were the ones inside the circles. Initially, the idea was to use a region-growing algorithm by using the lesion center only. However, the attempted methods were not effective, since there was always the need to tune in extremely sensitive thresholds, which was not the direction intended for this project.

6.2.2 Image processing results

The same example from each MRI scan group described in Chapter 5 will be provided. Thus, patient 349 will be again representative of group A, patient 93 of group B, patient 79 of group C and patient 894 of group D, since the intra-group homogeneity is considerably higher than the inter-group one. For each one, the FLAIR, T1 and PD density scan results will be presented, as each one required a different atlas sequence as a reference. With this distribution, all case scenarios are approached.

6.2.2.1 Top and bottom head limitation

In group A, more specifically patient 349 regarding FLAIR scan, it is possible to observe in Figures 6.29-6.32 that the head delimitation process was successful. The slices were correctly chosen in both cases (top and bottom) and the graph results are coherent as it exists a logical correlation shape in the graphs where the maximum value is clearly distinct from the rest.

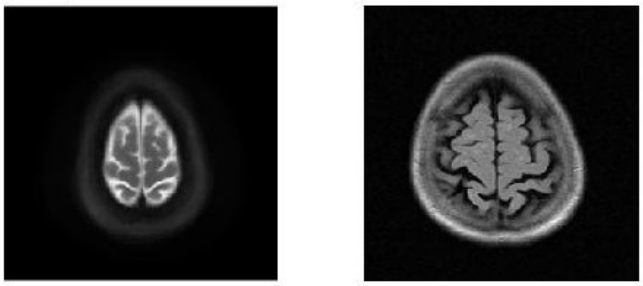

Figure 6.29: Top head slice selected for patient 349, FLAIR sequence.

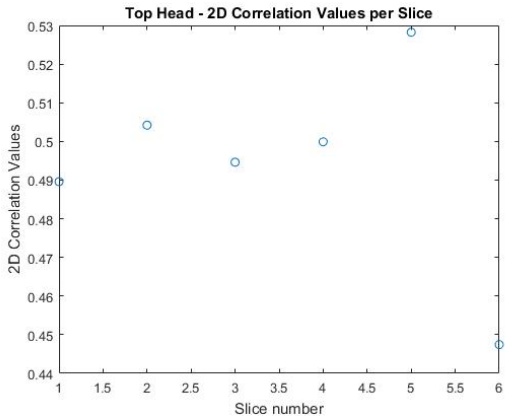

Figure 6.30: Top head slice 2D correlation values graph for patient 349, FLAIR sequence.

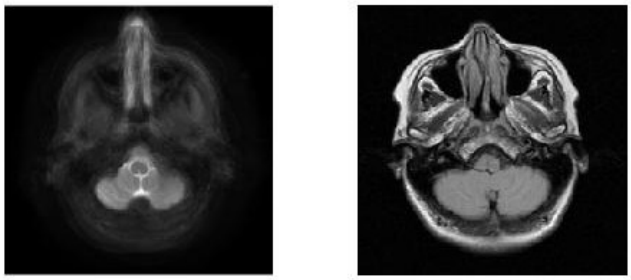

Figure 6.31: Bottom head slice selected for patient 349, FLAIR sequence.

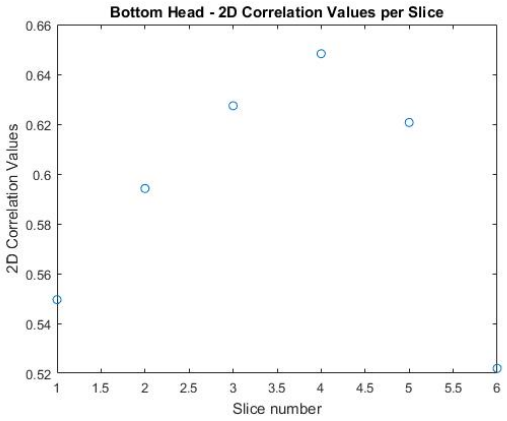

Figure 6.32: Bottom head slice 2D correlation values graph for patient 349, FLAIR sequence.

In group B, more specifically patient 93 regarding FLAIR scan, it is possible to observe in Figures 6.33-6.36 that the head delimitation process was successful. The slices were correctly chosen in both cases (top and bottom) and the graph results are coherent as it exists a logical correlation shape in the graphs where the maximum value is clearly distinct from the rest.

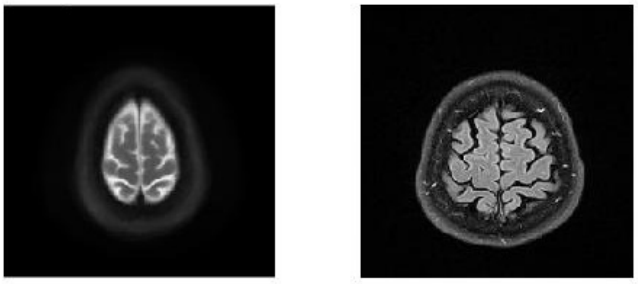

Figure 6.33: Top head slice selected for patient 93, FLAIR sequence.

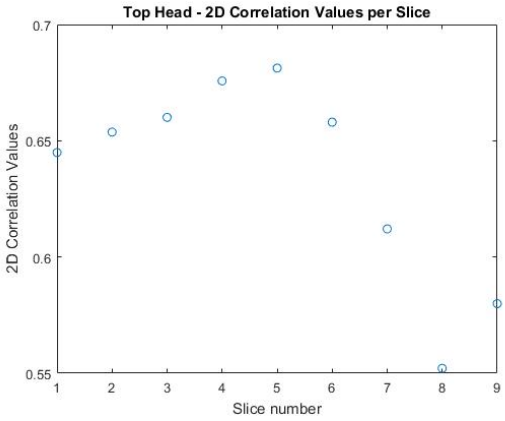

Figure 6.34: Top head slice 2D correlation values graph for patient 93, FLAIR sequence.

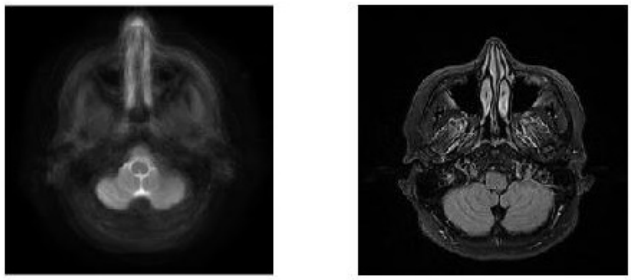

Figure 6.35: Bottom head slice selected for patient 93, FLAIR sequence.

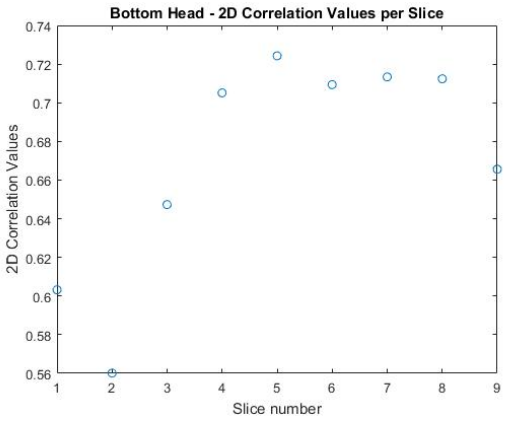

Figure 6.36: Bottom head slice 2D correlation values graph for patient 93, FLAIR sequence.

In group C, more specifically patient 79 regarding FLAIR scan, it is possible to observe in Figures 6.37-6.40 that the head delimitation process had some constraints. For the higher limit, the slices were correctly chosen and the graph results are

coherent as it exists a logical correlation shape in the graph where the maximum value is clearly distinct from the rest. However, for the bottom delimitation, it is possible to check that the graph shape has two peaks, where it should have only one. The chosen slice process could be better in this case. However, one can see that it is not a unsatisfactory performance though.

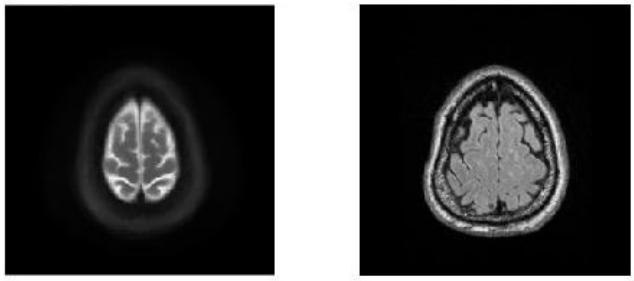

Figure 6.37: Top head slice selected for patient 79, FLAIR sequence.

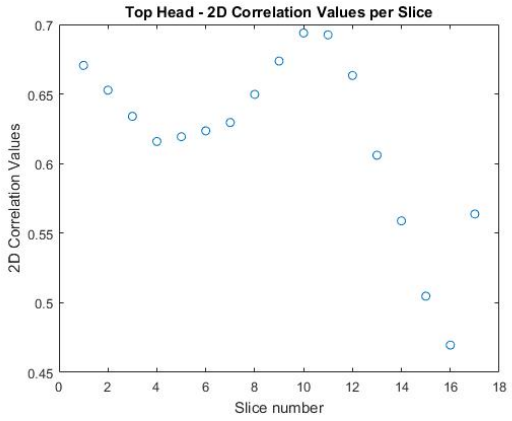

Figure 6.38: Top head slice 2D correlation values graph for patient 79, FLAIR sequence.

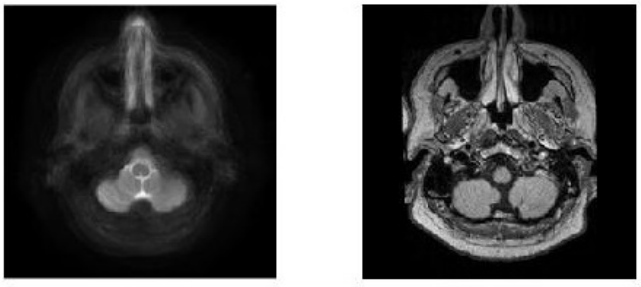

Figure 6.39: Bottom head slice selected for patient 79, FLAIR sequence.

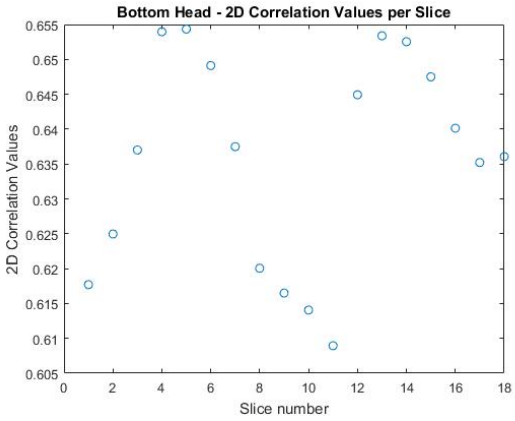

Figure 6.40: Bottom head slice 2D correlation values graph for patient 79, FLAIR sequence.

In group D, more specifically patient 894 regarding FLAIR scan, it is possible to observe in Figures 6.41-6.44 that the head delimitation process was successful. The slices were correctly chosen in both cases (top and bottom) and the graph results are coherent as it exists a logical correlation shape in the graphs where the maximum value is clearly distinct from the rest.

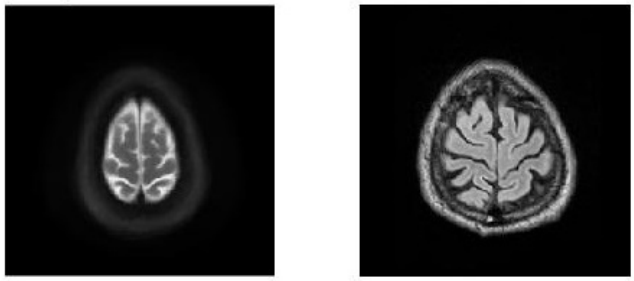

Figure 6.41: Top head slice selected for patient 894, FLAIR sequence.

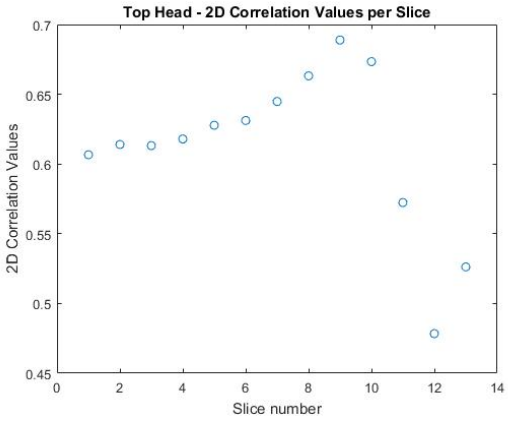

Figure 6.42: Top head slice 2D correlation values graph for patient 894, FLAIR sequence.

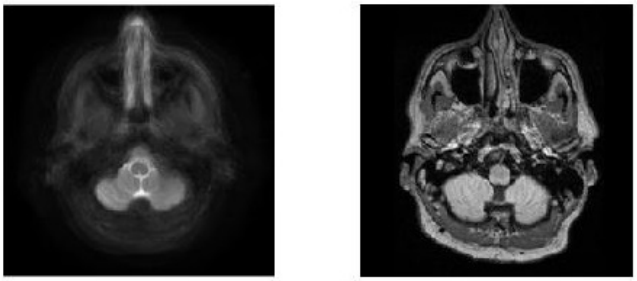

Figure 6.43: Bottom head slice selected for patient 894, FLAIR sequence.

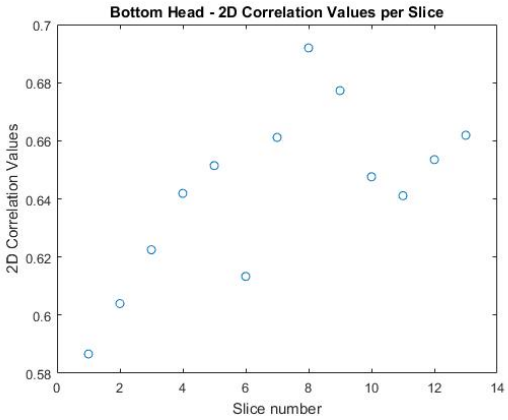

Figure 6.44: Bottom head slice 2D correlation values graph for patient 894, FLAIR sequence.

To conclude, the head delimitation with respect to FLAIR scans was successful. Despite the constraints presented for the bottom delimitation in group C, the output it is a satisfactory result. One can readily see this slide is relatively near to the ideal one.

In group A, more specifically patient 349 regarding T1 scan, it is possible to observe in Figures 6.45-6.48 that the head delimitation process was successful for the bottom delimitation. Despite the graph shape, the top slice had not a fully successful performance. It would have been considered more effective if a lower slice would have been chosen. However, the chosen slice is not distant from the ideal one.

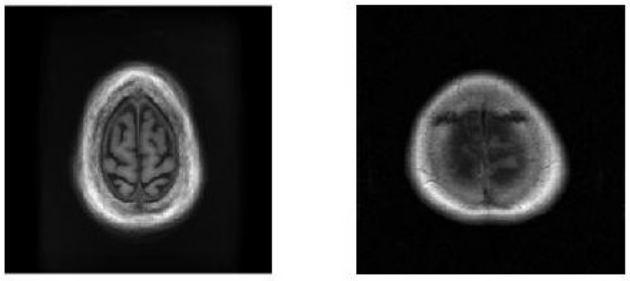

Figure 6.45: Top head slice selected for patient 349, T1 sequence.

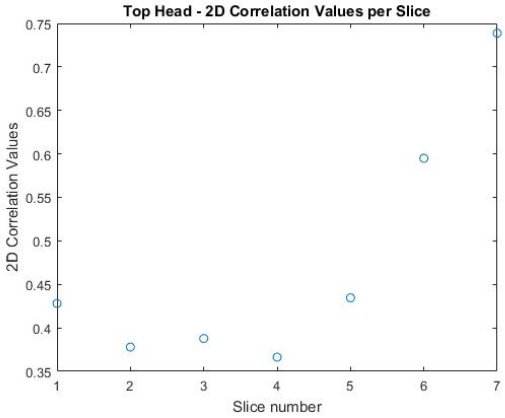

Figure 6.46: Top head slice 2D correlation values graph for patient 349, T1 sequence.

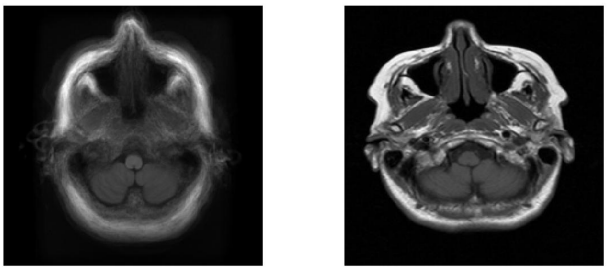

Figure 6.47: Bottom head slice selected for patient 349, T1 sequence.

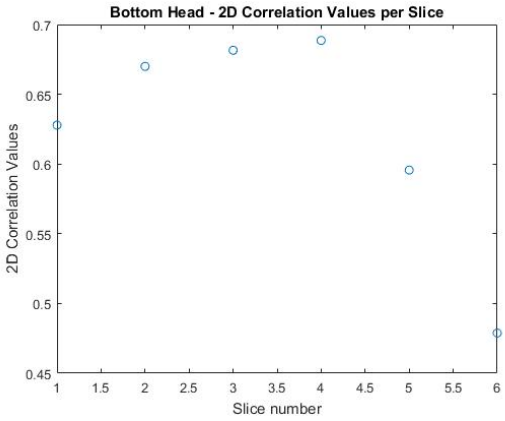

Figure 6.48: Bottom head slice 2D correlation values graph for patient 349, T1 sequence.

In group B, more specifically patient 93 regarding T1 scan, it is possible to observe in Figures 6.49-6.52 that the head delimitation process had some constraints. For the top delimitation, the slices were correctly chosen. However, for the bottom delimitation, it is possible to check that the assigned slice should have been a higher one. The graph shape shows logical results, nevertheless. As checked before, despite the wrong slice has been assigned, it is not distant from the desired one.

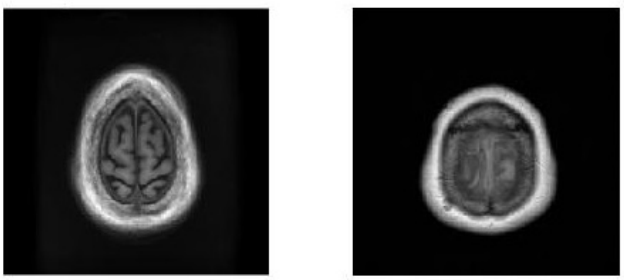

Figure 6.49: Top head slice selected for patient 93, T1sequence.

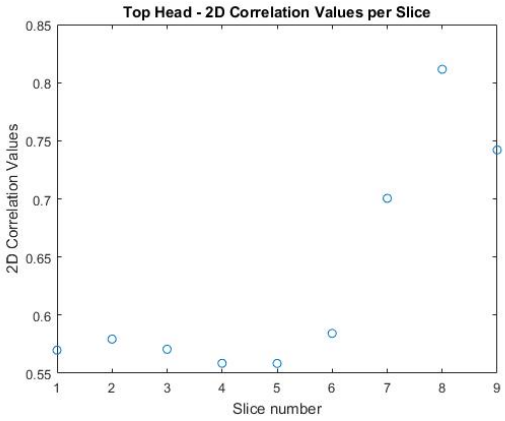

Figure 6.50: Top head slice 2D correlation values graph for patient 93, T1 sequence.

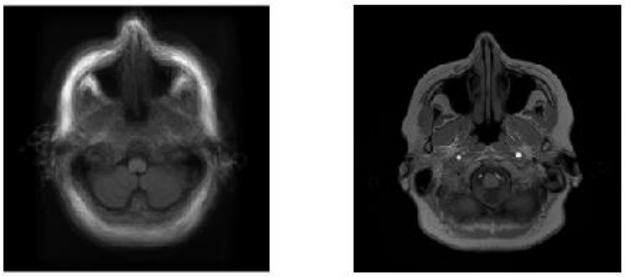

Figure 6.51: Bottom head slice selected for patient 93, T1 sequence.

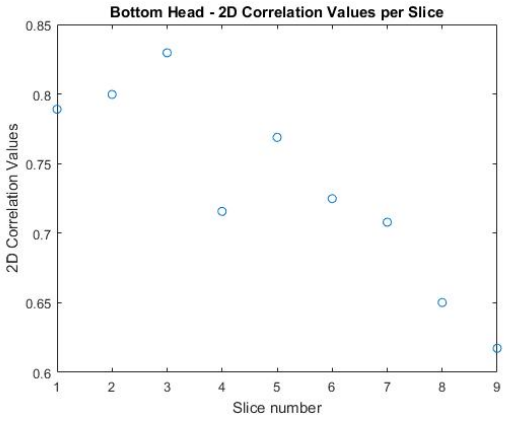

Figure 6.52: Bottom head slice 2D correlation values graph for patient 93, T1 sequence.

In group C, more specifically patient 79 regarding T1 scan, it is possible to observe in Figures 6.53-6.56 that the top delimitation process had some constraints. For the top delimitation, the process could have had a more satisfactory output,

despite not being distant from the desired one. This failure can be interpreted in the correlation graph as there were three slices with very similar values. The bottom delimitation procedure was successful.

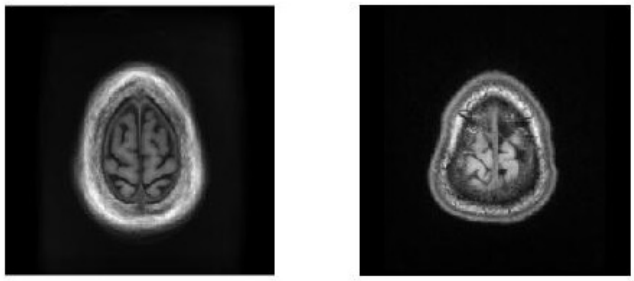

Figure 6.53: Top head slice selected for patient 79, T1 sequence.

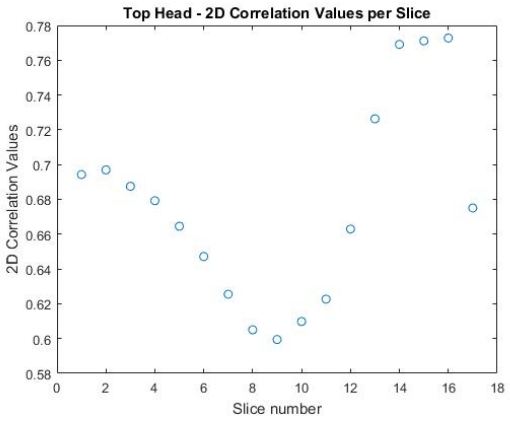

Figure 6.54: Top head slice 2D correlation values graph for patient 79, T1 sequence.

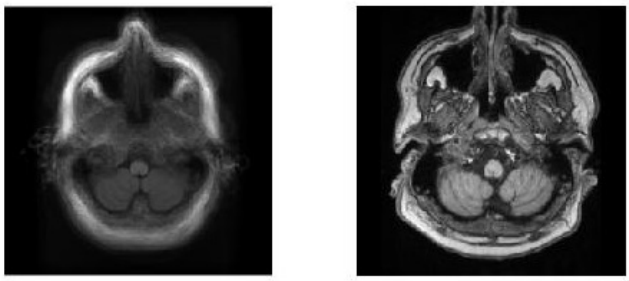

Figure 6.55: Bottom head slice selected for patient 79, T1 sequence.

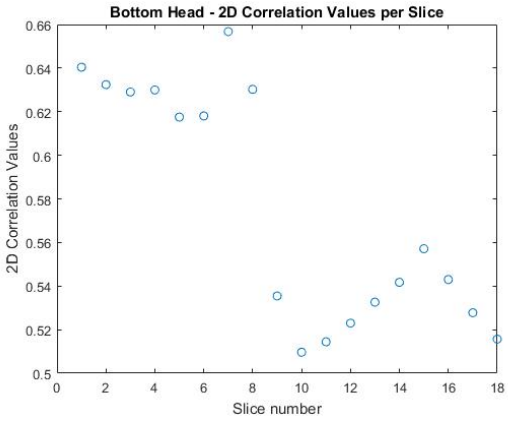

Figure 6.56: Bottom head slice 2D correlation values graph for patient 79, T1 sequence.

In group D, more specifically patient 894 regarding T1 scan, it is possible to observe in Figures 6.57-6.60 that both delimitation processes were successful.

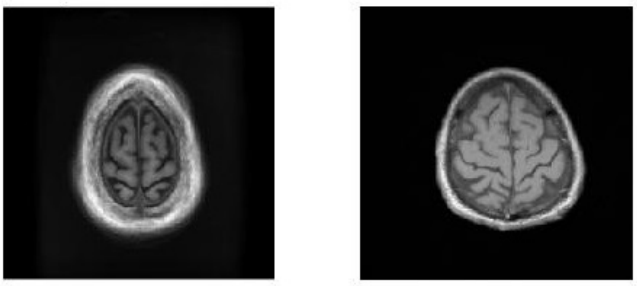

Figure 6.57: Top head slice selected for patient 894, T1 sequence.

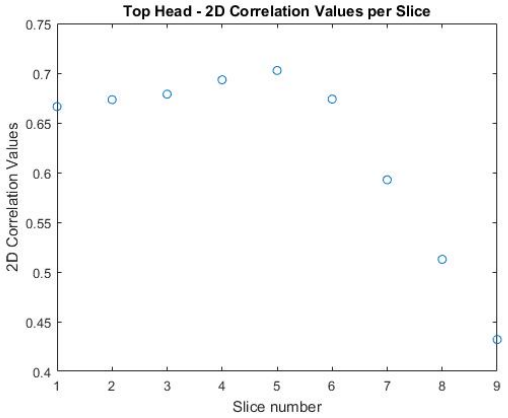

Figure 6.58: Top head slice 2D correlation values graph for patient 894, T1 sequence.

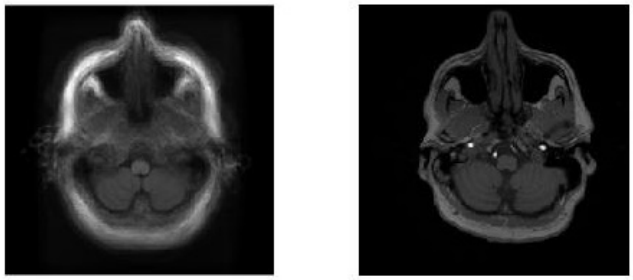

Figure 6.59: Bottom head slice selected for patient 894, T1 sequence.

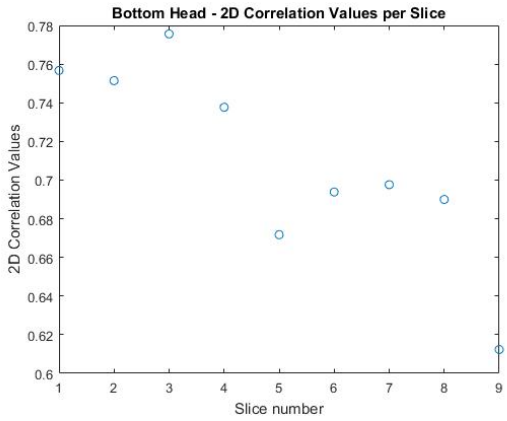

Figure 6.60: Bottom head slice 2D correlation values graph for patient 894, T1 sequence.

As a conclusion, the head delimitation regarding T1 scans was successful. There were more obstacles than with FLAIR scans. However, when the final output is not ideal, is not unsatisfactory either. These obstacles were verified in both delimitation processes.

In group A, more specifically patient 349 regarding PD scan, it is possible to observe in Figures 6.61-6.64 that both delimitation processes were successful.

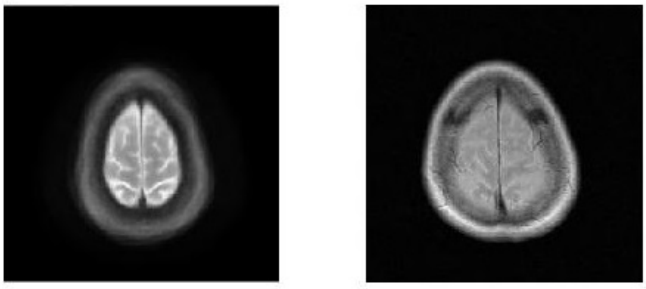

Figure 6.61: Top head slice selected for patient 349, PD sequence.

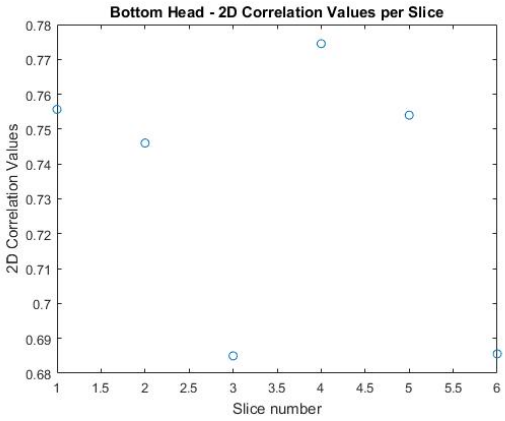

Figure 6.62: Top head slice 2D correlation values graph for patient 349, PD sequence.

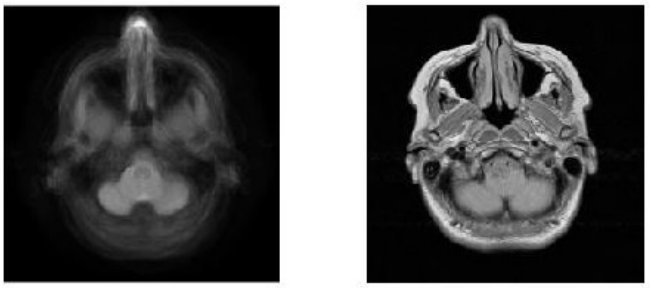

Figure 6.63: Bottom head slice selected for patient 349, PD sequence.

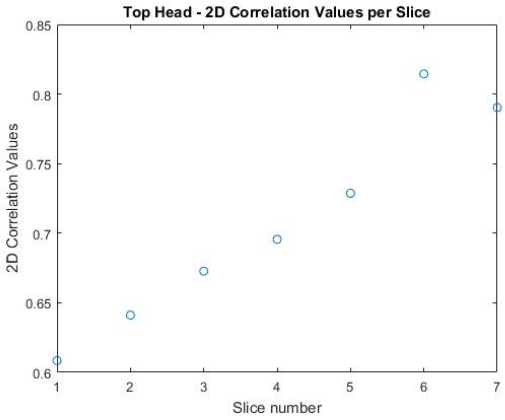

Figure 6.64: Bottom head slice 2D correlation values graph for patient 349, PD sequence.

In group B, more specifically patient 93 regarding PD scan, it is possible to observe in Figures 6.65-6.68 that top head delimitation process was successful.

The bottom delimitation, however, was not successful despite the correlation graph shape. A higher slice should have been chosen.

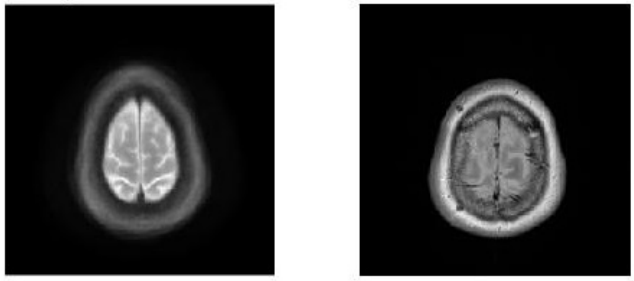

Figure 6.65: Top head slice selected for patient 93, PD sequence.

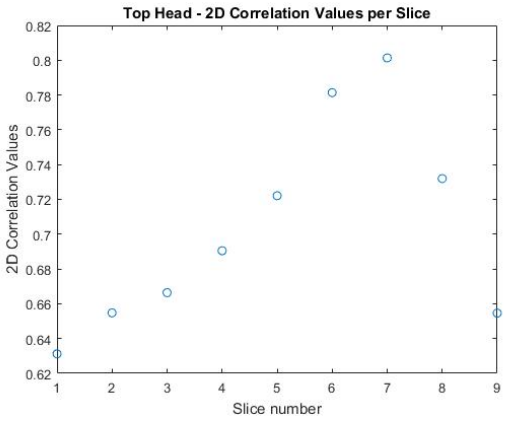

Figure 6.66: Top head slice 2D correlation values graph for patient 93, PD sequence.

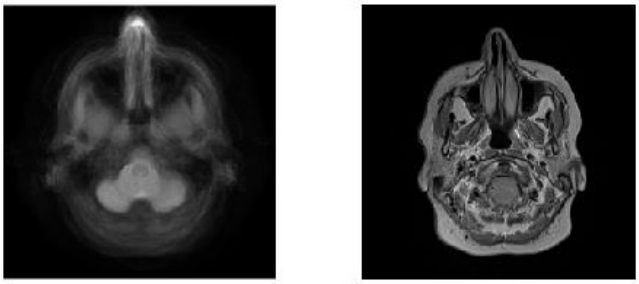

Figure 6.67: Bottom head slice selected for patient 93, PD sequence.

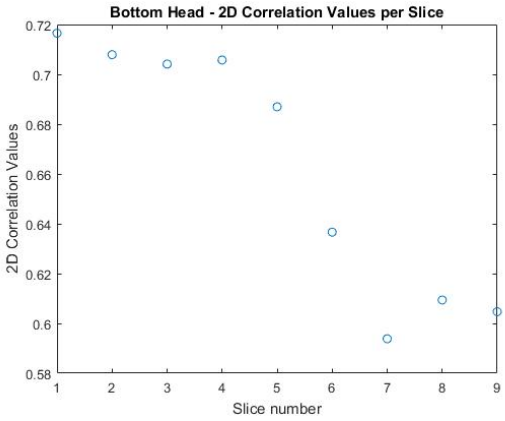

Figure 6.68: Bottom head slice 2D correlation values graph for patient 93, PD sequence.

In group C, more specifically patient 79 regarding PD scan, it is possible to observe in Figures 6.69-6.72 that top head delimitation process was successful. The bottom delimitation, however, was not successful despite the correlation graph shape (Figure 6.72). A higher slice number should have been chosen.

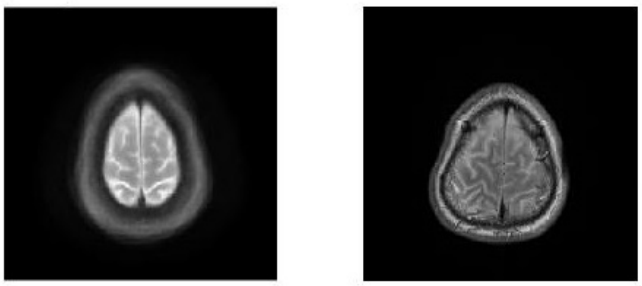

Figure 6.69: Top head slice selected for patient 79, PD sequence.

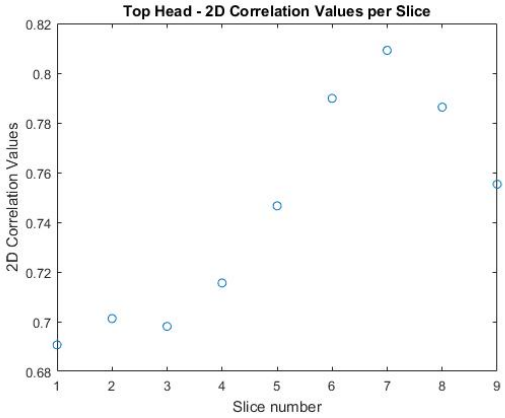

Figure 6.70: Top head slice 2D correlation values graph for patient 79, PD sequence.

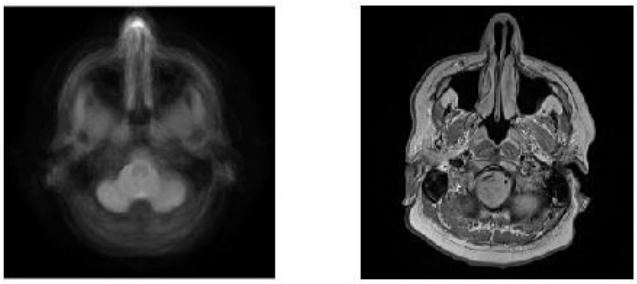

Figure 6.71: Bottom head slice selected for patient 79, PD sequence.

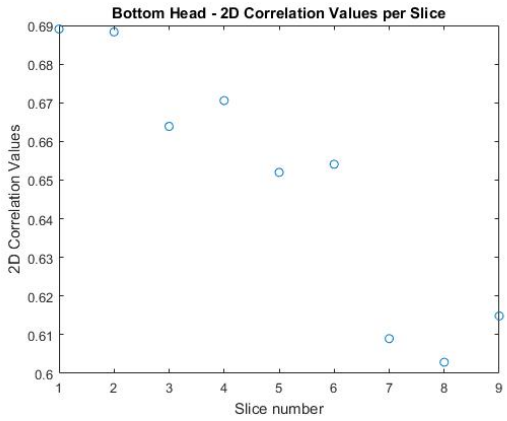

Figure 6.72: Bottom head slice 2D correlation values graph for patient 79, PD sequence.

In group D, more specifically patient 894 regarding PD scan, it is possible to observe in Figures 6.73-6.76 that both delimitation processes were successful.

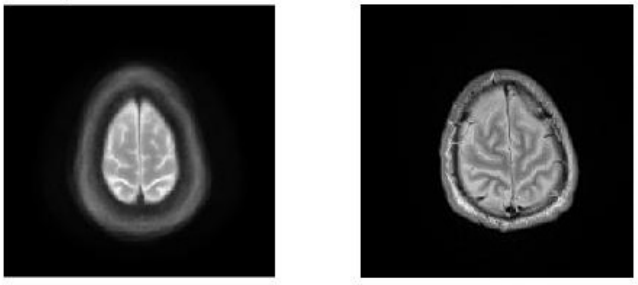

Figure 6.73: Top head slice selected for patient 894, PD sequence.

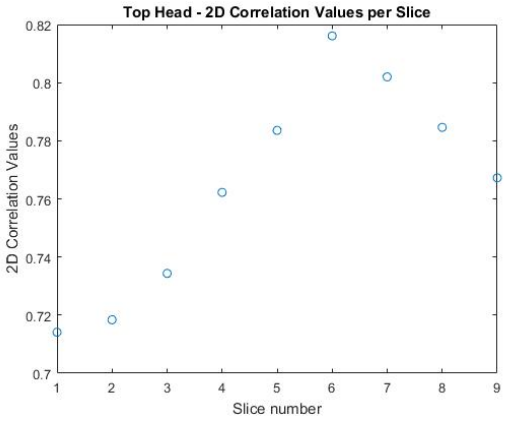

Figure 6.74: Top head slice 2D correlation values graph for patient 894, PD sequence.

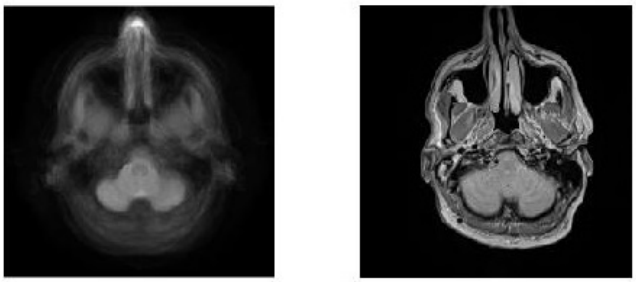

Figure 6.75: Bottom head slice selected for patient 894, PD sequence.

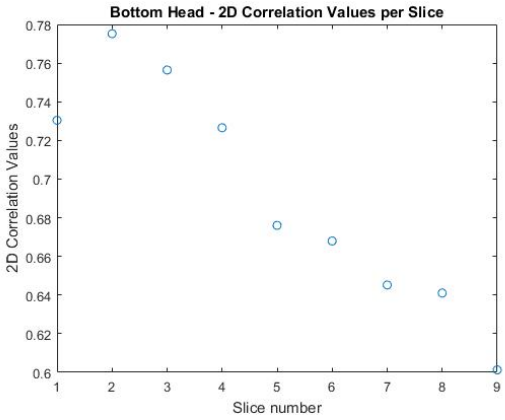

Figure 6.76: Bottom head slice 2D correlation values graph for patient 894, PD sequence.

Regarding PD scans, the results were similar when compared to FLAIR ones. In general terms, the head delimitation processes were successful.

By analyzing PD, T1 and FLAIR scans simultaneously, one can see that Group D outperformed the rest, which was not expected. Group A had the second best

performance while B and C performances were tied. Despite the brightness and contrast levels of Group D, it was possible to achieve a good performance. With this, it is known that the image adjusting and registration process were critical for its success. However, it is important to notice that this is one of the first steps of the image processing. In order to achieve conclusions, one must not only look at all intermediate steps but also at the final output.

6.2.2.2 Slice atlas/sequence assignment

In group A, more specifically patient 349 regarding FLAIR scan, it is possible to see in Figures 6.77 and 6.78 that the general slice assignment was successful. However, one can see that there are two slices slightly out of phase regarding the ventricles position.

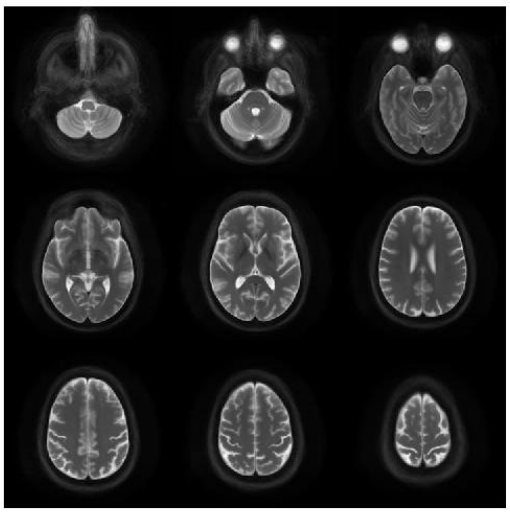

Figure 6.77: Atlas slices of the atlas/sequence slice assignment, for patient 349, FLAIR sequence. Pair slices only.

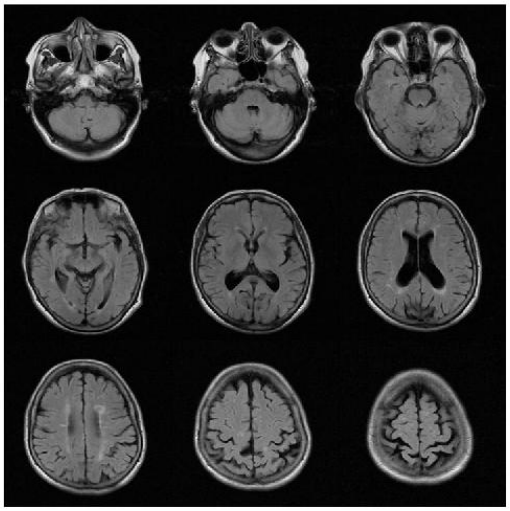

Figure 6.78: Sequence slices of the atlas/sequence slice assignment, for patient 349, FLAIR sequence. Pair slices only.

In group B, more specifically patient 93 regarding FLAIR scan, it is possible to see in Figures 6.79 and 6.80 that the slice assignment was successful.

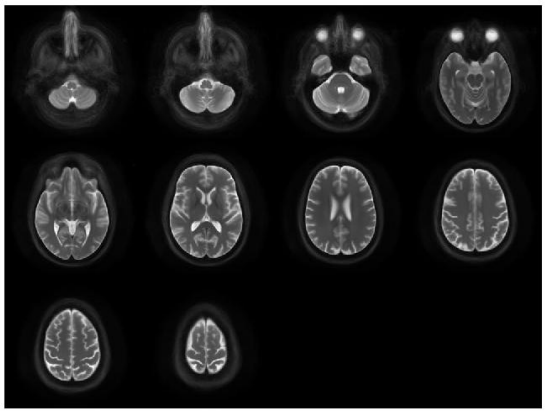

Figure 6.79: Atlas slices of the atlas/sequence slice assignment, for patient 93, FLAIR sequence. Slices that are multiple of 3 only.

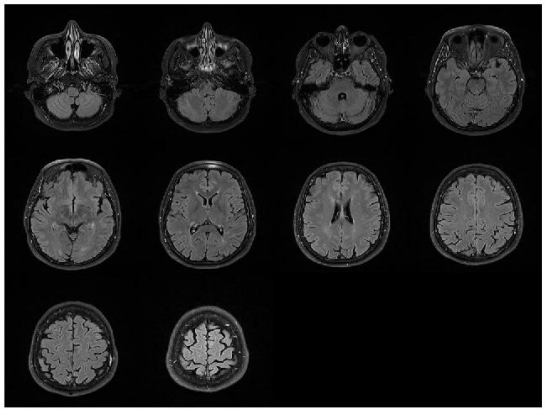

Figure 6.80: Sequence slices of the atlas/sequence slice assignment, for patient 93, FLAIR sequence. Slices that are multiple of 3 only.

In group C, more specifically patient 79 regarding FLAIR scan, it is possible to see in Figures 6.81 and 6.82 that the general slice assignment was successful. However, one can see that there is clearly one slice out of phase regarding the ventricles thickness.

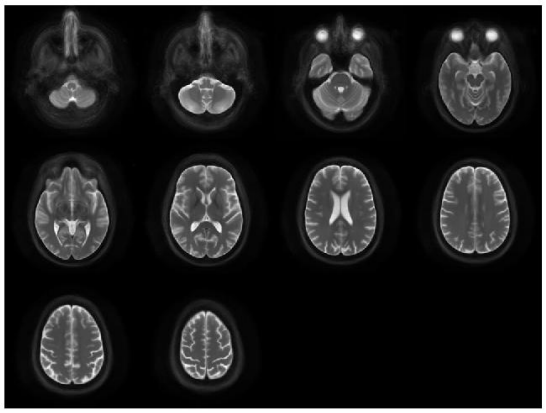

Figure 6.81: Atlas slices of the atlas/sequence slice assignment, for patient 79, FLAIR sequence. Slices that are multiple of 6 only.

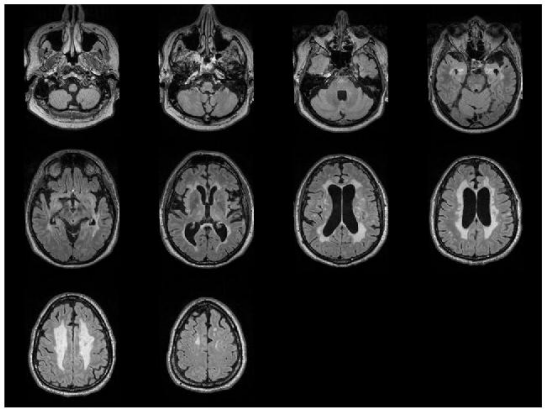

Figure 6.82: Sequence slices of the atlas/sequence slice assignment, for patient 79, FLAIR sequence. Slices that are multiple of 6 only.

In group D, more specifically patient 894 regarding FLAIR scan, it is possible to see in Figures 6.83 and 6.84 that the slice assignment was successful.

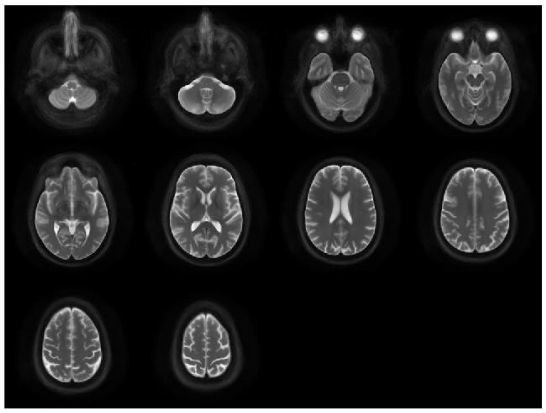

Figure 6.83: Atlas slices of the atlas/sequence slice assignment, for patient 894, FLAIR sequence. Slices that are multiple of 4 only.

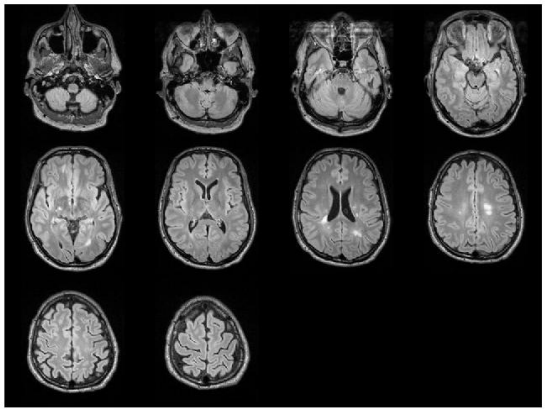

Figure 6.84: Sequence slices of the atlas/sequence slice assignment, for patient 894, FLAIR sequence. Slices that are multiple of 4 only.

Regarding the FLAIR scans, the slice assignment was successful, where the only obstacles observed were the ones regarding ventricles position and thickness. However, as already mentioned, this is also patient-dependent, since it is possible to have different structure brain proportions. In these cases, the slice assignment method used does not work so effectively. However, it provides an effective spatial matching in general terms.

In group A, more specifically patient 349 regarding T1 scan, it is possible to see in Figures 6.85 and 6.86 that the general slice assignment was successful.

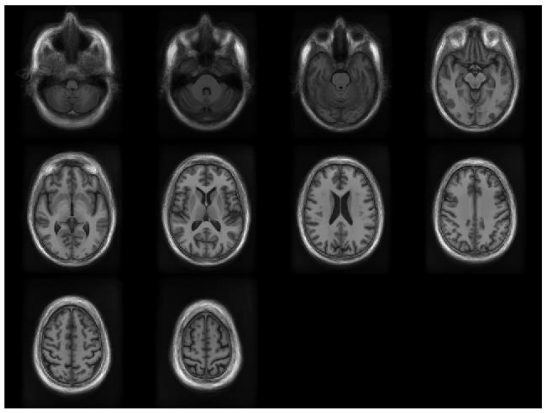

Figure 6.85: Atlas slices of the atlas/sequence slice assignment, for patient 349, T1 sequence. Pair slices only.

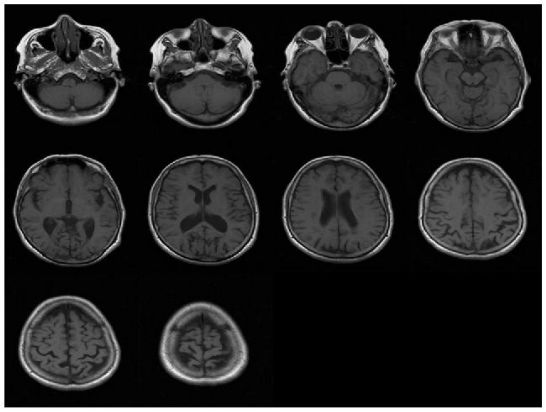

Figure 6.86: Sequence slices of the atlas/sequence slice assignment, for patient 349, T1 sequence. Pair slices only.

In group B, more specifically patient 93 regarding T1 scan, it is possible to see in Figures 6.87 and 6.88 that the general slice assignment was successful. However, there is a slice out of phase regarding ventricles position, once again.

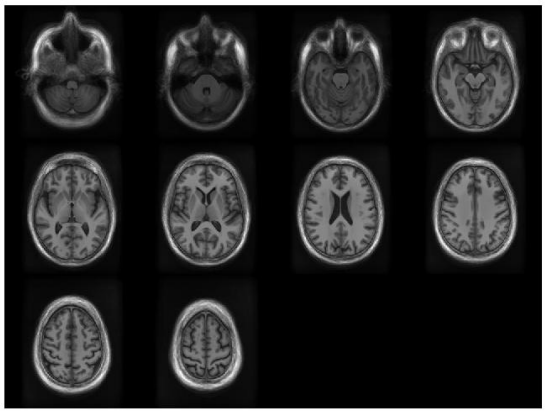

Figure 6.87: Atlas slices of the atlas/sequence slice assignment, for patient 93, T1 sequence. Slices that are multiple of 3 only.

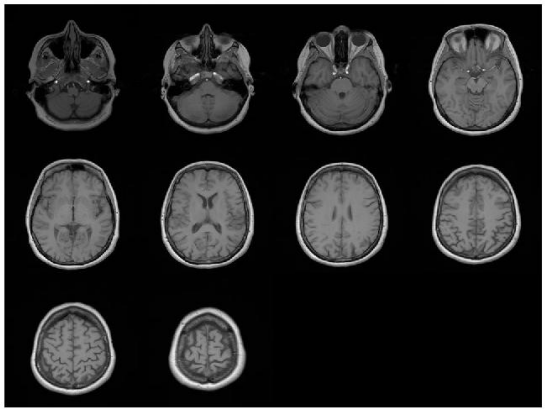

Figure 6.88: Sequence slices of the atlas/sequence slice assignment, for patient 93, T1 sequence. Slices that are multiple of 3 only.

In group C, more specifically patient 79 regarding T1 scan, it is possible to see in Figures 6.89 and 6.90 that the general slice assignment was successful. However, there are two slices out of phase regarding ventricles position and its thickness.

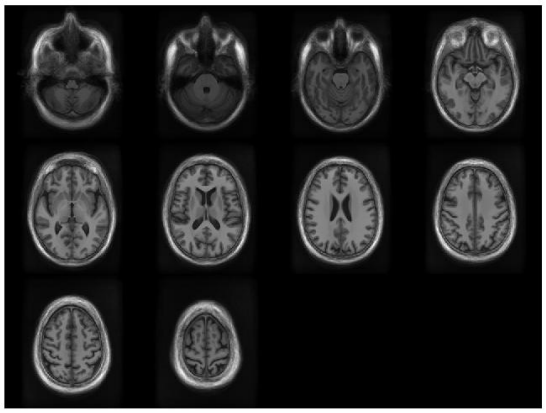

Figure 6.89: Atlas slices of the atlas/sequence slice assignment, for patient 79, T1 sequence. Slices that are multiple of 6 only.

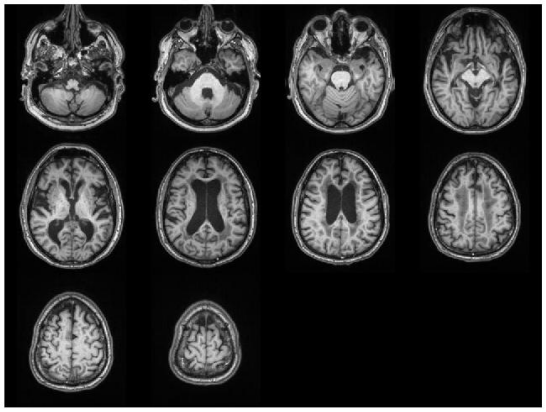

Figure 6.90: Sequence slices of the atlas/sequence slice assignment, for patient 79, T1 sequence. Slices that are multiple of 6 only.

In group D, more specifically patient 894 regarding T1 scan, it is possible to see in Figures 6.91 and 6.92 that the general slice assignment was successful.

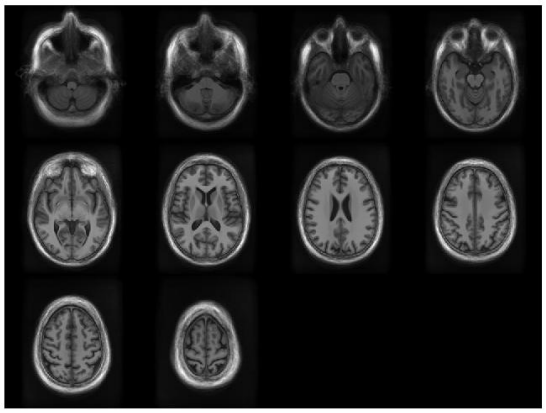

Figure 6.91: Atlas slices of the atlas/sequence slice assignment, for patient 894, T1 sequence. Slices that are multiple of 3 only.

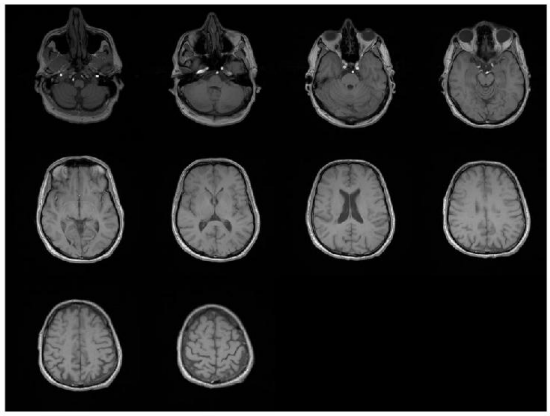

Figure 6.92: Sequence slices of the atlas/sequence slice assignment, for patient 894, T1 sequence. Slices that are multiple of 3 only.

Regarding T1 scans, the situation was similar to the one found in FLAIR scans. The obstacles found were related to the ventricles position and thickness.

In group A, more specifically patient 349 regarding PD scan, it is possible to see in Figures 6.93 and 6.94 that the general slice assignment was successful.

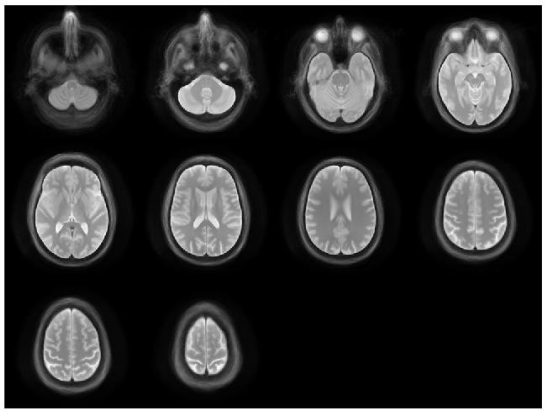

Figure 6.93: Atlas slices of the atlas/sequence slice assignment, for patient 349, PD sequence. Pair slices only.

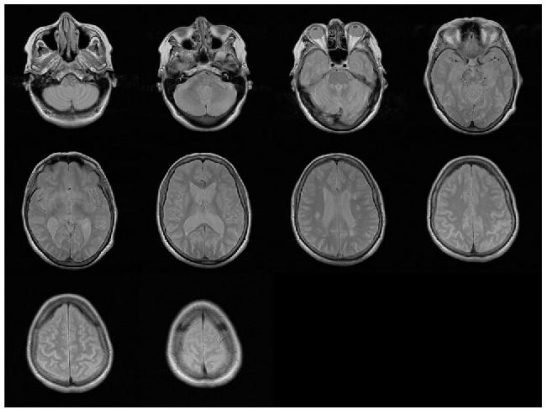

Figure 6.94: Sequence slices of the atlas/sequence slice assignment, for patient 349, PD sequence. Pair slices only.

In group B, more specifically patient 93 regarding PD scan, it is possible to see in Figures 6.95 and 6.96 that the general slice assignment was successful. However, the first three shown slices show a reasonable performance at the beginning. Nevertheless, in the rest of the slices, the output is the desired one. This can be interpreted due to this patient performance at the previous task in PD scans (top and bottom head limitation) as the bottom head slice chosen was not the most adequate.

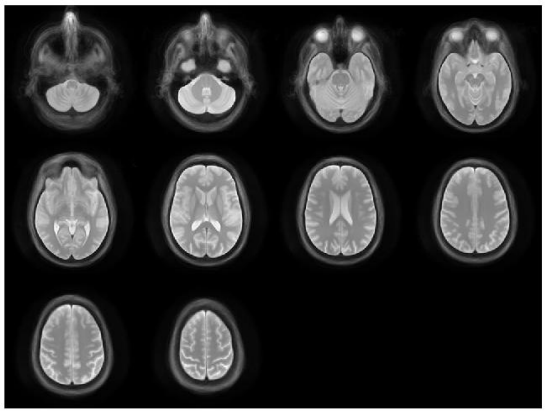

Figure 6.95: Atlas slices of the atlas/sequence slice assignment, for patient 93, PD sequence. Slices that are multiple of 3 only.

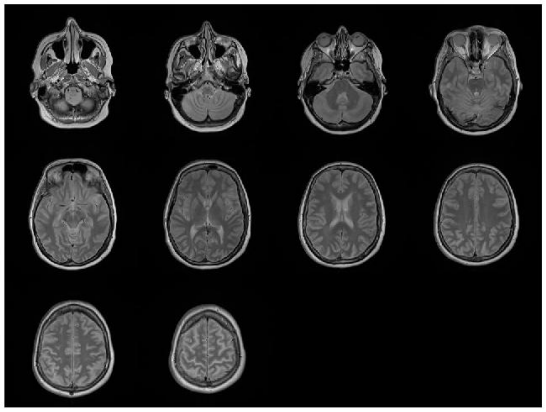

Figure 6.96: Sequence slices of the atlas/sequence slice assignment, for patient 93, PD sequence. Slices that are multiple of 3 only.

In group C, more specifically patient 79 regarding PD scan, it is possible to see in Figures 6.97 and 6.98 that the ventricle thickness is still a significant obstacle in this case, as verified in the other scans with the same patient.

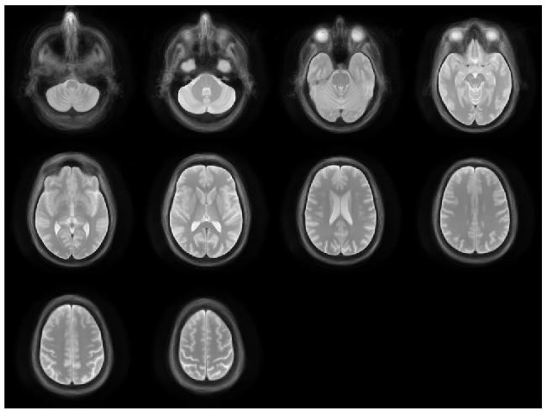

Figure 6.97: Atlas slices of the atlas/sequence slice assignment, for patient 79, PD sequence. Slices that are multiple of 3 only.

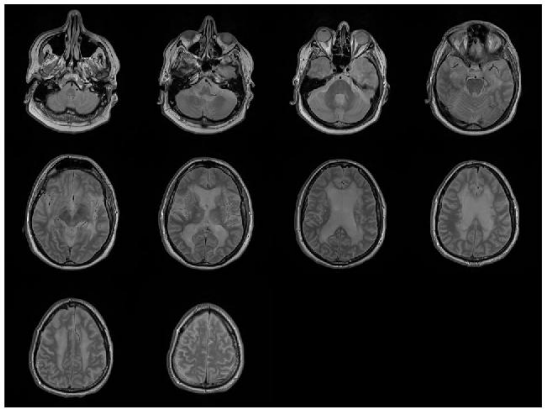

Figure 6.98: Sequence slices of the atlas/sequence slice assignment, for patient 79, PD sequence. Slices that are multiple of 3 only.

In group D, more specifically patient 894 regarding PD scan, it is possible to see in Figures 6.99 and 6.100 that the general slice assignment was successful. However, there is one slice out of phase regarding ventricles thickness.

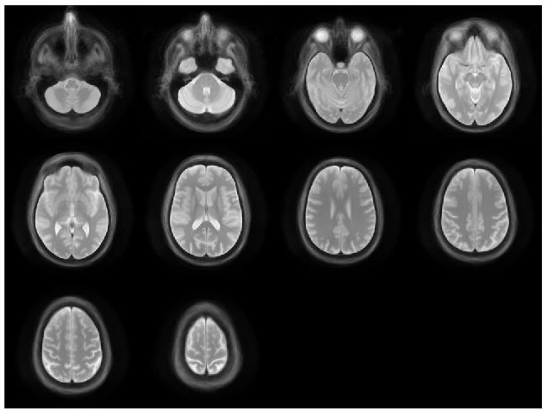

Figure 6.99: Atlas slices of the atlas/sequence slice assignment, for patient 894, PD sequence. Slices that are multiple of 3 only.

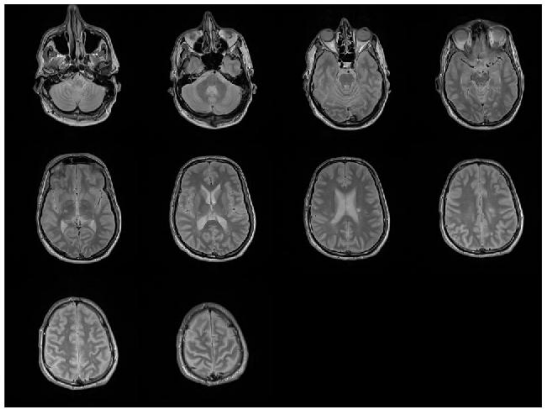

Figure 6.100: Sequence slices of the atlas/sequence slice assignment, for patient 894, PD sequence. Slices that are multiple of 3 only.

In a general form, the slice assignment process was successful since most of the slices assigned are the desired ones. When it is not the case, the desirable slice is not distant from the one chosen. These results are valid for an MRI scan at any modality, which is very interesting since it can be considered an effective and computationally efficient processing method. However, there are cases, such as the group C, that can be more complex. As the head is not shown entirely at the beginning of the head in most scans of this group, this might have led to bottom delimitation problems, affecting afterward the slice assignment task. However, it is very interesting to see how this procedure can recover the problems at the starting slices by choosing the correct slices towards higher positions.

6.2.2.3 Image registration

In image registration, it is not straightforward to evaluate and compare registration performances among different scans and modalities. The 2D correlation value could be an interesting metric, however it would not be precise due to the heterogeneity of the brain regarding non-interesting structures. Thus, the correlation value would not account only for the brain registration but also for the totality of the image, taking into account contrast, brightness and noise differences. This was proved since it was verified that, even in the best registration scenario, the correlation value never reached high values (never higher than 0.70, for example). In the slice assignment procedure, it was easier to evaluate since it is easy to compare visually the important brain structures and their positions.

Regarding intergroup performance, it is also very interesting to see that the methods allowed to overcome the announced problems. This can be a major step

when it comes to interpreting the reality: the possibility to have MRI scans from the same patient with complete different image properties due to different protocols and MRI scan machines.

Regarding the four mentioned patients regarding FLAIR scans, it is possible to see in Figures 6.101-6.108 that the registration was successful. Although it is not perfect, the important parts were registered adequately. By looking at the T1 scans (Figures 6.110-6.116) and at the PD scans (Figures 6.118-6.124), one can see the final output was satisfactory.

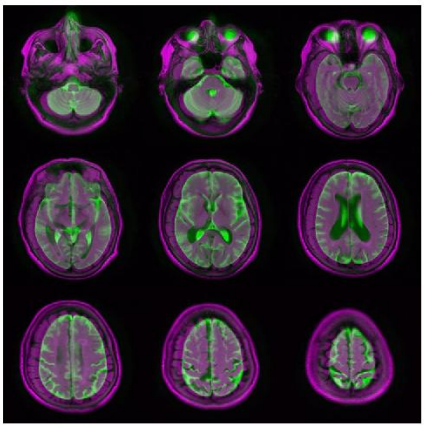

Figure 6.101: Atlas/sequence slices paired before registration process, for patient 349, FLAIR sequence. Pair slices only.

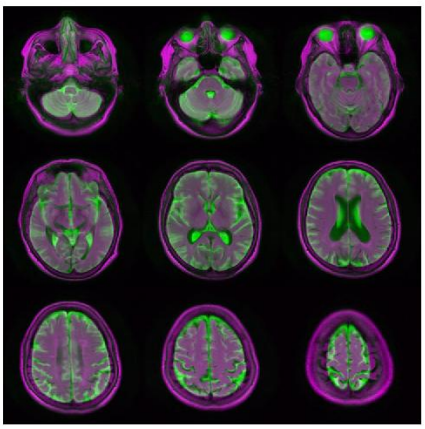

Figure 6.102: Atlas/sequence slices paired after registration process, for patient 349, FLAIR sequence. Pair slices only.

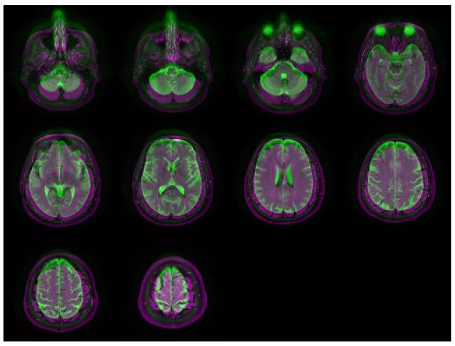

Figure 6.103: Atlas/sequence slices paired before registration process, for patient 93, FLAIR sequence. Slices that are multiple of 3 only.

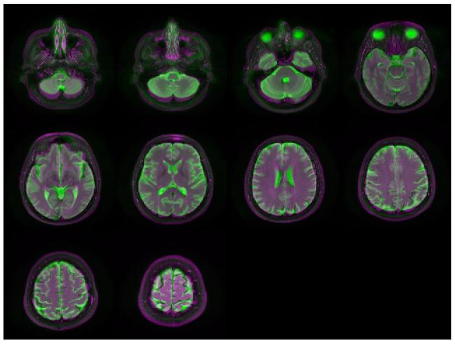

Figure 6.104: Atlas/sequence slices paired after registration process, for patient 93, FLAIR sequence. Slices that are multiple of 3 only.

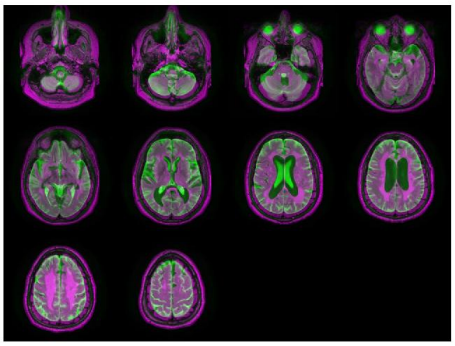

Figure 6.105: Atlas/sequence slices paired before registration process, for patient 79, FLAIR sequence. Slices that are multiple of 6 only.

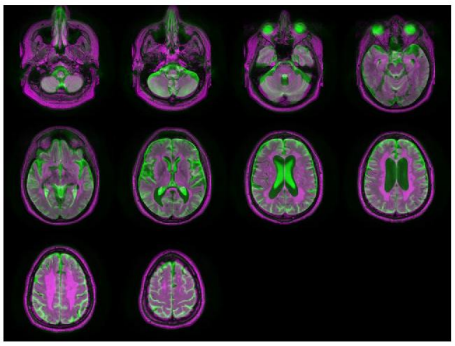

Figure 6.106: Atlas/sequence slices paired after registration process, for patient 79, FLAIR sequence. Slices that are multiple of 6 only.

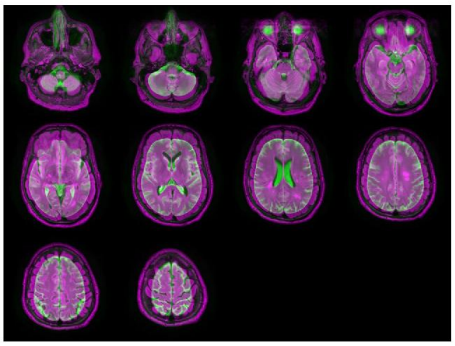

Figure 6.107: Atlas/sequence slices paired before registration process, for patient 894, FLAIR sequence. Slices that are multiple of 4 only.

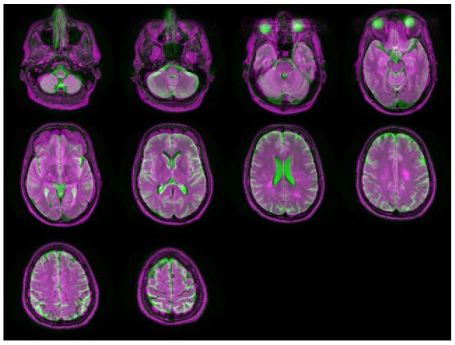

Figure 6.108: Atlas/sequence slices paired after registration process, for patient 894, FLAIR sequence. Slices that are multiple of 4 only.

Regarding the four mentioned patients regarding T1 scans, it is possible to see in Figures 6.109-6.116 that the registration was successful.

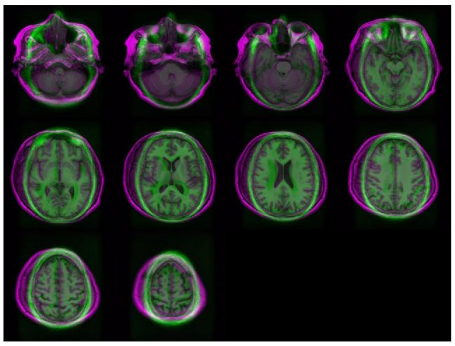

Figure 6.109: Atlas/sequence slices paired before registration process, for patient 349, T1 sequence. Pair slices only.

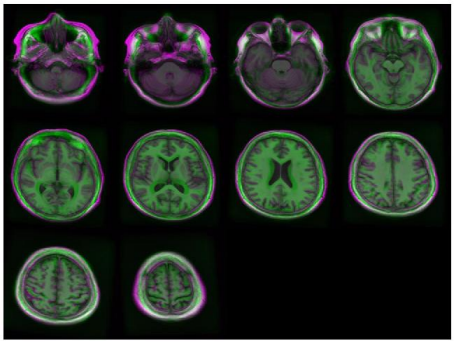

Figure 6.110: Atlas/sequence slices paired after registration process, for patient 349, T1 sequence. Pair slices only.

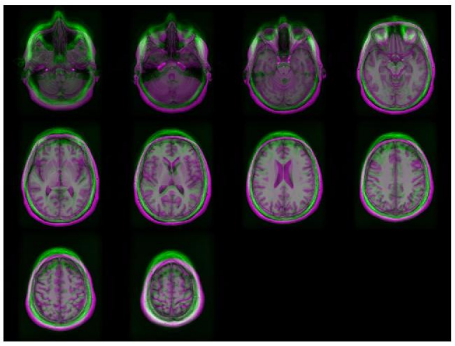

Figure 6.111: Atlas/sequence slices paired before registration process, for patient 93, T1 sequence. Slices that are multiple of 3 only.

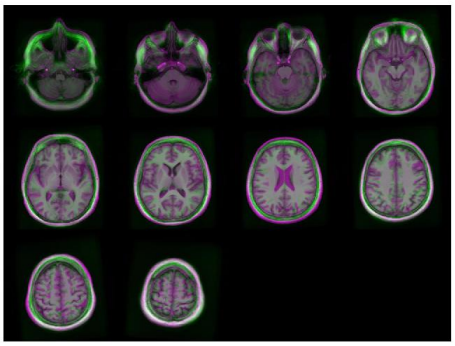

Figure 6.112: Atlas/sequence slices paired after registration process, for patient 93, T1 sequence. Slices that are multiple of 3 only.

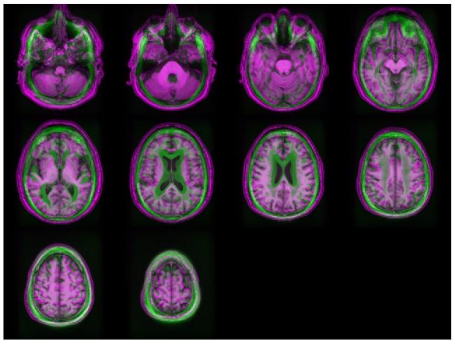

Figure 6.113: Atlas/sequence slices paired before registration process, for patient 79, T1 sequence. Slices that are multiple of 6 only.

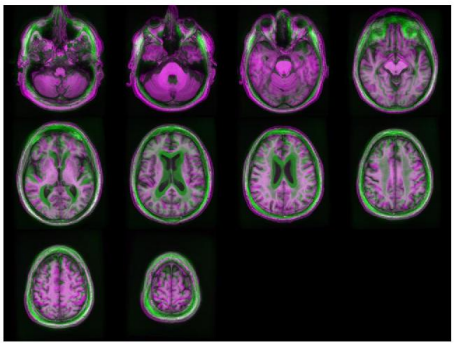

Figure 6.114: Atlas/sequence slices paired after registration process, for patient 79, T1 sequence. Slices that are multiple of 6 only.

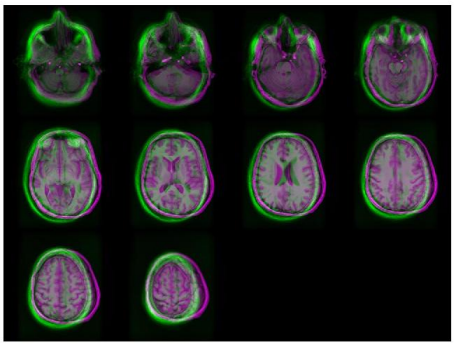

Figure 6.115: Atlas/sequence slices paired before registration process, for patient 894, T1 sequence. Slices that are multiple of 3 only.

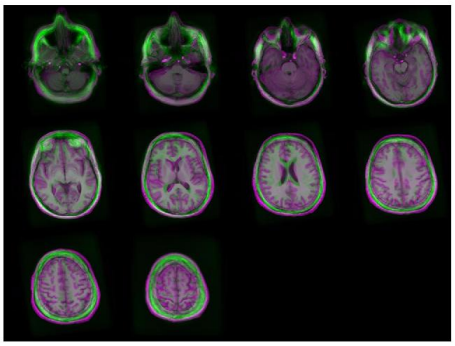

Figure 6.116: Atlas/sequence slices paired after registration process, for patient 894, T1 sequence. Slices that are multiple of 3 only.

Regarding the four mentioned patients regarding FLAIR scans, it is possible to see in Figures 6.117-6.124 that the registration was successful.

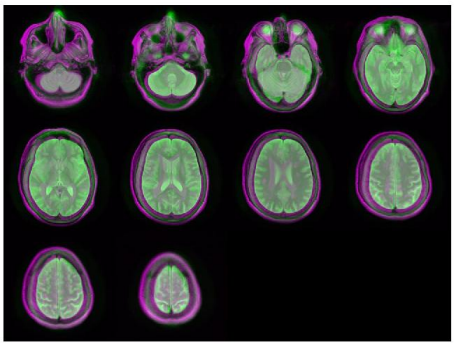

Figure 6.117: Atlas/sequence slices paired before registration process, for patient 349, PD sequence. Pair slices only.

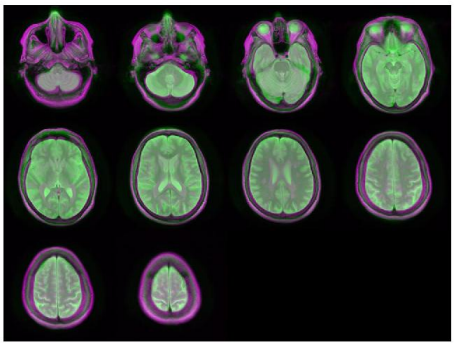

Figure 6.118: Atlas/sequence slices paired after registration process, for patient 349, PD sequence. Pair slices only.

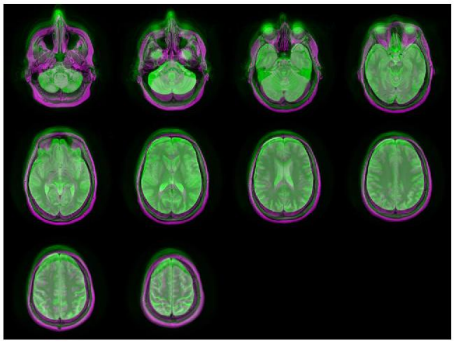

Figure 6.119: Atlas/sequence slices paired before registration process, for patient 93, PD sequence. Slices that are multiple of 3 only.

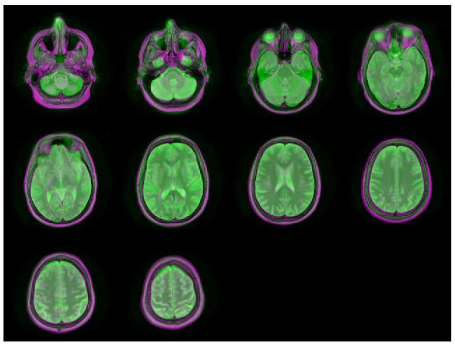

Figure 6.120: Atlas/sequence slices paired after registration process, for patient 93, PD sequence. Slices that are multiple of 3 only.

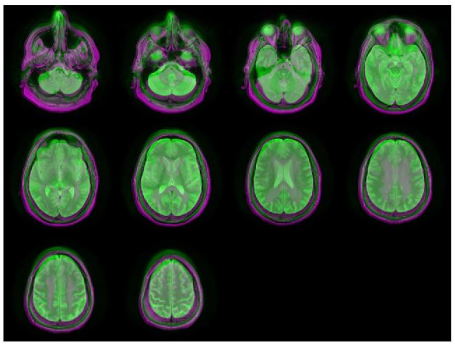

Figure 6.121: Atlas/sequence slices paired before registration process, for patient 79, PD sequence. Slices that are multiple of 3 only.

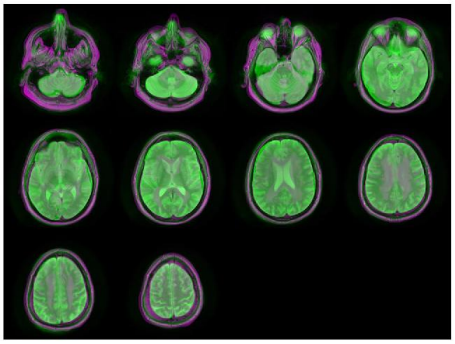

Figure 6.122: Atlas/sequence slices paired after registration process, for patient 79, PD sequence. Slices that are multiple of 3 only.

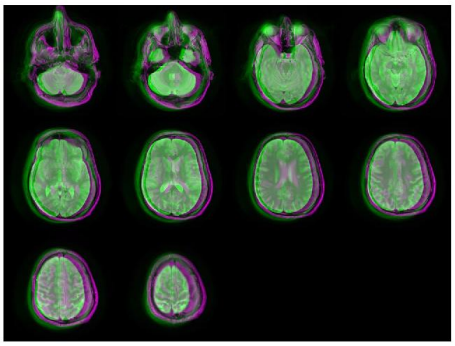

Figure 6.123: Atlas/sequence slices paired before registration process, for patient 894, T1 sequence. Slices that are multiple of 3 only.

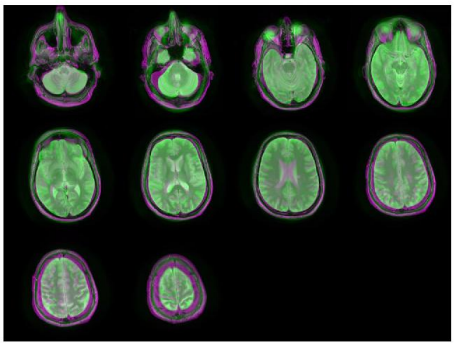

Figure 6.124: Atlas/sequence slices paired after registration process, for patient 894, T1 sequence. Slices that are multiple of 3 only.

6.2.3 Feature extraction

It is possible to proceed to the feature extraction process. As the final steps of the image processing were different for the lesion manual labeling databases and for the *MRI total head* database, there was the need to individualize both feature extraction methods. However, the main ideas were the same. As mentioned for the *MRI total head* database, the extracted features had as origin defined head regions where there was not a previous knowledge about lesion existence. On the other hand, for the lesion databases, features were extracted only from regions classified by the physicians as lesions.

6.2.3.1 MRI Total Head database

There are available different sequences extracted directly from the real MRI scan: brain only sequence, non-brain sequence structures and total sequence. With the rest of the atlas tools, there was possible to extract three more regarding the tissue nature: CSF, GM and WM. For this, it was used the atlas that characterized the brain as background, CSF, GM and WM.

The same principle was applied to the anatomical atlases, where it was possible to make a sequence for each individualized region of each atlas. However, in these regions, some extra measures were required. As known, these atlas tools suffered the same registration process that the total head sequence atlas did, making some approximations and artifact misguidances. In order to avoid some made discrepancies, these anatomical atlases previously suffered a numerical round process followed by an image opening procedure. This opening procedure was made with a disk of one pixel of diameter.

This was performed for every available sequence: brain only sequence, non-brain sequence, total sequence, GM sequence, WM sequence, CSF sequence and for each anatomical atlas region sequence. This process was performed for any modality: T1, T1-Gde, T2, Flair and PD, as shown in Figure 6.125. The main concepts behind the feature extraction were:

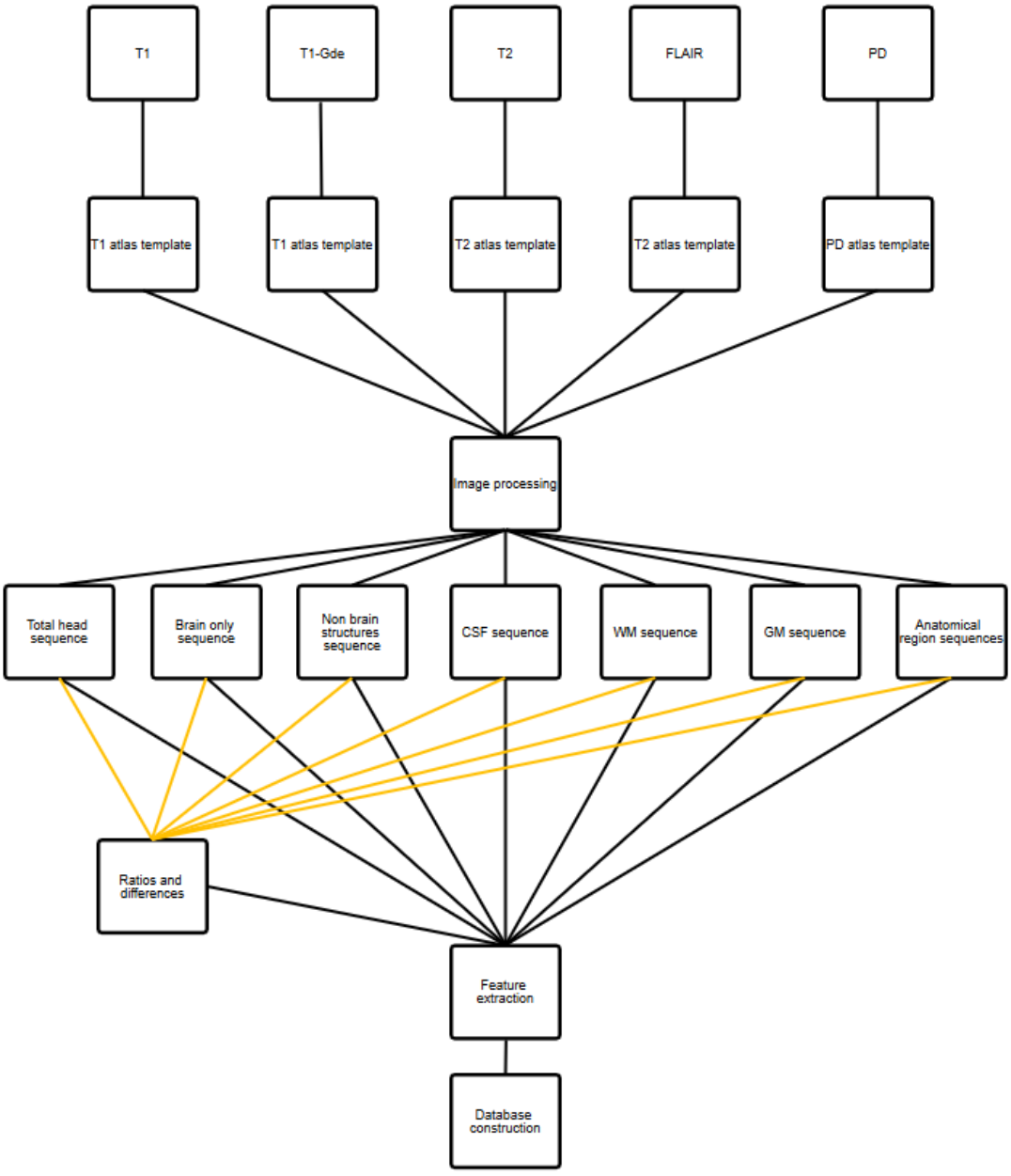

Figure 6.125: Full procedure pipeline for the construction of the *MRI whole head* database.

1. **Area**: exploratory method in order to check if there are modified areas due

to the presence of lesions.

2. **Fast Fourier Transform (FFT)**: by decomposing an image into its sine and cosine components and entering frequency domain, some new discriminative factors may arise.
3. **Color histogram**: lesions are easily distinguished in the MRI scans by their intensity differences regarding non-lesion tissues. Thus, image intensity histogram can be interesting.
4. **Symmetry**: lesion placement is not symmetrical as a lesion can appear at any brain part. Thus, if a brain has lesions, the symmetry will be naturally affected.
5. **Gray Level Co-Occurrence Matrix (GLCM) properties**: GLCM is a statistical method of examining texture by considering the spatial relationship of pixels. This way, non-lesion tissues and lesion tissues will possess different GLCM property values. Thus, local variations, homogeneity, joint probability occurrence of certain pixels and uniformity will be measured.
6. **Entropy**: the measurement of the order of an image. A brain with a higher number of lesions will theoretically have a higher entropy value as its information amount is greater.
7. **Raw features**: related to pixel intensity. As physicians tend to do this process automatically due to pixel intensity, this kind of procedure will also be attempted.

The extracted features with pixel intensity as the main concept are:

1. **Mean area**: the sum of the area calculated in each slice divided by the total number of slices.
2. **Median area**: the median of all area slices.
3. **Std area**: the standard deviation of all area slices.

In the extracted FFT features, it waas firstly computed for each slice the respective log-normalized FFT spectrum. In other words, the 2D FFT of each slice was computed and then log-divided by its DC mean-component. The final output, regarding all slices, was named as volume_fft. Its symmetrical part was also removed. The extracted features were:

1. **Mean_mean fft**: the mean value of the volume_ftt mean.
2. **Std_mean fft**: the standard deviation value of the volume_ftt mean.
3. **Median_mean fft**: the median value of the volume_ftt mean.
4. **Mean_std fft**: the mean value of the volume_ftt standard deviation.
5. **Median_std fft**: the median value of the volume_ftt standard deviation.

6. **Std_std fft**: the standard deviation value of the volume_ftt standard deviation.
7. **Mean_median fft**: the mean value of the volume_ftt median.
8. **Median_median fft**: the median value of the volume_ftt median.
9. **Std_median fft**: the standard deviation value of the volume_ftt median.
10. **Mean_intensity fft**: the mean intensity value at mean intensity frequency of all volume_fft slices.
11. **Median_intensity fft**: the median intensity value at median intensity frequency of all volume_fft slices.
12. **Mean_intensity_freq fft**: the mean intensity frequency of volume_fft.
13. **Median_intensity_freq fft**: the median intensity frequency of volume_fft.

The extracted features with color histogram as the main concept were:

1. **Mean_histogram_(1:20)**: 20 features, each for each histogram bin, since the histogram was divided in 20 bins. Each feature is the mean value of the respective bin.
2. **Median_histogram_(1:20)**: 20 features, each for each histogram bin, since the histogram was divided in 20 bins. Each feature is the median value of the respective bin.
3. **Bin_location_mean_mean histogram**: the mean bin location regarding the mean intensity.
4. **Bin_location_median_mean histogram**: the median bin location regarding the mean intensity.
5. **Bin_location_mean_median histogram**: the mean bin location regarding the median intensity.
6. **Bin_location_median_median histogram**: the median bin location regarding the median intensity.
7. **Std_median histogram**: the standard deviation of the median histogram.
8. **Std_mean histogram**: the standard deviation of the mean histogram.
9. **Std_bin_location_mean histogram**: the standard deviation of the bin location regarding the mean intensity.
10. **Std_bin_location_median histogram**: the standard deviation of the bin location regarding the median intensity.
11. **Std_histogram_(1:20)**: 20 features, each for each histogram bin, since the histogram was divided in 20 bins. Each feature is the standard deviation of the respective bin.
12. **Median_std histogram**: the median value of the standard deviations values

regarding all intensity values.

13. **Mean_std histogram**: the mean value of the standard deviations values regarding all intensity values.
14. **Std_std histogram**: the standard deviatin value of the standard deviations values regarding all intensity values.
15. **Bin_location_median_std histogram**: the median bin location regarding the standard deviation of the intensity.
16. **Bin_location_mean_std histogram**: the median bin location regarding the standard deviation of the intensity.
17. **Bin_location_max_std histogram**: the max bin location regarding the standard deviation of the intensity.

The extracted features with symmetry as the main concept were:

1. **Mean_symmetry_lr**: mean symmetry value of all slices regarding a vertical axis.
2. **Median_symmetry_lr**: median symmetry value of all slices regarding a vertical axis.
3. **Std_symmetry_lr**: standard deviation symmetry value of all slices regarding a vertical axis.
4. **Mean_symmetry_ud**: mean symmetry value of all slices regarding an horizontal axis.
5. **Median_symmetry_ud**: median symmetry value of all slices regarding an horizontal axis.
6. **Std_symmetry_ud**: standard deviation value of all slices regarding an horizontal axis.

The extracted features with GLCM properties as the main concept were:

1. **Mean_contrast_glcm**: mean contrast value of all slices.
2. **Median_contrast_glcm**: median contrast value of all slices.
3. **Std_contrast_glcm**: standard deviation contrast value of all slices.
4. **Mean_correlation_glcm**: mean correlation value of all slices.
5. **Median_correlation_glcm**: median correlation value of all slices.
6. **Std_correlation_glcm**: standard deviation correlation value of all slices.
7. **Mean_energy_glcm**: mean energy value of all slices.
8. **Median_energy_glcm**: median energy value of all slices.
9. **Std_energy_glcm**: standard deviation energy value of all slices.
10. **Max_energy_glcm**: maximum energy value of all slices.
11. **Min_energy_glcm**: minimum energy value of all slices.

12. **Mean_homogeneity_glcm**: mean homogeneity value of all slices.
13. **Median_homogeneity_glcm**: median homogeneity value of all slices.
14. **Std_homogeneity_glcm**: standard deviation homogeneity value of all slices.
15. **Max_homogeneity_glcm**: maximum homogeneity value of all slices.
16. **Min_homogeneity_glcm**: minimum homogeneity value of all slices.

The extracted features with entropy as the main concept were:

1. **Volumetric_entropy**: sum of all entropy slices.
2. **Mean_entropy**: mean entropy value.
3. **Median_entropy**: median entropy value.
4. **Std_entropy**: standard deviation entropy value.
5. **Max_entropy**: maximum entropy value.
6. **Min_entropy**: minimum entropy value.

The extracted features with raw feature extraction as the main concept were:

1. **Raw_mean_mean**: mean value of the mean pixel intensity.
2. **Raw_median_mean**: median value of the mean pixel intensity.
3. **Raw_std_mean**: standard deviation of the mean pixel intensity.
4. **Raw_mean_median**: mean value of the median pixel intensity.
5. **Raw_median_median**: median value of the median pixel intensity.
6. **Raw_std_median**: standard deviation of the median pixel intensity.
7. **Raw_mean_std**: mean value of the standard deviation pixel intensity.
8. **Raw_median_std**: median value of the standard deviation pixel intensity.
9. **Raw_std_std**: standard deviation of the standard deviation pixel intensity.

The feature extraction did not stop here. As the number of samples was reduced and it was desirable to explore the fastest way the largest number of different features, several ones were calculated by combining them. In other words, there were features extracted by combining different ones through the use of simple mathematical operations as subtraction and division.

Thus, with all the features extracted, ratios and differences were also calculated and used as features. Here are the combinations performed:

1. **A1_BO_ratio(diff)**: Anatomical Volume I/(-)Brain only sequence (for all regions from anatomical map I).
2. **A1_NB_ratio(diff)**: Anatomical Volume I/(-)Non brain structures sequence (for all regions from anatomical map I).
3. **A1_WB_ratio(diff)**: Anatomical Volume I/(-)Total head sequence (for all regions from anatomical map I).
4. **A1_CSF_ratio(diff)**: Anatomical Volume I/(-)CSF sequence (for all regions

from anatomical map I).

5. **A1_GM_ratio(diff)**: Anatomical Volume I/(-)GM sequence (for all regions from anatomical map I).
6. **A1_WM_ratio(diff)**: Anatomical Volume I/(-)WM sequence (for all regions from anatomical map I).
7. **A2_BO_ratio(diff)**: Anatomical Volume II/(-)Brain only sequence (for all regions from anatomical map II).
8. **A2_NB_ratio(diff)**: Anatomical Volume II/(-)Non brain structures sequence (for all regions from anatomical map II).
9. **A2_WB_ratio(diff)**: Anatomical Volume II/(-)Total head sequence (for all regions from anatomical map II).
10. **A2_CSF_ratio(diff)**: Anatomical Volume II/(-)CSF sequence (for all regions from anatomical map II).
11. **A2_GM_ratio(diff)**: Anatomical Volume II/(-)GM sequence (for all regions from anatomical map II).
12. **A2_WM_ratio(diff)**: Anatomical Volume II/(-)WM sequence (for all regions from anatomical map II)
13. **Raw_CSF_brain_ratio(diff)**: CSF sequence/(-) Total head sequence.
14. **Raw_GM_brain_ratio(diff)**: GM sequence/(-) Total head sequence.
15. **Raw_WM_brain_ratio(diff)**: WM sequence/(-) Total head sequence.
16. **Raw_CSF_BO_ratio(diff)**: CSF sequence/(-) Brain only sequence.
17. **Raw_GM_BO_ratio(diff)**: GM sequence/(-) Brain only sequence.
18. **Raw_WM_BO_ratio(diff)** WM sequence/(-) Brain only sequence.
19. **Raw_CSF_NB_ratio(diff)**: CSF sequence/(-)Non brain structures sequence.
20. **Raw_GM_NB_ratio(diff)**: GM sequence/(-)Non brain structures sequence.
21. **Raw_WM_NB_ratio(diff)**: WM sequence/(-)Non brain structures sequence.

6.2.3.2 Manual lesion labeling

As mentioned, the last processing steps were different regarding which database was desirable to build. The base features extracted for all databases are the same. In *One lesion one sample* database case, the extracted features were directly the ones from the mentioned database. In *One study one sample* database case, the used features were calculated using *One lesion one sample* database features. In *One patient one sample* database, the used features are calculated using *One study one sample* database, as it can be seen in Figures 6.126 and 6.127. The CSF, GM, WM, tissue maps and anatomical maps were also used to extract features from lesions.

The other sequences, such as the brain and non-brain structures, were not needed for natural reasons (brain lesions).

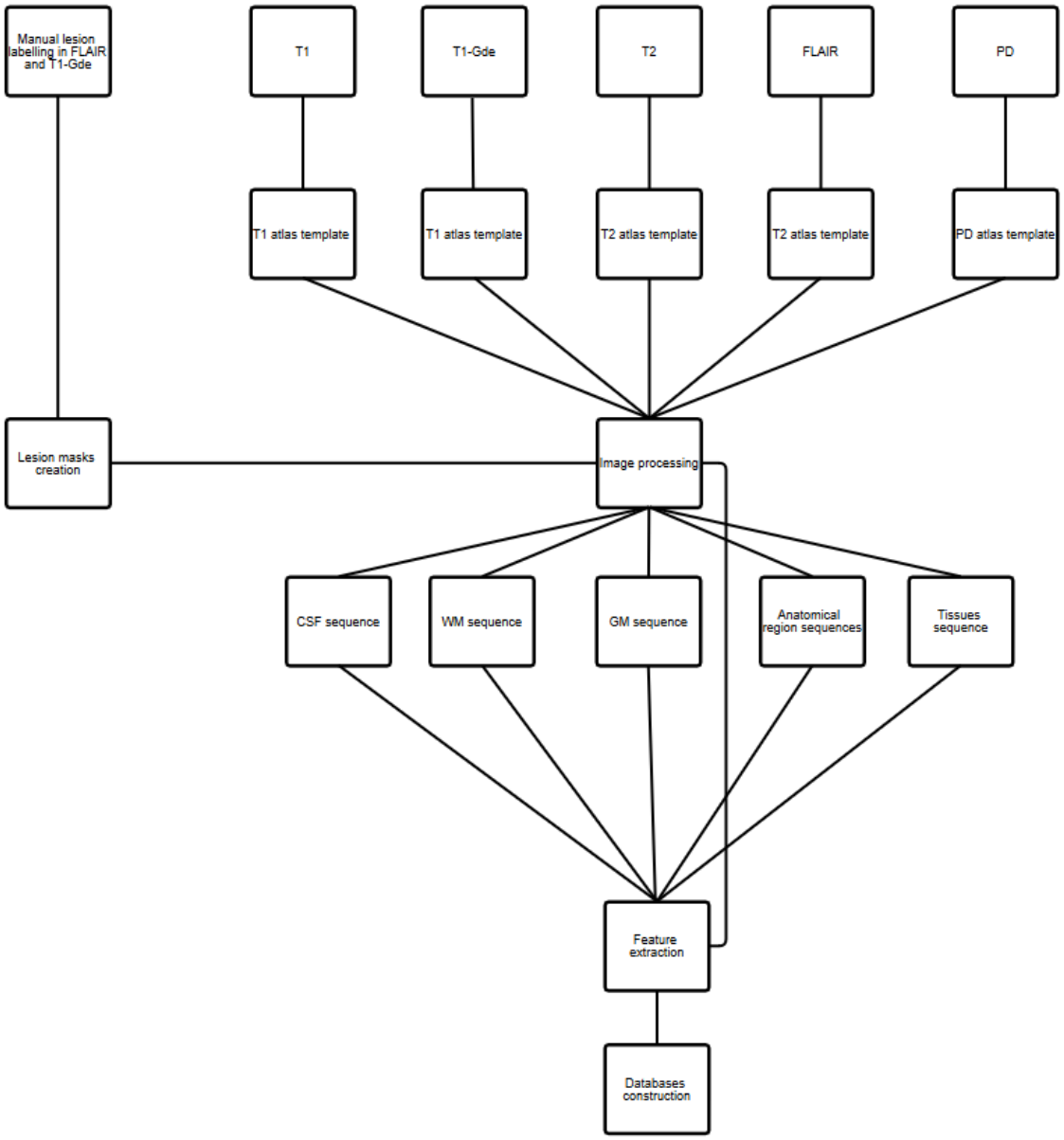

Figure 6.126: Full procedure pipeline from image processing untill database creation for lesion databases.

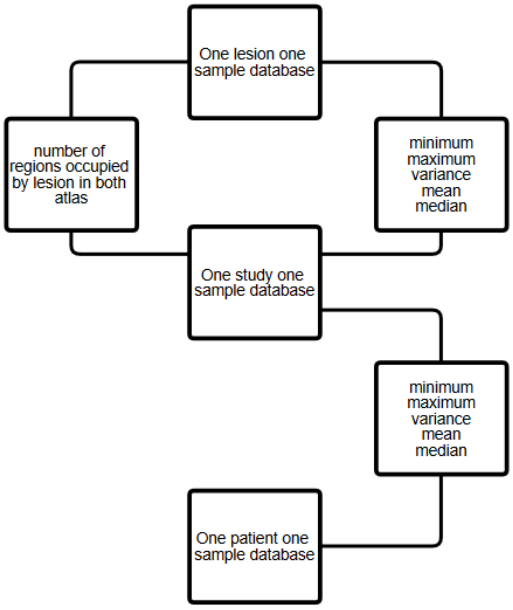

Figure 6.127: Lesion databases creation method.

As the features were extracted directly from lesions, they differed from the M*RI total head* database ones. Some concept ideas were excluded in this case since it was verified that its output always was a NaN or an infinite value, such as the FFT case. Regarding entropy and symmetry, theoreticaly it does not make sense to retrieve related features since the extracted characteristics were only regarding the lesions themselves. Thus, the main ideas behind the feature extraction were:

1. **Shape**: it is interesting to have an opportunity to study the influence of the lesion shape as these constitute characteristics easily extracted.
2. **Positioning**: it is also interesting to be able to study the influence of the lesion positioning.
3. **Pixel intensity**: the most intuitive characteristics that one can extract. The ones that make possible to automatically identify a region as a potential lesion.
4. **Histogram**: the same reason why the intensity values will be extracted.
5. **GLCM properties**: it is interesting to have an opportunity to perform texture analysis regarding the lesion regions only.

The extracted features with shape as the main concept are:

1. **Lesion area/slice_area**: lesion area divided by the skull slice area.
2. **Major axis length/slice_perimeter**: the major axis length divided by the skull slice perimeter.
3. **Minor axis length/slice_perimeter**: the inner axis length divided by the skull slice perimeter.

4. **Eccentricity**: eccentricity is a parameter associated with the conic section, where it can be interpreted as the measure of how much the conic section deviates from a circular shape. Thus, a perfect circle has 0 value of eccentricity.
5. **Orientation**: the absolute of the angle between the x-axis and the major axis of the ellipse that has the same second-moments as the region.
6. **ConvexArea/slice_area**: the number of pixels inside the convex hull specified by the lesion divided by the skull slice area.
7. **EquivDiameter/slice_perimeter**: diameter of a circle with the same area as the region divided by the skull slice perimeter.
8. **Solidity**: the proportion of pixels in the convex hull that is also in the region.
9. **Extent**: the ratio of pixels in the region to pixels in the total bounding box.
10. **Perimeter/slice_perimeter**: the perimeter divided by the skull slice perimeter.

The extracted features with positioning as the main concept were:

1. **Refspace**: the position value regarding the relative spatial position vector.
2. **Distance to the centre of skull**: the Euclidean distance to the centre of the skull slice.

The extracted features with pixel intensity as the main concept are:

1. **Mean pixel intensity/slice_meanPixel**: mean lesion pixel intensity divided by the skull slice mean pixel intensity.
2. **Median pixel intensity/slice_meanPixel**: median lesion pixel intensity divided by the skull slice mean pixel intensity.
3. **Max pixel intensity/slice_meanPixel**: maximum lesion pixel intensity divided by the skull slice mean pixel intensity.
4. **Min pixel intensity/slice_meanPixel**: minimum lesion pixel intensity divided by the skull slice mean pixel intensity.
5. **Var pixel intensity/slice_meanPixel**: variance of the lesion pixel intensity divided by the skull slice mean pixel intensity.

The extracted features with GLCM propoerties as the main concept were:

1. **Lesion contrast/slice contrast**: lesion contrast normalized by the skull slice contrast.
2. **Lesion correlation/slice correlation**: lesion correlation normalized by the skull slice correlation.
3. **Lesion energy/slice energy**: lesion energy normalized by the skull slice energy.
4. **Lesion homogeneity/slice homogeneity**: lesion homogeneity normalized

by the skull slice homogeneity.

As mentioned, GM, WM and CSF atlas sequences were also used. With these, other features were extracted related to the lesion location. For each one, the extracted features were:

1. **Squares numbers lesion region 90%/total region with 90**: number of pixels occupied by the lesion where the probability of a certain tissue (GM, WM, CSF) is at least 90% divided by the total number of pixels with at least 90%.
2. **Mean tissue prob**: the mean probability value regarding the tissue probability pixels occupied by the lesion.
3. **Median tissue prob**: the median probability value regarding the tissue probability pixels occupied by the lesion.
4. **Var tissue prob**: the variance of the probability value regarding the tissue probability pixels occupied by the lesion.
5. **Max tissue prob**: the maximum probability value regarding the tissue probability pixels occupied by the lesion.
6. **Min tissue prob**: the minimum probability value regarding the tissue probability pixels occupied by the lesion.

The extracted features related to the atlas tissue map were:

1. **Belongs to the 3 tissues**: binary feature, it the lesion occupies pixels of the three possible tissues.
2. **Percentage of GM**: the percentage of pixels occupied by the lesion belonging to GM.
3. **Percentage of WM**: the percentage of pixels occupied by the lesion belonging to WM.
4. **Percentage of CSF**: the percentage of pixels occupied by the lesion belonging to CSF.
5. **Belongs mostly to GM**: binary feature, if the majority of pixels occupy GM tissue.
6. **Belongs mostly to WM**: binary feature, if the majority of pixels occupy WM tissue.
7. **Belongs mostly to CSF**: binary feature, if the majority of pixels occupy CSF tissue.

The extracted features related to the atlas anatomical maps for each region were:

1. **Lesion in the region**: binary feature, if at least one lesion pixel occupies the

anatomical region in question.

2. **Ratio on the region affected by lesion**: the number of lesion pixels that occupy the anatomical region divided by the total area in pixels of the region.
3. **Mean pixel intensity**: the mean pixel intensity of the pixels that occupy the anatomical region in question.
4. **Median pixel intensity**: the median pixel intensity of the pixels that occupy the anatomical region in question.
5. **Var pixel intensity**: the variance of the pixel intensity of the pixels that occupy the anatomical region in question.
6. **Max pixel intensity**: the maximum pixel intensity of the pixels that occupy the anatomical region in question.
7. **Min pixel intensity**: the minimum pixel intensity of the pixels that occupy the anatomical region in question.

As seen in Figure 6.127, *One study one sample* database was constructed by using *One lesion one sample* database features and performing some calculations with them. Thus, *One study one sample* can be seen as the interpretation of all lesion features at the same time regarding a study. To do this, the minimum, maximum, variance, mean and median of all lesion features are calculated and turned into the *One study one sample* features. Besides these, it is also calculated the number of regions that a certain lesion occupies in both anatomical maps, separately.

The same mechanism was applied to *One study one* database to build the*One patient one sample* database. The mean, median, variance, minimum and maximum were applied to the existing features and used as the new features for the new database.

6.3 Feature selection

In this project, the amount of initial features was very large when compared to the number of samples. As known, this could have led to overfitting problems, due to the curse of dimensionality. Thus, it was necessary to reduce them in order to have a reduced set of discriminative ones. Besides, if one would work with the complete set of features, not only it would have overfitting problems but it would also be very complex to obtain an interpretation (clinical or not).

The used strategy to evaluate the features discriminative power consisted in a series of tests as a first step. Afterwards, a correlation between features was performed in order to avoid redundancy (if two features had a very high correlation,

only one was needed since they provided the same information). Depending on the number of features that remained when compared to the number of samples, an extra step was made. One of the feature tests used in the first step was used as final selection in order to reduce them to a minimal number. The criteria for the selection of the used test consisted in being directly related to the classification process. Thus, theoretically it is the test that will ensure the best set of features regarding classification performance. The pipeline scheme of the feature selection can be seen in Figure 6.128, which was used for all clinical databases.

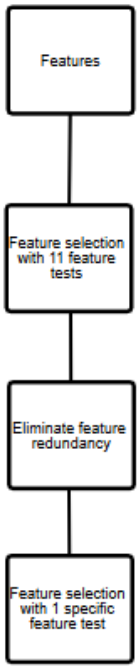

Figure 6.128: Feature selection scheme for all clinical databases.

Regarding image databases, since the number of features was significantly higher, the computation task would be tremendously heavy if one would apply the same procedure. Thus, to the clinical feature selection pipeline, a previous step is added: features had a first selection regarding its correlation to label and its performance in Kruskal-Wallis test. As it was needed some robust test and since it was impossible to use one that used the whole set of features simultaneously, there was the need to choose one that evaluated each feature independently. As a consequence, it was decided to use two. The correlation with the label offered a good measure of how directly was the discriminative power regarding the feature. Besides, it is not a parametric test, not assuming a Gaussian distribution over the data (as several tests do). This can be seen in Figure 6.129:

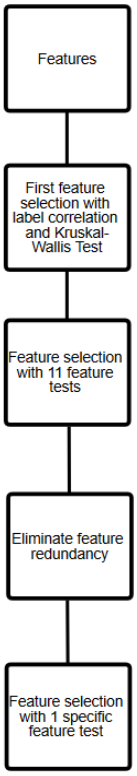

Figure 6.129: Feature selection scheme for all image databases.

The used feature tests are:

1. **Boxplot visualization**: test A.
2. **Kruskal-Wallis test**: test B.
3. **Correlation with label**: test C.
4. **F-score**: test D.
5. **Feature and label AUC**: test E.
6. **Minimum redundancy maximum relevance test**: test F.
7. **ReliefF algorithm**: test G.
8. **Decision tree feature importance**: test H.
9. **Ansari-Bradley test**: test I.
10. **Two sample Kolmogorov-Smirnov test**: test J.
11. **Wilcoxon rank sum test**: test L.

Boxplot is a method that makes able to evaluate graphically the discriminative power of a feature. Boxplots are non-parametric, since they display the variation of samples without making any assumptions regarding its statistical distribution. The spaces between the different box parts are directly related to data dispersion. A feature was considered to have discriminative power when its boxes (one box for

each class) did not intersect. By other words, when the first quartile of one box was higher than the third one of the other box.

Kruskal-Wallis is also a non-parametric test to verify if two samples come from the same distribution. These samples can have different sizes. As Kruskal-Wallis is a statistical test, the α value used as threshold was 0.05. Thus, it is possible to deny the null hypothesis if p-value $< \alpha$.

Correlation with the label is an intuitive feature as it provides a direct feature relation regarding the label. The used threshold value was 0.25 due to the observed results.

F-score is directly related to the mean differences between the two classes and their standard deviation. Features with good discriminative power will have a high F-score value, where the used threshold is 0.1 due to the observed results. Higher the difference of the means and lower the standard deviation of each one, higher is the F-score value, as it can be seen in the following equation, where X_0 and X_1 represent the data belonging to each class (0 and 1):

$$Fscore = \frac{(mean(X_0) - mean(X_1))^2}{std(X_0)^2 + std(X_1)^2}.$$

It is possible to create a Receiver Operator Characteristic (ROC) curve specifically for every feature. A ROC curve is created by plotting the true positive rate against false positive rate by changing the feature threshold regarding a classification decision. The AUC is the area under the ROC curve. The higher its value, the greater is the feature predictive value. An area of value 1 represents a perfect feature, where an area of 0.5 represents a random behavior. The used threshold for the AUC was 0.65 due to the observed results.

Minimum Redundancy Maximum Relevance (mRMR) is an algorithm that takes as input the whole set of features, ranking them by its discriminative power and intra-correlation. This way, the top-ranked features will not only have the higher discriminative power but also the lowest redundancy regarding the rest of the features. Relevance can be calculated with F-statistic or mutual information, regarding feature nature (continuous/discrete) and redundancy can be calculated by using Pearson correlation coefficient or mutual information, regarding feature nature once again [77].

ReliefF is a feature selection algorithm used in binary classification. This takes as input the whole set of features, ranking them by its discriminative power. However, it does not take into account the possibility of information redundancy. ReliefF was used by applicating it in a regression with k nearest neighbors as it was used MATLAB relieff function. It was used a K=3.

Decision tree feature importance is a very interesting test as it is directly re-

lated to the classification process (a decision tree is a classification algorithm). In this test, a fitted binary classification tree is created based on the whole set of features. Afterwards, the feature importance of each one is calculated by analyzing the tree structure. Besides, it is also an interesting test since decision trees are easily interpreted.

Ansari-Bradley, Two-sample Kolmogorov-Smirnov and Wilcoxon rank sum are all statistical tests, where each of them has a null hypothesis. Similarly to the Kruskal-Wallis, Ansari-Bradley test, the threshold value (α) for rejecting the null hypothesis is 0.05. Ansari-Bradleys null hypothesis test is that the data in the two classes come from the same distribution. The two sample Kolmogorov-Smirnov null hypothesis test is that the data in the two classes come from the same continuous distribution. Wilcoxon rank sum null hypothesis test is that the data in the two classes are samples from continuous distributions with equal medians.

It was naturally expected that no feature would get a score of value 11 (to each passed test is attributed 1 point) as some tests are for certain types of features (parametric/non-parametric, continuous/discrete). The goal of this feature selection step was to select the ones that had a relatively higher score regarding the others. The goal with this set of tests is was explore all possibilities and to analyze each feature from different perspectives.

6.4 Supervised learning

After the set of features was chosen for each database regarding each label, supervised learning algorithms were performed in order to evaluate the predictors quality. As the number of samples was reduced in all databases, except *One lesion one sample* database, it was desired to test these cases in the most variable situations. It was a valid path to give an insight on how the model would generalize to a set of independent datasets and cases. If one case is succeeded in different conditions, the level of trust in the given results is naturally higher. Besides, trying different methods also reduces some existing bias, since some cases can have outstanding performances due to certain data circumstances.

This is the reason why three different partition methods were attempted: K-Fold with K=10, LOO and the traditional one (70:30 ratio). Dimensionality reduction was also an approach method, in order to check if the results would improve or not with it. The used dimensionality reduction technique was PCA. For the same reasons, there were tested 11 different classification algorithms: decision tree, Linear Discriminant Analysis (LDA), Quadratic Discriminant Analysis (QDA), Sup-

port Vector Machine (SVM), K-Nearest Neighbors (KNN) with K=1,3 and 5, Naive Bayes classifier, Generalized Linear Model (GLM) regression and minimum distance classifier with Euclidean and Mahalanobis distance. Thus, all combinations were tested, as shown in Figure 6.130.

Afterwards, the results were analyzed regarding different metrics calculated with a confusion matrix and with a ROC curve.

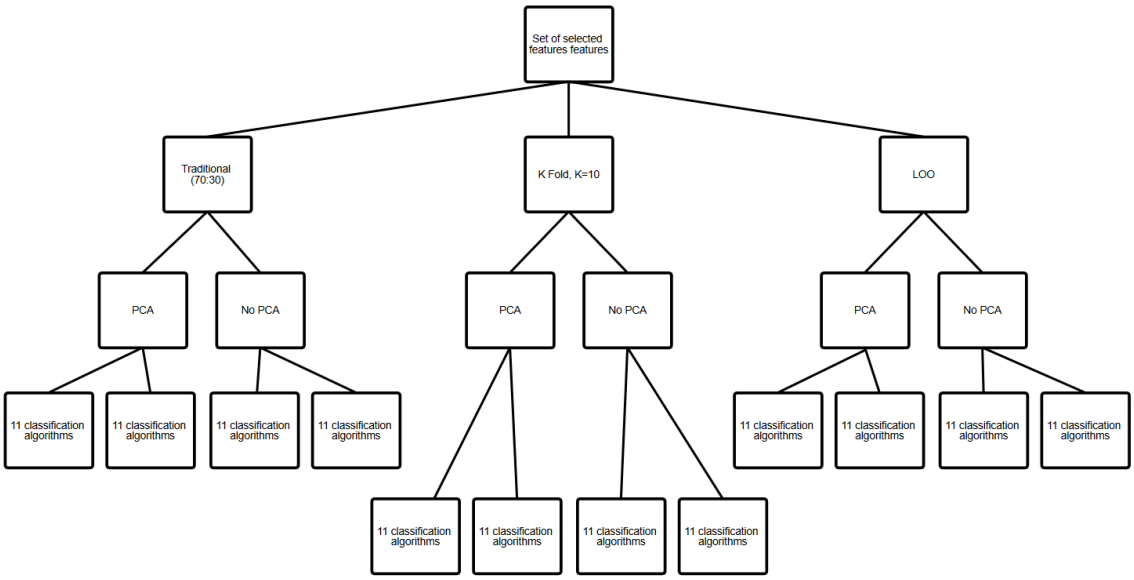

Figure 6.130: The scheme of the supervised learning procedure.

6.4.1 Partition methods

The most common method for partition the data is to consider 70% of data for training and the other 30% for testing. As it is the classical approach, it was used. However, as already mentioned, the number of samples of the existing databases is reduced. Due to the randomness of the training/test set, some performances may be extremely good or bad due to a certain selection for each set. So, in order to avoid these discrepancies, this process was repeated 100 times and its results were averaged. This partition method does not seem to be the most adequate for a reduced number of samples.

K-Fold 10 is a more appropriate method for a reduced number of samples. In k-Fold partitioning, the dataset is divided into k equal-sized groups. Again, this division is random. While one of the k groups will be used as the test set, the others k-1 will constitute the training set. This process is repeated k times in order to every k group to be the train set. As the dataset is small, by experimenting

different combinations of training and test samples, a more insight will be provided. Besides, this process was repeated 100 times and its results were averaged. This method is considered to be more appropriate since it theoretically allows a deeper use of the existing samples as there are performed k different combinations per step.

Leave One Out (LOO) partition method can be seen as a particular method of K-Fold, where K=number of samples. Thus, all samples are used as the test set individually while the rest (all samples except the selected one) constitutes the training set. In this case, since there are no random set attributions, the process was not repeated for each sample.

6.4.2 Dimensionality reduction

Principal Component Analysis (PCA) is a statistical procedure where a set of observations are transformed into a set of values linearly uncorrelated variables, commonly named principal components. The amount of principal components is the same as features. This transformation is performed by analyzing the direction and orientation where the existing variance will be the highest. Thus, the first principal component will have the largest possible variable. After the first, every orthogonal component will be evaluated and selected the one with the highest variance, and so on. A common procedure in PCA analysis is to discard the principal components having the least quantity of information. In other words, the ones that possess the lowest variance value.

In this thesis, the number of principal components was choosed according to the relative amount of information (0.85 as threshold). In other words, the variance of all principal components is summed and a cumulative sum operation is performed from the first to the last components. When the amount of information divided by the total reaches a significant value regarding the number of components (3/4), no more components are selected. This number of components was taken into account due to the database size, in order to reduce overfitting. 0.85 was the commonest threshold that complied with this number of principal components. This technique is interesting because it is a path to reduce the number of features and therefore to reduce overfitting risk.

However, since PCA constitutes a transformation in the data, features lose its original meaning, since a principal component is constituted by several weights of different features.

6.4.3 Classification algorithms

Decision trees go from observations (represented in the branches) to conclusions about a sample value (a certain class of a label, represented in the leaves). These mentioned observations are simple conditions, where a threshold is used upon a feature. For example, the condition feature $x > 0.5$ will result in a bifurcation. A tree is constructed by evaluating the set of features regarding the class, resulting in several branches until leaves are reached. As a final output, an interpretable scheme with a tree shape is presented as an algorithm to predict new data. The advantage of trees, besides the real world intuitive interpretation, it is the possibility to analyze all sample cases and to decide the most important ones. This decision criteria can be variate, where entropy is commonly an used one. The used decision tree was the one created with the default definitions of MATLAB function *fitctree*.

LDA, besides being a classification algorithm, is also a dimensionality reduction technique, where it projects multidimensional data into a 1D space. In other words, LDA natively projects multidimensional data into a C-1 dimension, where C is the number of classes. This means that, for binary problems, it projects the data into 1 dimension. However, LDA is a supervised learning technique, while PCA does not take into account the labels (its procedures are based only on data intrinsic properties). The data is projected with the goal of increasing the distance between the two class means and with the goal of minimizing the intra-class variance. QDA has a similar procedure, however, instead of projecting the data into a linear space, it is projected into a quadratic one (2D).

The goal of KNN is the application of a database where new data is labeled simply regarding the training samples position. Thus, to predict a new point, the k nearest points of the point to be predicted are chosen, where the predicted label is the most common between these. K should not be even in order to exclude the possibility to have equally common labels regarding the k nearest points. KNN was performed with K=1, 3 and 5 as these are odd numbers. Besides, the K value must not be large in order to be sensitive to the points localizations. Thus, these 3 values were tested to verify how the algorithm reacts to different levels of noise and position sensitivity.

SVM algorithms project the training set in a high dimensional space through the use of a kernel function. The non-linear data suffers a transformation in a way that a line (discriminative hyperplane) can be generated to separate the existing classes. This class distance must be maximized. Some samples are used to define separation margins and to define the decision hyperplane. These samples are named

support vectors. The data to be tested is, therefore, projected into the high dimensionality space created with the training set where it will be classified according to its localization regarding the discriminative hyperplane. These calculations are performed with a kernel function, where the Radial Basis Function (RBF) was the used one. A standard SVM algorithm has the objective of finding a space were is possible to be drawn a plane able to separate the existing classes.

Naive Bayes classifier is different from all the presented algorithms so far as it is not essentially dependent in the spatial distribution of the samples. This classifier has statistical ideas as the main concept since it is considered a conditional probability model. By taking into the account the Bayes theorem, it is possible to decompose the conditional probability into the multiplication of the prior probability and likelihood divided by the evidence. Since the evidence is a constant value, the core of this algorithm is present in the multiplication operation. By assuming conditional independence of all features, the model gets simplified and intuitive. This model is combined with a decision rule, where the most common it is to choose the one with the higher probability (argmax operation).

A regression analysis was made with GLM. GLM consists in a flexible generalization of a standard linear regression. With the GLM trained, a regression is made by applying a decision criteria regarding a chosen threshold. The chosen threshold was 0.5 as it is the most common one applied in standard linear regressions.

In the minimum distance classifier, the distance of a new point is measured regarding the medium feature value of each class of the training set. The predicted class will be the one that ensured the lowest distance to the new point. In this project, two different metrics were tested: Euclidean and Mahalanobis distances. The difference between these two distances, in practical terms, is that Mahalanobis distance is independent of feature scaling.

6.4.4 Evaluation metrics

With the given results and with the real labels, a confusion matrix was calculated for each case. As all problems were binary, this matrix will always be a 2×2 one, indicating the number of false positives, false negatives, true positives and true positives. With this matrix, it is possible to calculate some metrics in order to have a deeper insight regarding a certain performance. True positives and true negatives represent the successfully predicted cases, while false positives and negatives represent the failed ones. The calculated metrics were:

1. **Specificity**: the ratio of successfully classified negative predicted cases re-

garding all negative ones.

2. **Sensitivity**: the ratio of successfully classified positive predicted cases regarding all positive ones.
3. **PPV**: the ratio of successfully classified positive predicted cases regarding all cases predicted as positive.
4. **NPV**: the ratio of successfully classified negative predicted cases regarding all cases predicted as negative.
5. **Accuracy**: the ratio of successfully classified predicted cases.

The ROC curve is also an interesting output regarding the predicting results. As mentioned in the feature selection procedure, it is a graphical plot that illustrates the capacity of a binary classifier regarding the decision threshold variation. This curve is created by changing the threshold value in order to find all labeling decision cases. For each threshold value, the true positive rate and false positive rate are calculated. In fact, the true positive rate it is commonly known as sensitivity and false positive rate can be calculated by (1-specificity). The AUC is an interesting estimator regarding the ROC as it provides an overall view regarding the performance with every threshold value. The ideal case is the one where both classes are totally linearly separatable by a certain threshold value. In this case, the AUC has value 1. The higher the AUC value, higher the performance.

Chapter 7

Results

Since the results were very extense, an evaluation system was created in order to make them simpler to interpret. Since these have a significant variability due to the use of different datasets, partition methods, classifiers and sets of features, it was decided to grade the overall performance among labels. The best-graded labels were the ones explored in a deeper level as the degree of trust in them is logically higher.

As it can be seen, the existing labels are all correlated in a certain way, since are all EDSS-related (except label *msCourse*). Thus, among the best ranked-labels, the most common features were highlighted as a sign of coherence in these processes. In other words, if a feature was described as a good predictor in several different databases and different labels, it was considered to be an influent factor for MS disease progression evaluation.

Two overall performance methods were used, one using AUC (area under the curve) and the other using the set of classification performance measures (Specificity, Sensibility, PPV, NPV, Accuracy).

The AUC performance method consisted in attributing 1 point to a classifier whose AUC is higher than 0.69, 2 points to higher than 0.79 and 3 points to values higher than 0.89 (Table E.2 in Appendix V). If the performance was obtained using the 70:30 ratio partition method, it was multiplied by 1, by 2 with k-Fold method and by 3 with LOO method (Table E.3 in Appendix V). The total score of a set of features to a certain label is the sum of points of all the classifiers within the same database. This way, the performance had the influence of the different partition methods and was considered to be better if the set of features evaluated had a

higher number of classifiers performing effectively.

The method using classification performance measures consisted in attributing 1 point to a classifier if the lowest stat (specificity or sensibility or PPV or NPV or accuracy) was higher than 0.49, 2 points if higher than 0.59, 3 points if higher than 0.69, 4 points if higher than 0.79, 5 points if higher than 0.89 (Table E.2 in Appendix V). Similarly to the AUC performance method, the points were multiplied (Table E.3 in Appendix V) regarding the partition method.

With these two performance methods, the most trustful paths in order to explore were found. The classification performances measures can be found in Appendix V.

7.1 Performance metric analysis

With the obtained results on different databases, an overall integration of the scores was made. With this, aiming to find the most reliable set of features/set of labels in order to make a deeper analysis afterward to get some insights about MS progression.

In each database, the three highest scored labels were selected (the ones in bold in each table) and attributed points, according to Table 7.1.

The analysis is agglomerative as it starts by grouping the database scoring according to the source of data (clinical or image origin). In the image databases, there is a separation between the lesion source and the total MRI source. Then, an overall one is calculated, where the result score is the sum of all databases scores (tables 7.6 and 7.13). Two alternatives of overall metrics are also calculated, using again the system of Table 7.1, one gathering all databases (tables 7.7 and 7.14) and another with the all image databases, all clinical databases and the already mentioned overall one (tables 7.8 and 7.15).

Table 7.1: The evaluation metric used with the labels rank.

Position	**Score**
1st	3 points
2nd	2 points
3rd	1 point

7.1.1 AUC performance method analysis

7.1.1.1 Image databases

Table 7.2: The label scoring of the *MRI total head* database with AUC performance method.

Label	Score
msCourse	**1**
highestEDSS	**3**
currentEDSS	0
nextEDSS	0
first2EDSS	0
tendencyEDSS	0
mediumEDSS	**2**

Table 7.3: The label scoring of the lesions database with AUC performance method.

Label	Score
msCourse	0
highestEDSS	**5**
currentEDSS	0
nextEDSS	**5**
first2EDSS	0
tendencyEDSS	0
mediumEDSS	0

Table 7.4: The label scoring of all image source databases with AUC performance method.

Label	Score
msCourse	1
highestEDSS	**8**
currentEDSS	0
nextEDSS	**5**
first2EDSS	0
tendencyEDSS	0
mediumEDSS	**2**

7.1.1.2 Clinical databases

Table 7.5: The label scoring of all clinical source databases with AUC performance method.

Label	Score
msCourse	3
highestEDSS	**16**
currentEDSS	1
nextEDSS	**10**
first2EDSS	4
tendencyEDSS	0
mediumEDSS	**9**

7.1.1.3 Performance ensembling

Table 7.6: The label scoring of all databases with AUC performance method.

Label	Score
msCourse	4
highestEDSS	**24**
currentEDSS	1
nextEDSS	**15**
first2EDSS	4
tendencyEDSS	0
mediumEDSS	**11**

Table 7.7: The label scoring of all databases with the position score system using AUC performance method.

Label	Score
msCourse	1
highestEDSS	**15**
currentEDSS	0
nextEDSS	**9**
first2EDSS	0
tendencyEDSS	0
mediumEDSS	**5**

Table 7.8: The label scoring of the ensemble of all databases, all image databases and all clinical databases with the position score system using AUC performance method.

Label	Score
msCourse	0
highestEDSS	**9**
currentEDSS	0
nextEDSS	**6**
first2EDSS	0
tendencyEDSS	0
mediumEDSS	**3**

7.1.2 Stats performance method analysis

7.1.2.1 Image databases

Table 7.9: The label scoring of the *MRI total head* database with Stats performance method.

Label	Score
msCourse	0
highestEDSS	**3**
current	0
nextEDSS	**1**
first2EDSS	0
tendencyEDSS	0
mediumEDSS	**2**

Table 7.10: The label scoring of the lesions database with stats performance method.

Label	Score
msCourse	1
highestEDSS	**6**
currentEDSS	0
nextEDSS	**5**
first2EDSS	1
tendencyEDSS	0
mediumEDSS	**5**

Table 7.11: The label scoring of all image source databases with stats performance method.

Label	Score
msCourse	1
highestEDSS	**9**
currentEDSS	0
nextEDSS	**6**
first2EDSS	1
tendencyEDSS	0
mediumEDSS	**7**

7.1.2.2 Clinical databases

Table 7.12: The label scoring of all clinical source databases with stats performance method.

Label	Score
msCourse	0
highestEDSS	**12**
currentEDSS	0
nextEDSS	**5**
first2EDSS	0
tendencyEDSS	0
mediumEDSS	**8**

7.1.2.3 Performance ensembling

Table 7.13: The label scoring of all databases with stats performance method.

Label	Score
msCourse	5
highestEDSS	**33**
currentEDSS	0
nextEDSS	**13**
first2EDSS	4
tendencyEDSS	0
mediumEDSS	**16**

Table 7.14: The label scoring of all databases with the position score system using stats performance method.

Label	Stats
msCourse	0
highestEDSS	**15**
currentEDSS	0
nextEDSS	**6**
first2EDSS	0
tendencyEDSS	0
mediumEDSS	**10**

Table 7.15: The label scoring of the ensemble of all databases, all image databases and all clinical databases with the position score system using stats performance method.

Label	Score
msCourse	0
highestEDSS	**9**
currentEDSS	0
nextEDSS	**3**
first2EDSS	0
tendencyEDSS	0
mediumEDSS	**6**

7.1.3 Best scored labels

By analyzing the results by both metrics, it's possible to see a coherence in the results: the top 3 best ranked labels were in both cases the *highestEDSS*, *mediumEDSS*, *nextEDSS*, where the *highestEDSS* takes always the first place. With the AUC performance method, *mediumEDSS* takes second place and *nextEDSS* third, while on the stats performance method, they switch positions.

In order to focus the attention on these three cases, the information regarding them and the set of features will be displayed again, making easier the following interpretations and calculations.

7.1.3.1 *HighestEDSS*

Table 7.16: Overview of the performance of *highestEDSS* label. The best performances are in bold.

Database	Label	Stats method score	AUC method score
MRI Total Head	highestEDSS>3	131	24
MRI Total Head	highestEDSS>5	0	0
One sample one lesion	highestEDSS>3	0	0
One sample one lesion	highestEDSS>5	0	0
One sample one lesion ensemble	highestEDSS>3	0	0
One sample one lesion ensemble	highestEDSS>5	0	0
One sample one study	highestEDSS>3	61	4
One sample one study	highestEDSS>5	0	2
One sample one patient	highestEDSS>3	109	0
One sample one patient	highestEDSS>5	not performed	not performed
Static_Normal	**highestEDSS>3**	**231**	45
Static_Normal	highestEDSS>5	not performed	not performed
Static_Investigation	highestEDSS>3	110	14
Static_Investigation	highestEDSS>5	not performed	not performed
Groundzero_Normal	highestEDSS>3	145	20
Groundzero_Normal	highestEDSS>5	not performed	not performed
Groundzero_Investigation	highestEDSS>3	71	0
Groundzero_Investigation	highestEDSS>5	not performed	not performed
Momentaneous_Normal	highestEDSS>3	189	82
Momentaneous_Normal	highestEDSS>5	not performed	80
Momentaneous_Investigation	highestEDSS>3	146	61
Momentaneous_Investigation	highestEDSS>5	110	63
Momentaneous_Past_Normal	**highestEDSS>3**	**233**	**124**
Momentaneous_Past_Normal	**highestEDSS>5**	118	**92**
Momentaneous_Past_Investigation	**highestEDSS>3**	**283**	**142**
Momentaneous_Past_Investigation	highestEDSS>5	126	90

The set of features for each clinical database for *highestEDSS* label:

1. ***Static* Standard for *highestEDSS*>3**: EDSS Medium Value/year, EDSS 1st year, No Years.
2. ***Static* Standard for *highestEDSS*>5**: not performed.
3. ***Static* Investigation for *highestEDSS*>3**: MS Course, No Years, Pyramidal first 2 years.
4. ***Static* Investigation for *highestEDSS*>5**: not performed.
5. ***Groundzero* Standard for *highestEDSS*>3**: Optic Pathways, Ms Course, EDSS.
6. ***Groundzero* Standard for *highestEDSS*>5**: not performed.
7. ***Groundzero* Investigation for *highestEDSS*>3**: Time since onset, Relapse Age.
8. ***Groundzero* Investigation for *highestEDSS*>5**: not performed.
9. ***Momentaneous* Standard for *highestEDSS*>3**: Years since Onset, Last EDSS.
10. ***Momentaneous* Standard for *highestEDSS*>5**: MS Course, Years since Onset, Last EDSS, Gender.
11. ***Momentaneous* Investigation for *highestEDSS*>3**: Spinal Cord, Age Visit, Years since Onset.
12. ***Momentaneous* Investigation for *highestEDSS*>5**: Spinal Cord, MS Course, Age Visit, Gender.
13. ***Momentaneous with past* Standard for *highestEDSS*>3**: Age Visit, EDSS Medium Value/Year, Average Treatment 2 first years.
14. ***Momentaneous with past* Standard for *highestEDSS*>5**: Optic Pathways, EDSS Medium Value/Year, Pyramidal first 2 years, Corticosteroids 1st year.
15. ***Momentaneous with past* Investigation for *highestEDSS*>3**: Spinal Cord, Age Visit, Years since Onset, Nb of visits per Year, Sensory ratio, Corticosteroids Ratio.
16. ***Momentaneous with past* Investigation for *highestEDSS*>5**: Optic Pathways, Pyramidal first 2 years, Corticosteroids 1st year.

The databases with the highest score belong to clinical origins, where the *Momentaneous with past* takes the first and second place of maximum scores. The investigation method seems to achieve better results, which is a very interesting fact, since it does not include EDSS-related features. The *Static* database also has an interesting performance.

7.1.3.2 *MediumEDSS*

Table 7.17: Overview of the performance of *mediumEDSS* label. The best performances are in bold.

Database	Label	Stats method score	AUC method score
MRI Total Head	mediumEDSS>3	48	20
MRI Total Head	mediumEDSS>5	0	0
One sample one lesion	mediumEDSS>3	6	0
One sample one lesion	mediumEDSS>5	0	0
One sample one lesion ensemble	mediumEDSS>3	0	0
One sample one lesion ensemble	mediumEDSS>5	0	0
One sample one study	mediumEDSS>3	10	0
One sample one study	mediumEDSS>5	not performed	not performed
One sample one patient	mediumEDSS>3	76	0
One sample one patient	mediumEDSS>5	10	0
Static_Normal	mediumEDSS>3	100	20
Static_Normal	mediumEDSS>5	not performed	not performed
Static_Investigation	mediumEDSS>3	66	5
Static_Investigation	mediumEDSS>5	not performed	not performed
Groundzero_Normal	mediumEDSS>3	38	20
Groundzero_Normal	mediumEDSS>5	not performed	not performed
Groundzero_Investigation	mediumEDSS>3	18	0
Groundzero_Investigation	mediumEDSS>5	not performed	not performed
Momentaneous_Normal	**mediumEDSS>3**	**189**	**115**
Momentaneous_Normal	mediumEDSS>5	not performed	not performed
Momentaneous_Investigation	**mediumEDSS>3**	**132**	**83**
Momentaneous_Investigation	mediumEDSS>5	not performed	not performed
Momentaneous_Past_Normal	**mediumEDSS>3**	**104**	**73**
Momentaneous_Past_Normal	mediumEDSS>5	not performed	not performed
Momentaneous_Past_Investigation	mediumEDSS>3	104	62
Momentaneous_Past_Investigation	mediumEDSS>5	not performed	not performed

The set of features for each clinical database for *mediumEDSS* label:

1. ***Static* Standard for *mediumEDSS*>3**: EDSS 1st year, Ratio nb EDSS increase, No Years.
2. ***Static* Standard for *mediumEDSS*>5**: not performed.
3. ***Static* Investigation for *mediumEDSS*>3**: Gender, Age of Onset, Nb of visits first 2 years, Pyramidal first 2 years, No Years.
4. ***Static* Investigation for *mediumEDSS*>5**: not performed.
5. ***Groundzero* Standard for *mediumEDSS*>3**: Spinal Cord, CNS Pyramidal Tract, Brainstem-Cerebellum, Time since onset.
6. ***Groundzero* Standard for *mediumEDSS*>5**: not performed.

7. ***Groundzero* Investigation for *mediumEDSS*>3**: Gender, Age of Onset, Nb of visits first 2 years, Pyramidal first 2 years, No Years.
8. ***Groundzero* Investigation for *mediumEDSS*>5**: not performed.
9. ***Momentaneous* Standard for *mediumEDSS*>3**: Age of Diagnosis, Years from Onset to Diagnosis, Years since Onset, Last EDSS.
10. ***Momentaneous* Standard for *mediumEDSS*>5**: not performed.
11. ***Momentaneous* Investigation for *mediumEDSS*>3**: Age of Diagnosis, MS Course, Years since Onset.
12. ***Momentaneous* Investigation for *mediumEDSS*>5**: not performed.
13. ***Momentaneous with past* Standard for *mediumEDSS*>3**: Ratio nb EDSS increase, Last EDSS.
14. ***Momentaneous with past* Standard for *mediumEDSS*>5**: not performed.
15. ***Momentaneous with past* Investigation for *mediumEDSS*>3**: Spinal Cord, MS Course, No Years, Pyramidal ratio, Pyramidal first 2 years.
16. ***Momentaneous with past* Investigation for *mediumEDSS*>5**: not performed.

The databases with the highest score belong to clinical origins, where the *Momentaneous* and *Momentaneous with past* take the first three places. The investigation procedure occupies the second place, which is a very interesting fact since it does not include direct EDSS-related features.

7.1.3.3 NextEDSS

Table 7.18: Overview of the performance of *nextEDSS* label. The best performances are in bold.

Database	Label	Stats method score	AUC method score
MRI Total Head	nextEDSS>3	42	4
MRI Total Head	nextEDSS>5	6	0
One sample one lesion	nextEDSS>3	0	0
One sample one lesion	nextEDSS>5	0	0
One sample one lesion ensemble	nextEDSS>3	1	0
One sample one lesion ensemble	nextEDSS>5	0	0
One sample one study	nextEDSS>3	10	4
One sample one study	nextEDSS>5	19	2
One sample one patient	nextEDSS>3	not performed	not performed
One sample one patient	nextEDSS>5	not performed	not performed
Static_Normal	nextEDSS>3	not performed	not performed
Static_Normal	nextEDSS>5	not performed	not performed
Static_Investigation	nextEDSS>3	not performed	not performed
Static_Investigation	nextEDSS>5	not performed	not performed
Groundzero_Normal	nextEDSS>3	not performed	not performed
Groundzero_Normal	nextEDSS>5	not performed	not performed
Groundzero_Investigation	nextEDSS>3	not performed	not performed
Groundzero_Investigation	nextEDSS>5	not performed	not performed
Momentaneous_Normal	**nextEDSS>3**	**146**	**122**
Momentaneous_Normal	nextEDSS>5	92	50
Momentaneous_Investigation	nextEDSS>3	136	94
Momentaneous_Investigation	nextEDSS>5	6	6
Momentaneous_Past_Normal	**nextEDSS>3**	**179**	**123**
Momentaneous_Past_Normal	nextEDSS>5	98	59
Momentaneous_Past_Investigation	**nextEDSS>3**	**148**	**109**
Momentaneous_Past_Investigation	nextEDSS>5	32	21

The set of features for each clinical database for *nextEDSS* label:

1. ***Static* Standard for *nextEDSS*>3**: not performed.
2. ***Static* Standard for *nextEDSS*>5**: not performed.
3. ***Static* Investigation for *nextEDSS*>3**: not performed.
4. ***Static* Investigation for *nextEDSS*>5**: not performed.
5. ***Groundzero* Standard for *nextEDSS*>3**: not performed.
6. ***Groundzero* Standard for *nextEDSS*>5**: not performed.
7. ***Groundzero* Investigation for *nextEDSS*>3**: not performed.
8. ***Groundzero* Investigation for *nextEDSS*>5**: not performed.
9. ***Momentaneous* Standard for *nextEDSS*>3**: Years since Onset, Last

EDSS.

10. ***Momentaneous* Standard for *nextEDSS*>5**: MS Course, Years since Onset, Last EDSS, Gender.
11. ***Momentaneous* Investigation for *nextEDSS*>3**: Spinal Cord, Age Visit, Years since Onset.
12. ***Momentaneous* Investigation for *nextEDSS*>5**: Spinal Cord, MS Course, Age Visit, Gender.
13. ***Momentaneous with past* Standard for *nextEDSS*>3**: Optic Pathways, EDSS Medium Value/year, EDSS first 2 years std, Relapses Per Year, Visual 1 ratio
14. ***Momentaneous with past* Standard for *nextEDSS*>5**: EDSS Medium Value/Year, EDSS first 2 years, EDSS std/year, Last EDSS.
15. ***Momentaneous wth past* Investigation for *nextEDSS*>3**: MS Course, No Years, Pyramidal first 2 years, Visual 1 ratio, Average Duration.
16. ***Momentaneous with past* Investigation for *nextEDSS*>5**: Optic Pathways, No Years, Pyramidal first 2 years, Sensory 1 ratio, Average Duration.

The databases with the highest score belong to clinical origins, where the *Momentaneous with past* and *Momentaneous* take the first three places. The investigation procedure occupies the half of the second and third place, which is an interesting fact since it does not include direct EDSS-related features.

7.1.4 Clinical feature analysis

Some features like Spinal Cord, MS Course, Gender, Pyramidal First 2 years, Visual Ratio, EDSS-related features, Optical Pathways, Sensory Ratio and No Year appeared in different databases and in different labels, showing some potential in order to be MS disease progression predictors. Some of them, as the MS Course, No Years, Gender and EDSS-related features are previously considered obvious. Patients with SP type tend to have worst prognostics. MS is related to gender, since women are more affected by this condition when compared to men. The more years a patient suffers from MS, the more likely its EDSS is larger. However, others may not be that obvious, like Spinal Cord, Pyramidal First 2 Years, Visual Ratio, Optical Pathways and Sensory Ratio.

In the next tables (Tables 7.19-7.45), the presence of the mentioned features is counted in order to evaluate their discriminative power, regarding the different labels.

7.1.4.1 In highestEDSS label

Table 7.19: The presence of Spinal Cord feature in the best set of features for label *highestEDSS*.

Total of studies it appear	Standard procedure	Investigation procedure
3	0	3
For highestEDSS >3		
2	0	2
For highestEDSS >5		
1	0	1

Table 7.20: The presence of Pyramidal first 2 Years feature in the best set of features for label *highestEDSS*.

Total of studies it appear	Standard procedure	Investigation procedure
3	1	2
For highestEDSS >3		
1	0	1
For highestEDSS >5		
2	1	1

Table 7.21: The presence of Optical Pathways feature in the best set of features for label *highestEDSS*.

Total of studies it appear	Standard procedure	Investigation procedure
3	2	1
For highestEDSS >3		
1	1	0
For highestEDSS >5		
2	1	1

Table 7.22: The presence of MS Course feature in the best set of features for label *highestEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
3	1	2
For highestEDSS >3		
1	0	1
For highestEDSS >5		
2	1	1

Table 7.23: The presence of Visual Ratio feature in the best set of features for label *highestEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
0	0	0
For highestEDSS >3		
0	0	0
For highestEDSS >5		
0	0	0

Table 7.24: The presence of Sensory Ratio feature in the best set of features for label *highestEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
1	0	1
For highestEDSS >3		
1	0	1
For highestEDSS >5		
0	0	0

Table 7.25: The presence of Gender feature in the best set of features for label *highestEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
2	0	1
For highestEDSS >3		
0	0	0
For highestEDSS >5		
1	0	1

Table 7.26: The presence of EDSS-related features in the best set of features for label *highestEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
7	7	1
For highestEDSS >3		
5	5	0
For highestEDSS >5		
2	2	0

Table 7.27: The presence of No Years feature in the best set of features for label *highestEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
2	0	1
For highestEDSS >3		
2	0	1
For highestEDSS >5		
0	0	0

7.1.4.2 In mediumEDSS label

Table 7.28: The presence of Spinal Cord feature in the best set of features for label *mediumEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
2	0	1
For highestEDSS >3		
2	0	1
For highestEDSS >5		
0	0	0

Table 7.29: The presence of Pyramidal first 2 years feature in the best set of features for label *mediumEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
3	0	3
For highestEDSS >3		
3	0	3
For highestEDSS >5		
0	0	0

Table 7.30: The presence of Optical Pathways feature in the best set of features for label *mediumEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
0	0	0
For highestEDSS >3		
0	0	0
For highestEDSS >5		
0	0	0

Table 7.31: The presence of MS Course feature in the best set of features for label *mediumEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
2	0	2
For highestEDSS >3		
2	0	2
For highestEDSS >5		
0	0	0

Table 7.32: The presence of Visual ratio feature in the best set of features for label *mediumEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
0	0	0
For highestEDSS >3		
0	0	0
For highestEDSS >5		
0	0	0

Table 7.33: The presence of Sensory ratio feature in the best set of features for label *mediumEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
0	0	0
For highestEDSS >3		
0	0	0
For highestEDSS >5		
0	0	0

Table 7.34: The presence of Gender feature in the best set of features for label *mediumEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
2	0	2
For highestEDSS >3		
2	0	2
For highestEDSS >5		
0	0	0

Table 7.35: The presence of EDSS-related features in the best set of features for label *mediumEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
4	4	0
For highestEDSS >3		
4	4	0
For highestEDSS >5		
0	0	0

Table 7.36: The presence of No Year feature in the best set of features for label *mediumEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
4	0	3
For highestEDSS >3		
4	0	3
For highestEDSS >5		
0	0	0

7.1.4.3 In nextEDSS label

Table 7.37: The presence of Spinal Cord feature in the best set of features for label *nextEDSS*.

Total of studies it appear	Standard procedure	Investigation procedure
2	0	2
For highestEDSS >3		
1	0	1
For highestEDSS >5		
1	0	1

Table 7.38: The presence of Pyramidal First 2 years feature in the best set of features for label *nextEDSS*.

Total of studies it appear	Standard procedure	Investigation procedure
2	0	2
For highestEDSS >3		
1	0	1
For highestEDSS >5		
1	0	1

Table 7.39: The presence of Optic Pathways feature in the best set of features for label *nextEDSS*.

Total of studies it appear	Standard procedure	Investigation procedure
2	0	1
For highestEDSS >3		
1	0	0
For highestEDSS >5		
1	0	1

Table 7.40: The presence of MS Course feature in the best set of features for label *nextEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
2	0	1
For highestEDSS >3		
1	0	1
For highestEDSS >5		
1	0	0

Table 7.41: The presence of Visual Ratio feature in the best set of features for label *nextEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
2	0	1
For highestEDSS >3		
2	0	1
For highestEDSS >5		
0	0	0

Table 7.42: The presence of Sensory Ratio feature in the best set of features for label *nextEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
1	0	1
For highestEDSS >3		
0	0	0
For highestEDSS >5		
1	0	1

Table 7.43: The presence of Gender feature in the best set of features for label *nextEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
1	0	1
For highestEDSS >3		
0	0	0
For highestEDSS >5		
1	0	1

Table 7.44: The presence of EDSS-related features in the best set of features for label *nextEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
8	8	0
For highestEDSS >3		
3	3	0
For highestEDSS >5		
5	5	0

Table 7.45: The presence of No Years feature in the best set of features for label *nextEDSS*.

Total of studies it appear	**Standard procedure**	**Investigation procedure**
2	0	2
For highestEDSS >3		
1	0	1
For highestEDSS >5		
1	0	1

7.1.4.4 Data interpretation

If one decides to integrate the feature information regarding all highlighted features, it is possible to construct a hierarchy of feature presence with to the obtained results. Features as Spinal Cord, MS Course, Pyramidal First 2 years, EDSS-related features and No Years are present at least one time in the studies made with the labels considered to be trustful (*highestEDSS*, *nextEDSS*, *mediumEDSS*). Features as Sensory Ratio and Optical Pathways appear in studies of two of these labels (*nextEDSS* and *highestEDSS*). At least, Visual Ratio only appears in studies of one label (*nextEDSS*).

By analyzing the number of presences of each feature in all cases, some interesting facts come across. The results seem trustful since EDSS feature related appear as the most important (a score of 19 in Table 7.46). Gender, No Years and MS Course, which are obvious predictors of the disease progression, also appear with a good score (6,8 and 7, respectively). However, some surprise features also appear with a very interesting score: Spinal Cord with 7 points and Pyramidal First 2 Years with 8 points.

When comparing these feature presences of labeling for > 3 studies only (Table 7.47), the best-ranked features are EDSS feature related (12 points), No Years (7

points) and Spinal Cord and Pyramidal First 2 Years (5 points each). Features like Gender and MS Course scored 3 and 4 points, respectively.

When comparing these feature presences of labeling for > 5 studies only (Table 7.48), one can see the results are significantly worst. No feature was present in any set for predicting *mediumEDSS*$>$ 5 properly. The best-ranked features are EDSS-related features (7 points), Pyramidal First 2 years, Optical Pathways and MS Course (3 points each).

If one explores the EDSS-related features (Table 7.49) will understand that the best predictor is, in fact, the last EDSS value of a patient, with a score of 8 points. The second best is EDSS Medium Value/Year with 5 points. It is interesting to note that Pyramidal First 2 Years achieved the same points with the same criteria (8 points as well) and that Spinal Cord achieved 7 points.

Table 7.46: The general overview of the feature presence in the studies performed with labels *highestEDSS*, *nextEDSS* and *mediumEDSS*.

Feature	nextEDSS	highestEDSS	mediumEDSS	Total
Spinal Cord	2	3	2	**7**
Pyramidal First 2 Years	2	3	3	**8**
Optical Pathways	2	3	0	5
MS Course	2	3	2	7
Visual Ratio	2	0	0	2
Sensory Ratio	1	1	0	2
Gender	2	2	2	6
EDSS-related features	8	7	4	**19**
No Years	2	2	2	**8**

Table 7.47: The general overview of the feature presence in the studies performed with labels *highestEDSS*> 3, *nextEDSS*> 3 and *mediumEDSS*> 3.

Feature	nextEDSS	highestEDSS	mediumEDSS	Total
Spinal Cord	1	2	2	**5**
Pyramidal First 2 Years	1	1	3	**5**
Optical Pathways	1	1	0	2
MS Course	1	1	2	4
Visual Ratio	2	0	0	2
Sensory Ratio	0	1	0	1
Gender	1	0	2	3
EDSS-related features	3	5	4	**12**
No Years	1	2	4	**7**

Table 7.48: The general overview of the feature presence in the studies performed with labels *highestEDSS*> 5, *nextEDSS*> 5 and *mediumEDSS*> 5.

Feature	nextEDSS	highestEDSS	mediumEDSS	Total
Spinal Cord	1	1	0	**2**
Pyramidal First 2 Years	1	2	0	**3**
Optical Pathways	1	2	0	**3**
MS Course	1	2	0	**3**
Visual Ratio	0	0	0	0
Sensory Ratio	1	0	0	1
Gender	1	1	0	**2**
EDSS-related features	5	2	0	**7**
No Years	1	0	0	1

Table 7.49: The general overview of the EDSS-related features presence in the studies performed with labels *highestEDSS*, *nextEDSS* and *mediumEDSS*.

Feature	nextEDSS	highestEDSS	mediumEDSS	Total
EDSS medium Value/year	2	3	0	**5**
EDSS/ Last EDSS	3	3	2	**8**
EDSS 1st Year	0	1	0	1
Ratio Nb EDSS Increase	0	0	1	1
EDSS first 2 Years std	1	0	0	1
EDSS first 2 Years	1	0	0	1
EDSS std Year	1	0	1	1

7.1.5 Image features

Since clinic and image are different sources of data, it is reasonable to separate their results. Not only due to the origin itself but also due to the results obtained, where it is possible to evidence a better understanding of MS progression through the use of clinical descriptors. With the different set of features for all image databases with each label, an analysis was made, counting the used regions, modalities and the tissues used in features. Since the features have a larger variety of options, this was the chosen path, in order to get a briefer insight. In the region tables (Tables 7.51-7.59), the common features for different labels appear in bold.

7.1.5.1 In highestEDSS label

Table 7.50: The different set of features of all image databases for label *highestEDSS*.

Database	Label	Features
MRI Total Head	highestEDSS>3	164_A1_CSF_ratio_T2_max_entropy, 22_A1_WM_diff_FLAIR_max_entropy
MRI Total Head	highestEDSS>5	22_A1_WM_ratio_FLAIR_bin_location_median_median histogram
One sample one lesion	highestEDSS>3	Orientation,Var Pixel Intensity/slice_meanPixel, WM_squares numbers lesion region 90%/total,region with 90, T1_Var Pixel Intensity/slice_meanPixel, T1_gdeVar,Pixel Intensity/slice_meanPixel
One sample one lesion	highestEDSS>5	Solidity, Max Pixel Intensity/slice_meanPixel, T2_Mean Pixel Intensity/slice_meanPixel, T2_Min Pixel Intensity/slice_meanPixel, T1_gdeMean Pixel Intensity/slice_meanPixel, T1_gdeMax Pixel Intensity/slice_meanPixel, DP_Mean Pixel Intensity/slice_meanPixel, DP_Max Pixel Intensity/slice_meanPixel, DP_Min Pixel,Intensity/slice_meanPixel
One sample one study	highestEDSS>3	Var_Solidity, Mean_GM_min tissue prob, Var_GM_min tissue prob, Mean_Anatomical_I_162_lesion in,the region, Max_Anatomical_I_162_ratio on,region affected by lesion, Var_Anatomical_I_162_ratio on,region affected by lesion, Mean_Anatomical_I_162_ratio on,region affected by lesion, Var_Anatomical_I_162_median pixel,intensity, Max_Anatomical_I_162_lesion in the,region, Max_Anatomical_I_162_max,pixel intensity
One sample one study	highestEDSS>5	Var_Anatomical_II_39_mean,pixel intensity, Var_Anatomical_I_122_median pixel intensity, Mean_Anatomical_II_39_lesion in,the region
One sample one patient	highestEDSS>3	Max_Max_Anatomical_I_29_ratio on region affected by lesion, Mean_Var_Anatomical_II_40_var pixel intensity, Var_Max_Anatomical_II_40_var pixel intensity, Mean_Mean_Anatomical_II_40_var pixel,intensity, Var_Var_Anatomical_II_40_var pixel intensity
One sample one patient	highestEDSS>5	Not performed

Table 7.51: The region count of ones used in features for all image databases for label *highestEDSS*.

Region	Count
22	**2**
164	**1**
29	1
39	4
40	4
122	1
162	7

Table 7.52: The tissue count of ones used in features for all image databases for label *highestEDSS*.

Tissue	Count
WM	4
GM	2
CSF	1

Table 7.53: The modality count of ones used in features for all image databases for label *highestEDSS*.

Modality	Count
Flair	2
T1 Gde	5
T1	2
PD	6
T2	3

7.1.5.2 In mediumEDSS label

Table 7.54: The different set of features of all image databases for label *mediumEDSS*.

Database	Label	Features
MRI Total Head	mediumEDSS>3	66_A1_BO_ratio_T2_std_entropy, 121_A1_BO_ratio_T2_raw_std__mean, 48_A1_CSF_ratio_T2_std_energy_glcm, 92_A1_CSF_ratio_T2_mean_std,histogram, 22_A1_WM_diff_FLAIR_max_entropy, 22_A1_WM_ratio_FLAIR_max_entropy, 85_A1_WM_ratio_FLAIR_max_entropy
MRI Total Head	mediumEDSS>5	48_A1_BO_diff_T2_raw_std__mean, 48_A1_BO_ratio_T2_raw_mean_mean, 48_A1_BO_ratio_T2_raw_std__mean, 61_A1_BO_ratio_T2_raw_std__mean, Anatomical_31_DP_mean_histogram_18, Anatomical_31_DP_std_histogram_18
One sample one lesion	mediumEDSS>3	T2_Mean,Pixel Intensity/slice_meanPixel, T2_Min Pixel,Intensity/slice_meanPixel, T1_Mean Pixel,Intensity/slice_meanPixel, T1_Min Pixel,Intensity/slice_meanPixel, T1_gdeMean Pixel,Intensity/slice_meanPixel, T1_gdeMin Pixel,Intensity/slice_meanPixel, DP_Mean Pixel,Intensity/slice_meanPixel
One sample one lesion	mediumEDSS>5	Solidity, WM_mean tissue prob, T2_Mean Pixel Intensity/slice_meanPixel, T2_Min Pixel Intensity/slice_meanPixel, T1_Mean Pixel Intensity/slice_meanPixel, T1_Max Pixel Intensity/slice_meanPixel, T1_Min Pixel Intensity/slice_meanPixel, T1_Median Pixel Intensity/slice_meanPixel, T1_gdeMax Pixel Intensity/slice_meanPixel, T1_gdeMedian Pixel Intensity/slice_meanPixel, DP_Median,Pixel Intensity/slice_meanPixel
One sample one study	mediumEDSS>3	Var_Solidity, Mean_Anatomical_II_408_mean pixel intensity, Mean_Anatomical_II_408_median pixel intensity, Mean_Anatomical_II_408_min pixel intensity, Var_Anatomical_II_408_min pixel intensity, Max_Anatomical_II_408_mean pixel intensity, Max_Anatomical_II_408_median pixel intensity, Mean_Anatomical_II_408_lesion,in the region
One sample one study	mediumEDSS>5	Not performed
One sample one patient	mediumEDSS>3	Max_Mean_RefSpace, Max_Median_RefSpace, Var_Var_Anatomical_I_31_var pixel,intensity, Max_Mean_Anatomical_I_25_ratio on,region affected by lesion, Mean_Var_Anatomical_I_25_ratio on,region affected by lesion, Mean_Var_Anatomical_I_29_ratio on,region affected by lesion, Max_Var_Anatomical_I_31_mean pixel intensity, Mean_Max_Anatomical_I_31_var,pixel intensity
One sample one patient	mediumEDSS>5	Max_Max_Anatomical_II_14_ratio on region affected by lesion, Max_Mean_Anatomical_I_43_lesion in the region, Max_Mean_Anatomical_I_43_max pixel intensity, Max_Var_Anatomical_I_43_mean pixel intensity, Max_Var_Anatomical_I_31_mean pixel intensity, Max_Var_Anatomical_I_31_min pixel intensity, Max_Max_Anatomical_II_54_ratio on region,affected by lesion, Max_Mean_Anatomical_I_43_mean,pixel intensity

Table 7.55: The region count of ones used in features for all image databases for label *mediumEDSS*.

Region	Count
66	1
121	1
48	4
92	1
22	**2**
85	1
61	1
31	6
25	2
14 (Anatomical map II)	1
43	4
29	**1**

Table 7.56: The tissue count of ones used in features for all image databases for label *mediumEDSS*.

Tissue	Count
WM	5
GM	0
CSF	2

Table 7.57: The modality count of ones used in features for all image databases for label *mediumEDSS*.

Modality	Count
Flair	3
T1 Gde	5
T1	11
PD	5
T2	15

7.1.5.3 In nextEDSS label

Table 7.58: The different set of features of all image databases for label *nextEDSS*.

Database	Label	Features
MRI Total Head	nextEDSS>3	164_A1_CSF_ratio_T2_max_entropy, 22_A1_WM_diff_FLAIR_max_entropy
MRI Total Head	nextEDSS>5	22_A1_WM_ratio_FLAIR_bin_location_median_median histogram
One sample one lesion	nextEDSS>3	T1_gdeVar Pixel,Intensity/slice_meanPixel
One sample one lesion	nextEDSS>5	RefSpace, Mean Pixel Intensity/slice_meanPixel, Max Pixel Intensity/slice_meanPixel, T2_Mean Pixel Intensity/slice_meanPixel, T2_Min Pixel Intensity/slice_meanPixel, T1_Mean Pixel Intensity/slice_meanPixel, T1_Min Pixel Intensity/slice_meanPixel, T1_gdeMax Pixel Intensity/slice_meanPixel, T1_gdeMin Pixel Intensity/slice_meanPixel, T1_gdeMedian Pixel Intensity/slice_meanPixel, DP_Mean Pixel Intensity/slice_meanPixel, DP_Max Pixel Intensity/slice_meanPixel
One sample one study	nextEDSS>3	Var_GM_min tissue prob, Max_GM_min tissue prob, Var_Anatomical_I_21_var pixel intensity, Mean_Anatomical_I_21_var pixel intensity, Max_Anatomical_I_29_ratio on region affected,by lesion, Mean_Anatomical_I_29_var pixel intensity, Max_Anatomical_I_29_var pixel intensity, Var_Anatomical_I_42_var pixel,intensity, Var_Anatomical_I_21_ratio on,region affected by lesion, Var_Var,Pixel Intensity/slice_meanPixel
One sample one study	nextEDSS>5	Median_T1_Var,Pixel Intensity/slice_meanPixel, Var_GM_min tissue prob, Max_GM_min tissue prob, Max_Anatomical_I_21_var pixel,intensity, Max_GM_mean tissue prob, Var_Anatomical_I_21_var pixel,intensity, Var_Anatomical_I_29_ratio on region affected by lesion, Mean_Anatomical_I_21_var pixel,intensity, Var_Anatomical_I_29_var pixel intensity, Max_Anatomical_I_29_ratio on region affected by lesion, Mean_Anatomical_I_29_var pixel intensity, Mean_Anatomical_I_42_var pixel,intensity, Mean_Anatomical_I_29_ratio on,region affected by lesion,Var_Var,Pixel Intensity/slice_meanPixel
One sample one patient	nextEDSS>3	Not performed
One sample one patient	nextEDSS>5	Not performed

Table 7.59: The region count of ones used in features for all image databases for label *nextEDSS*.

Region	Count
22	2
21	6
29	5
42	1
164	1

Table 7.60: The tissue count of ones used in features for all image databases for label *nextEDSS*.

Tissue	Count
WM	2
GM	5
CSF	1

Table 7.61: The modality count of ones used in features for all image databases for label *nextEDSS*.

Modality	Count
Flair	7
T1 Gde	8
T1	5
PD	4
T2	4

7.1.5.4 Data interpretation

Since the performance results are not as good as the clinical ones, the degree of trust in the obtained interpretations is smaller. The region 22 (right superior frontal gyrus) and 29 (left middle orbitofrontal gyrus) appear in at least one study of each label. The region 22 appears always in the set of features for studies in the *MRI Total Head* database. The region 29 appears in *One sample one study* and in *One sample one patient* databases. Region 164 (right putamen) appears in studies of two different labels (*nextEDSS* and *highestEDSS*) in *MRI Total Head* database.

When it comes to modality count, it is possible to form a hierarchy (Table 7.62) using the already mentioned position system for attributing points (3 points

for first place, 2 points for second and 1 point for third one). However, the results were not as clear as in other situations. In the modality, T1-Gde appears to have a better performance, however, with PD, T2 and T1 (4 points, 4 points and 3 points respectively) the performance seemed to be similar.

When it comes to tissue count, the hierarchy is clearer (Table 7.63) and makes it possible to verify some already known facts about MS lesion exploration, as the importance of analyzing the WM regions. GM also appears better than CSF, which was also a given fact before the start of the study.

Table 7.62: Overall modality count for labels *nextEDSS*, *mediumEDSS* and *highestEDSS*.

Modality	**Count**
Flair	2
T1 Gde	**6**
T1	3
PD	4
T2	4

Table 7.63: Overall tissue count for labels *nextEDSS*, *mediumEDSS* and *highestEDSS*.

Tissue	**Count**
WM	**8**
GM	6
CSF	4

Chapter 8

Discussion

In this chapter, the most pertinent topics touched in this thesis are here discussed. Despite the fact that the goal of this master's dissertation was to study the progression of MS disease, some general aspects regarding this condition were not approached. Epidemiology appears to be a very interesting factor, however, it was impossible to study its influence, since all patients were not only caucasian but also born and live in Europe.

MS diagnosis could have been a very interesting aspect, however, this was impossible due to the time-consuming tasks of retrieving the MRI scans from CHUC's database. Naturally, all of the selected patients suffered from MS condition. For handling a diagnosis situation, it would be necessary to have non-MS patients in the database. This situation, however, would have been very interesting not only to study the diagnosis of MS/healthy but also between MS/other neurologic condition. NMO is a particular case, where there is a significant number of patients suffering from this condition.

PP form was not accounted due to the minimal number of patients suffering from it and because it is very distinct from the other two forms, RR and SP. These last two are quite interesting as all patients start with RR form, evolving or not to SP. This particularity constitutes a strong reason for focusing on the first years of MS manifestations. Although the results regarding label *msCourse* were not considered as trustful as the ones with labels *nextEDSS*, *highestEDSS* and *mediumEDSS*, there is a latent curiosity remaining regarding RR/SP distinction. As SP form is known to be more severe, intuitively confirmed by checking the EDSS, there must be an intrinsic relation between the last three mentioned labels and *msCourse*.

Therapy was also an excluded factor from this dissertation as it is not a straightforward aspect. A physician prescribes necessarily a stronger drug to a patient with a more severe condition. In a certain way, the used therapy constitutes an evaluation of the MS patient progression performed by the physician. The only way to properly study therapy influence would have been with a different database, where all patients or groups of patients would have very similarly MS progressions and taken different drugs. Besides the difficulty inherent to the patient's selection and MRI retrieval, this hypothetical database would not offer the same conditions to study the disease progression in a general form.

EDSS turned out to be the most important analyzed and explored factor, which is logical as it is the global scale used to evaluate the physical condition of an MS patient. As the disease tracking was attempted through machine learning algorithms, there was the necessity of transforming the EDSS into intervals. For a more simple process, all case scenarios were approached in binary situations. Using an EDSS of 5 as threshold was an intuitive and natural decision. Not only constitutes an equal division into the scale but also symbolizes the difference between severe/smooth affected mobility. However, there was not a reasonable number of samples in some created databases that possessed an EDSS value higher or equal to 5. This was the reason why sometimes some studies regarding EDSS labels with value 5 as threshold were not performed. Using value 3 as threshold, the problem of non-sufficient samples was surpassed. The decision to use this value also as threshold was advised by Doctor Sónia Batista as it can be interesting for physicians.

Exploring MS progression with simultaneously two different thresholds was very interesting as it provided a deeper insight despite the obstacles found. This exploration could have been made in several forms, however, the one performed was chosen in order to highlight one of the thresholds (5). Thus, instead of performing the initial feature selection for each label for values 3 and 5 as thresholds, it was only made for 5. By doing this, this threshold was clearly highlighted, since it provided an extra degree of trust to the selected features in terms of severity.

8.1 State of the Art

The state of the art turned out to be a very interesting inspiration for this work, especially since there are very specific approaches for MRI brain image processing. At the beginning, it was expected to be possible to use several techniques and algorithms mentioned. Nevertheless, it was not possible. Many algorithms are already included in MRI analysis software or in programming language packages,

as the case of the Python language, originally considered for the image processing procedure. This was not possible as many of the MRI scans were not compatible with these tools. In other words, most of the preprocessing steps in some scans had as output not processed images but only missing values. Software algorithms were decided not to be used. Besides constituting a black box at some point, it would not have been an automatic procedure, as pretended. It still would have been possible to develop the existing algorithms, however, that would have been a hard time-consuming task. Thus, by checking the existing algorithms, the core ideas for the used image processing were developed, such as the top/bottom head limitation, image registering and atlas use.

Although the great volume of investigation performed regarding lesion segmentation, this theme was not deeply explored. In fact, it was attempted to build a machine learning procedure for lesion detecting through lesion/non-lesion distinction. For this, extra regions (non-lesion ones) were labeled by the author and the same features were also extracted from them. These regions that were labeled presented very similar characteristics in terms of pixel intensity, shape and localization regarding lesions. This was not described in this dissertation since the results were not satisfactory. Despite the labeled non-lesion regions were seen as "hard" ones, there is a high degree of trust in the used labeling. The labeling process was performed by two neuroradiologists while looking at the respective scan reports (performed by other neuroradiologist).

As a consequence, the proposed procedure evolved from automatic to semi-automatic, where a physician lesion labeling was needed. It can be seen as a compromise made between effort (by the physician) and performance (by the algorithm). Thus, the physician only takes part in the beginning stage of the process by delineating the lesion regions. It was also attempted to reduce the physician effort by only being necessary to choose one point of each lesion. Ideally, with the selected point, it would have been possible to delineate the respective lesion through the use of a region growing algorithm. However, the results were not satisfactory as well, as it was needed to tune several thresholds regarding different scans and modalities.

Some aspects regarding lesion segmentation were not taken into account, as types of lesions due to contrast (focal/diffuse lesions), which seems a very interesting path for a future work. However, contrast and lesion localization were deeply approached. A method of deepening this analysis regarding lesions would be to integrate longitudinal scans, which were not used since it could not be found horizontal sequences in atlases. Another compelling approach seemed to be the exploration of the atlases anatomical maps and tissue maps as features from lesions and non-

lesions were extracted directly from certain specific regions. This way, a detailed brain investigation was obtained.

Regarding clinical data, as seen, there are a reduced number of studies that integrated this source of data. By integrating pattern recognition techniques and machine learning concepts, the analysis goes significantly beyond the main tools used with clinical data, such as correlations and statistical tests. EDSS is the most used information regarding this source of data, existing already some interesting findings. As checked not only in this project but also in the state of the art, there is evidence of a stronger correlation between clinical manifestations and several brain factors in the first years.

8.2 Dataset description

A big limitation of this project is the database size (36 patients). Despite the reduced number, it was a hard time-consuming task due to the existing problems in CHUC's database. The clinical data curation was a hard task as the original one was in a significant raw condition. This part of the project happens to be an accurate representation of the existing problems in this kind of investigation work. Due to missing data, there were some engaging features that were excluded related to family clinical history, to concomitant diseases, to CSF and related to evoked potentials exam, since there are already known by the physicians to be influent factors.

Besides these limitations, there is also one not mentioned directly until now. As known, the EDSS values are regarding patient visits, routine or not. If it is a routine one, the EDSS is regarding the normal condition of the patient. However, if not, it is most probably regarding a relapse. If it is a relapse, this value can increase abnormally and then decay to values that correspond the normal progression condition of the patient. Naturally, the existence of relapses will naturally influence the EDSS-related labels. The advantage of this is having an indirect influence of the number of registered relapses taken into account in the labels. The disadvantage is the fact of not existing a separation of EDSS values for relapses and non-relapses. This, however, could have been done but there would be a tremendous reduction in the number of samples of the database. As the number of samples in the *Momentaneous* and in the *Momentaneous with past* databases is 87 and 46 of them are routine ones, there would have been a database reduction of 41 samples, by other words, an approximate reduction of 47%.

The heterogeneity of the MRI scans was a considerable obstacle, since the procedure, MRI machine, slice thickness, number of slices of each scan affected deeply

this step. Besides, despite the similarity of protocols regarding some groups of scans, the image quality may not be similar. As consequence, the division of MRI scans regarding the image quality is a more practical approach since it can be more useful in terms of evaluating the performance of image processing. This image processing performance evaluation was not a simple task due to the inexistence of proper metrics. Although there are several image metrics that can make a quantification of the sequences/atlas similarity, the information given would not be trustful. An MRI scan has a tremendous complexity due to the existing heterogeneity between brains. Besides, one must remember that an MRI scan also shows all non-brain structures and, as known, even the brain structures can have different proportions. These facts are taken into account in the metrics output, adultering the real performance value. Thus, an optimal image processing can have a lower 2D correlation value with the atlas regarding a bad one, for example. By attributing groups regarding the FLAIR sequence quality, it is simpler to visualize the overall process. To do this division group, it was chosen the FLAIR sequence since it was the one used for the lesion labeling. Therefore, it was primordial to guarantee the best performance possible, as the study of certain brain regions, tissues and structures was a priority as well.

8.3 Experimental procedure

As the number of patients was reduced, there was a special need to have more information. Thus, in order to increase the quantity of data and to explore the largest number of possible situations, the raw database was treated in order to provide different natures of information. It was possible to build 3 dynamic databases. One with the existing information from each patient at the beginning of the MS onset (*Groundzero*) and two regarding specific moments of each patient (*Momentaneous* and *Momentaneous with past*). Nevertheless, it was also possible to create the Static database, containing all existing information regarding each patient. This one has a curious factor: all features were normalized in order to be possible to compare patients with a different number of years passed since onset. This way, a new patient can be introduced in the database, while its features are continuously updated with the passage of time, which is the optimal situation for a hospital database.

In order to explore in a deeper level, several labels were created: *tendencyEDSS*, *msCourse*, *nextEDSS*, *mediumEDSS*, *highestEDSS* and *first2EDSS*, where the EDSS-related labels were thresholded at 3 and 5. Despite its differences, they are all indirectly related. Higher the EDSS value, the more probable it is to pass the chosen threshold. Besides, *msCourse* is indirectly related to EDSS as previously

mentioned. *TendencyEDSS*, however, it is a complicated issue. Curiously, the results were coherent with the non-routine visits: it was expected a bad performance since the tendency had also taken into account the relapses. From all the used labels, the *tendencyEDSS* is the most affected by this factor, without any doubt. Nevertheless, it would have been curious to have a good performance. If so, a deeper analysis would have been done, in order to check if it was possible to predict an upcoming relapse or not. For the lesion databases, the same principles were performed. For the *MRI total head* database, only the principle of the different labels was applied. Due to this being a time-consuming task and since the major focus was on the lesions themselves and the clinical data, the *MRI total head* database was not unwrapped into different ones. Due to the given results with this database, it is a very interesting approach for future work to develop this database into static and dynamic and evaluate the performance.

Regarding the image processing, the overall performance was good. It is impossible to achieve optimal performance in every case, specially because each human possesses a different brain in terms of structure ratios and dimensions. In general terms, the results were satisfactory and, most important, there was not any unreasonable output. It is with a good degree of trust that is possible to claim that the algorithm was able to surpass brightness, contrast and image registration obstacles without great difficulty.

As this dissertation has an exploratory perspective, the feature extraction was a detailed procedure. In clinical terms, due to the findings of the first years of MS manifestation, many interesting characteristics were transformed into features by analyzing its behavior not only during all moments but also specially during the first year and the during the first two years. Regarding MRI scans, features from concept ideas as FFT, color histogram, symmetry, entropy and pixel intensity were retrieved. The novelty of this procedure in this dissertation is its extraction from not only the brain as a total structure but also from different small brain regions and defined tissues as GM, WM and CSF.

Volumes were not used, only areas, due to the existing difficulties regarding a different number of slices, slice thickness and spacing between slices. Another obstacle was the characterization of a lesion as a 3D structure. It can be a complicated issue due to differences in slice thickness and inter-modality differences. Thus, in order to avoid this, each region was assumed as a 2D structure.

Regarding the feature selection method, the goal of having a first feature selection with several different tests was to be able to compare the features regarding its overall behavior. It was never expected that a feature would pass in every test as

some are specifically made for certain types of data. This way, a selection through these tests was always performed by comparing a feature performance with all the other features performance. This feature selection was performed by steps not only due to the large number of features but also to understand the hierarchy of them in terms of performance. The last feature selection step is performed with a decision tree so it can happen the optimal selection in order to best succeed in the classification step.

Forcing the called investigation procedure was also an interesting approach as clinically obvious features were previously deleted. Only the ones with direct influence, such as the EDSS-related ones. Therefore, features like Spinal Cord and Gender, for example, were still considered. This is important to have a reference of its discriminative power regarding novelty features so that a reasonable comparison can be performed.

The principles used for the multi-labeling use and for the different natures of database construction were the same used for the classification process: to go the furthest possible in analyzing the data. Thus, to have a higher degree of trust and to explore the data in the deepest way, three different partition methods, a possibility of dimensionality reduction and eleven classifiers were combined. The classifiers' selection was based on their properties and on their simplicity. As the number of samples in every database is reduced, the classifiers must be simple as well due to overfitting and to be simple to interpret. Decision trees and SVM's have the advantage of being easy to interpret clinically and to visually describe its process. LDA and QDA have the advantage of transforming the data into a simpler one. GLM ables the model fitting of any order and transforms it into a regression. KNN takes into account the number of training samples in specific positions. The Naive Bayes classifier, contrary to the other classifiers, is not based in geometric properties but in statistical ones. The minimum distance classifiers are the simplest ones, measuring the distance of a point to the centroid of each class. However, it is important to denote that not always was possible to apply all classifiers. For example, with QDA and Naive Bayes, frequently it was impossible since one of the classes had 0 variance and these two algorithms needed that both class variances would be non-null. Regarding GLM fitting, not always it was possible to transform the fitted model into a regression.

Several metrics were used to evaluate the performances by calculating the confusion matrix and the ROC curve. With the confusion matrix, several metrics were calculated and integrated in order to have an overall insight of several aspects. With the ROC curve, the AUC was calculated in order to have an overall insight as well.

In a certain way, the ROC curve is able to provide a more detailed information of the data separation regarding the two different classes. The confusion matrix is more directed to the final classification performance.

8.4 Results

As seen in the Appendices, the results are constituted by more than 400 tables, each one regarding a database, a label, a partition method and the usage or not of dimensionality reduction method. It is a tremendously hard task to be able to interpret these tables by just looking at them. Thus, to make this process simpler, objective and in order to unify all studies performed, a scoring system was created. By doing this, an assumption of all studies being related was developed, which was an interesting view of the disease progression by assembling many case scenarios simultaneously. The first taken step was to evaluate the performances and to choose the labels that are associated with the best performances. By using only these, the degree of trust in the next interpretations was naturally higher since a certain level of doubt was eliminated.

Two simple systems were created, one for the confusion matrix metrics and the other for the AUC value. Higher is the value of these, higher are the attributed points to each classifier performance. To these points, another system was applied taking into account the partition method. As the number of samples of each database is reduced, it was given more importance to the partition method that explore the deepest the dataset. Thus, to LOO method it was attributed 3 points as N-1 sets of N-1 training samples were tested, where N is the number of samples. To K-Fold 10 method it was attributed 2 points as 10 different training datasets were testes. Finally, to the 30:70 ratio method it was attributed 1 point. The partition method score was multiplied by the one obtained in the classifier's performance.

With the obtained performances, another classification system was used regarding relative classification of the labels for the same database. In other words, in a defined database, the first classified label got 3 points, the second one 2 points and the third one 1 point. As seen by the results, the labels that outperformed were *highestEDSS*, *nextEDSS* and *mediumEDSS*. In these, a high degree of trust was taken into account regarding these mentioned ones. With these, a feature search of the most discriminative ones was performed. This was able to be made since as mentioned already, the whole set of databases and labels was seen and interpreted as a unified system. By counting the number of features in the different datasets of these three mentioned labels, it was possible to build an hierarchy of feature

importance/discriminatory power.

Thus, in the clinical data, the results were satisfactory. As obvious and theoretically expected, the EDSS-related features were the most predictive. Features like the number of years that a patient suffers from MS, initial MS manifestations related to spinal Cord, MS course and even gender had optimal performances, being already expected as well. This was very important to confirm that the study, in fact, is totally coherent with the clinic established ideas of MS progression. The engaging part of the results is the other features: Pyramidal First 2 Years, Spinal Cord, Optical Pathways, Sensorial Ratio and Visual Ratio, specially the first three because their attributed points were significantly higher.

At first sight, Pyramidal First 2 Years seems to be logical as well and, in fact, it is. As known, the Pyramidal tract is responsible for the mobility, which is a tremendously important factor in the EDSS scale. Besides, as seen in [17], the Pyramidal FS is the most involved in the determination of the EDSS with 84.9% of involvement. What makes this feature so interesting is that it is only regarding the first two years of MS manifestation. Thus, the known importance of the Pyramidal tract regarding the EDSS scale and the findings on a more significant cause-effect relationship in the first two years of MS manifestation, makes this feature a very pertinent one. Not only because of the separated given facts but also because it merged them into one unified fact. As known, the Pyramidal ratio was used as feature for the first year, the first two and for its totality of data and the chosen one was always the one regarding the first two years. As this feature was also tested in patients with more than two years of tracking, it can be interpreted as a crutial factor for the future disease progression.

Spinal cord is a different case. When showing these results to Doctor Sónia Batista, it was mentioned that this fact is an empirical evidence. Patients that showed MS initial manifestations at spinal cord level are likely to have a more severe disease progression. However, there were no studies or reasons that could explain it. As said, it is an empirical evidence, which also is satisfactory and provides extra confidence levels in the obtained results.

Optical pathways feature had a slightly reduced performance when compared to Spinal cord and Pyramidal First 2 Years features, however, it was still considered to be relevant. There is no concrete clinic evidence or findings besides this paper for this source of feature. So, some extra investigation must be done in order to understand how it can affect MS progression. Visual Ratio and Sensory Ratio only had 2 points, so the degree of trust in them is considered to be not relevant for this dissertation. However, it can still be interesting to see how it would be its

performance in a deeper study with a bigger database.

In the image databases, the same principles were applied. However, with some changes. Instead of counting the features themselves, the tissues and regions were the ones counted. As the number of features was tremendously high, another strategy had to be chosen. By taking this path, 2 regions from Anatomical Map I were present in studies regarding the three labels: regions 22 (right superior frontal gyrus) and 99 (left middle orbitofrontal gyrus) (Figures 8.1 and 8.2).

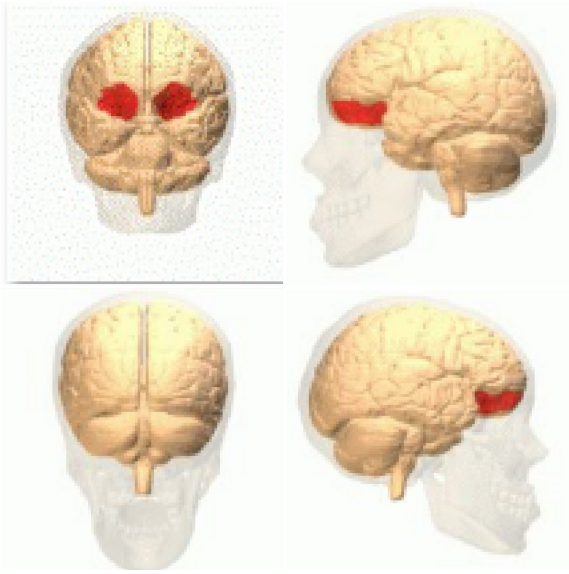

Figure 8.1: Orbitofrontal gyrus region [14].

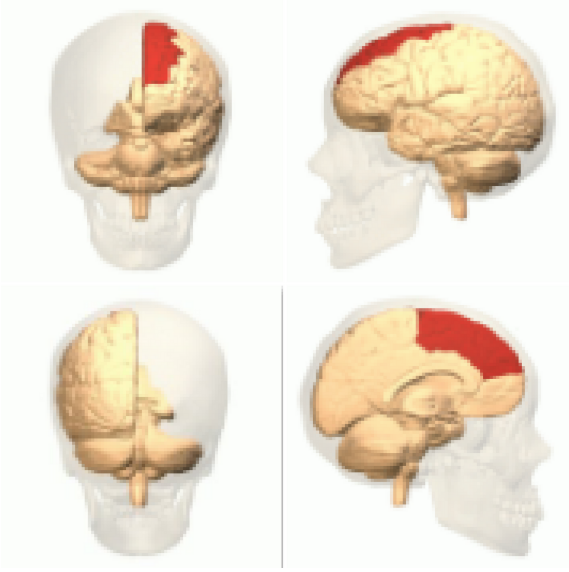

Figure 8.2: Left superior frontal gyrus [15].

As there are not any evidence or findings of MS disease progression at any specific brain region, these findings cannot be compared to any other studies. Besides,

the features are not the same in some studies, but only the region in question. This issue needs to be addressed more deeply in a future work. The degree of trust in the image results is not the same as the ones in clinical data. Besides the fact that there are no evidence of cause-effect relationships by other authors and no clinical empirical facts, the overall results of the classifiers were not as good as the clinical ones.

However, the results seem quite engaging, since the tissue predictive power turned out to be the one predicted, which is very coherent to clinical evidence. white matter was considered to be the most predictive tissue, grey matter the second one and cerebrospinal fluid the third one. This fact provides to the image results some degree of trust.

A very intriguing fact was the obtained results at the modalities predictive power. T1-Gde was the sequence with most predictive power, followed by T2 and PD. FLAIR sequence was the one considered to have less predictive power, which is intriguing since it was in this sequence that the manual labeling was performed. Besides, clinically it is one of the most helpful sequences in terms of deciding if a certain region is a lesion or not. The fact of T1-Gde having the best discriminative power is also very interesting as it provides contrast to the recent lesions. With this modality, it is taken into account a temporal factor that other sequences cannot take advantage of.

8.5 Exploratory activity

In order to clarify the interpretations regarding the obtained results at a clinical level, some post exploration was performed. As mentioned, the whole set of databases and labels was visualized as a unified system and, therefore, was interpreted as all the labels being indirectly related. In order to verify the level of trust in this unification, especially regarding label MS course since a soon prediction of SP course would be tremendously interesting, the correlations between the labels were calculated. The SP course prediction has a special interest not only due to the difficulty of physicians at predicting it at the beginning of onset but also due to the time nature of the extracted features of Pyramidal first 2 years, Spinal cord and Optical pathways: two of them are retrieved at the MS diagnosis moment and the first one only needs the first two years. With this fact, it would be ideal for a physician to have a course prediction within a temporal space of 2 years only with every patient.

However, as seen in Tables 8.1 and 8.2, the correlation values between *msCourse*

and the other labels is not satisfactory. Thus, the idea of only working with the best-ranked labels due to a certain degree of trust was, indeed, a reasonable move to walk towards a unified system. With the correlation results, the idea of testing these features with the MS course was left apart, since the necessary conditions were not reunited. To fully deepen and to clarify completely this question, the same procedure was made in the *Momentaneous* databases, separating it into two different ones: one regarding relapses visits only and other regarding routine visits only. The results showed a week relationship between *msCourse* and the other labels again, excluding for completely this working line. The correlation values between the other labels oscillated but maintained its relationship in a general way.

Table 8.1: The label correlation values between *mediumEDSS*, *nextEDSS*, *highestEDSS* and *msCourse* in the clinical databases.

Labels	Static		Momentaneous (and with past)		Groundzero	
	label>3	label>5	label>3	label>5	label>3	label>5
mediumEDSS & msCourse	0.79	0.52	0.67	0.39	0.48	0.11
nextEDSS & msCourse	NA	NA	0.69	0.46	NA	NA
highestEDSS & msCourse	0.59	0.44	0.46	0.63	0.59	0.52
mediumEDSS & nextEDSS	NA	NA	0.88	0.51	NA	NA
mediumEDSS & highestEDSS	0.79	0.35	0.75	0.42	0.59	0.46
highestEDSS & nextEDSS	NA	NA	0.68	0.73	NA	NA

Table 8.2: The label correlation values between *mediumEDSS*, *nextEDSS*, *highestEDSS* and *msCourse* in the *Momentaneous* databases, regarding relapse visits and routine ones.

Labels	Relapse		Routine	
	label>3	label>5	label>3	label>5
mediumEDSS & msCourse	0.72	0.62	0.63	0.07
nextEDSS & msCourse	0.61	0.48	0.75	0.45
highestEDSS & msCourse	0.45	0.70	0.47	0.58
mediumEDSS & nextEDSS	0.86	0.52	0.91	0.49
mediumEDSS & highestEDSS	0.68	0.42	0.80	0.43
highestEDSS & nextEDSS	0.67	0.82	0.70	0.65

Afterwards, the three highlighted features were tested regarding this performed bifurcation made in the *Momentaneous with past* database (relapse visits and routine visits). The correlation between feature and label, AUC of ROC curve between feature and label and the scatterplot visualization were performed for the whole totality of the database and for each bifurcation for all three labels, as seen in Tables 8.3, 8.4 and 8.5.

By analyzing the following tables, one can see that the routine bifurcation had not only better results than the relapse bifurcation but also than the database with

Table 8.3: Analysis of Pyramidal First 2 years feature regarding the *Momentaneous with past* database and both bifurcations regarding relapse visits and routine visits.

Metrics/Labels		Relapse & Routine			Relapse			Routine		
		highestEDSS	nextEDSS	mediumEDSS	highestEDSS	nextEDSS	mediumEDSS	highestEDSS	nextEDSS	mediumEDSS
Correlation	label>3	0.40	0.58	0.57	0.26	0.42	0.41	0.53	0.68	0.71
	label>5	0.67	0.43	0.21	0.60	0.45	0.18	0.77	0.44	0.25
AUC	label>3	0.73	0.81	0.80	0.48	0.58	0.54	0.82	0.86	0.89
	label>5	0.82	0.66	0.58	0.61	0.65	0.44	0.91	0.68	0.62

Table 8.4: Analysis of Spinal cord feature regarding the *Momentaneous with past* database and both bifurcations regarding relapse visits and routine visits.

Metrics/Labels		Relapse & Routine			Relapse			Routine		
		highestEDSS	nextEDSS	mediumEDSS	highestEDSS	nextEDSS	mediumEDSS	highestEDSS	nextEDSS	mediumEDSS
Correlation	label>3	0.16	0.28	0.30	0.23	0.03	0.06	0.37	0.46	0.35
	label>5	0.31	0.31	0.30	0.09	0.21	0.28	0.51	0.39	0.33
AUC	label>3	0.66	0.65	0.58	0.63	0.52	0.47	0.69	0.74	0.68
	label>5	0.65	0.64	0.60	0.55	0.60	0.60	0.73	0.67	0.61

no bifurcations, in the 3 feature cases. These were the theoretically expected results as relapses are unpredictable. It is extremely hard to not only predict a relapse but also to guess its severity. Thus, the 3 highlighted features lose discriminative power regarding the relapse bifurcation. With only routine visits, their discriminative power increases, confirming its potential for MS disease progression and tracking.

An intriguing factor is the fact of the overall feature results are coherent with the feature discriminative power selection regarding all databases: the best is the Pyramidal First 2 years, the second best is Spinal cord and Optic pathways appears at last. As expected, the existence of spinal cord initial MS manifestations is correlated positively with the EDSS increase. By other words, with the presence of spinal cord initial MS manifestations, higher is the probability of the patient having a more severe progression. The same principle is confirmed with pyramidal tract signs in the first 2 years.

By looking at the scatterplots, more specific conclusions can be retrieved. If one visualizes the scatterplots of Pyramidal first 2 years for the *highestEDSS*>3 and *highestEDSS*>5, intuitively will check the feature power (Figures 8.3 and 8.4). The most interesting regarding the feature when it comes to scatterplotting is its comparison with the relapse bifurcation: it becomes a stronger relation regarding the strongest relapse severity a patient can suffer (Figures 8.5 and 8.6). This feature seems to be more discriminative with labels with threshold 3 than with 5.

By looking at the Spinal cord scatterplots, it is intuitive to see it is an important factor to a severe disease progression, specially regarding labels thresholded with EDSS value 5 (Figures 8.7-8.12). However, this is seen in the complete dataset, in the complete one and in each bifurcation.

The Optical pathways feature is the opposite, which was intuitively noticed

Table 8.5: Analysis of Optical pathways feature regarding the *Momentaneous with past* database and both bifurcations regarding relapse visits and routine visits.

Metrics/Labels		Relapse & Routine			Relapse			Routine		
		highestEDSS	nextEDSS	mediumEDSS	highestEDSS	nextEDSS	mediumEDSS	highestEDSS	nextEDSS	mediumEDSS
Correlation	label>3	0.41	0.32	0.33	0.40	0.27	0.31	0.42	0.37	0.34
	label>5	0.25	0.21	0.14	0.24	0.20	0.14	0.25	0.22	0.15
AUC	label>3	0.20	0.27	0.27	0.19	0.31	0.26	0.21	0.24	0.27
	label>5	0.34	0.37	0.43	0.33	0.38	0.43	0.35	0.37	0.44

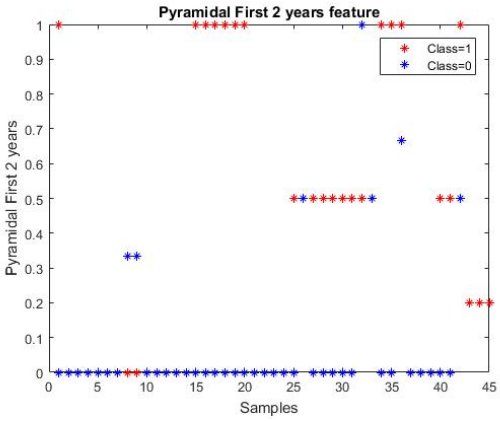

Figure 8.3: Scatterplot with feature Pyramidal First 2 years with the complete *Momentaneous* database for the label *highestEDSS*>3.

since all correlation values were negative. This can be seen easily in the scatterplots regarding this feature (Figures 8.13, 8.14 and 8.15). If a patient has an MS initial manifestation at the optic pathways levels, the disease progression will be certainly less severe. This is seen in all datasets tested: the complete one and each bifurcation.

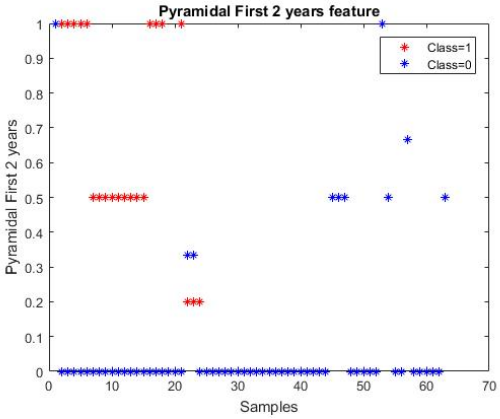

Figure 8.4: Scatterplot with feature Pyramidal First 2 years with the complete *Momentaneous* database for the label *highestEDSS*> 5.

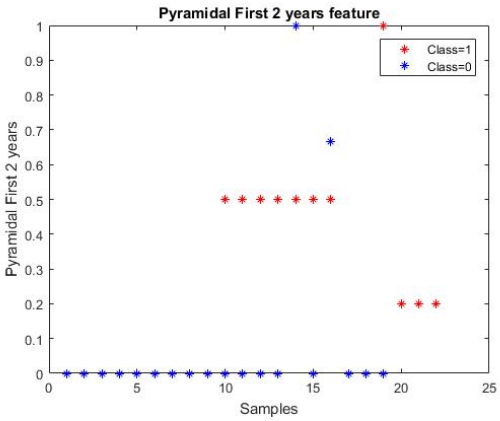

Figure 8.5: Scatterplot with feature Pyramidal First 2 years with the relapse bifurcation database for the label *highestEDSS*> 3.

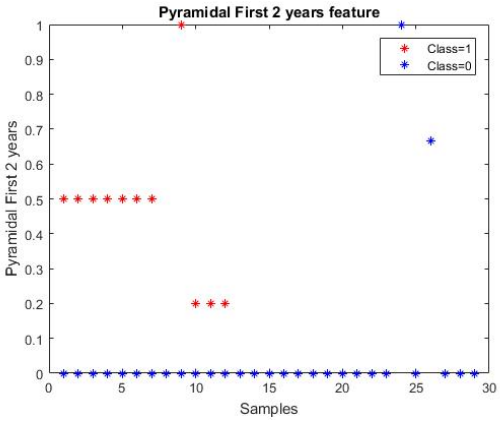

Figure 8.6: Scatterplot with feature Pyramidal First 2 years with the relapse bifurcation database for the label *highestEDSS*> 5.

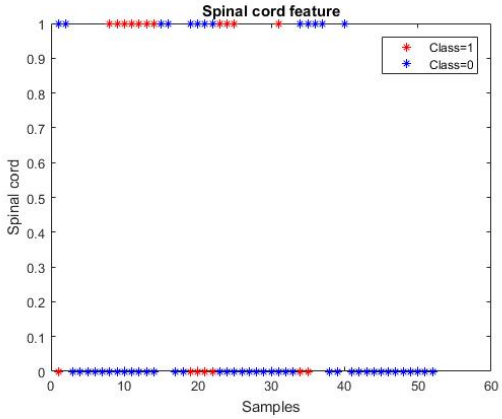

Figure 8.7: Scatterplot with feature Spinal Cord with the complete *Momentaneous* database for the label *mediumEDSS*>3.

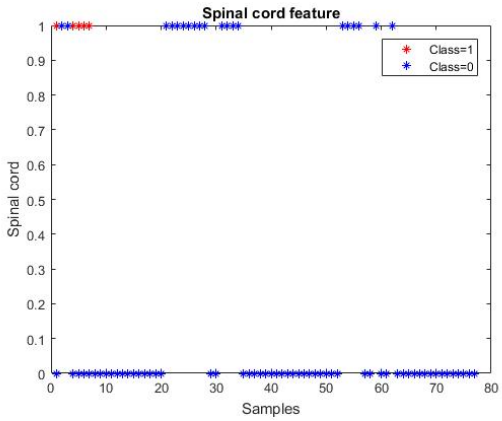

Figure 8.8: Scatterplot with feature Spinal Cord with the complete *Momentaneous* database for the label *mediumEDSS*>5.

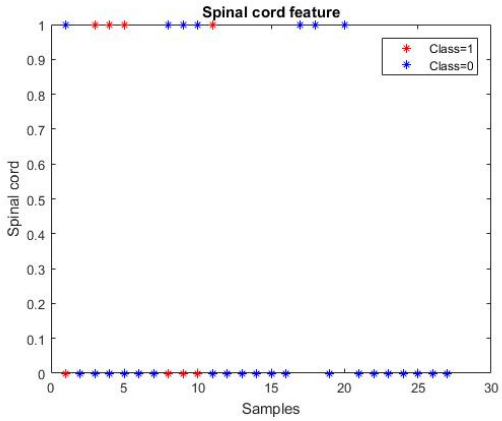

Figure 8.9: Scatterplot with feature Spinal Cord with the relapse bifurcation database for the label *nextEDSS*>3.

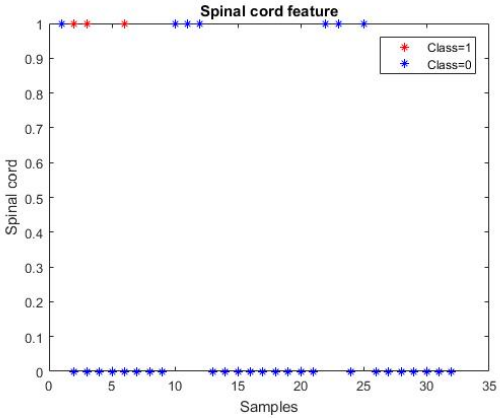

Figure 8.10: Scatterplot with feature Spinal Cord with the relapse bifurcation database for the label *nextEDSS*>5.

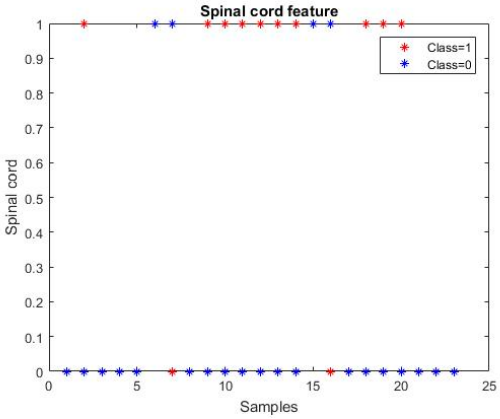

Figure 8.11: Scatterplot with feature Spinal Cord with the routine bifurcation database for the label *highestEDSS*>3.

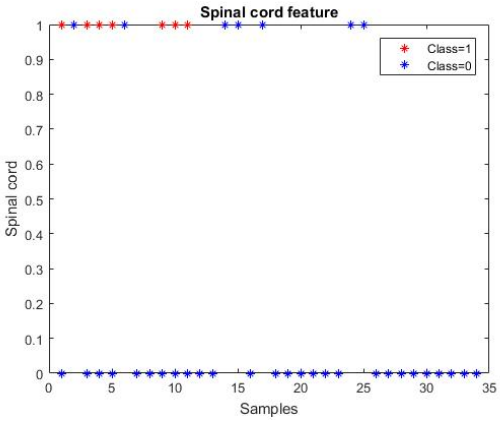

Figure 8.12: Scatterplot with feature Spinal Cord with the routine bifurcation database for the label *highestEDSS*>5.

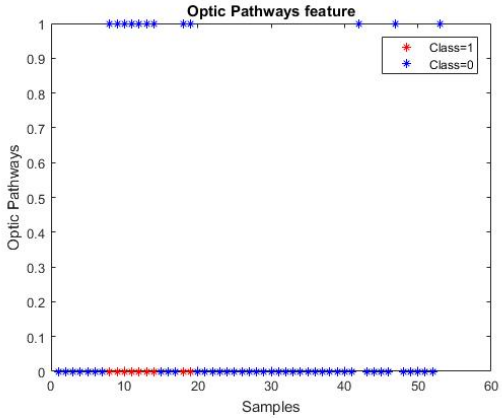

Figure 8.13: Scatterplot with feature Optical Pathways with the complete *Momentaneous* database for the label *nextEDSS*> 3.

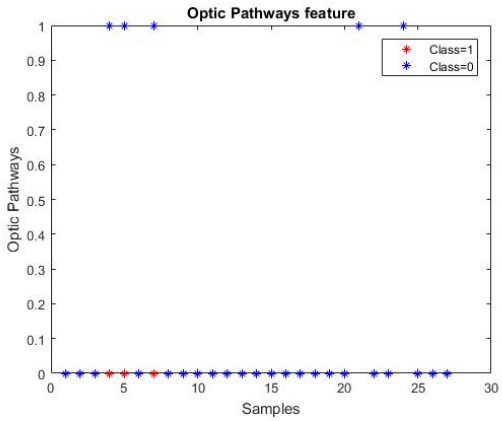

Figure 8.14: Scatterplot with feature Optical Pathways with the relapse bifurcation database for the label *nextEDSS*> 3.

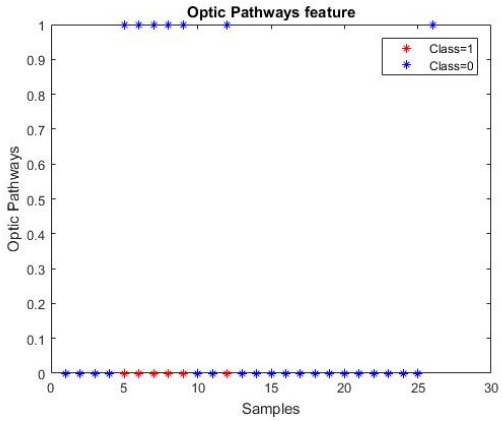

Figure 8.15: Scatterplot with feature Optical Pathways with the routine bifurcation database for the label *nextEDSS*> 3.

Chapter 9

Conclusion

The goal of this project was to evaluate and predict MS progression with an original database from Centro Hospitalar Universitário de Coimbra curated by the author. As already known before this dissertation, this was not an easy task, which is proved by the fact of not existing a gold standard algorithm to perform this process.

In order to evaluate and study the disease progression, it was desired to build a robust algorithm against different metrics, enabling quantification of the disease progression. Thus, as a product of assembling clinical and algorithmic knowledge, biological, heuristic and clinical rules would be required in order to be more than a simple mathematical model. In other words, a clinical perspective had to be attributed to the model. To make it easy to apply in the daily physician life, it would have to be automatic and standardized.

As seen, not all objectives were accomplished. In fact, the evaluation and prediction of MS progression was performed with an original database and with an automatic procedure for clinical data. However, regarding the imaging part, the obtained algorithm is a semi-automatic process, since previous lesion manual labeling is required. A method for lesion detection was attempted but the results were not satisfactory. Thus, it was decided that performance should not be sacrificed significantly, but rather to have a time-consuming task initially.

Clinical data has a stronger predictive power when compared to image data, which is natural since imaging features are extractions with a strong mathematical basis and with a reasonable clinical one. Besides, it does not exist an actual consense regarding the best image features, which can show the real complexity of this task.

Predicting and studying progression was not the only task, discovering some new unknown patterns was another goal, which led to the most interesting part of the job, according to the author's point of view. At clinical level it was possible to show 3 interesting features that may be relevant for progression assessment: the ratio of times there were MS manifestations at the pyramidal tract in the first 2 years (Pyramidal First 2 Years feature), MS initial manifestations at spinal cord level (Spinal Cord feature) and at the optic pathways (Optic Pathways feature). The most interesting part of these 3 is the temporality factor: the first one only needs the first 2 years of MS onset and the other two are immediately extracted at the onset moment. As they can be acquired in a relative fast way, they become interesting and useful in life applications for a future prediction.

An attractive fact about the results was the presence of the most clinical obvious and already known predictors: EDSS-related, gender, MS course and number of years with MS. This provides a certain degree of trust to the obtained results as it is significantly coherent with clinical knowledge. Spinal cord was already an empirical fact known by the doctors, which is now mathematically proven. As it was possible to explore deeper the features influence, the *Momentaneous* database was bifurcated into relapse/routine visits in order to fully comprehend MS progression. Despite the unpredictability of relapses, spinal cord MS initial manifestations and pyramidal tract evidences in the first 2 years showed to be influent factors, and not only in non-relapse disease progression.

Regarding the obtained results at imaging level, since there are no findings related to any brain region, it is very hard and risky to assume an interpretation with the same degree of confidence. Since the number of features was significantly larger, the strategy was also different, as the feature counting was performed not by the feature itself but by the tissue/region in question. Besides, the image results were not as good as the clinical ones. Nevertheless, the most reliable labels obtained with only the imaging results were the same 3: *highestEDSS*, *nextEDSS* and *mediumEDSS*. The most appealing parts of the imaging procedure were the new MRI simple processing method and the extensive feature extraction regarding tissue extraction and brain structures.

The greatest obstacle of this dissertation was the database curation due to the spent time retrieving the MRI scans, the significant quantity of missing data regarding some important features and, as naturally, the number of patients (36). Lower the number of patients, theoretically lower is the representativity of the population. Besides, most of the algorithms applied may not work properly with such reduced number of samples. In order to fight this problem, the database was handled in mul-

tiple perspectives, with multiple goals and with multiple metrics. Another appealing technique used in order to accomplish this multiple perspective was the visualization and comprehension of the multiple created databases as a unified system of the MS progression.

However, this is not simple, since a physician must be able to fully understand this process in order to evaluate it with a clinical view. This perception of a unified system is not totally correct, as stated by Doctor Sónia Batista. Some ways of how the data was handled seemed to a physician a mathematical process only and not clinical. Ratios, standard variations of certain features may lose its clinical meaning. For example, by using a medium EDSS or the highest EDSS achieved value as labels, a clinical value meaning is lost since EDSS values are respective to both relapses and routines in the database. Besides, these are metrics never used in real life. The extra exploration performed in Chapter 8, besides guaranteeing the cause-effect relationship of the mentioned features, also had as objective the increase of the existing clinical meaning and application.

Making a clear bridge between the mathematical and clinical concepts can be extremely complicated as clinical points of view have completely different rules than the ones in computation. Besides, the complexity of the image processing and pattern recognition algorithms make the communication task even harder, since the number of calculations performed may be a big obstacle to lose the clinical sense.

This dissertation opens paths to many research fronts, not only to improve the algorithms and procedure themselves but also to keep adding samples to the database in order to verify if the same results are still obtained. Studying in a deeper way these 3 clinical features and to verify the 2 obtained brain regions seems a very natural evolution of this work. However, there are always other issues equally interesting, such as different labels, different approaches for the same original database or even different backbones and alternative ways of interpreting the same results.

Bibliography

[1] R. A. Marrie, "Environmental risk factors in multiple sclerosis aetiology," *The Lancet Neurology*, vol. 3, no. 12, pp. 709–718, 2004.

[2] K. Rejdak, S. Jackson, and G. Giovannoni, "Multiple sclerosis: a practical overview for clinicians," *British medical bulletin*, vol. 95, no. 1, pp. 79–104, 2010.

[3] A. Webb, *Introduction to biomedical imaging*. Wiley-Interscience, 2003.

[4] H. S. MS, "Edss scale," 2015. [Web; accessed in 19/12/2017].

[5] M. R. I. M. of the Brain and S. Basics, "Magnetic resonance imaging (mri) of the brain and spine: Basics," 2017. [Web; accessed in 20/12/2017].

[6] D. García-Lorenzo, S. Francis, S. Narayanan, D. L. Arnold, and D. L. Collins, "Review of automatic segmentation methods of multiple sclerosis white matter lesions on conventional magnetic resonance imaging," *Medical image analysis*, vol. 17, no. 1, pp. 1–18, 2013.

[7] D. García-Lorenzo, S. Francis, S. Narayanan, D. L. Arnold, and D. L. Collins, "Review of automatic segmentation methods of multiple sclerosis white matter lesions on conventional magnetic resonance imaging," *Medical image analysis*, vol. 17, no. 1, pp. 1–18, 2013.

[8] B. F. Hutton and M. Braun, "Software for image registration: algorithms, accuracy, efficacy," in *Seminars in nuclear medicine*, vol. 33, pp. 180–192, Elsevier, 2003.

[9] K. Boesen, K. Rehm, K. Schaper, S. Stoltzner, R. Woods, E. Lüders, and D. Rottenberg, "Quantitative comparison of four brain extraction algorithms," *NeuroImage*, vol. 22, no. 3, pp. 1255–1261, 2004.

[10] O. Freifeld, H. Greenspan, and J. Goldberger, "Multiple sclerosis lesion detection using constrained gmm and curve evolution," *Journal of Biomedical Imaging*, vol. 2009, p. 14, 2009.

[11] R. He and P. A. Narayana, "Automatic delineation of gd enhancements on magnetic resonance images in multiple sclerosis," *Medical physics*, vol. 29, no. 7,

pp. 1536–1546, 2002.

[12] N. Shiee, P.-L. Bazin, A. Ozturk, D. S. Reich, P. A. Calabresi, and D. L. Pham, "A topology-preserving approach to the segmentation of brain images with multiple sclerosis lesions," *NeuroImage*, vol. 49, no. 2, pp. 1524–1535, 2010.

[13] C. A. Cocosco, V. Kollokian, R. K.-S. Kwan, G. B. Pike, and A. C. Evans, "Brainweb: Online interface to a 3d mri simulated brain database," in *NeuroImage*, Citeseer, 1997.

[14] D. C. f. L. S. D. Wikipedia, "Orbital gyrus animation," 2010.

[15] D. C. f. L. S. D. Wikipedia, "Superior frontal gyrus animation," 2010.

[16] C. H. Polman, S. C. Reingold, B. Banwell, M. Clanet, J. A. Cohen, M. Filippi, K. Fujihara, E. Havrdova, M. Hutchinson, L. Kappos, *et al.*, "Diagnostic criteria for multiple sclerosis: 2010 revisions to the mcdonald criteria," *Annals of neurology*, vol. 69, no. 2, pp. 292–302, 2011.

[17] J. F. Kurtzke, "Rating neurologic impairment in multiple sclerosis an expanded disability status scale (edss)," *Neurology*, vol. 33, no. 11, pp. 1444–1444, 1983.

[18] G. DeLuca, G. Ebers, and M. Esiri, "Axonal loss in multiple sclerosis: a pathological survey of the corticospinal and sensory tracts," *Brain*, vol. 127, no. 5, pp. 1009–1018, 2004.

[19] M. M. Goldenberg, "Multiple sclerosis review," *Pharmacy and Therapeutics*, vol. 37, no. 3, p. 175, 2012.

[20] D. A. Hafler, "Multiple sclerosis," *The Journal of Clinical Investigation*, vol. 113, no. 6, pp. 789–794, March 2004.

[21] N. Koch-Henriksen and P. S. Sørensen, "The changing demographic pattern of multiple sclerosis epidemiology," *The Lancet Neurology*, vol. 9, no. 5, pp. 520–532, 2010.

[22] G. C. Ebers, "Environmental factors and multiple sclerosis," *The Lancet Neurology*, vol. 7, no. 3, pp. 268–277, 2008.

[23] S. W. Courtney, *All About Multiple Sclerosis*. Multiple Sclerosis Association of America, 3 ed., 2006.

[24] F. D. Lublin, S. C. Reingold, J. A. Cohen, G. R. Cutter, P. S. Sørensen, A. J. Thompson, J. S. Wolinsky, L. J. Balcer, B. Banwell, F. Barkhof, *et al.*, "Defining the clinical course of multiple sclerosis the 2013 revisions," *Neurology*, vol. 83, no. 3, pp. 278–286, 2014.

[25] B. A. Cohen, "Current and emerging treatment strategies for multiple sclerosis,"

[26] A. Gajofatto and M. D. Benedetti, "Treatment strategies for multiple sclerosis:

when to start, when to change, when to stop?," *World Journal of Clinical Cases: WJCC*, vol. 3, no. 7, p. 545, 2015.

[27] P. Suetens, *Fundamentals of Medical Imaging*. Katholieke Universiteit Leuven, 2 ed., 2009.

[28] R. B. Lufkin, *The MRI manual*. Mosby Incorporated, 1998.

[29] P. Reimer, P. M. Parizel, J. F. Meaney, and F. A. Stichnoth, *Clinical MR Imaging: A practical approach 3rd Edition*. No. 1, Springer, 2010.

[30] J. W. Peterson, L. Bö, S. Mörk, A. Chang, and B. D. Trapp, "Transected neurites, apoptotic neurons, and reduced inflammation in cortical multiple sclerosis lesions," *Annals of neurology*, vol. 50, no. 3, pp. 389–400, 2001.

[31] A. Carass, S. Roy, A. Jog, J. L. Cuzzocreo, E. Magrath, A. Gherman, J. Button, J. Nguyen, F. Prados, C. H. Sudre, *et al.*, "Longitudinal multiple sclerosis lesion segmentation: Resource and challenge," *NeuroImage*, vol. 148, pp. 77–102, 2017.

[32] M. Filippi, M. Horsfield, A. Campi, S. Mammi, C. Pereira, and G. Comi, "Resolution-dependent estimates of lesion volumes in magnetic resonance imaging studies of the brain in multiple sclerosis," *Annals of neurology*, vol. 38, no. 5, pp. 749–754, 1995.

[33] B. Fischl, "Freesurfer," *Neuroimage*, vol. 62, no. 2, pp. 774–781, 2012.

[34] R. He and P. A. Narayana, "Global optimization of mutual information: application to three-dimensional retrospective registration of magnetic resonance images," *Computerized Medical Imaging and Graphics*, vol. 26, no. 4, pp. 277–292, 2002.

[35] M. Jenkinson, P. Bannister, M. Brady, and S. Smith, "Improved optimization for the robust and accurate linear registration and motion correction of brain images," *Neuroimage*, vol. 17, no. 2, pp. 825–841, 2002.

[36] B. R. Sajja, S. Datta, R. He, M. Mehta, R. K. Gupta, J. S. Wolinsky, and P. A. Narayana, "Unified approach for multiple sclerosis lesion segmentation on brain mri," *Annals of biomedical engineering*, vol. 34, no. 1, pp. 142–151, 2006.

[37] A. Klein, J. Andersson, B. A. Ardekani, J. Ashburner, B. Avants, M.-C. Chiang, G. E. Christensen, D. L. Collins, J. Gee, P. Hellier, *et al.*, "Evaluation of 14 nonlinear deformation algorithms applied to human brain mri registration," *Neuroimage*, vol. 46, no. 3, pp. 786–802, 2009.

[38] X. Lladó, A. Oliver, M. Cabezas, J. Freixenet, J. C. Vilanova, A. Quiles, L. Valls, L. Ramió-Torrentà, and À. Rovira, "Segmentation of multiple sclerosis lesions in brain mri: a review of automated approaches," *Information Sciences*, vol. 186, no. 1, pp. 164–185, 2012.

[39] Z. Hou, "A review on mr image intensity inhomogeneity correction," *International Journal of Biomedical Imaging*, vol. 2006, 2006.

[40] S. Datta, B. R. Sajja, R. He, R. K. Gupta, J. S. Wolinsky, and P. A. Narayana, "Segmentation of gadolinium-enhanced lesions on mri in multiple sclerosis," *Journal of Magnetic Resonance Imaging*, vol. 25, no. 5, pp. 932–937, 2007.

[41] K. Van Leemput, F. Maes, D. Vandermeulen, A. Colchester, and P. Suetens, "Automated segmentation of multiple sclerosis lesions by model outlier detection," *IEEE transactions on medical imaging*, vol. 20, no. 8, pp. 677–688, 2001.

[42] Y. Wu, S. K. Warfield, I. L. Tan, W. M. Wells, D. S. Meier, R. A. van Schijndel, F. Barkhof, and C. R. Guttmann, "Automated segmentation of multiple sclerosis lesion subtypes with multichannel mri," *NeuroImage*, vol. 32, no. 3, pp. 1205–1215, 2006.

[43] H. Greenspan, A. Ruf, and J. Goldberger, "Constrained gaussian mixture model framework for automatic segmentation of mr brain images," *IEEE transactions on medical imaging*, vol. 25, no. 9, pp. 1233–1245, 2006.

[44] D. García-Lorenzo, S. Prima, D. L. Collins, D. Arnold, S. P. Morrissey, and C. Barillot, "Combining robust expectation maximization and mean shift algorithms for multiple sclerosis brain segmentation," in *MICCAI workshop on Medical Image Analysis on Multiple Sclerosis (validation and methodological issues)(MIAMS'2008)*, pp. 82–91, 2008.

[45] Y. Zhang, "Mri texture analysis in multiple sclerosis," *Journal of Biomedical Imaging*, vol. 2012, p. 2, 2012.

[46] B. J. Bedell and P. A. Narayana, "Automatic segmentation of gadolinium-enhanced multiple sclerosis lesions," *Magnetic resonance in medicine*, vol. 39, no. 6, pp. 935–940, 1998.

[47] A.-O. Boudraa, S. M. R. Dehak, Y.-M. Zhu, C. Pachai, Y.-G. Bao, and J. Grimaud, "Automated segmentation of multiple sclerosis lesions in multispectral mr imaging using fuzzy clustering," *Computers in biology and medicine*, vol. 30, no. 1, pp. 23–40, 2000.

[48] S. Saha and S. Bandyopadhyay, "A new point symmetry based fuzzy genetic clustering technique for automatic evolution of clusters," *Information Sciences*, vol. 179, no. 19, pp. 3230–3246, 2009.

[49] A. P. Dempster, N. M. Laird, and D. B. Rubin, "Maximum likelihood from incomplete data via the em algorithm," *Journal of the royal statistical society. Series B (methodological)*, pp. 1–38, 1977.

[50] J. A. S. Bricq, C. Collet, "Ms lesion segmentation based on hidden markov chains," *Mult. Scler. Lesion Segm. Challenge*, pp. 1–9, 2008.

[51] M. Prastawa and G. Gerig, "Automatic ms lesion segmentation by outlier detection and information theoretic region partitioning," *Grand Challenge Work.: Mult. Scler. Lesion Segm. Challenge*, pp. 1–8, 2008.

[52] X. Tomas and S. K. Warfield, "Fully-automatic generation of training points for automatic multiple sclerosis segmentation," *Work Med Image Anal Mult Scler*, pp. 5–14, 2009.

[53] D.-J. Kroon, E. van Oort, and C. Slump, "Multiple sclerosis detection in multispectral magnetic resonance images with principal components analysis," 2008.

[54] D. Goldberg-Zimring, A. Achiron, S. Miron, M. Faibel, and H. Azhari, "Automated detection and characterization of multiple sclerosis lesions in brain mr images," *Magnetic resonance imaging*, vol. 16, no. 3, pp. 311–318, 1998.

[55] P. Anbeek, K. L. Vincken, and M. A. Viergever, "Automated ms-lesion segmentation by k-nearest neighbor classification," *MIDAS J*, 2008.

[56] J. Morra, Z. Tu, A. Toga, and P. Thompson, "Automatic segmentation of ms lesions using a contextual model for the miccai grand challenge," *Multiple Sclerosis Lesion Segmentation Challenge*, pp. 1–7, 2008.

[57] E. Geremia, O. Clatz, B. H. Menze, E. Konukoglu, A. Criminisi, and N. Ayache, "Spatial decision forests for ms lesion segmentation in multi-channel magnetic resonance images," *NeuroImage*, vol. 57, no. 2, pp. 378–390, 2011.

[58] A. Cerasa, E. Bilotta, A. Augimeri, A. Cherubini, P. Pantano, G. Zito, P. Lanza, P. Valentino, M. C. Gioia, and A. Quattrone, "A cellular neural network methodology for the automated segmentation of multiple sclerosis lesions," *Journal of neuroscience methods*, vol. 203, no. 1, pp. 193–199, 2012.

[59] S. Valverde, M. Cabezas, E. Roura, S. González-Villà, D. Pareto, J. C. Vilanova, L. Ramió-Torrentà, À. Rovira, A. Oliver, and X. Lladó, "Improving automated multiple sclerosis lesion segmentation with a cascaded 3d convolutional neural network approach," *NeuroImage*, vol. 155, pp. 159–168, 2017.

[60] T. Brosch, L. Y. Tang, Y. Yoo, D. K. Li, A. Traboulsee, and R. Tam, "Deep 3d convolutional encoder networks with shortcuts for multiscale feature integration applied to multiple sclerosis lesion segmentation," *IEEE transactions on medical imaging*, vol. 35, no. 5, pp. 1229–1239, 2016.

[61] D. L. Collins, A. P. Zijdenbos, V. Kollokian, J. G. Sled, N. J. Kabani, C. J. Holmes, and A. C. Evans, "Design and construction of a realistic digital brain phantom," *IEEE transactions on medical imaging*, vol. 17, no. 3, pp. 463–468, 1998.

[62] S. K. Warfield, K. H. Zou, and W. M. Wells, "Simultaneous truth and performance level estimation (staple): an algorithm for the validation of image

segmentation," *IEEE transactions on medical imaging*, vol. 23, no. 7, pp. 903–921, 2004.

[63] M. Bosc, F. Heitz, J.-P. Armspach, I. Namer, D. Gounot, and L. Rumbach, "Automatic change detection in multimodal serial mri: application to multiple sclerosis lesion evolution," *Neuroimage*, vol. 20, no. 2, pp. 643–656, 2003.

[64] J. D. Rodriguez, A. Perez, D. Arteta, D. Tejedor, and J. A. Lozano, "Using multidimensional bayesian network classifiers to assist the treatment of multiple sclerosis," *IEEE Transactions on Systems, Man, and Cybernetics, Part C (Applications and Reviews)*, vol. 42, no. 6, pp. 1705–1715, 2012.

[65] A. Feinstein, L. Kartsounis, D. H. Miller, B. D. Youl, and M. A. Ron, "Clinically isolated lesions of the type seen in multiple sclerosis: a cognitive, psychiatric, and mri follow up study.," *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 55, no. 10, pp. 869–876, 1992.

[66] A. Boiko, G. Vorobeychik, D. Paty, V. Devonshire, D. Sadovnick, *et al.*, "Early onset multiple sclerosis a longitudinal study," *Neurology*, vol. 59, no. 7, pp. 1006–1010, 2002.

[67] P. A. Brex, O. Ciccarelli, J. I. O'riordan, M. Sailer, A. J. Thompson, and D. H. Miller, "A longitudinal study of abnormalities on mri and disability from multiple sclerosis," *New England Journal of Medicine*, vol. 346, no. 3, pp. 158–164, 2002.

[68] J. Sastre-Garriga, G. T. Ingle, D. T. Chard, M. Cercignani, L. Ramió-Torrentà, D. H. Miller, and A. J. Thompson, "Grey and white matter volume changes in early primary progressive multiple sclerosis: a longitudinal study," *Brain*, vol. 128, no. 6, pp. 1454–1460, 2005.

[69] G. Tedeschi, D. Dinacci, L. Lavorgna, A. Prinster, G. Savettieri, A. Quattrone, P. Livrea, C. Messina, A. Reggio, G. Servillo, *et al.*, "Correlation between fatigue and brain atrophy and lesion load in multiple sclerosis patients independent of disability," *Journal of the neurological sciences*, vol. 263, no. 1, pp. 15–19, 2007.

[70] R. Zivadinov, J. Sepcic, D. Nasuelli, R. De Masi, L. M. Bragadin, M. Tommasi, S. Zambito-Marsala, R. Moretti, A. Bratina, M. Ukmar, *et al.*, "A longitudinal study of brain atrophy and cognitive disturbances in the early phase of relapsing-remitting multiple sclerosis," *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 70, no. 6, pp. 773–780, 2001.

[71] A. Crimi, O. Commowick, A. Maarouf, J.-C. Ferré, E. Bannier, A. Tourbah, I. Berry, J.-P. Ranjeva, G. Edan, and C. Barillot, "Predictive value of imaging markers at multiple sclerosis disease onset based on gadolinium-and uspio-

enhanced mri and machine learning," *PloS one*, vol. 9, no. 4, p. e93024, 2014.

[72] A. Minneboo, F. Barkhof, C. H. Polman, B. M. Uitdehaag, D. L. Knol, and J. A. Castelijns, "Infratentorial lesions predict long-term disability in patients with initial findings suggestive of multiple sclerosis," *Archives of neurology*, vol. 61, no. 2, pp. 217–221, 2004.

[73] Y. Zhao, B. C. Healy, D. Rotstein, C. R. Guttmann, R. Bakshi, H. L. Weiner, C. E. Brodley, and T. Chitnis, "Exploration of machine learning techniques in predicting multiple sclerosis disease course," *PloS one*, vol. 12, no. 4, p. e0174866, 2017.

[74] D. W. Shattuck, M. Mirza, V. Adisetiyo, C. Hojatkashani, G. Salamon, K. L. Narr, R. A. Poldrack, R. M. Bilder, and A. W. Toga, "Construction of a 3d probabilistic atlas of human cortical structures," *Neuroimage*, vol. 39, no. 3, pp. 1064–1080, 2008.

[75] T. Rohlfing, N. M. Zahr, E. V. Sullivan, and A. Pfefferbaum, "The sri24 multichannel atlas of normal adult human brain structure," *Human brain mapping*, vol. 31, no. 5, pp. 798–819, 2010.

[76] J. C. Mazziotta, A. W. Toga, A. Evans, P. Fox, and J. Lancaster, "A probabilistic atlas of the human brain: Theory and rationale for its development: The international consortium for brain mapping (icbm)," *Neuroimage*, vol. 2, no. 2, pp. 89–101, 1995.

[77] M. Radovic, M. Ghalwash, N. Filipovic, and Z. Obradovic, "Minimum redundancy maximum relevance feature selection approach for temporal gene expression data," *BMC bioinformatics*, vol. 18, no. 1, p. 9, 2017.

Appendices

Chapter A

Appendix I - EDSS grading Functional Systems

Table A.1: FS Pyramidal grading system [17].

Grade	**Meaning**
0	Normal
1	Abnormal signs without disability
2	Minimal disability
3	Mild or moderate paraparesis or hemiparesis
4	Marked paraparesis or hemiparesis; moderate quadriparesis or monoplegia
5	Paraplegia, hemiplegia or marked quadriparesis
6	Quadriplegia
V	Unknown

Table A.2: FS Cerebellar grading system [17].

Grade	Meaning
0	Normal
1	Abnormal signs without disability
2	Mild ataxia
3	Moderate truncal or limb ataxia
4	Severe ataxia, all limbs
5	Unable to perform coordinated movements due to ataxia
V	Unknown
X	Used after each number when weakness (grade 3+ on pyramidal) interferes with testing

Table A.3: FS Brain Stem grading system [17].

Grade	Meaning
0	Normal
1	Signs only
2	Moderate nystagmus or other mild disability
3	Severe nystagmus, marked extraocular weakness, or moderate disability of other cranial nerves
4	Marked dysarthria or other marked disability
5	Inability to swallow or speak
V	Unknown

Table A.4: FS Sensory grading system [17].

Grade	Meaning
0	Normal
1	Vibration or figure-writing decrease only, in one or two limbs
2	Mild decrease in touch or pain or position sense, and/or moderate decrease in vibration in one or two limbs; or vibratory decrease alone in three or four limbs
3	Moderate decrease in touch or pain or position sense, and/or essentially lost vibration in one or two limbs; or mild decrease in touch or pain and/or moderate decrease in all proprioreceptive tests in three or four limbs
4	Marked decrease in touch or pain or loss of proprioception, alone or ocmbined, in one or two limbs; or moderate decrease in touch or pain and/or severe proprioception for most of the body below the head
5	Loss of sensation in one or two limbs; or moderate decrease in touch or pain and/or loss of proprioception for most of the body below the hand
6	Sensation essentially lost below the head
V	Unknown

Table A.5: FS Bowel & Bladder grading system [17].

Grade	Meaning
0	Normal
1	Mild Urinary hesitancy, urgency or retention
2	Moderate hesitancy, urgency, retention of bowel or bladder, or rare urinary incontinence
3	Frequent urinary incontinence
4	In need of almost constant catheterization
5	Loss of bladder function
6	Loss of bowel and bladder function
V	Unknown

Table A.6: FS Visual grading system [17].

Grade	Meaning
0	Normal
1	Scotoma with visual acuity (corrected) better than 20/30
2	Worse eye with scotoma with maximal visual acuity (corrected) of 20/30 to 20/59
3	Worse eye with large scotoma, or moderate decrease in fields, but with maximal visual acuity (corrected) of 20/60 to 20/99
4	Worse eye with marked decrease of fields and maximal visual acuity (corrected) of 20/100 to 20/200; grade 3 plus maximal acuity of better eye of 20/60 or less.
5	Worse eye with maximal visual acuity (corrected) less than 20/200; grade 4 plus maximal acuity of better eye of 20/60 or less
6	Grade 5 plus maximal visual acuity of better eye of 20/60 or less
V	Unknown
X	Is added to grades 0 to 6 for presence of temporal pallor

Table A.7: FS Cerebral grading system [17].

Grade	Meaning
0	Normal
1	Mood alteration only
2	Mild decrease in mentation
3	Moderate decrease in mentation
4	Marked decrease in mentation (chronic brain syndrome - moderate)
5	Dementia or chronic brain syndrome - severe or incompetent
V	Unknown

Table A.8: FS Other grading system [17].

Grade	Meaning
0	None
1	Any other neurologic findings attributed to MS
V	Unknown

Chapter B

Appendix II - Clinical databases description

The clinical databases are here described with the maximum detail. Not only each feature is explained but also the normalization process is explained.

B.1 Static database

B.1.1 Identification sheet

From Identification sheet, the *Static* database is constituted by the following features (binary features were transformed into 1/0):

Pathways

1. **Gender**: equal to the raw feature description described in Chapter 5.
2. **Age of onset**: the age at which MS started to manifest.
3. **Supratentorial**: equal to the raw feature description described in Chapter 5.
4. **Optic**: equal to the raw feature description described in Chapter 5.
5. **Brainstem-Cerebellum**: equal to the raw feature description described in Chapter 5.
6. **Spinal Cord**: equal to the raw feature description described in Chapter 5.
7. **Age of diagnosis**: the age at which the patient was diagnosed with MS.
8. **Years from onset to diagnosis**: years passed from onset to diagnosis.
9. **Clinical findings**: equal to the raw feature description described in Chapter

5.

10. **MRI**: equal to the raw feature description described in Chapter 5.
11. **Evoked potentials**: equal to the raw feature description described in Chapter 5.
12. **CSF**: equal to the raw feature description described in Chapter 5.
13. **Age at SP diagnosis**: equal to the raw feature description described in Chapter 5.
14. **Years from onset to diagnosis SP**: time passed since MS onset and SP diagnosis.
15. **MS Course**: equal to the raw feature description described in Chapter 5.
16. **Active**: equal to the raw feature description described in Chapter 5.

The feature normalization process occurred in the following form:

1. **Gender**: no need for normalization process.
2. **Age of onset**: it was decided to normalize the feature using as maximum value 50 years old. This way, if a patient has an onset age superior to 50, its feature value will be 1. In this thesis, the target patients have onset ages of from 20 to approximately 40 years old.
3. **Supratentorial**: no need for normalization process.
4. **Optic Pathways**: no need for normalization process.
5. **Brainstem-Cerebellum**: no need for normalization process.
6. **Spinal Cord**: no need for normalization process.
7. **Age of diagnosis**: it was decided to use as normalization factor the same value as used in age of onset (50).
8. **Years from onset to diagnosis**: it was used 20 years as normalization factor since this feature has a tremendous variability.
9. **Clinical findings**: no need for normalization process.
10. **MRI**: no need to normalization process.
11. **Evoked potentials**: no need for normalization process.
12. **CSF**: no need for normalization process.
13. **Age at SP diagnosis**: it was used 60 years old as value, since there were patients with more than 50 years old when SP was diagnosed.
14. **Years from onset to diagnosis SP**: it was used 25 years as normalization factor since this feature has a tremendous variability and since its maximum value surpasses the 20 years value used as limit in feature "years from onset to diagnosis".
15. **MS Course**: no need for normalization process.

16. **Active**: no need for normalization process.

B.1.2 Visits sheet

From Visits sheet, the *Static* database is constituted by the following features:

1. **Nb of visits per year**: the average of visits made per year.
2. **Nb of visits 1st year**: the number of visits made in the first year.
3. **Nb of visits first 2 years**: the number of visits made in the first 2 years.
4. **Suspected Relapses ratio per year**: the average of the annual numbers of suspected relapses regarding all visits made to the clinic.
5. **Suspected relapses ratio 1st year**: the average of suspected relapses regarding the first year the patient visited the clinic.
6. **Suspected relapses ratio first 2 years**: the average of suspected relapses regarding the first two years the patient visited the clinic.
7. **EDSS medium value/year**: the average value of the anual EDSS medium values values regarding all visits made to the clinic.
8. **EDSS 1st year**: the average value of all EDSS values regarding the first year the patient visited the clinic.
9. **EDSS first 2 years**: the average value of all EDSS values regarding the first two years the patient visited the clinic.
10. **EDSS std/year**: the standard deviation of the annual EDSS medium values.
11. **EDSS 1st year std**: the standard deviation of the EDSS values regarding the first year the patient visited the clinic.
12. **EDSS first 2 years std**: the standard deviation of the EDSS values regarding the first two years the patient visited the clinic.
13. **EDSS medium variation/year**: the average value of all annual EDSS variations per year regarding all visits made to the clinic.
14. **EDSS medium variation 1st year**: the medium variation of EDSS values regarding the first year the patient has visited the clinic.
15. **EDSS medium variation first 2 years**: the medium variation of EDSS values regarding the first year the patient has visited the clinic.
16. **EDSS std of variation/year**: the standard deviation of the annual EDSS variations regarding all visits made to the clinic.
17. **EDSS std of variation 1st year**: the standard deviation of the EDSS variations regarding the first year the patient visited the clinic.
18. **EDSS std of variation first 2 years**: the standard deviation of the EDSS

variations regarding the first 2 years the patient visited the clinic.

19. **EDSS increase 1st year**: the ratio of times the EDSS value has increased from consecutive visits regarding the first year the patient has visited the clinic.
20. **EDSS increase first 2 years**: the ratio of times the EDSS value has increased from consecutive visits regarding the first two years the patient has visited the clinic.
21. **Ratio nb EDSS increase**: the ratio of times the EDSS value has increased from consecutive visits regarding all visits made to the clinic.
22. **Ratio nb EDSS decrease**: the ratio of times the EDSS value has decreased from consecutive visits regarding all visits made to the clinic.
23. **Ratio nb EDSS decrease 1st year**: the ratio of times the EDSS value has decreased from consecutive visits regarding the first year the patient has visited the clinic.
24. **Ratio nb EDSS decrease first 2 years**: the ratio of times the EDSS value has decreased from consecutive visits regarding the first two years the patient has visited the clinic.
25. **Routine visits ratio**: the ratio of routine visits regarding all visits made to the clinic.
26. **Routine visits ratio 1st year**: the ratio of routine visits regarding the first year the patient has visited the clinic.
27. **Routine visits first 2 years**: the ratio of routine visits regarding the first two years the patient has visited the clinic.
28. **No years**: the number of years the patient.

The feature normalization process occurred in the following form:

1. **Nb of visits per year**: the normalization factor was 3 visits per year since it was the maximum registered.
2. **Nb of visits 1st year**: the normalization factor mas 3 visits since it was the maximum registered.
3. **Nb of visits first 2 years**: the normalization factor mas 5 visits since it was the maximum registered.
4. **Suspected Relapses ratio per year**: the normalization factor was 3 suspected relapses since it is the maximum integer in order to normalize the data between 0 and 1.
5. **Suspected relapses ratio 1st year**: the normalization factor was 3 suspected relapses since it is the maximum registered.
6. **Suspected relapses ratio first 2 years**: the normalization factor was 5

suspected relapses since it is the maximum registered.

7. **EDSS medium value/year**: the normalization factor was 10 since the EDSS scale maximum value is 10.
8. **EDSS 1st year**: the normalization factor was 10 since the EDSS scale maximum value is 10.
9. **EDSS first 2 years**: the normalization factor was 10 since the EDSS scale maximum value is 10.
10. **EDSS std/year**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
11. **EDSS 1st year std**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
12. **EDSS first 2 years std**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
13. **EDSS medium variation/year**: the normalization factor was 2 since it is the maximum integer in order to normalize the data between 0 and 1.
14. **EDSS medium variation 1st year**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
15. **EDSS medium variation first 2 years**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
16. **EDSS std of variation/year**: the normalization factor was 2 since it is the maximum integer in order to normalize the data between 0 and 1.
17. **EDSS std of variation 1st year**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
18. **EDSS std of variation first 2 years**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
19. **EDSS increase 1st year**: no need for normalization process.
20. **EDSS increase first 2 years**:no need for normalization process.
21. **Ratio nb EDSS increase**: no need for normalization process.
22. **Ratio nb EDSS decrease**: no need for normalization process.
23. **Ratio nb EDSS decrease 1st year**: no need to normalization process.
24. **Ratio nb EDSS decrease first 2 years**: no need for normalization process.
25. **Routine visits ratio**: no need for normalization process.
26. **Routine visits ratio 1st year**: no need for normalization process.
27. **Routine visits first 2 years**: no need for normalization process.
28. **No years**: the normalization factor was 32, due to the maximum of number

of years registered in the relapses sheet in No years feature.

B.1.3 Relapses sheet

From Relapses sheet, the *Static* database is constituted by the following features:

1. **Relapses per year**: the average of the annual numbers of relapses regarding all relapses.
2. **Relapses 1st year**: the number of relapses regarding the first year the patient suffered relapses.
3. **Relapses first 2 years**: the number of relapses regarding the first two years the patient suffered relapses.
4. **Pyramidal Ratio**: the ratio of times there were MS manifestations in the pyramidal tract due to a relapse regarding all relapses.
5. **Pyramidal 1st year**: the ratio of times there were MS manifestations related to the pyramidal tract due to a relapse regarding the first year a patient suffered relapses.
6. **Pyramidal first 2 years**: the ratio of times there were MS manifestations related to the pyramidal tract due to a relapse regarding the first two years a patient suffered relapses.
7. **Brain Stem ratio**: the ratio of times there were MS manifestations related to the brain stem due to a relapse regarding all relapses.
8. **Brain Stem 1st year**: the ratio of times there were MS manifestations related to the brain stem due to a relapse regarding the first year a patient suffered relapses.
9. **Brain Stem first 2 years**: the ratio of times there were MS manifestations related to the brain stem due to a relapse regarding the first two years a patient suffered relapses.
10. **Bowel ratio**: the ratio of times there were MS manifestations related to the bowel and bladder due to a relapse regarding all relapses.
11. **Bowel 1st year**: the ratio of times there were MS manifestations related to the bowel and bladder due to a relapse regarding the first year a patient suffered relapses.
12. **Bowel first 2 years**: the ratio of times there were MS manifestations related to the bowel and bladder due to a relapse regarding the first two years a patient suffered relapses.
13. **Neuropsycho ratio**: the ratio of times there were MS manifestations related

to the neuropsycho functions due to a relapse regarding all relapses.

14. **Neuropsycho 1st year**: the ratio of times there were MS manifestations related to the neuropsycho functions due to a relapse regarding the first year a patient suffered relapses.
15. **Neuropsycho first 2 years**: the ratio of times there were MS manifestations related to the bowel and bladder due to a relapse regarding the first two years a patient suffered relapses.
16. **Cerebellum ratio**: the ratio of times there were MS manifestations related to the cerebellum due to a relapse regarding all relapses.
17. **Cerebellum 1st year**: the ratio of times there were MS manifestations related to the cerebellum due to a relapse regarding the first year a patient suffered relapses.
18. **Cerebellum 2 years**: the ratio of times there were MS manifestations related to the cerebellum due to a relapse regarding the first two years a patient suffered relapses.
19. **Visual ratio**: the ratio of times there were MS manifestations related to visual functions due to a relapse regarding all relapses.
20. **Visual 1st year**: the ratio of times there were MS manifestations related to visual functions due to a relapse regarding the first year a patient suffered relapses.
21. **Visual first 2 years**: the ratio of times there were MS manifestations related to visual functions due to a relapse regarding the first two years a patient suffered relapses.
22. **Sensory ratio**: the ratio of times there were MS manifestations related to sensory functions due to a relapse regarding all relapses.
23. **Sensory 1st year**: the ratio of times there were MS manifestations related to sensory functions due to a relapse regarding the first year a patient suffered relapses.
24. **Sensory first 2 years**: the ratio of times there were MS manifestations related to sensory functions due to a relapse regarding the first two years a patient suffered relapses.
25. **Corticosteroids Ratio**: the ratio of times corticosteroids were used as treatment relapse treatment regarding all relapses.
26. **Corticosteroids/year**: the average of the annual ratios of corticosteroids use as relapse treatment.
27. **Corticosteroids 1st year**: the ratio of corticosteroids use regarding the first

year the patient suffered relapses.

28. **Corticosteroids first 2 years**: the ratio of corticosteroids use regarding the first two years the patient suffered relapses.
29. **Average treatment intensity**: the average treatment intensity regarding relapse treatment regarding all relapses. No corticosteroids use has value 0, hydrocortisone use has value 1, methylprednisolone has value 2 and plasmapheresis value 3.
30. **Average treatment 1st year**: the average treatment intensity regarding relapse treatment regarding the first year the patient suffered relapses. No corticosteroids use has value 0, hydrocortisone use has value 1, methylprednisolone has value 2 and plasmapheresis value 3.
31. **Average treatment first 2 years**: the average treatment intensity regarding relapse treatment regarding the first two years the patient suffered relapses. no corticosteroids use has value 0, hydrocortisone use has value 1, methylprednisolone has value 2 and plasmapheresis value 3.
32. **Average duration**: the average duration in days of corticosteroids treatment regarding all relapses.
33. **Average duration 1st year**: the average duration in days of corticosteroids use treatment regarding the first year the patient suffered relapses.
34. **Average duration first 2 years**: the average duration in days of corticosteroids use treatment regarding the first two years the patient suffered relapses.

The feature normalization process occurred in the following form:

1. **Relapses per year**: the normalization factor was 4, since it is the maximum integer in order to normalize the data between 0 and 1.
2. **Relapses 1st year**: the normalization factor was 4, since the maximum value registered was 3. Value 3 was not chosen since the normalization factor in feature relapses per year is 4.
3. **Relapses first 2 years**: the normalization factor was 6, since the maximum value registered was 6.
4. **Pyramidal Ratio**: no need to normalization process.
5. **Pyramidal 1st year**: no need to normalization process.
6. **Pyramidal first 2 years**: no need to normalization process.
7. **Brain Stem ratio**: no need to normalization process.
8. **Brain Stem 1st year**: no need to normalization process.
9. **Brain Stem first 2 years**: no need to normalization process.
10. **Bowel ratio**: no need to normalization process.

11. **Bowel 1st year**: no need to normalization process.
12. **Bowel first 2 years**: no need to normalization process.
13. **Neuropsycho ratio**: no need to normalization process.
14. **Neuropsycho 1st year**: no need to normalization process.
15. **Neuropsycho first 2 years**: no need to normalization process.
16. **Cerebellum ratio**: no need to normalization process.
17. **Cerebellum 1st year**: no need to normalization process.
18. **Cerebellum 2 years**: no need to normalization process.
19. **Visual ratio**: no need to normalization process.
20. **Visual 1st year**: no need to normalization process.
21. **Visual first 2 years**: no need to normalization process.
22. **Sensory ratio**: no need to normalization process.
23. **Sensory 1st year**: no need to normalization process.
24. **Sensory first 2 years**: no need to normalization process.
25. **Corticosteroids Ratio**: no need to normalization process.
26. **Corticosteroids/year**: no need to normalization process.
27. **Corticosteroids 1st year**: no need to normalization process.
28. **Corticosteroids first 2 years**:no need to normalization process.
29. **Average treatment intensity**: the normalization factor was 3, since it is the maximum possible value (plasmapheresis treatment).
30. **Average treatment 1st year**: the normalization factor was 3, since it is the maximum possible value (plasmapheresis treatment).
31. **Average treatment first 2 years**: the normalization factor was 3, since it is the maximum possible value (plasmapheresis treatment).
32. **Average duration**: the normalization factor was 10, since it is the maximum registered value. Besides, it is not benefic to do a corticosteroids treatment for a long period.
33. **Average duration 1st year**: the normalization factor was 10, since it is the maximum registered value. Besides, it is not benefic to do a corticosteroids treatment for a long period.
34. **Average duration first 2 years**: the normalization factor was 10, since it is the maximum registered value. Besides, it isn not benefic to do a corticosteroids treatment for a long period.

B.2 Groundzero database

B.2.1 Identification sheet

From Identification sheet, the *Groundzero* database is constituted by the following features:

1. **Gender**: equal to the raw feature description described in Chapter 5.
2. **Age of onset**: the age at which MS started to manifest.
3. **Supratentorial**: equal to the raw feature description described in Chapter 5.
4. **Optic Pathways**: equal to the raw feature description described in Chapter 5.
5. **Brainstem-Cerebellum**: equal to the raw feature description described in Chapter 5.
6. **Spinal Cord**: equal to the raw feature description described in Chapter 5.
7. **Age of diagnosis**: the age at which the patient was diagnosed with MS.
8. **Years from onset to diagnosis**: years passed from onset to diagnosis.
9. **Clinical findings**: equal to the raw feature description described in Chapter 5.
10. **MRI**: equal to the raw feature description described in Chapter 5.
11. **Evoked potentials**: equal to the raw feature description described in Chapter 5.
12. **CSF**: equal to the raw feature description described in Chapter 5.
13. **Age at SP diagnosis**: equal to the raw feature description described in Chapter 5.
14. **Years from onset to diagnosis SP**: time passed since MS onset and SP diagnosis.

The feature normalization process occurred in the following form:

1. **Gender**: no need for normalization process.
2. **Age of onset**: it was decided to normalize the feature using as maximum value 50 years old. This way, if a patient has an onset age superior to 50, its feature value will be 1. In this thesis, the target patients have onset ages of from 20 to approximately 40 years old.
3. **Supratentorial**: no need for normalization process.
4. **Optic Pathways**: no need for normalization process.
5. **Brainstem-Cerebellum**: no need for normalization process.
6. **Spinal Cord**: no need for normalization process.

7. **Age of diagnosis**: it was decided to use as normalization factor the same value as used in the age of onset (50).
8. **Years from onset to diagnosis**: it was used 20 years as normalization factor since this feature has a tremendous variability.
9. **Clinical findings**: no need for normalization process.
10. **MRI**: no need to normalization process.
11. **Evoked potentials**: no need for normalization process.
12. **CSF**: no need for normalization process.
13. **Age at SP diagnosis**: it was used 60 years old as value since there were patients with more than 50 years old when SP was diagnosed.

B.2.2 Visits sheet

From Visits sheet, the *Groundzero* database is constituted by the following features:

1. **Visit age**: the patient's age when suffered the first relapse.
2. **Routine**: if the first visit to the clinic was a routine one.
3. **Suspected relapse**: if in the first visit to the clinic there were suspicions of an upcoming relapse.
4. **EDSS**: the EDSS value at the first visit to the clinic.

The feature normalization process occurred in the following form:

1. **Visit age**: the normalization factor was 60, since the maximum registered value is 55.
2. **Routine**: no need to normalization process.
3. **Suspected relapse**: no need to normalization process.
4. **EDSS**: the normalization factor is 10, since it is the maximum value of the EDSS scale.

B.2.3 Relapses sheet

From Relapses sheet, the *Groundzero* database is constituted by the following features:

1. **Relapse age**: the patient's age at the moment of the first relapse.
2. **Time since onset**: the time that has passed from MS onset to the first relapse.
3. **CNS Pyramidal tract**: if there were MS initial manifestations related to the pyramidal tract.

4. **CNS Brain Stem**: if there were MS initial manifestations related to the brain stem.
5. **CNS Bowel Bladder**: if there were MS initial manifestations related to the bowel and bladder.
6. **CNS Neuropsycho functions**: if there were MS initial manifestations related to neuropsycho functions.
7. **CNS Cerebellum**: if there were MS initial manifestations related to the cerebellum.
8. **CNS Visual functions**: if there MS initial manifestations related to visual functions.
9. **CNS Sensory functions**: if there MS initial manifestations related to sensory functions.
10. **Hospital**: if there was the need to be internalized at the hospital during the first appointment.
11. **Ambulatory**: if the patient seriously harmed its ambulatory capacity during the first appointment.
12. **Corticosteroids**: if the patient had corticosteroids treatment at the moment of the first appointment.
13. **Treatment name**: the corticosteroids treatment used at the moment of the first relapse. No corticosteroids use has value 0, hydrocortisone use has value 1, methylprednisolone has value 2 and plasmapheresis value 3.
14. **Duration Days**: the corticosteroids treatment duration in days.

The feature normalization process occurred in the following form:

1. **Relapse age**: the normalization factor was 60, since the maximum registered value is 55.
2. **Time since onset**: the normalization factor was 20, since the maximum registered value is 19.
3. **CNS Pyramidal tract**: no need to normalization process.
4. **CNS Brain Stem**: no need to normalization process.
5. **CNS Bowel Bladder**: no need to normalization process.
6. **CNS Neuropsycho functions**: no need to normalization process.
7. **CNS Cerebellum**: no need to normalization process.
8. **CNS Visual functions**: no need to normalization process.
9. **CNS Sensory functions**: no need to normalization process.
10. **Hospital**: no need to normalization process.
11. **Ambulatory**: no need to normalization process.

12. **Corticosteroids**: no need to normalization process.
13. **Treatment name**: the normalization factor was 3, since it is the maximum possible value (plasmapheresis treatment).
14. **Duration Days**: the normalization factor was 10, since it is the maximum registered value. Besides, it is not benefic to do a corticosteroids treatment for a long period.

B.3 Momentaneous database

B.3.1 Identification sheet

From Identification sheet, the *Momentaneous* database is constituted by the following features:

1. **Gender**: equal to the raw feature description described in Chapter 5.
2. **Age of onset**: the age at which MS started to manifest.
3. **Supratentorial**: equal to the raw feature description described in Chapter 5.
4. **Optic Pathways**: equal to the raw feature description described in Chapter 5.
5. **Brainstem-Cerebellum**: equal to the raw feature description described in Chapter 5.
6. **Spinal Cord**: equal to the raw feature description described in Chapter 5.
7. **Age of diagnosis**: the age at which the patient was diagnosed with MS.
8. **Years from onset to diagnosis**: years passed from onset to diagnosis.
9. **Clinical findings**: equal to the raw feature description described in Chapter 5.
10. **MRI**: equal to the raw feature description described in Chapter 5.
11. **Evoked potentials**: equal to the raw feature description described in Chapter 5.
12. **CSF**: equal to the raw feature description described in Chapter 5.
13. **Age at SP diagnosis**: equal to the raw feature description described in Chapter 5.
14. **Years from onset to diagnosis SP**: time passed since MS onset and SP diagnosis.
15. **MS Course**: equal to the raw feature description described in Chapter 5.
16. **Active**: equal to the raw feature description described in Chapter 5.
17. **Age visit**: patient's age at the moment of the visit to the clinic.

18. **Years since onset**: the time passed from onset to the moment of the visit to the clinic.

The feature normalization process occurred in the following form:

1. **Gender**: no need to normalization process.
2. **Age of onset**: it was decided to normalize the feature using as maximum value 50 years old. This way, if a patient has an onset age superior to 50, its feature value will be 1. In this thesis, the target patients have onset ages of from 20 to approximately 40 years old.
3. **Supratentorial**: no need for normalization process.
4. **Optic Pathways**: no need for normalization process.
5. **Brainstem-Cerebellum**: no need for normalization process.
6. **Spinal Cord**: no need for normalization process.
7. **Age of diagnosis**: it was decided to use as normalization factor the same value as used in age of onset (50).
8. **Years from onset to diagnosis**: it was used 20 years as normalization factor since this feature has a tremendous variability.
9. **Clinical findings**: no need for normalization process.
10. **MRI**: no need for normalization process.
11. **Evoked potentials**: no need for normalization process.
12. **CSF**: no need for normalization process.
13. **Age at SP diagnosis**: it was used 60 years old as value since there were patients with more than 50 years old when SP was diagnosed.
14. **Years from onset to diagnosis SP**: it was used 25 years as normalization factor since this feature has a tremendous variability and since its maximum value surpasses the 20 years value used as the limit in feature "years from onset to diagnosis".
15. **MS Course**: no need to normalization process.
16. **Active**: no need to normalization process.
17. **Age visit**: the normalization factor was 70 since the maximum registered value is 66.
18. **Years since onset**: the normalization was 35 since the maximum registered value is 31.

B.3.2 Visits sheet

From Visits sheet, the *Momentaneous* database is constituted by the following features:

1. **Last routine**: if the last visit to the clinic was a routine one.
2. **Last suspected**: ifonn the last visit to the clinic there were suspicions of an upcoming relapse.
3. **Last EDSS**: the EDSS value at the last visit to the clinic.
4. **Last weakness**: if in the last visit to the clinic there were MS manifestations of cerebral weakness.
5. **Last sympton**: if in the last visit to the clinic there were MS manifestations of visual symptons.

The feature normalization process occured in the following form:

1. **Last routine**: no need for normalization process.
2. **Last suspected**: no need for normalization process.
3. **Last EDSS**: the normalization factor is 10, since it is the maximum value of the EDSS scale.
4. **Last weakness**: no need for normalization process.
5. **Last sympton**: no need for normalization process.

B.3.3 Relapses sheet

From Relapses sheet, the *Momentaneous* database is constituted by the following features:

1. **Last Pyramidal**: if there were MS manifestations related to the pyramidal tract regarding the last relapse.
2. **Last Brain Stem**: if there were MS manifestations related to the brain stem due regarding the last relapse.
3. **Last Bowel Bladder**: if there were MS manifestations related to the bowel and bladder regarding the last relapse.
4. **Last Neuropsycho functions**: if there were MS manifestations related to neuropsycho functions regarding the last relapse.
5. **Last Cerebellum**: if there were MS manifestations related to the cerebellum regarding the last relapse.
6. **Last Visual functions**: if there were MS manifestations related to visual functions regarding the last relapse.
7. **Last Sensory functions**: if there were MS manifestations related to sensory

functions regarding the last relapse.

8. **Last hospital**: if there was the need to be internalized at the hospital during the last relapse.
9. **Last ambulatory**: f the patient seriously harmed its ambulatory capacity during the last relapse.
10. **Last corticosteroids**: if the patient had corticosteroids treatment at the moment of the last relapse.
11. **Last treatment name**: the corticosteroids treatment used at the moment of the last relapse. No corticosteroids use has value 0, hydrocortisone use has value 1, methylprednisolone has value 2 and plasmapheresis value 3.
12. **Last duration Days**: the corticosteroids treatment duration in days.

The feature normalization process occurred in the following form:

1. **Last Pyramidal**: no need for normalization process.
2. **Last Brain Stem**: no need for normalization process.
3. **Last Bowel Bladder**: no need for normalization process.
4. **Last Neuropsycho functions**: no need for normalization process.
5. **Last Cerebellum**: no need for normalization process.
6. **Last Visual functions**: no need for normalization process.
7. **Last Sensory functions**: no need for normalization process.
8. **Last hospital**: no need for normalization process.
9. **Last ambulatory**: no need for normalization process.
10. **Last corticosteroids**: no need for normalization process.
11. **Last treatment name**: the normalization factor was 3, since it is the maximum possible value (plasmapheresis treatment).
12. **Last duration Days**: the normalization factor was 10, since it is the maximum registered value. Besides, it is not benefic to do a corticosteroids treatment for a long period.

B.4 Momentaneous with past database

B.4.1 Identification sheet

From Identification sheet, the *Momentaneous with past* database is constituted by the following features:

1. **Gender**: equal to the raw feature description described in Chapter 5.
2. **Age of onset**: the age at which MS started to manifest.

3. **Supratentorial**: equal to the raw feature description described in Chapter 5.
4. **Optic Pathways**: equal to the raw feature description described in Chapter 5.
5. **Brainstem-Cerebellum**: equal to the raw feature description described in Chapter 5.
6. **Spinal Cord**: equal to the raw feature description described in Chapter 5.
7. **Age of diagnosis**: the age at which the patient was diagnosed with MS.
8. **Years from onset to diagnosis**: years passed from onset to diagnosis.
9. **Clinical findings**: equal to the raw feature description described in Chapter 5.
10. **MRI**: equal to the raw feature description described in Chapter 5.
11. **Evoked potentials**: equal to the raw feature description described in Chapter 5.
12. **CSF**: equal to the raw feature description described in Chapter 5.
13. **Age at SP diagnosis**: equal to the raw feature description described in Chapter 5.
14. **Years from onset to diagnosis SP**: time passed since MS onset and SP diagnosis.
15. **MS Course**: equal to the raw feature description described in Chapter 5.
16. **Active**: equal to the raw feature description described in Chapter 5.
17. **Age visit**: patient's age at the moment of the visit to the clinic.
18. **Years since onset**: the time passed from onset to the moment of the visit to the clinic.

The feature normalization process occurred in the following form:

1. **Gender**: no need for normalization process.
2. **Age of onset**: it was decided to normalize the feature using as maximum value 50 years old. This way, if a patient has an onset age superior to 50, its feature value will be 1. In this thesis, the target patients have onset ages of from 20 to approximately 40 years old.
3. **Supratentorial**: no need for normalization process.
4. **Optic Pathways**: no need for normalization process.
5. **Brainstem-Cerebellum**: no need for normalization process.
6. **Spinal Cord**: no need for normalization process.
7. **Age of diagnosis**: it was decided to use as normalization factor the same value as used in age of onset (50).
8. **Years from onset to diagnosis**: it was used 20 years as normalization factor

since this feature has a tremendous variability.

9. **Clinical findings**: no need for normalization process.
10. **MRI**: no need for normalization process.
11. **Evoked potentials**: no need for normalization process.
12. **CSF**: no need for normalization process.
13. **Age at SP diagnosis**: it was used 60 years old as value, since there were patients with more than 50 years old when SP was diagnosed.
14. **Years from onset to diagnosis SP**: it was used 25 years as normalization factor since this feature has a tremendous variability and since its maximum value surpasses the 20 years value used as the limit in feature "years from onset to diagnosis".
15. **MS Course**: no need for normalization process.
16. **Active**: no need for normalization process.
17. **Age visit**: the normalization factor was 70 since the maximum registered value is 66.
18. **Years since onset**: the normalization was 35 since the maximum registered value is 31.

B.4.2 Visits sheet

From Visits sheet, the *Momentaneous with past* database is constituted by the following features:

1. **Nb of visits per year**: the average of visits made per year.
2. **Nb of visits 1st year**: number of visits made in the first year.
3. **Nb of visits first 2 years**: number of visits made in the first 2 years.
4. **Suspected Relapses ratio per year**: the average of the annual numbers of suspected relapses regarding all visits made to the clinic.
5. **Suspected relapses ratio 1st year**: the average of suspected relapses regarding the first year the patient visited the clinic.
6. **Suspected relapses ratio first 2 years**: the average of suspected relapes regarding the first two years the patient visited the clinic.
7. **EDSS medium value/year**: the average value of the annual EDSS medium values regarding all visits made to the clinic.
8. **EDSS 1st year**: the average value of all EDSS values regarding the first year the patient visited the clinic.
9. **EDSS first 2 years**: the average value of all EDSS values regarding the first

two years the patient visited the clinic.

10. **EDSS std/year**: the standard deviation of the annual EDSS medium values.
11. **EDSS 1st year std**: the standard deviation of the EDSS values regarding the first year the patient visited the clinic.
12. **EDSS first 2 years std**: the standard deviation of the EDSS values regarding the first two years the patient visited the clinic.
13. **EDSS medium variation/year**: the average value of all annual EDSS variations per year regarding all visits made to the clinic.
14. **EDSS medium variation 1st year**: the medium variation of EDSS values regarding the first year the patient has visited the clinic.
15. **EDSS medium variation first 2 years**:
16. **EDSS medium variation first 2 years**: the medium variation of EDSS values regarding the first year the patient has visited the clinic.
17. **EDSS std of variation/year**: the standard deviation of the annual EDSS variations regarding all visits made to the clinic.
18. **EDSS std of variation 1st year**: the standard deviation of the EDSS variations regarding the first year the patient visited the clinic.
19. **EDSS std of variation first 2 years**: the standard deviation of the EDSS variations regarding the first 2 years the patient visited the clinic.
20. **EDSS increase 1st year**: the ratio of times the EDSS value has increased from consecutive visits regarding the first year the patient has visited the clinic.
21. **EDSS increase first 2 years**: the ratio of times the EDSS value has increased from consecutive visits regarding the first two years the patient has visited the clinic.
22. **Ratio nb EDSS increase**: the ratio of times the EDSS value has increased from consecutive visits regarding all visits made to the clinic.
23. **Ratio nb EDSS decrease**: the ratio of times the EDSS value has decreased from consecutive visits regarding all visits made to the clinic.
24. **Ratio nb EDSS decrease 1st year**: the ratio of times the EDSS value has decreased from consecutive visits regarding the first year the patient has visited the clinic.
25. **Ratio nb EDSS decrease first 2 years**: the ratio of times the EDSS value has decreased from consecutive visits regarding the first two years the patient has visited the clinic.
26. **Routine visits ratio**: the ratio of routine visits regarding all visits made to the clinic.

27. **Routine visits ratio 1st year**: the ratio of routine visits regarding the first year the patient has visited the clinic.
28. **Routine visits first 2 years**: the ratio of routine visits regarding the first two years the patient has visited the clinic.
29. **No years**: the number of years the patient.
30. **Last routine**: if the last visit to the clinic was a routine one.
31. **Last suspected**: if on the last visit to the clinic there were suspicions of an upcoming relapse.
32. **Last EDSS**: the EDSS value at the last visit to the clinic.
33. **Last weakness**: if on the last visit to the clinic there were manifestations related to cerebral weakness.
34. **Last sympton**: if on the last visit to the clinic there were manifestations related to visual symptons.

The feature normalization process occurred in the following form:

1. **Nb of visits per year**: the normalization factor was 3 visits per year since it was the maximum registered.
2. **Nb of visits 1st year**: the normalization factor mas 3 visits, since it was the maximum registered.
3. **Nb of visits first 2 years**: the normalization factor mas 5 visits since it was the maximum registered.
4. **Suspected Relapses ratio per year**: the normalization factor was 3 suspected relapses since it is the maximum integer in order to normalize the data between 0 and 1.
5. **Suspected relapses ratio 1st year**: the normalization factor was 3 suspected relapses since it is the maximum registered.
6. **Suspected relapses ratio first 2 years**: the normalization factor was 5 suspected relapses since it is the maximum registered.
7. **EDSS medium value/year**: the normalisation factor was 10 since the EDSS scale maximum value is 10.
8. **EDSS 1st year**: the normalization factor was 10 since the EDSS scale maximum value is 10.
9. **EDSS first 2 years**: the normalization factor was 10 since the EDSS scale maximum value is 10.
10. **EDSS std/year**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
11. **EDSS 1st year std**: the normalization factor was 3 since it is the maximum

integer in order to normalize the data between 0 and 1.

12. **EDSS first 2 years std**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
13. **EDSS medium variation/year**: the normalization factor was 2 since it is the maximum integer in order to normalize the data between 0 and 1.
14. **EDSS medium variation 1st year**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
15. **EDSS medium variation first 2 years**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
16. **EDSS std of variation/year**: the normalization factor was 2 since it is the maximum integer in order to normalize the data between 0 and 1.
17. **EDSS std of variation 1st year**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
18. **EDSS std of variation first 2 years**: the normalization factor was 3 since it is the maximum integer in order to normalize the data between 0 and 1.
19. **EDSS increase 1st year**: no need for normalization process.
20. **EDSS increase first 2 years**:no need for normalization process.
21. **Ratio nb EDSS increase**: no need for normalization process.
22. **Ratio nb EDSS decrease**: no need for normalization process.
23. **Ratio nb EDSS decrease 1st year**: no need for normalization process.
24. **Ratio nb EDSS decrease first 2 years**: no need for normalization process.
25. **Routine visits ratio**: no need for normalization process.
26. **Routine visits ratio 1st year**: no need for normalization process.
27. **Routine visits first 2 years**: no need for normalization process.
28. **No years**: the normalisation factor was 32, due to the maximum of number of years registered in the relapses sheet in No years feature.
29. **Last routine**: no need for normalization process.
30. **Last suspected**: no need for normalization process.
31. **Last EDSS**: the normalization factor is 10 since it is the maximum value of the EDSS scale.
32. **Last weakness**: no need for normalization process.
33. **Last sympton**: no need for normalization process.

B.4.3 Relapses sheet

From Relapses sheet, the *Momentaneous with past* database is constituted by the following features:

1. **Relapses per year**: the average of the annual numbers of relapses regarding all relapses.
2. **Relapses 1st year**: the number of relapses regarding the first year the patient suffered relapses.
3. **Relapses first 2 years**: the number of relapses regarding the first two years the patient suffered relapses.
4. **Pyramidal Ratio**: the ratio of times there were MS manifestations in the pyramidal tract due to a relapse regarding all relapses.
5. **Pyramidal 1st year**: the ratio of times there were MS manifestations related to the pyramidal tract due to a relapse regarding the first year a patient suffered relapses.
6. **Pyramidal first 2 years**: the ratio of times there were MS manifestations related to the pyramidal tract due to a relapse regarding the first two years a patient suffered relapses.
7. **Brain Stem ratio**: the ratio of times there were MS manifestations related to the brain stem due to a relapse regarding all relapses.
8. **Brain Stem 1st year**: the ratio of times there were MS manifestations related to the brain stem due to a relapse regarding the first year a patient suffered relapses.
9. **Brain Stem first 2 years**: the ratio of times there were MS manifestations related to the brain stem due to a relapse regarding the first two years a patient suffered relapses.
10. **Bowel ratio**: the ratio of times there were MS manifestations related to the bowel and bladder due to a relapse regarding all relapses.
11. **Bowel 1st year**: the ratio of times there were MS manifestations related to the bowel and bladder due to a relapse regarding the first year a patient suffered relapses.
12. **Bowel first 2 years**: the ratio of times there were MS manifestations related to the bowel and bladder due to a relapse regarding the first two years a patient suffered relapses.
13. **Neuropsycho ratio**: the ratio of times there were MS manifestations related to the neuropsycho functions due to a relapse regarding all relapses.
14. **Neuropsycho 1st year**: the ratio of times there were MS manifestations

related to the neuropsycho functions due to a relapse regarding the first year a patient suffered relapses.

15. **Neuropsycho first 2 years**: the ratio of times there were MS manifestations related to the bowel and bladder due to a relapse regarding the first two years a patient suffered relapses.
16. **Cerebellum ratio**: the ratio of times there were MS manifestations related to the cerebellum due to a relapse regarding all relapses.
17. **Cerebellum 1st year**: the ratio of times there were MS manifestations related to the cerebellum due to a relapse regarding the first year a patient suffered relapses.
18. **Cerebellum 2 years**: the ratio of times there were MS manifestations related to the cerebellum due to a relapse regarding the first two years a patient suffered relapses.
19. **Visual ratio**: the ratio of times there were MS manifestations related to visual functions due to a relapse regarding all relapses.
20. **Visual 1st year**: the ratio of times there were MS manifestations related to visual functions due to a relapse regarding the first year a patient suffered relapses.
21. **Visual first 2 years**: the ratio of times there were MS manifestations related to visual functions due to a relapse regarding the first two years a patient suffered relapses.
22. **Sensory ratio**: the ratio of times there were MS manifestations related to sensory functions due to a relapse regarding all relapses.
23. **Sensory 1st year**: the ratio of times there were MS manifestations related to sensory functions due to a relapse regarding the first year a patient suffered relapses.
24. **Sensory first 2 years**: the ratio of times there were MS manifestations related to sensory functions due to a relapse regarding the first two years a patient suffered relapses.
25. **Corticosteroids Ratio**: the ratio of times corticosteroids were used as treatment relapse treatment regarding all relapses.
26. **Corticosteroids/year**: the average of the annual ratios of corticosteroids use as relapse treatment.
27. **Corticosteroids 1st year**: the ratio of corticosteroids use regarding the first year the patient suffered relapses.
28. **Corticosteroids first 2 years**: the ratio of corticosteroids use regarding the

first two years the patient suffered relapses.

29. **Average treatment intensity**: the average treatment intensity regarding relapse treatment regarding all relapses. No corticosteroids use has value 0, hydrocortisone use has value 1, methylprednisolone has value 2 and plasmapheresis value 3.
30. **Average treatment 1st year**: the average treatment intensity regarding relapse treatment regarding the first year the patient suffered relapses. No corticosteroids use has value 0, hydrocortisone use has value 1, methylprednisolone has value 2 and plasmapheresis value 3.
31. **Average treatment first 2 years**: the average treatment intensity regarding relapse treatment regarding the first two years the patient suffered relapses. no corticosteroids use has value 0, hydrocortisone use has value 1, methylprednisolone has value 2 and plasmapheresis value 3.
32. **Average duration**: the average duration in days of corticosteroids treatment regarding all relapses.
33. **Average duration 1st year**: the average duration in days of corticosteroids use treatment regarding the first year the patient suffered relapses.
34. **Average duration first 2 years**: the average duration in days of corticosteroids use treatment regarding the first two years the patient suffered relapses.
35. **Last Pyramidal**: if there were MS manifestations related to the pyramidal tract regarding the last visit.
36. **Last Brain Stem**: if there were MS manifestations related to the brain stem due regarding the last visit.
37. **Last Bowel Bladder**: if there were MS manifestations related to the bowel and bladder regarding the last visit.
38. **Last Neuropsycho functions**: if there were MS manifestations related to neuropsycho functions regarding the last visit.
39. **Last Cerebellum**: if there were MS manifestations related to the cerebellum regarding the last visit.
40. **Last Visual functions**: if there were MS manifestations related to visual functions regarding the last visit.
41. **Last Sensory functions**: if there were MS manifestations related to sensory functions regarding the last visit.
42. **Last hospital**: if there was the need to be internalized at the hospital during the last visit.
43. **Last ambulatory**: if the patient seriously harmed its ambulatory capacity

during the last visit.

44. **Last corticosteroids**: if the patient had corticosteroids treatment at the moment of the last visit.
45. **Last treatment name**: the corticosteroids treatment used at the moment of the last relapse. No corticosteroids use has value 0, hydrocortisone use has value 1, methylprednisolone has value 2 and plasmapheresis value 3.
46. **Last duration Days**: the corticosteroids treatment duration in days.

The feature normalization process occurred in the following form:

1. **Relapses per year**: the normalization factor was 4, since it is the maximum integer in order to normalize the data between 0 and 1.
2. **Relapses 1st year**: the normalization factor was 4, since the maximum value registered was 3. Value 3 was not chosen since the normalization factor in feature relapses per year is 4.
3. **Relapses first 2 years**: the normalization factor was 6, since the maximum value registered was 6.
4. **Pyramidal Ratio**: no need for normalization process.
5. **Pyramidal 1st year**: no need for normalization process.
6. **Pyramidal first 2 years**: no need for normalization process.
7. **Brain Stem ratio**: no need for normalization process.
8. **Brain Stem 1st year**: no need for normalization process.
9. **Brain Stem first 2 years**: no need for normalization process.
10. **Bowel ratio**: no need for normalization process.
11. **Bowel 1st year**: no need for normalization process.
12. **Bowel first 2 years**: no need for normalization process.
13. **Neuropsycho ratio**: no need for normalization process.
14. **Neuropsycho 1st year**: no need for normalization process.
15. **Neuropsycho first 2 years**: no need for normalization process.
16. **Cerebellum ratio**: no need for normalization process.
17. **Cerebellum 1st year**: no need for normalization process.
18. **Cerebellum 2 years**: no need for normalization process.
19. **Visual ratio**: no need for normalization process.
20. **Visual 1st year**: no need for normalization process.
21. **Visual first 2 years**: no need for normalization process.
22. **Sensory ratio**: no need for normalization process.
23. **Sensory 1st year**: no need for normalization process.

24. **Sensory first 2 years**: no need for normalization process.
25. **Corticosteroids Ratio**: no need for normalization process.
26. **Corticosteroids/year**: no need for normalization process.
27. **Corticosteroids 1st year**: no need for normalization process.
28. **Corticosteroids first 2 years**:no need for normalization process.
29. **Average treatment intensity**: the normalization factor was 3 since it is the maximum possible value (plasmapheresis treatment).
30. **Average treatment 1st year**: the normalization factor was 3 since it is the maximum possible value (plasmapheresis treatment).
31. **Average treatment first 2 years**: the normalization factor was 3 since it is the maximum possible value (plasmapheresis treatment).
32. **Average duration**: the normalization factor was 10 since it is the maximum registered value. Besides, it is not benefic to do a corticosteroids treatment for a long period.
33. **Average duration 1st year**: the normalization factor was 10 since it is the maximum registered value. Besides, it is not benefic to do a corticosteroids treatment for a long period.
34. **Average duration first 2 years**: the normalization factor was 10 since it is the maximum registered value. Besides, it is not benefic to do a corticosteroids treatment for a long period.
35. **Last Pyramidal**: no need for normalization process.
36. **Last Brain Stem**: no need for normalization process.
37. **Last Bowel Bladder**: no need for normalization process.
38. **Last Neuropsycho functions**: no need for normalization process.
39. **Last Cerebellum**: no need for normalization process.
40. **Last Visual functions**: no need for normalization process.
41. **Last Sensory functions**: no need for normalization process.
42. **Last hospital**: no need for normalization process.
43. **Last ambulatory**: no need for normalization process.
44. **Last corticosteroids**: no need for normalization process.
45. **Last treatment name**: the normalization factor was 3, since it is the maximum possible value (plasmapheresis treatment).
46. **Last duration Days**: the normalization factor was 10, since it is the maximum registered value. Besides, it is not benefic to do a corticosteroids treatment for a long period.

Chapter C

Appendix III - Experimental procedure

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
4	20	22	0.09	0.18
5	21	24	0.13	0.21
4	22	24	0.08	0.17
4	22	24	0.08	0.17
3	31	35	0.11	0.09
7	63	70	0.10	0.10
7	63	70	0.10	0.10
7	63	70	0.10	0.10
3	31	35	0.11	0.09
6	33	37	0.11	0.16
6	33	37	0.11	0.16
6	33	37	0.11	0.16
6	33	37	0.11	0.16
6	33	37	0.11	0.16
6	33	37	0.11	0.16
6	33	37	0.11	0.16

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
6	33	37	0.11	0.16
4	32	35	0.09	0.11
4	32	35	0.09	0.11
5	31	35	0.11	0.14
5	31	35	0.11	0.14
5	31	35	0.11	0.14
4	31	35	0.11	0.11
5	41	45	0.09	0.11
4	31	35	0.11	0.11
5	40	45	0.11	0.11
4	31	35	0.11	0.11
2	18	20	0.10	0.10
2	18	20	0.10	0.10
2	18	20	0.10	0.10
2	18	20	0.10	0.10
3	18	20	0.10	0.15
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
5	31	35	0.11	0.14
4	31	35	0.11	0.11
5	31	35	0.11	0.14
5	31	35	0.11	0.14
5	31	35	0.11	0.14
4	18	20	0.10	0.20
3	18	20	0.10	0.15
3	18	20	0.10	0.15
3	18	20	0.10	0.15
3	19	20	0.05	0.15
3	18	20	0.10	0.15
4	20	22	0.09	0.18

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
3	18	20	0.10	0.15
2	19	20	0.05	0.10
2	18	20	0.10	0.10
2	18	20	0.10	0.10
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
3	19	22	0.14	0.14
3	19	22	0.14	0.14
3	19	22	0.14	0.14
3	19	22	0.14	0.14
3	19	22	0.14	0.14
9	35	40	0.13	0.23
9	35	40	0.13	0.23
9	35	40	0.13	0.23
9	35	40	0.13	0.23
9	35	40	0.13	0.23
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
3	19	22	0.14	0.14
4	21	40	0.48	0.10
5	31	36	0.14	0.14
5	31	36	0.14	0.14
5	31	36	0.14	0.14
5	31	36	0.14	0.14
5	31	36	0.14	0.14
6	31	35	0.11	0.17
6	31	35	0.11	0.17
6	31	35	0.11	0.17
6	31	35	0.11	0.17

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
6	31	35	0.11	0.17
6	31	35	0.11	0.17
2	18	20	0.10	0.10
2	18	20	0.10	0.10
2	18	20	0.10	0.10
2	18	20	0.10	0.10
2	18	20	0.10	0.10
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
3	18	20	0.10	0.15
3	18	20	0.10	0.15
3	18	20	0.10	0.15
3	18	20	0.10	0.15
3	18	20	0.10	0.15
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
4	22	24	0.08	0.17
4	22	24	0.08	0.17
4	22	24	0.08	0.17
4	22	24	0.08	0.17
5	30	35	0.14	0.14
7	58	65	0.11	0.11

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
5	30	35	0.14	0.14
7	58	65	0.11	0.11
5	30	35	0.14	0.14
3	21	22	0.05	0.14
3	21	22	0.05	0.14
3	21	22	0.05	0.14
3	21	22	0.05	0.14
3	21	22	0.05	0.14
8	35	40	0.13	0.20
8	35	40	0.13	0.20
8	35	40	0.13	0.20
8	35	40	0.13	0.20
8	35	40	0.13	0.20
3	32	35	0.09	0.09
3	32	35	0.09	0.09
3	32	35	0.09	0.09
6	62	65	0.05	0.09
6	62	65	0.05	0.09
4	32	35	0.09	0.11
4	32	35	0.09	0.11
6	43	45	0.04	0.13
6	43	45	0.04	0.13
6	33	37	0.11	0.16
6	33	37	0.11	0.16
6	33	37	0.11	0.16
6	33	37	0.11	0.16
6	33	37	0.11	0.16
4	31	35	0.11	0.11
4	31	35	0.13	0.11
5	39	45	0.13	0.11
5	39	45	0.13	0.11
4	31	35	0.11	0.11
4	21	22	0.05	0.18

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	21	22	0.05	0.18
3	19	22	0.14	0.14
3	19	22	0.14	0.14
3	19	22	0.14	0.14
3	19	22	0.14	0.14
3	19	22	0.14	0.14
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
6	33	37	0.11	0.16
13	127	140	0.09	0.09
13	127	140	0.09	0.09
13	127	140	0.09	0.09
6	33	37	0.11	0.16
5	22	24	0.08	0.21
5	22	24	0.08	0.21
5	22	24	0.08	0.21
5	22	24	0.08	0.21
5	22	24	0.08	0.21
4	33	35	0.06	0.11
4	33	35	0.06	0.11
4	33	35	0.06	0.11
6	57	65	0.12	0.09

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
6	57	65	0.12	0.09
6	57	65	0.12	0.09
3	19	20	0.05	0.15
3	19	20	0.05	0.15
3	19	20	0.05	0.15
3	19	20	0.05	0.15
3	19	20	0.05	0.15
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	19	20	0.05	0.20
4	19	20	0.05	0.20
4	19	20	0.05	0.20
4	19	20	0.05	0.20
4	19	20	0.05	0.20
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
4	22	24	0.08	0.17
4	22	24	0.08	0.17
4	22	24	0.08	0.17
4	22	24	0.08	0.17
4	22	24	0.08	0.17
4	22	24	0.08	0.17
4	22	24	0.08	0.17
4	22	24	0.08	0.17
4	22	24	0.08	0.17
4	22	24	0.08	0.17
4	22	24	0.08	0.17
5	31	35	0.11	0.14

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
2	20	22	0.09	0.09
2	20	22	0.09	0.09
2	20	22	0.09	0.09
2	20	22	0.09	0.09
2	20	22	0.09	0.09
4	33	37	0.11	0.11
4	33	37	0.11	0.11
4	33	37	0.11	0.11
4	33	37	0.11	0.11
4	33	37	0.11	0.11
3	31	37	0.16	0.08
3	31	37	0.16	0.08
7	64	70	0.09	0.10
7	64	70	0.09	0.10
7	64	70	0.09	0.10
5	30	35	0.14	0.14
5	30	35	0.14	0.14
5	30	35	0.14	0.14
6	22	24	0.08	0.25
6	22	24	0.08	0.25
6	22	24	0.08	0.25
6	22	24	0.08	0.25
6	22	24	0.08	0.25
5	31	35	0.11	0.14
5	31	35	0.11	0.14
8	60	65	0.08	0.12
3	20	20	0.00	0.15
3	20	20	0.00	0.15
3	20	20	0.00	0.15
3	20	20	0.00	0.15
3	20	20	0.00	0.15
3	21	22	0.05	0.14
3	21	22	0.05	0.14

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
3	21	22	0.05	0.14
3	21	22	0.05	0.14
3	21	22	0.05	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
4	20	24	0.17	0.17
4	20	24	0.17	0.17
4	20	24	0.17	0.17
4	20	24	0.17	0.17
4	20	24	0.17	0.17
3	30	35	0.14	0.09
3	30	35	0.14	0.09
3	30	35	0.14	0.09
9	45	50	0.10	0.18
9	45	50	0.10	0.18
5	32	37	0.14	0.14
5	32	37	0.14	0.14
5	32	37	0.14	0.14
5	40	45	0.11	0.11
5	40	45	0.11	0.11
4	20	20	0.00	0.20
5	20	24	0.17	0.21
3	20	24	0.17	0.13
3	20	24	0.17	0.13
3	20	24	0.17	0.13
5	39	46	0.15	0.11
12	66	78	0.15	0.15
5	31	35	0.11	0.14
5	31	35	0.11	0.14
4	38	45	0.16	0.09

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
4	38	45	0.16	0.09
4	38	45	0.16	0.09
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	21	22	0.05	0.18
2	20	24	0.17	0.08
2	20	24	0.17	0.08
2	20	24	0.17	0.08
2	20	24	0.17	0.08
2	20	24	0.17	0.08
4	35	40	0.13	0.10
4	35	40	0.13	0.10
3	18	20	0.10	0.15
3	18	20	0.10	0.15
3	18	20	0.10	0.15
3	18	20	0.10	0.15
4	19	22	0.14	0.18
4	19	22	0.14	0.18
4	19	22	0.14	0.18
3	19	20	0.05	0.15
3	19	20	0.05	0.15
3	19	20	0.05	0.15
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
5	31	35	0.11	0.14
5	31	35	0.11	0.14
7	58	65	0.11	0.11
4	19	23	0.17	0.17

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
6	32	37	0.14	0.16
6	32	37	0.14	0.16
6	32	37	0.14	0.16
6	32	37	0.14	0.16
6	32	37	0.14	0.16
10	60	70	0.14	0.14
5	30	35	0.14	0.14
5	30	35	0.14	0.14
10	60	70	0.14	0.14
10	60	70	0.14	0.14
3	21	24	0.13	0.13
3	21	24	0.13	0.13
3	21	24	0.13	0.13
3	21	24	0.13	0.13
3	21	24	0.13	0.13
12	48	60	0.20	0.20
12	48	60	0.20	0.20
12	48	60	0.20	0.20
12	48	60	0.20	0.20
12	48	60	0.20	0.20
6	33	37	0.11	0.16
6	33	37	0.11	0.16
6	33	37	0.11	0.16
6	33	37	0.11	0.16
6	33	37	0.11	0.16
5	31	35	0.11	0.14
5	31	35	0.11	0.14
5	31	35	0.11	0.14
5	31	35	0.11	0.14
5	31	35	0.11	0.14
6	29	35	0.17	0.17
6	29	35	0.17	0.17
6	29	35	0.17	0.17

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
6	29	35	0.17	0.17
6	29	35	0.17	0.17
5	31	35	0.11	0.14
5	31	35	0.11	0.14
5	31	35	0.11	0.14
16	47	55	0.15	0.29
6	37	45	0.18	0.13
5	20	22	0.09	0.23
5	20	22	0.09	0.23
5	20	22	0.09	0.23
5	20	22	0.09	0.23
5	20	22	0.09	0.23
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
7	39	45	0.13	0.16
7	39	45	0.13	0.16
5	40	35	0.14	0.14
5	40	35	0.14	0.14
5	40	35	0.14	0.14
5	57	65	0.12	0.08
5	57	65	0.12	0.08
5	57	65	0.12	0.08
2	29	35	0.17	0.06
2	29	35	0.17	0.06
3	19	20	0.05	0.15
3	19	20	0.05	0.15
3	19	20	0.05	0.15
3	19	20	0.05	0.15
3	19	20	0.05	0.15
4	21	22	0.05	0.18

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	21	24	0.13	0.17
4	30	35	0.14	0.11
4	30	35	0.14	0.11
8	58	65	0.11	0.12
8	58	65	0.11	0.12
8	58	65	0.11	0.12
4	22	25	0.12	0.16
4	22	25	0.12	0.16
4	22	25	0.12	0.16
4	22	25	0.12	0.16
4	22	25	0.12	0.16
5	31	35	0.11	0.14
5	31	35	0.11	0.14
5	31	35	0.11	0.14
6	41	45	0.09	0.13
6	41	45	0.09	0.13
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14
3	20	22	0.09	0.14

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
3	20	22	0.09	0.14
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	21	22	0.05	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
4	20	22	0.09	0.18
5	30	35	0.14	0.14
5	30	35	0.14	0.14
5	30	35	0.14	0.14
5	30	35	0.14	0.14
5	30	35	0.14	0.14
5	30	35	0.14	0.14
5	30	35	0.14	0.14
5	30	35	0.14	0.14
5	30	35	0.14	0.14
5	30	35	0.14	0.14
5	20	24	0.17	0.21
5	20	24	0.17	0.21
5	20	24	0.17	0.21
5	20	24	0.17	0.21
5	20	24	0.17	0.21
9	62	70	0.11	0.13
9	62	70	0.11	0.13
9	62	70	0.11	0.13
6	31	35	0.11	0.17
6	31	35	0.11	0.17
6	32	35	0.09	0.17
6	32	35	0.09	0.17

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	Top Slice	Number of Slices	Bottom-Start	End-Top
6	32	35	0.09	0.17
6	40	45	0.11	0.13
6	40	45	0.11	0.13
4	30	35	0.14	0.11
4	30	35	0.14	0.11
4	30	35	0.14	0.11
7	58	65	0.11	0.11
7	58	65	0.11	0.11
6	31	35	0.11	0.17
6	31	35	0.11	0.17
8	58	65	0.11	0.12
8	58	65	0.11	0.12
8	58	65	0.11	0.12
5	32	35	0.09	0.14
5	32	35	0.09	0.14
5	32	35	0.09	0.14
6	41	45	0.09	0.13
6	41	45	0.09	0.13
5	31	35	0.11	0.14
5	31	35	0.11	0.14
5	31	35	0.11	0.14
5	31	35	0.11	0.14
5	31	35	0.11	0.14
5	22	25	0.12	0.20
5	22	25	0.12	0.20
5	22	25	0.12	0.20
5	22	25	0.12	0.20
5	22	25	0.12	0.20
5	31	36	0.14	0.14
5	31	36	0.14	0.14
5	31	36	0.14	0.14
6	40	46	0.13	0.13
6	40	46	0.13	0.13

Table C.1: Study performed with CHUC's database for determination of a security search interval for top and head limit slices.

Bottom Slice	**Top Slice**	**Number of Slices**	**Bottom-Start**	**End-Top**
6	40	46	0.13	0.13

Chapter D

Appendix IV - Machine learning results

The machine learning results are here presented. In order to do so, these are split by the origin set, type of procedure and label in question. Classification results will be the output (supervised), in order to provide final conclusions regarding the actual prediction power of groups of features and to explore the potential of certain labels. In some cases, the intermediate feature selection process will be displayed in order to have a deeper understanding oh the predictors influence and power. These are only shown in the situations chosen to study more deeply (in labels *highestEDSS*, *mediumEDSS* and *nextEDSS* in the clinical databases), since they are more trustful because the performances were clearly better.

These steps were performed with and without PCA. The best results (where sensibility, specificity, negative predictive value, positive predictive value and accuracy are all above 50%) are in bold.

Besides this procedure, there is also a deeper investigation, since features can have a medical point of view. This way, the investigation procedure presents extra studies about a more specific group of features, where some of the standard procedure set are excluded for being already clinically very obvious predictors. This way, the main concern in these try-outs it is to come across with new factors and predictors that might open doors to new investigation paths.

Since these are very extense, a code name system was constructed to name the tables, regarding the data set, partition method and label. The code system is constituted by Used Database_Standard or Investigation_Partition Method_Label.

If PCA is applied, the term PCA is written between the partition method and the label. The 70:30 ratio partition method was named as traditional in the present tables.

D.1 Clinic Data

D.1.1 Static Set

D.1.1.1 Standard procedure

For label *msCourse* (0/1 - RR-SP):
Final Features: EDSS Medium Value/Year.

Table D.1: Static_Standard_Traditional_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.85	0.76	0.71	0.62	0.68	0.76	0.77	0.85	0.85	0.86
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
100.00	**100.00**	66.67	66.67	33.33	33.33	**66.67**	66.67	**100.00**	**100.00**	**100.00**
16.67	**83.33**	77.78	77.78	83.33	88.89	**88.89**	77.78	**83.33**	**83.33**	**83.33**
100.00	**100.00**	93.33	93.33	88.24	88.89	**94.12**	93.33	**100.00**	**100.00**	**100.00**
16.67	**50.00**	33.33	33.33	25.00	33.33	**50.00**	33.33	**50.00**	**50.00**	**50.00**
28.57	**85.71**	76.19	76.19	76.19	80.95	**85.71**	76.19	**85.71**	**85.71**	**85.71**
Confusion Matrix										
3 15 0 3	15 3 0 3	14 4 1 2	14 4 1 2	15 3 2 1	16 2 2 1	16 2 1 2	14 4 1 2	15 3 0 3	15 3 0 3	15 3 0 3

Table D.2: Static_Standard_Traditional_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.51	0.50	0.49	0.50	0.50	0.51	0.50	0.50	0.50
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN
14.29	14.29	14.29	14.29	14.29	14.29	14.29	14.29	14.29	14.29	14.29
14.29	14.29	14.29	14.29	14.29	14.29	14.29	14.29	14.29	14.29	14.29
Confusion Matrix										
0 18 0 3	0 18 0 3	0 18 0 3	0 18 0 3	0 18 0 3	0 18 0 3	0 18 0 3	0 18 0 3	0 18 0 3	0 18 0 3	0 18 0 3

Table D.3: Static_Standard_kFold_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	0.64	0.64	0.55	0.63	0.60	0.53	0.62	0.64	0.47	0.66
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
63.64	**81.82**	**81.82**	**63.64**	**81.82**	**72.73**	**54.55**	**72.73**	**81.82**	**54.55**	**90.91**
88.46	**88.46**	**92.31**	**92.31**	**88.46**	**88.46**	**92.31**	**92.31**	**88.46**	**84.62**	**84.62**
85.19	**92.00**	**92.31**	**85.71**	**92.00**	**88.46**	**82.76**	**88.89**	**92.00**	**81.48**	**95.65**
70.00	**75.00**	**81.82**	**77.78**	**75.00**	**72.73**	**75.00**	**80.00**	**75.00**	**60.00**	**71.43**
81.08	**86.49**	**89.19**	**83.78**	**86.49**	**83.78**	**81.08**	**86.49**	**86.49**	**75.68**	**86.49**
Confusion Matrix										
23 3	23 3	24 2	24 2	23 3	23 3	24 2	24 2	23 3	22 4	22 4
4 7	2 9	2 9	4 7	2 9	3 8	5 6	3 8	2 9	5 6	1 10

Table D.4: Static_Standard_kFold_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.64	0.69	0.69	0.55	0.50	0.70	0.71	0.69	0.69	0.71	0.71
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
81.82	**90.91**	**90.91**	**63.64**	**54.55**	**90.91**	**90.91**	**90.91**	**90.91**	**100.00**	**100.00**
88.46	**92.31**	**92.31**	**88.46**	**88.46**	**92.31**	**88.46**	**92.31**	**92.31**	**92.31**	**92.31**
92.00	**96.00**	**96.00**	**85.19**	**82.14**	**96.00**	**95.83**	**96.00**	**96.00**	**100.00**	**100.00**
75.00	**83.33**	**83.33**	**70.00**	**66.67**	**83.33**	**76.92**	**83.33**	**83.33**	**84.62**	**84.62**
86.49	**91.89**	**91.89**	**81.08**	**78.38**	**91.89**	**89.19**	**91.89**	**91.89**	**94.59**	**94.59**
Confusion Matrix										
23 3	24 2	24 2	23 3	23 3	24 2	23 3	24 2	24 2	24 2	24 2
2 9	1 10	1 10	4 7	5 6	1 10	1 10	1 10	1 10	0 11	0 11

Table D.5: Static_Standard_LOO_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.47	0.48	0.52	0.47	0.35	0.36	0.48	0.47	0.43	0.43
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
27.27	27.27	27.27	27.27	27.27	9.09	9.09	27.27	27.27	18.18	27.27
76.92	65.38	69.23	76.92	65.38	61.54	65.38	69.23	65.38	69.23	57.69
71.43	68.00	69.23	71.43	68.00	61.54	62.96	69.23	68.00	66.67	65.22
33.33	25.00	27.27	33.33	25.00	9.09	10.00	27.27	25.00	20.00	21.43
62.16	54.05	56.76	62.16	54.05	45.95	48.65	56.76	54.05	54.05	48.65
Confusion Matrix										
20 6	17 9	18 8	20 6	17 9	16 10	17 9	18 8	17 9	18 8	15 11
8 3	8 3	8 3	8 3	8 3	10 1	10 1	8 3	8 3	9 2	8 3

Table D.6: Static_Standard_LOO_msCourse

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.64	0.69	0.69	0.55	0.50	0.70	0.71	0.69	0.69	0.51	0.51
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
36.36	27.27	27.27	18.18	27.27	27.27	36.36	27.27	27.27	36.36	36.36
69.23	65.38	65.38	69.23	76.92	65.38	65.38	65.38	65.38	65.38	65.38
72.00	68.00	68.00	66.67	71.43	68.00	70.83	68.00	68.00	70.83	70.83
33.33	25.00	25.00	20.00	33.33	25.00	30.77	25.00	25.00	30.77	30.77
59.46	54.05	54.05	54.05	62.16	54.05	56.76	54.05	54.05	56.76	56.76
Confusion Matrix										
18 8 7 4	17 9 8 3	17 9 8 3	18 8 9 2	20 6 8 3	17 9 8 3	17 9 7 4	17 9 8 3	17 9 8 3	17 9 7 4	17 9 7 4

First feature selection process for *mediumEDSS*:

Table D.7: Static_Feature_Selection_Identification_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Gender	0	1	1	1	1	1	1	1	0	0	1	**8**
Age of Onset	0	0	0	0	1	0	1	1	0	0	0	**3**
Optic Pathways	0	0	0	1	0	0	0	0	0	0	0	1
Brainstem-Cerebellum	0	0	0	0	0	1	0	0	0	0	0	1
Spinal Cord	0	0	0	0	0	1	1	0	0	0	0	**2**
Age of Diagnosis	0	1	1	1	1	0	0	0	0	0	1	**5**
Years from Onset to Diagnosis	1	0	1	1	1	0	0	1	0	1	1	**7**
MRI	0	0	0	0	0	0	1	0	0	0	0	1
CSF	0	0	0	0	0	1	0	0	0	0	0	1
Active	0	0	0	0	0	0	1	0	0	0	0	1

Selected features: Gender, Age of Onset, Spinal Cord, Age of Diagnosis, Years from Onset to Diagnosis.

Table D.8: Static_Feature_Selection_Visits_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Nb of visits per Year	0	0	0	1	0	0	0	0	0	0	0	1
Nb of Visits 1st Year	0	0	1	1	0	0	0	0	0	0	0	**2**
Nb of visits first 2 years	1	1	1	1	0	0	0	0	0	1	1	**6**
Suspected Relapses Ratio per year	0	0	0	1	0	0	0	0	0	0	0	1
Suspected Relapses Ratio 1st year	0	0	0	1	0	0	0	0	0	0	0	1
Suspected Relapses Ratio first 2 years	1	1	1	1	0	0	0	0	0	1	1	**6**
EDSS 1st year	1	1	1	1	1	0	1	1	0	0	1	**8**
EDSS std/year	1	1	1	0	1	0	1	0	0	0	1	**6**
EDSS 1st year std	0	0	0	0	0	0	1	1	0	0	0	**2**
EDSS first 2 years std	0	0	0	0	0	0	1	0	0	0	0	1
EDSS medium variation/Year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS medium variation 1st year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS medium variation first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
EDSS std of variation/year	0	0	0	0	1	0	1	0	0	0	0	**2**
EDSS std of variation 1st year	0	0	0	0	0	0	1	1	0	0	0	**2**
EDSS std of variation first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
EDSS Increase 1st Year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS Increase first 2 years	0	1	1	1	1	0	0	0	0	0	1	**5**
Ratio nb EDSS increase	0	1	1	1	1	0	1	0	0	1	1	**7**
Ratio nb EDSS decrease first 2 years	0	1	1	1	0	0	1	0	0	1	1	**6**
Routine Visits first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
No Years	0	0	1	1	1	0	0	0	0	0	0	**3**

Selected features: Nb of Visits 1st Year, Nb of visits first 2 years, Suspected

Relapses Ratio first 2 years, EDSS 1st year, EDSS std/year, EDSS 1st year std, EDSS std of variation/year, EDSS std of variation 1st year. EDSS increase first 2 years, Ratio nb EDSS increase, Ratio nb EDSS decrease first 2 years.

Table D.9: Static_Feature_Selection_Relapses_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Relapses first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Pyramidal ratio	0	1	1	1	1	0	0	1	0	0	1	**6**
Pyramidal 1st year	0	0	0	0	0	1	0	0	0	0	0	1
Pyramidal first 2 years	0	1	1	1	1	0	0	1	1	1	1	**8**
BrainStem 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Brain Stem first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Neuropsycho 1st year	0	0	0	0	0	0	0	0	1	1	0	**2**
Visual ratio	0	0	0	0	0	0	1	0	0	0	0	1
Visual 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Visual first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Sensory ratio	1	1	1	1	0	0	1	1	0	0	1	**7**
Sensory 1st year	0	0	0	0	0	1	0	0	0	0	0	1
Sensory first 2 years	0	0	0	0	0	1	0	0	0	0	0	1
Corticosteroids Ratio	0	0	0	0	0	1	0	0	0	0	0	1
Corticosteroids 1st year	0	0	0	0	0	1	0	0	0	0	0	1
Corticosteroids first 2 years	0	0	0	0	0	1	0	0	0	0	0	1
Average Duration	0	0	0	0	0	0	0	1	0	0	0	1
No Years	0	0	1	1	1	0	1	1	1	1	0	**7**

Selected features: Pyramidal ratio, Pyramidal first 2 years, Neuropsycho 1st year, Sensory ratio, No Years.

For label *mediumEDSS* (0/1 - $(< 3)/(\geq 3)$**):**

Final Features: EDSS 1st Year, Ratio nb EDSS increase, Number of Years

Table D.10: Static_Standard_Traditional_PCA_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.77	0.74	0.68	0.62	0.67	0.66	0.72	0.77	0.75	0.75
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
75.00	**75.00**	**75.00**	75.00	75.00	75.00	75.00	**75.00**	**75.00**	**75.00**	**75.00**
54.55	**81.82**	**72.73**	54.55	45.45	54.55	63.64	**81.82**	**81.82**	**81.82**	**81.82**
85.71	**90.00**	**88.89**	85.71	83.33	85.71	87.50	**90.00**	**90.00**	**90.00**	**90.00**
37.50	**60.00**	**50.00**	37.50	33.33	37.50	42.86	**60.00**	**60.00**	**60.00**	**60.00**
60.00	**80.00**	**73.33**	60.00	53.33	60.00	66.67	**80.00**	**80.00**	**80.00**	**80.00**
Confusion Matrix										
6 5 1 3	9 2 1 3	8 3 1 3	6 5 1 3	5 6 1 3	6 5 1 3	7 4 1 3	9 2 1 3	9 2 1 3	9 2 1 3	9 2 1 3

Table D.11: Static_Standard_Traditional_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.50	0.66	0.67	0.55	0.59	0.64	0.77	0.50	0.50	0.50
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
50.00	100.00	**50.00**	75.00	25.00	25.00	**50.00**	**100.00**	100.00	100.00	100.00
63.64	0.00	**81.82**	63.64	90.91	81.82	**81.82**	**63.64**	0.00	0.00	0.00
77.78	NaN	**81.82**	87.50	76.92	75.00	**81.82**	**100.00**	NaN	NaN	NaN
33.33	26.67	**50.00**	42.86	50.00	33.33	**50.00**	**50.00**	26.67	26.67	26.67
60.00	26.67	**73.33**	66.67	73.33	66.67	**73.33**	**73.33**	26.67	26.67	26.67
Confusion Matrix										
7 4	0 11	9 2	7 4	10 1	9 2	9 2	7 4	0 11	0 11	0 11
2 2	0 4	2 2	1 3	3 1	3 1	2 2	0 4	0 4	0 4	0 4

Table D.12: Static_Standard_kFold_PCA_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.59	0.56	0.17	0.63	0.44	0.45	0.48	NA	0.60	0.57
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
53.33	**60.00**	**53.33**	6.67	**66.67**	40.00	40.00	46.67	NA	**73.33**	**60.00**
77.27	**90.91**	**86.36**	77.27	**77.27**	72.73	72.73	86.36	NA	**81.82**	**86.96**
70.83	**76.92**	**73.08**	54.84	**77.27**	64.00	64.00	70.37	NA	**81.82**	**76.92**
61.54	**81.82**	**72.73**	16.67	**66.67**	50.00	50.00	70.00	MA	**73.33**	**75.00**
67.57	**78.38**	**72.97**	48.65	**72.97**	59.46	59.46	70.27	NA	**78.38**	**76.32**
Confusion Matrix										
17 5	20 2	19 3	17 5	17 5	16 6	16 6	19 3	NA	18 4	20 3
7 8	6 9	7 8	14 1	5 10	9 6	9 6	8 7	NA	4 11	6 9

Table D.13: Static_Standard_kFold_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.77	0.63	0.69	0.70	0.58	0.71	0.60	0.72	0.64	0.62	0.71
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
86.67	**66.67**	**80.00**	**80.00**	**60.00**	**80.00**	**60.00**	**80.00**	**66.67**	**66.67**	**80.00**
90.91	**86.36**	**86.36**	**81.82**	**81.82**	**90.91**	**95.45**	**90.91**	**86.36**	**86.36**	**81.82**
90.91	**79.17**	**86.36**	**85.71**	**75.00**	**86.96**	**77.78**	**86.96**	**79.17**	**79.17**	**85.71**
86.67	**76.92**	**80.00**	**75.00**	**69.23**	**85.71**	**90.00**	**85.71**	**76.92**	**76.92**	**75.00**
89.19	**78.38**	**83.78**	**81.08**	**72.97**	**86.49**	**81.08**	**86.49**	**78.38**	**78.38**	**81.08**
Confusion Matrix										
20 2	19 3	19 3	18 4	18 4	20 2	21 1	20 2	19 3	19 3	18 4
2 13	5 10	3 12	3 12	6 9	3 12	6 9	3 12	5 10	5 10	3 12

Table D.14: Static_Standard_LOO_PCA_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.40	0.41	0.45	0.73	0.40	0.57	0.57	0.43	0.41	0.40	0.41
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
26.67	20.00	26.67	26.67	26.67	40.00	40.00	20.00	20.00	26.67	20.00
54.55	63.64	63.64	95.45	54.55	72.73	72.73	68.18	63.64	54.55	63.64
52.17	53.85	56.00	65.63	52.17	64.00	64.00	55.56	53.85	52.17	53.85
28.57	27.27	33.33	80.00	28.57	50.00	50.00	30.00	27.27	28.57	27.27
43.24	45.95	48.65	67.57	43.24	59.46	59.46	48.65	45.95	43.24	45.95
Confusion Matrix										
12 10	14 8	14 8	21 1	12 10	16 6	16 6	15 7	14 8	12 10	14 8
11 4	12 3	11 4	11 4	11 4	9 6	9 6	12 3	12 3	11 4	12 3

Table D.15: Static_Standard_LOO_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.58	0.54	0.61	0.56	0.60	0.52	0.60	0.58	0.54	0.54	0.51
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
53.33	40.00	**53.33**	53.33	46.67	40.00	40.00	**53.33**	40.00	40.00	46.67
63.64	68.18	**68.18**	59.09	72.73	63.64	77.27	**63.64**	68.18	68.18	54.55
66.67	62.50	**68.18**	65.00	66.67	60.87	65.38	**66.67**	62.50	62.50	60.00
50.00	46.15	**53.33**	47.06	53.85	42.86	54.55	**50.00**	46.15	46.15	41.18
59.46	56.76	**62.16**	56.76	62.16	54.05	62.16	**59.46**	56.76	56.76	51.35
Confusion Matrix										
14 8	15 7	15 7	13 9	16 6	14 8	17 5	14 8	15 7	15 7	12 10
7 8	9 6	7 8	7 8	8 7	9 6	9 6	7 8	9 6	9 6	8 7

For label *mediumEDSS* (0/1 - $(<5)/(\geq 5)$**):**

The via pattern recognition study was not performed since the number of patients with *mediumEDSS*≥ 5 was minimal.

First feature selection process for *highestEDSS*:

Table D.16: Static_Feature_Selection_Identification_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Gender	0	0	0	1	0	1	0	0	0	0	0	2
Age of Onset	0	0	0	1	0	0	1	0	0	0	0	2
Optic Pathways	0	1	1	0	0	0	0	0	1	0	1	**4**
Brainstem-Cerebellum	0	0	0	0	0	1	1	0	0	0	0	2
Spinal Cord	0	0	1	1	0	1	1	0	0	0	0	**4**
Age of Diagnosis	0	0	1	1	1	0	0	0	0	0	0	3
Years from Onset to Diagnosis	0	0	0	0	0	0	0	1	0	0	0	1
Evoked Potentials	0	0	0	0	0	1	0	0	0	0	0	1
CSF	0	0	0	0	0	1	0	0	0	0	0	1
Age at SP Diagnosis	0	1	1	1	1	0	1	1	1	1	1	**9**
Years from Diagnosis to SP	0	1	1	1	1	0	0	0	1	1	1	**7**
Years from Diagnosis to Onset	0	1	1	1	1	0	0	0	1	1	1	**7**
MS Course	0	1	1	1	1	1	1	0	1	1	1	**9**

Selected features: Optic Pathways, Spinal-Cord, Age at SP Diagnosis, Years from Diagnosis to SP, Years from Diagnosis to Onset, MS Course.

Table D.17: Static_Feature_Selection_Visits_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Nb of visits first 2 years	4	1	1	1	1	0	0	0	0	0	0	**4**
Suspected Relapses Ratio first 2 years	7	1	1	1	1	0	0	0	0	0	0	**4**
EDSS Medium Value/year	8	1	1	1	1	1	0	1	1	0	1	**9**
EDSS 1st year	9	1	1	1	1	1	0	1	1	0	1	**9**
EDSS first 2 years	10	1	1	1	1	1	0	1	0	0	1	**8**
EDSS std/year	11	1	1	1	1	1	0	1	0	0	1	**8**
EDSS 1st year std	12	0	0	0	0	0	0	1	0	0	0	1
EDSS first 2 years std	13	0	0	0	0	0	0	1	0	0	0	1
EDSS medium variation/Year	14	0	0	0	0	0	0	1	0	0	0	1
EDSS medium variation 1st year	15	0	0	0	0	0	0	1	0	0	0	1
EDSS medium variation first 2 years	16	0	0	0	0	0	0	1	0	0	0	1
EDSS std of variation/year	17	0	0	0	0	0	0	1	0	0	0	1
EDSS std of variation 1st year	18	0	0	0	0	0	0	1	0	0	0	1
EDSS std of variation first 2 years	19	0	0	0	0	0	0	1	0	0	0	1
EDSS Increase 1st Year	20	0	0	0	0	0	0	1	0	0	0	1
EDSS Increase first 2 years	**21**	**0**	**1**	**1**	**1**	**1**	**0**	**0**	**0**	**0**	**0**	**5**
Ratio nb EDSS increase	**22**	**0**	**1**	**1**	**1**	**1**	**0**	**1**	**0**	**0**	**1**	**7**
Ratio nb EDSS decrease 1st year	24	0	0	1	1	0	0	1	0	0	0	3
Ratio nb EDSS decrease first 2 years	25	0	0	0	1	0	0	1	0	0	0	2
Routine Visits Ratio 1st Year	27	0	0	0	0	0	1	0	0	0	0	1
No Years	**29**	**1**	**1**	**1**	**1**	**1**	**0**	**0**	**1**	**0**	**1**	**8**

Selected features: Nb of visits first 2 years, Suspected Relapses Ratio first 2 years, EDSS Medium Value/year, EDSS 1st year, EDSS first 2 years, EDSS std/year, EDSS Increase first 2 years, Ratio nb EDSS increase, No Years.

Table D.18: Static_Feature_Selection_Relapses_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Relapses Per Year	0	0	0	0	0	0	0	1	0	0	0	1
Relapses first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Pyramidal ratio	0	1	1	0	1	0	0	1	0	0	1	**5**
Pyramidal 1st year	0	0	0	0	0	1	0	0	0	0	0	1
Pyramidal first 2 years	0	1	1	0	1	0	0	0	1	0	1	**5**
BrainStem 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Brain Stem first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Neuropsycho ratio	0	0	0	0	0	0	1	1	0	0	0	2
Neuropsycho 1st year	0	0	0	0	0	0	0	0	1	0	0	1
Neuropsycho first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Cerebellum ratio	0	0	0	1	0	0	0	0	0	0	0	1
Visual ratio	0	0	0	0	0	0	1	0	0	0	0	1
Visual first 2 years	0	0	0	1	0	0	1	0	0	0	0	2
Sensory ratio	0	0	0	1	0	0	0	0	0	0	0	1
Sensory 1st year	0	0	0	0	0	1	0	0	0	0	0	1
Corticosteroids Ratio	0	0	0	0	0	1	0	0	0	0	0	1
Corticosteroids 1st year	0	0	0	0	0	1	0	0	0	0	0	1
Corticosteroids first 2 years	0	0	0	0	0	1	0	0	0	0	0	1
Average Duration	0	0	0	0	0	0	1	0	0	0	0	1
Average Duration first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
No Years	0	0	0	1	1	0	1	1	1	0	0	**5**

Selected features: Pyramidal ratio, Pyramidal first 2 years, No Years.

For label *highestEDSS* (0/1 - (< 3)/(≥ 3)):

Final Features: EDSS Medium Value/Year, EDSS 1st Year, Number of Years

Table D.19: Static_Standard_Traditional_PCA_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.65	0.79	0.79	0.74	0.78	0.77	0.78	0.79	0.79	0.80	0.80
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
80.00	**60.00**	**80.00**	**60.00**	**80.00**	**80.00**	**60.00**	**80.00**	**60.00**	**60.00**	**60.00**
50.00	**87.50**	**87.50**	**75.00**	**75.00**	**87.50**	**87.50**	**87.50**	**87.50**	**87.50**	**87.50**
80.00	**77.78**	**87.50**	**75.00**	**85.71**	**87.50**	**77.78**	**87.50**	**77.78**	**77.78**	**77.78**
50.00	**75.00**	**80.00**	**60.00**	**66.67**	**80.00**	**75.00**	**80.00**	**75.00**	**75.00**	**75.00**
61.54	**76.92**	**84.62**	**69.23**	**76.92**	**84.62**	**76.92**	**84.62**	**76.92**	**76.92**	**76.92**
Confusion Matrix										
4 4 1 4	7 1 2 3	7 1 1 4	6 2 2 3	6 2 1 4	7 1 1 4	7 1 2 3	7 1 1 4	7 1 2 3	7 1 2 3	7 1 2 3

Table D.20: Static_Standard_Traditional_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.50	0.50	0.51	0.50	0.50	0.50	0.50
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN
38.46	38.46	38.46	38.46	38.46	38.46	38.46	38.46	38.46	38.46	38.46
38.46	38.46	38.46	38.46	38.46	38.46	38.46	38.46	38.46	38.46	38.46
Confusion Matrix										
0 8 0 5	0 8 0 5	0 8 0 5	0 8 0 5	0 8 0 5	0 8 0 5	0 8 0 5	0 8 0 5	0 8 0 5	0 8 0 5	0 8 0 5

Table D.21: Static_Standard_kFold_PCA_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.64	0.64	0.67	0.65	0.72	0.72	0.65	0.63	0.64	0.64	0.65
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
70.59	**64.71**	**70.59**	**70.59**	**82.35**	**82.35**	**70.59**	**64.71**	**64.71**	**64.71**	**66.67**
85.00	**95.00**	**80.00**	**85.00**	**90.00**	**90.00**	**85.00**	**85.00**	**95.00**	**95.00**	**95.00**
77.27	**76.00**	**76.19**	**77.27**	**85.71**	**85.71**	**77.27**	**73.91**	**76.00**	**76.00**	**76.00**
80.00	**91.67**	**75.00**	**80.00**	**87.50**	**87.50**	**80.00**	**78.57**	**91.67**	**91.67**	**92.31**
78.38	**81.08**	**75.68**	**78.38**	**86.49**	**86.49**	**78.38**	**75.68**	**81.08**	**81.08**	**81.58**
Confusion Matrix										
17 3 5 12	19 1 6 11	16 4 5 12	17 3 5 12	18 2 3 14	18 2 3 14	17 3 5 12	17 3 6 11	19 1 6 11	19 1 6 11	19 1 6 12

Table D.22: Static_Standard_kFold_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.79	0.72	0.78	0.79	0.79	0.80	0.79	0.81	NA	0.80	0.75
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
94.12	**76.47**	**94.12**	**94.12**	**94.12**	**94.12**	**94.12**	**100.00**	NA	**88.24**	**76.47**
95.00	**95.00**	**95.00**	**95.00**	**95.00**	**95.00**	**95.00**	**95.00**	NA	**95.00**	**95.00**
95.00	**82.61**	**95.00**	**95.00**	**95.00**	**95.00**	**95.00**	**100.00**	NA	**90.48**	**82.61**
94.12	**92.86**	**94.12**	**94.12**	**94.12**	**94.12**	**94.12**	**94.44**	NA	**93.75**	**92.86**
94.59	**86.49**	**94.59**	**94.59**	**94.59**	**94.59**	**94.59**	**97.30**	NA	**91.89**	**86.49**
Confusion Matrix										
19 1	19 1	19 1	19 1	19 1	19 1	19 1	19 1	NA	19 1	19 1
1 16	4 13	1 16	1 16	1 16	1 16	1 16	0 17	NA	2 15	4 13

Table D.23: Static_Standard_LOO_PCA_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.67	0.72	0.70	0.67	0.70	0.70	0.67	0.68	0.72	0.53	0.56
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
58.82	**52.94**	**64.71**	**58.82**	**64.71**	**64.71**	**58.82**	**52.94**	**52.94**	35.29	41.18
75.00	**85.00**	**75.00**	**75.00**	**75.00**	**75.00**	**75.00**	**80.00**	**85.00**	70.00	70.00
68.18	**68.00**	**71.43**	**68.18**	**71.43**	**71.43**	**68.18**	**66.67**	**68.00**	56.00	58.33
66.67	**75.00**	**68.75**	**66.67**	**68.75**	**68.75**	**66.67**	**69.23**	**75.00**	50.00	53.85
67.57	**70.27**	**70.27**	**67.57**	**70.27**	**70.27**	**67.57**	**67.57**	**70.27**	54.05	56.76
Confusion Matrix										
15 5	17 3	15 5	15 5	15 5	15 5	15 5	16 4	17 3	14 6	14 6
7 10	8 9	6 11	7 10	6 11	6 11	7 10	8 9	8 9	11 6	10 7

Table D.24: Static_Standard_LOO_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.48	0.56	0.56	0.56	0.51	0.51	0.54	NA	0.65	0.65
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
47.06	35.29	**52.94**	**52.94**	**52.94**	47.06	47.06	**52.94**	NA	**58.82**	**52.94**
55.00	60.00	**60.00**	**60.00**	**60.00**	55.00	55.00	**55.00**	NA	**70.00**	**75.00**
55.00	52.17	**60.00**	**60.00**	**60.00**	55.00	55.00	**57.89**	NA	**66.67**	**65.22**
47.06	42.86	**52.94**	**52.94**	**52.94**	47.06	47.06	**50.00**	NA	**62.50**	**64.29**
51.35	48.65	**56.76**	**56.76**	**56.76**	51.35	51.35	**54.05**	NA	**64.86**	**64.86**
Confusion Matrix										
11 9	12 8	12 8	12 8	12 8	11 9	11 9	11 9	NA	14 6	15 5
9 8	11 6	8 9	8 9	8 9	9 8	9 8	8 9	NA	7 10	8 9

For label *highestEDSS* (0/1 - $(< 5)/(\geq 5)$**):**

The via pattern recognition study was not performed since the number of patients with *highestEDSS*≥ 5 was minimal.

For label *first2EDSS* (0/1 - $(< 3)/(\geq 3)$**):**

Final Features: EDSS 1st Year, Sensory 1 Ratio.

Table D.25: Static_Standard_Traditional_PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	0.72	0.68	0.57	0.51	0.58	0.64	0.68	0.72	0.73	0.72
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
66.67	66.67	66.67	33.33	33.33	33.33	66.67	66.67	66.67	66.67	66.67
35.00	65.00	65.00	70.00	60.00	70.00	66.67	65.00	65.00	65.00	65.00
87.50	92.86	92.86	87.50	85.71	87.50	93.33	92.86	92.86	92.86	92.86
13.33	22.22	22.22	14.29	11.11	14.29	22.22	22.22	22.22	22.22	22.22
39.13	65.22	65.22	65.22	56.52	65.22	66.67	65.22	65.22	65.22	65.22
Confusion Matrix										
7 13	13 7	13 7	14 6	12 8	14 6	14 7	13 7	13 7	13 7	13 7
1 2	1 2	1 2	2 1	2 1	2 1	1 2	1 2	1 2	1 2	1 2

Table D.26: Static_Standard_Traditional_first2EDSS< 3

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.52	0.58	0.58	0.60	0.60	0.64	0.64	0.60	0.58	0.68	0.68
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
10.00	20.00	25.00	30.00	30.00	30.00	30.00	35.00	20.00	40.00	15.00
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
14.29	15.79	16.67	17.65	17.65	17.65	17.65	18.75	15.79	20.00	15.00
21.74	30.43	34.78	39.13	39.13	39.13	39.13	43.48	30.43	47.83	26.09
Confusion Matrix										
2 18	4 16	5 15	6 14	6 14	6 14	6 14	7 13	4 16	8 12	3 17
0 3	0 3	0 3	0 3	0 3	0 3	0 3	0 3	0 3	0 3	0 3

Table D.27: Static_Standard_kFold_PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.33	0.35	0.35	0.29	0.52	0.47	0.33	0.34	0.34	0.56	0.49
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
30.00	30.00	30.00	30.00	**60.00**	**50.00**	30.00	30.00	30.00	**80.00**	60.00
77.78	85.19	81.48	92.59	**81.48**	**81.48**	81.48	81.48	85.19	**70.37**	70.37
75.00	76.67	75.86	78.13	**84.62**	**81.48**	75.86	75.86	76.67	**90.48**	82.61
33.33	42.86	37.50	60.00	**54.55**	**50.00**	37.50	37.50	42.86	**50.00**	42.86
64.86	70.27	67.57	75.68	**75.68**	**72.97**	67.57	67.57	70.27	**72.97**	67.57
Confusion Matrix										
21 6 7 3	23 4 7 3	22 5 7 3	25 2 7 3	22 5 4 6	22 5 5 5	22 5 7 3	22 5 7 3	23 4 7 3	19 8 2 8	19 8 4 6

Table D.28: Static_Standard_kFold_first2EDSS< 3

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.58	0.58	0.55	0.52	0.62	0.46	0.46	0.55	NA	0.58	0.64
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
80.00	**80.00**	**80.00**	**70.00**	**90.00**	**60.00**	**60.00**	**80.00**	NA	90.00	**90.00**
92.59	**96.30**	**96.30**	**96.30**	**96.30**	**96.30**	**100.00**	**100.00**	NA	62.96	**92.59**
92.59	**92.86**	**92.86**	**89.66**	**96.30**	**86.67**	**87.10**	**93.10**	NA	94.44	**96.15**
80.00	**88.89**	**88.89**	**87.50**	**90.00**	**85.71**	**100.00**	**100.00**	NA	47.37	**81.82**
89.19	**91.89**	**91.89**	**89.19**	**94.59**	**86.49**	**89.19**	**94.59**	NA	70.27	**91.89**
Confusion Matrix										
25 2 2 8	26 1 2 8	26 1 2 8	26 1 3 7	26 1 1 9	26 1 4 6	27 0 4 6	27 0 2 8	NA NA	17 10 1 9	25 2 1 9

Table D.29: Static_Standard_LOO_PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.42	0.41	0.46	0.44	0.38	0.33	0.41	0.42	0.58	0.63
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
20.00	10.00	10.00	10.00	20.00	10.00	0.00	10.00	10.00	60.00	60.00
74.07	77.78	74.07	85.19	66.67	66.67	70.37	74.07	77.78	59.26	70.37
71.43	70.00	68.97	71.88	69.23	66.67	65.52	68.97	70.00	80.00	82.61
22.22	14.29	12.50	20.00	18.18	10.00	0.00	12.50	14.29	35.29	42.86
59.46	59.46	56.76	64.86	54.05	51.35	51.35	56.76	59.46	59.46	67.57
Confusion Matrix										
20 7 8 2	21 6 9 1	20 7 9 1	23 4 9 1	18 9 8 2	18 9 9 1	19 8 10 0	20 7 9 1	21 6 9 1	16 11 4 6	19 8 4 6

Table D.30: Static_Standard_LOO_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.47	0.54	0.49	0.59	0.60	0.54	0.49	NA	0.60	0.57
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
30.00	20.00	30.00	20.00	40.00	30.00	20.00	20.00	NA	70.00	40.00
74.07	74.07	77.78	77.78	77.78	85.19	85.19	77.78	NA	55.56	74.07
74.07	71.43	75.00	72.41	77.78	76.67	74.19	72.41	NA	83.33	76.92
30.00	22.22	33.33	25.00	40.00	42.86	33.33	25.00	NA	36.84	36.36
62.16	59.46	64.86	62.16	67.57	70.27	67.57	62.16	NA	59.46	64.86
Confusion Matrix										
20 7	20 7	21 6	21 6	21 6	23 4	23 4	21 6	NA	15 12	20 7
7 3	8 2	7 3	8 2	6 4	7 3	8 2	8 2	NA	3 7	6 4

For label *first2EDSS* (0/1 - $(< 5)/(\geq 5)$):

The via pattern recognition study was not performed since the number of patients with *first2EDSS*≥ 5 was minimal.

D.1.1.2 Investigation procedure

In the investigation procedure, after excluding on purpose features that are already clinically obviously for a physician, a final feature test is made. The selected one was the evaluation of the features importance in order to build a decision tree (already used in previous tests).

For label *msCourse* (0/1 - RR/SP):

Features before selection: Age at Onset, Number of visits per year, Pyramidal ratio, Pyramidal 1st year, Pyramidal first 2 years.

Excluded features: EDSS Medium Value/year, EDSS 1st year, EDSS first 2 years, EDSS std/year.

Final Features:Age at Onset, Number of visits per year, Pyramidal 1 ratio.

Table D.31: Static_Investigation_Traditional_PCA_msCourse

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.56	0.64	0.63	0.57	0.56	0.60	0.58	0.64	0.64	0.64	0.63
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
33.33	66.67	66.67	66.67	33.33	33.33	33.33	33.33	66.67	66.67	66.67
77.78	72.22	72.22	61.11	77.78	88.89	94.44	88.89	72.22	72.22	72.22
87.50	92.86	92.86	91.67	87.50	88.89	89.47	88.89	92.86	92.86	92.86
20.00	28.57	28.57	22.22	20.00	33.33	50.00	33.33	28.57	28.57	28.57
71.43	71.43	71.43	61.90	71.43	80.95	85.71	80.95	71.43	71.43	71.43
Confusion Matrix										
14 4 2 1	13 5 1 2	13 5 1 2	11 7 1 2	14 4 2 1	16 2 2 1	17 1 2 1	16 2 2 1	13 5 1 2	13 5 1 2	13 5 1 2

Table D.32: Static_Investigation_Traditional_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.62	NA	0.52	0.46	0.56	0.59	0.63	0.62	0.59	0.60
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
66.67	66.67	NA	33.33	33.33	33.33	33.33	66.67	66.67	66.67	66.67
50.00	66.67	NA	66.67	44.44	77.78	83.33	55.56	66.67	38.89	66.67
90.00	92.31	NA	85.71	80.00	87.50	88.24	90.91	92.31	87.50	92.31
18.18	25.00	NA	14.29	9.09	20.00	25.00	20.00	25.00	15.38	25.00
52.38	66.67	NA	61.90	42.86	71.43	76.19	57.14	66.67	42.86	66.67
Confusion Matrix										
9 9	12 6	NA	12 6	8 10	14 4	15 3	10 8	12 6	7 11	12 6
1 2	1 2	NA	2 1	2 1	2 1	2 1	1 2	1 2	1 2	1 2

Table D.33: Static_Investigation_kFold_PCA_msCourse

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.34	0.32	0.39	0.20	0.31	0.29	0.27	0.34	0.30	0.50	0.45
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
27.27	27.27	36.36	18.18	18.18	27.27	18.18	27.27	27.27	**54.55**	45.45
76.92	92.31	84.62	92.31	69.23	88.46	92.31	84.62	92.31	**80.77**	76.92
71.43	75.00	75.86	72.73	66.67	74.19	72.73	73.33	75.00	**80.77**	76.92
33.33	60.00	50.00	50.00	20.00	50.00	50.00	42.86	60.00	**54.55**	45.45
62.16	72.97	70.27	70.27	54.05	70.27	70.27	67.57	72.97	**72.97**	67.57
Confusion Matrix										
20 6 8 3	24 2 8 3	22 4 7 4	24 2 9 2	18 8 9 2	23 3 8 3	24 2 9 2	22 4 8 3	24 2 8 3	21 5 5 6	20 6 6 5

Table D.34: Static_Investigation_kFold_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.32	0.39	0.37	0.02	0.33	0.33	0.27	0.37	0.37	0.55	0.45
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
27.27	36.36	36.36	0.00	27.27	27.27	25.00	36.36	36.36	**63.64**	45.45
73.08	92.31	92.31	100.00	80.77	80.77	88.46	92.31	92.31	**80.77**	73.08
70.37	77.42	77.42	70.27	72.41	72.41	71.88	77.42	77.42	**84.00**	76.00
30.00	66.67	66.67	NaN	37.50	37.50	50.00	66.67	66.67	**58.33**	41.67
59.46	75.68	75.68	70.27	64.86	64.86	68.42	75.68	75.68	**75.68**	64.86
Confusion Matrix										
19 7 8 3	24 2 7 4	24 2 7 4	26 0 11 0	21 5 8 3	21 5 8 3	23 3 9 3	24 2 7 4	24 2 7 4	21 5 4 7	19 7 6 5

Table D.35: Static_Investigation_LOO_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.45	0.44	0.47	0.34	0.50	0.44	0.56	0.49	0.44	0.48	0.48
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
18.18	9.09	18.18	0.00	27.27	9.09	18.18	18.18	9.09	27.27	27.27
73.08	84.62	76.92	88.46	73.08	84.62	88.46	80.77	84.62	69.23	69.23
67.86	68.75	68.97	67.65	70.37	68.75	71.88	70.00	68.75	69.23	69.23
22.22	20.00	25.00	0.00	30.00	20.00	40.00	28.57	20.00	27.27	27.27
56.76	62.16	59.46	62.16	59.46	62.16	67.57	62.16	62.16	56.76	56.76
Confusion Matrix										
19 7	22 4	20 6	23 3	19 7	22 4	23 3	21 5	22 4	18 8	18 8
9 2	10 1	9 2	11 0	8 3	10 1	9 2	9 2	10 1	8 3	8 3

Table D.36: Static_Investigation_LOO_msCourse

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.60	0.62	0.62	0.00	0.55	0.55	0.68	0.52	0.62	0.53	0.65
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
36.36	27.27	27.27	0.00	27.27	27.27	27.27	18.18	27.27	36.36	**54.55**
80.77	88.46	88.46	100.00	80.77	80.77	92.31	84.62	88.46	69.23	**76.92**
75.00	74.19	74.19	70.27	72.41	72.41	75.00	70.97	74.19	72.00	**80.00**
44.44	50.00	50.00	NaN	37.50	37.50	60.00	33.33	50.00	33.33	**50.00**
67.57	70.27	70.27	70.27	64.86	64.86	72.97	64.86	70.27	59.46	**70.27**
Confusion Matrix										
21 5 7 4	23 3 8 3	23 3 8 3	26 0 11 0	21 5 8 3	21 5 8 3	24 2 8 3	22 4 9 2	23 3 8 3	18 8 7 4	20 6 5 6

For label *mediumEDSS* (0/1 - $(< 3)/(\geq 3)$**):**

Features before selection: Gender, Age of Onset, Spinal Cord, Nb of Visits 1st Year, Nb of visits first 2 years, Number of Years, Pyramidal ratio, Pyramidal first 2 years, Sensory 1 ratio.

Excluded features: EDSS 1st year, EDSS std/year, EDSS 1st year std, EDSS std of variation/year, EDSS Increase first 2 years, Ratio nb EDSS increase, Ratio nb EDSS decrease first 2 years.

Final Features: Gender, Age of Onset, Nb of Visits first 2 Years, Pyramidal ratio, Number of years.

Table D.37: Static_Investigation_Traditional_PCA_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.73	0.71	0.64	0.63	0.62	0.59	0.67	0.73	0.73	0.75
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
75.00	**75.00**	**75.00**	75.00	75.00	75.00	75.00	50.00	**75.00**	**75.00**	**75.00**
45.45	**72.73**	**72.73**	54.55	54.55	54.55	54.55	72.73	**72.73**	**72.73**	**72.73**
83.33	**88.89**	**88.89**	85.71	85.71	85.71	85.71	80.00	**88.89**	**88.89**	**88.89**
33.33	**50.00**	**50.00**	37.50	37.50	37.50	37.50	40.00	**50.00**	**50.00**	**50.00**
53.33	**73.33**	**73.33**	60.00	60.00	60.00	60.00	66.67	**73.33**	**73.33**	**73.33**
Confusion Matrix										
5 6 1 3	8 3 1 3	8 3 1 3	6 5 1 3	6 5 1 3	6 5 1 3	6 5 1 3	8 3 2 2	8 3 1 3	8 3 1 3	8 3 1 3

Table D.38: Static_Investigation_Traditional_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.65	0.62	0.67	0.56	0.62	0.62	0.68	0.65	0.66	0.62
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
50.00	75.00	50.00	**75.00**	50.00	50.00	**50.00**	50.00	75.00	75.00	75.00
63.64	54.55	72.73	**72.73**	63.64	63.64	**81.82**	72.73	54.55	45.45	54.55
77.78	85.71	80.00	**88.89**	77.78	77.78	**81.82**	80.00	85.71	83.33	85.71
33.33	37.50	40.00	**50.00**	33.33	33.33	**50.00**	40.00	37.50	33.33	37.50
60.00	60.00	66.67	**73.33**	60.00	60.00	**73.33**	66.67	60.00	53.33	60.00
Confusion Matrix										
7 4 2 2	6 5 1 3	8 3 2 2	8 3 1 3	7 4 2 2	7 4 2 2	9 2 2 2	8 3 2 2	6 5 1 3	5 6 1 3	6 5 1 3

Table D.39: Static_Investigation_kFold_PCA_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.57	0.54	0.14	0.49	0.44	0.53	0.48	0.57	0.58	0.56
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
46.67	**60.00**	**53.33**	6.67	46.67	40.00	**53.33**	46.67	**60.00**	**66.67**	**60.00**
63.64	**90.91**	**81.82**	77.27	72.73	72.73	**72.73**	81.82	**90.91**	**72.73**	**86.36**
63.64	**76.92**	**72.00**	54.84	66.67	64.00	**69.57**	69.23	**76.92**	**76.19**	**76.00**
46.67	**81.82**	**66.67**	16.67	53.85	50.00	**57.14**	63.64	**81.82**	**62.50**	**75.00**
56.76	**78.38**	**70.27**	48.65	62.16	59.46	**64.86**	67.57	**78.38**	**70.27**	**75.68**
Confusion Matrix										
14 8 8 7	20 2 6 9	18 4 7 8	17 5 14 1	16 6 8 7	16 6 9 6	16 6 7 8	18 4 8 7	20 2 6 9	16 6 5 10	19 3 6 9

Table D.40: Static_Investigation_kFold_mediumEDSS< 3

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.53	0.57	0.49	0.58	0.49	0.62	0.57	0.56	NA	0.55	0.62
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
53.33	**60.00**	46.67	**60.00**	46.67	**66.67**	**53.33**	**53.33**	NA	**66.67**	**66.67**
63.64	**86.36**	81.82	**77.27**	68.18	**81.82**	**86.36**	**86.36**	NA	**68.18**	**86.36**
66.67	**76.00**	69.23	**73.91**	65.22	**78.26**	**73.08**	**73.08**	NA	**75.00**	**79.17**
50.00	**75.00**	63.64	**64.29**	50.00	**71.43**	**72.73**	**72.73**	NA	**58.82**	**76.92**
59.46	**75.68**	67.57	**70.27**	59.46	**75.68**	**72.97**	**72.97**	NA	**67.57**	**78.38**
Confusion Matrix										
14 8	19 3	18 4	17 5	15 7	18 4	19 3	19 3	NA	15 7	19 3
7 8	6 9	8 7	6 9	8 7	5 10	7 8	7 8	NA	5 10	5 10

Table D.41: Static_Investigation_LOO_PCA_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.58	0.54	0.57	0.50	0.54	0.57	0.52	0.56	0.54	0.58	0.56
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
53.33	33.33	40.00	13.33	40.00	40.00	40.00	33.33	33.33	**66.67**	**60.00**
63.64	72.73	72.73	86.36	68.18	72.73	63.64	77.27	72.73	**72.73**	**86.36**
66.67	61.54	64.00	59.38	62.50	64.00	60.87	62.96	61.54	**76.19**	**76.00**
50.00	45.45	50.00	40.00	46.15	50.00	42.86	50.00	45.45	**62.50**	**75.00**
59.46	56.76	59.46	56.76	56.76	59.46	54.05	59.46	56.76	**70.27**	**75.68**
Confusion Matrix										
14 8	16 6	16 6	19 3	15 7	16 6	14 8	17 5	16 6	16 6	19 3
7 8	10 5	9 6	13 2	9 6	9 6	9 6	10 5	10 5	5 10	6 9

Table D.42: Static_Investigation_LOO_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.51	0.50	0.35	0.46	0.40	0.45	0.47	0.51	0.43	0.48
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
46.67	33.33	26.67	20.00	33.33	26.67	26.67	26.67	33.33	40.00	33.33
59.09	68.18	72.73	50.00	59.09	54.55	63.64	68.18	68.18	45.45	63.64
61.90	60.00	59.26	47.83	56.52	52.17	56.00	57.69	60.00	52.63	58.33
43.75	41.67	40.00	21.43	35.71	28.57	33.33	36.36	41.67	33.33	38.46
54.05	54.05	54.05	37.84	48.65	43.24	48.65	51.35	54.05	43.24	51.35
Confusion Matrix										
13 9	15 7	16 6	11 11	13 9	12 10	14 8	15 7	15 7	10 12	14 8
8 7	10 5	11 4	12 3	10 5	11 4	11 4	11 4	10 5	9 6	10 5

For label *mediumEDSS* (0/1 - (< 5)/(≥ 5)):

The via pattern recognition study was not performed since the number of patients with *mediumEDSS*≥ 5 was minimal.

For label *highestEDSS* (0/1 - (< 3)/(≥ 3)):

Features before selection: Optic Pathways, Spinal Cord, MS Course, Number of years, Pyramidal 1 ratio, Pyramidal first 2 years, Neuropsycho 1 ratio, Visual first 2 years.

Excluded features: Nb of visits first 2 years, EDSS Medium Value/year, EDSS 1st year, EDSS first 2 years, EDSS std/year, EDSS Increase first 2 years, Ratio nb EDSS increase, Ratio nb EDSS decrease.

Final features: MS Course, Number of years, Pyramidal 1 ratio.

Table D.43: Static_Investigation_Traditional_PCA_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.73	0.76	0.72	0.66	0.66	0.66	0.71	0.74	0.76	0.76	0.75
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
60.00	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**
87.50	**87.50**	**75.00**	**75.00**	**62.50**	**75.00**	**87.50**	**75.00**	**87.50**	**87.50**	**87.50**
77.78	**77.78**	**75.00**	**75.00**	**71.43**	**75.00**	**77.78**	**75.00**	**77.78**	**77.78**	**77.78**
75.00	**75.00**	**60.00**	**60.00**	**50.00**	**60.00**	**75.00**	**60.00**	**75.00**	**75.00**	**75.00**
76.92	**76.92**	**69.23**	**69.23**	**61.54**	**69.23**	**76.92**	**69.23**	**76.92**	**76.92**	**76.92**
Confusion Matrix										
7 1 2 3	7 1 2 3	6 2 2 3	6 2 2 3	5 3 2 3	6 2 2 3	7 1 2 3	6 2 2 3	7 1 2 3	7 1 2 3	7 1 2 3

Table D.44: Static_Investigation_Traditional_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.73	0.76	0.72	0.66	0.66	0.66	0.71	0.74	0.76	0.76	0.75
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
60.00	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**	**60.00**
87.50	**87.50**	**75.00**	**75.00**	**62.50**	**75.00**	**87.50**	**75.00**	**87.50**	**87.50**	**87.50**
77.78	**77.78**	**75.00**	**75.00**	**71.43**	**75.00**	**77.78**	**75.00**	**77.78**	**77.78**	**77.78**
75.00	**75.00**	**60.00**	**60.00**	**50.00**	**60.00**	**75.00**	**60.00**	**75.00**	**75.00**	**75.00**
76.92	**76.92**	**69.23**	**69.23**	**61.54**	**69.23**	**76.92**	**69.23**	**76.92**	**76.92**	**76.92**
Confusion Matrix										
7 1 2 3	7 1 2 3	6 2 2 3	6 2 2 3	5 3 2 3	6 2 2 3	7 1 2 3	6 2 2 3	7 1 2 3	7 1 2 3	7 1 2 3

Table D.45: Static_Investigation_kFold_PCA_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.60	0.63	0.48	0.54	0.54	0.66	0.62	0.61	0.63	0.62	0.62
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
64.71	**64.71**	82.35	**52.94**	**52.94**	**70.59**	**64.71**	**64.71**	**64.71**	**64.71**	**64.71**
75.00	**95.00**	45.00	**75.00**	**75.00**	**80.00**	**80.00**	**75.00**	**95.00**	**90.00**	**95.00**
71.43	**76.00**	75.00	**65.22**	**65.22**	**76.19**	**72.73**	**71.43**	**76.00**	**75.00**	**76.00**
68.75	**91.67**	56.00	**64.29**	**64.29**	**75.00**	**73.33**	**68.75**	**91.67**	**84.62**	**91.67**
70.27	**81.08**	62.16	**64.86**	**64.86**	**75.68**	**72.97**	**70.27**	**81.08**	**78.38**	**81.08**
Confusion Matrix										
15 5 6 11	19 1 6 11	9 11 3 14	15 5 8 9	15 5 8 9	16 4 5 12	16 4 6 11	15 5 6 11	19 1 6 11	18 2 6 11	19 1 6 11

Table D.46: Static_Investigation_kFold_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.63	0.62	NA	0.73	0.65	0.64	0.64	NA	NA	0.60	0.65
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
70.59	**64.71**	NA	**82.35**	**70.59**	**64.71**	**64.71**	NA	NA	**58.82**	**64.71**
85.00	**90.00**	NA	**90.00**	**80.00**	**95.00**	**95.00**	NA	NA	**95.00**	**90.00**
77.27	**75.00**	NA	**85.71**	**76.19**	**76.00**	**76.00**	NA	NA	**73.08**	**75.00**
80.00	**84.62**	NA	**87.50**	**75.00**	**91.67**	**91.67**	NA	NA	**90.91**	**84.62**
78.38	**78.38**	NA	**86.49**	**75.68**	**81.08**	**81.08**	NA	NA	**78.38**	**78.38**
Confusion Matrix										
17 3	18 2	NA	18 2	16 4	19 1	19 1	NA	NA	19 1	18 2
5 12	6 11	NA	3 14	5 12	6 11	6 11	NA	NA	7 10	6 11

Table D.47: Static_Investigation_LOO_PCA_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.63	0.47	0.51	0.53	0.62	0.56	0.54	0.63	0.44	0.47
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
35.29	41.18	64.71	47.06	41.18	**52.94**	47.06	47.06	41.18	29.41	29.41
60.00	80.00	30.00	55.00	65.00	**70.00**	65.00	60.00	80.00	60.00	65.00
52.17	61.54	50.00	55.00	56.52	**63.64**	59.09	57.14	61.54	50.00	52.00
42.86	63.64	44.00	47.06	50.00	**60.00**	53.33	50.00	63.64	38.46	41.67
48.65	62.16	45.95	51.35	54.05	**62.16**	56.76	54.05	62.16	45.95	48.65
Confusion Matrix										
12 8	16 4	6 14	11 9	13 7	14 6	13 7	12 8	16 4	12 8	13 7
11 6	10 7	6 11	9 8	10 7	8 9	9 8	9 8	10 7	12 5	12 5

Table D.48: Static_Investigation_LOO_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.49	0.54	0.54	0.53	0.59	0.49	NA	0.63	0.56
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
41.18	35.29	47.06	47.06	47.06	35.29	41.18	47.06	NA	41.18	41.18
60.00	65.00	50.00	60.00	60.00	70.00	75.00	50.00	NA	80.00	70.00
54.55	54.17	52.63	57.14	57.14	56.00	60.00	52.63	NA	61.54	58.33
46.67	46.15	44.44	50.00	50.00	50.00	58.33	44.44	NA	63.64	53.85
51.35	51.35	48.65	54.05	54.05	54.05	59.46	48.65	NA	62.16	56.76
Confusion Matrix										
12 8	13 7	10 10	12 8	12 8	14 6	15 5	10 10	NA	16 4	14 6
10 7	11 6	9 8	9 8	9 8	11 6	10 7	9 8	NA	10 7	10 7

For label *highestEDSS* (0/1 - (< 5)/(≥ 5)):

The via pattern recognition study was not performed since the number of patients with *highestEDSS*≥ 5 was minimal.

Features before selection: Gender, Pyramidal 1 ratio, Pyramidal first 2 years, BrainStem 1st year, Visual 1 ratio, Visual first 2 years, Sensory 1 ratio.

Excluded features: EDSS 1st year, EDSS std/year, EDSS first 2 years std, EDSS Increase first 2 years, Ratio nb EDSS increase.

Final features: Pyramidal ratio, Sensory ratio.

Table D.49: Static_Investigation_Traditional__PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.70	0.66	0.57	0.56	0.60	0.63	0.63	0.70	0.70	0.69
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
66.67	66.67	66.67	33.33	33.33	66.67	66.67	66.67	66.67	66.67	66.67
35.00	65.00	60.00	75.00	75.00	65.00	65.00	65.00	65.00	65.00	65.00
87.50	92.86	92.31	88.24	88.24	92.86	92.86	92.86	92.86	92.86	92.86
13.33	22.22	20.00	16.67	16.67	22.22	22.22	22.22	22.22	22.22	22.22
39.13	65.22	60.87	69.57	69.57	65.22	65.22	65.22	65.22	65.22	65.22
Confusion Matrix										
7 13 1 2	13 7 1 2	12 8 1 2	15 5 2 1	15 5 2 1	13 7 1 2	13 7 1 2	13 7 1 2	13 7 1 2	13 7 1 2	13 7 1 2

Table D.50: Static_Investigation_Traditional_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.69	NA	0.58	0.51	0.61	0.65	0.66	0.69	0.67	0.68
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
66.67	66.67	NA	66.67	66.67	66.67	66.67	66.67	66.67	66.67	66.67
60.00	70.00	NA	50.00	45.00	50.00	50.00	55.00	55.00	65.00	65.00
92.31	93.33	NA	90.91	90.00	90.91	90.91	91.67	91.67	92.86	92.86
20.00	25.00	NA	16.67	15.38	16.67	16.67	18.18	18.18	22.22	22.22
60.87	69.57	NA	52.17	47.83	52.17	52.17	56.52	56.52	65.22	65.22
Confusion Matrix										
12 8 1 2	14 6 1 2	NA NA	10 10 1 2	9 11 1 2	10 10 1 2	10 10 1 2	11 9 1 2	11 9 1 2	13 7 1 2	13 7 1 2

Table D.51: Static_Investigation_kFold_PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.30	0.27	0.44	0.27	0.54	0.42	0.39	0.28	0.26	0.56	0.45
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
30.00	20.00	**50.00**	30.00	**60.00**	40.00	30.00	20.00	20.00	70.00	60.00
74.07	88.89	**81.48**	96.30	**77.78**	81.48	77.78	85.19	88.89	66.67	70.37
74.07	75.00	**81.48**	78.79	**84.00**	78.57	75.00	74.19	75.00	85.71	82.61
30.00	40.00	**50.00**	75.00	**50.00**	44.44	33.33	33.33	40.00	43.75	42.86
62.16	70.27	**72.97**	78.38	**72.97**	70.27	64.86	67.57	70.27	67.57	67.57
Confusion Matrix										
20 7	24 3	22 5	26 1	21 6	22 5	21 6	23 4	24 3	18 9	19 8
7 3	8 2	5 5	7 3	4 6	6 4	7 3	8 2	8 2	3 7	4 6

Table D.52: Static_Investigation_kFold_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.34	0.30	0.35	0.07	0.44	0.37	0.31	0.32	0.28	0.45	0.46
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
40.00	30.00	40.00	10.00	50.00	30.00	30.00	30.00	30.00	60.00	60.00
88.89	96.30	88.89	100.00	66.67	62.96	85.19	88.89	96.30	55.56	59.26
80.00	78.79	80.00	75.00	78.26	70.83	76.67	77.42	78.79	78.95	80.00
57.14	75.00	57.14	100.00	35.71	23.08	42.86	50.00	75.00	33.33	35.29
75.68	78.38	75.68	75.68	62.16	54.05	70.27	72.97	78.38	56.76	59.46
Confusion Matrix										
24 3 6 4	26 1 7 3	24 3 6 4	27 0 9 1	18 9 5 5	17 10 7 3	23 4 7 3	24 3 7 3	26 1 7 3	15 12 4 6	16 11 4 6

Table D.53: Static_Investigation_LOO_PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.46	0.57	0.63	0.55	0.54	0.59	0.44	0.46	0.52	0.47
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
30.00	10.00	30.00	20.00	40.00	30.00	40.00	10.00	10.00	50.00	30.00
81.48	85.19	81.48	92.59	70.37	77.78	77.78	81.48	85.19	55.56	62.96
75.86	71.88	75.86	75.76	76.00	75.00	77.78	70.97	71.88	75.00	70.83
37.50	20.00	37.50	50.00	33.33	33.33	40.00	16.67	20.00	29.41	23.08
67.57	64.86	67.57	72.97	62.16	64.86	67.57	62.16	64.86	54.05	54.05
Confusion Matrix										
22 5 7 3	23 4 9 1	22 5 7 3	25 2 8 2	19 8 6 4	21 6 7 3	21 6 6 4	22 5 9 1	23 4 9 1	15 12 5 5	17 10 7 3

Table D.54: Static_Investigation_LOO_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.63	0.58	0.88	0.63	0.63	0.60	0.58	0.63	0.44	0.44
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
20.00	20.00	20.00	10.00	60.00	60.00	30.00	20.00	20.00	40.00	40.00
85.19	92.59	88.89	100.00	70.37	70.37	85.19	88.89	92.59	44.44	44.44
74.19	75.76	75.00	75.00	82.61	82.61	76.67	75.00	75.76	66.67	66.67
33.33	50.00	40.00	100.00	42.86	42.86	42.86	40.00	50.00	21.05	21.05
67.57	72.97	70.27	75.68	67.57	67.57	70.27	70.27	72.97	43.24	43.24
Confusion Matrix										
23 4 8 2	25 2 8 2	24 3 8 2	27 0 9 1	19 8 4 6	19 8 4 6	23 4 7 3	24 3 8 2	25 2 8 2	12 15 6 4	12 15 6 4

For label *first2EDSS* (0/1 - (< 5)/(≥ 5)):

The via pattern recognition study was not performed since the number of patients with *first2EDSS*≥ 5 was minimal.

D.1.2 Ground zero Set

D.1.2.1 Standard procedure

For label *msCourse* (0/1 - RR/SP):

Final Features: Relapse age, Time since onset.

Table D.55: GroundZero_Standard_Traditional_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.66	0.60	0.58	0.55	0.56	0.58	0.65	0.66	0.51	0.50
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
100.00	66.67	66.67	66.67	66.67	66.67	33.33	66.67	66.67	33.33	33.33
11.11	66.67	44.44	50.00	44.44	50.00	72.22	72.22	66.67	61.11	55.56
100.00	92.31	88.89	90.00	88.89	90.00	86.67	92.86	92.31	84.62	83.33
15.79	25.00	16.67	18.18	16.67	18.18	16.67	28.57	25.00	12.50	11.11
23.81	66.67	47.62	52.38	47.62	52.38	66.67	71.43	66.67	57.14	52.38
Confusion Matrix										
2 16 0 3	12 6 1 2	8 10 1 2	9 9 1 2	8 10 1 2	9 9 1 2	13 5 2 1	13 5 1 2	12 6 1 2	11 7 2 1	10 8 2 1

Table D.56: GroundZero_Standard_Traditional_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.60	0.50	NA	0.56	0.59	0.60	0.59	NA	0.50	0.50	0.50
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
100.00	100.00	NA	100.00	66.67	100.00	100.00	NA	100.00	100.00	100.00
22.22	0.00	NA	16.67	33.33	27.78	22.22	NA	0.00	0.00	0.00
100.00	NaN	NA	100.00	85.71	100.00	100.00		NaN	NaN	NaN
17.65	14.29	NA	16.67	14.29	18.75	17.65	NA	14.29	14.29	14.29
33.33	14.29	NA	28.57	38.10	38.10	33.33	NA	14.29	14.29	14.29
Confusion Matrix										
4 14 0 3	0 18 0 3	NA NA	3 15 0 3	6 12 1 2	5 13 0 3	4 14 0 3	NA NA	0 18 0 3	0 18 0 3	0 18 0 3

Table D.57: GroundZero_Standard_kFold_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.37	0.38	0.37	0.07	0.27	0.29	0.13	0.42	NA	0.3603	0.3573
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
45.45	36.36	36.36	0.00	18.18	18.18	9.09	45.45	NA	36.36	36.36
88.46	80.77	84.62	92.31	73.08	84.62	88.46	80.77	NA	73.08	76.92
79.31	75.00	75.86	68.57	67.86	70.97	69.70	77.78	NA	73.08	74.07
62.50	44.44	50.00	0.00	22.22	33.33	25.00	50.00	NA	36.36	40.00
75.68	67.57	70.27	64.86	56.76	64.86	64.86	70.27	NA	62.16	64.86
Confusion Matrix										
23 3 6 5	21 5 7 4	22 4 7 4	24 2 11 0	19 7 9 2	22 4 9 2	23 3 10 1	21 5 6 5	NA NA	19 7 7 4	20 6 7 4

Table D.58: GroundZero_Standard_kFold_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.61	0.34	0.44	0.43	0.53	0.62	0.55	0.36	NA	0.49	0.60
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
72.73	36.36	45.45	45.45	**63.64**	**81.82**	**63.64**	36.36	NA	**54.55**	**72.73**
88.46	96.15	92.31	88.46	**84.62**	**88.46**	**88.46**	96.15	NA	**88.46**	**80.77**
88.46	78.13	80.00	79.31	**84.62**	**92.00**	**85.19**	78.13	NA	**82.14**	**87.50**
72.73	80.00	71.43	62.50	**63.64**	**75.00**	**70.00**	80.00	NA	**66.67**	**61.54**
83.78	78.38	78.38	75.68	**78.38**	**86.49**	**81.08**	78.38	NA	**78.38**	**78.38**
Confusion Matrix										
23 3 3 8	25 1 7 4	24 2 6 5	23 3 6 5	22 4 4 7	23 3 2 9	23 3 4 7	25 1 7 4	NA NA	23 3 5 6	21 5 3 8

Table D.59: GroundZero_Standard_LOO_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.62	0.60	0.63	0.52	0.60	0.76	0.34	0.71	0.60	0.60	0.60
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
18.18	9.09	9.09	9.09	18.18	18.18	0.00	9.09	9.09	36.36	36.36
84.62	69.23	73.08	92.31	73.08	80.77	88.46	65.38	69.23	80.77	80.77
70.97	64.29	65.52	70.59	67.86	70.00	67.65	62.96	64.29	75.00	75.00
33.33	11.11	12.50	33.33	22.22	28.57	0.00	10.00	11.11	44.44	44.44
64.86	51.35	54.05	67.57	56.76	62.16	62.16	48.65	51.35	67.57	67.57
Confusion Matrix										
22 4 9 2	18 8 10 1	19 7 10 1	24 2 10 1	19 7 9 2	21 5 9 2	23 3 11 0	17 9 10 1	18 8 10 1	21 5 7 4	21 5 7 4

Table D.60: GroundZero_Standard_LOO_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.61	0.49	0.47	0.48	0.47	0.48	0.56	0.61	0.38	0.38
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
27.27	18.18	18.18	18.18	27.27	27.27	27.27	18.18	18.18	9.09	18.18
65.38	92.31	80.77	76.92	69.23	65.38	69.23	88.46	92.31	69.23	53.85
68.00	72.73	70.00	68.97	69.23	68.00	69.23	71.88	72.73	64.29	60.87
25.00	50.00	28.57	25.00	27.27	25.00	27.27	40.00	50.00	11.11	14.29
54.05	70.27	62.16	59.46	56.76	54.05	56.76	67.57	70.27	51.35	43.24
Confusion Matrix										
17 9	24 2	21 5	20 6	18 8	17 9	18 8	23 3	24 2	18 8	14 12
8 3	9 2	9 2	9 2	8 3	8 3	8 3	9 2	9 2	10 1	9 2

First feature selection process for *highestEDSS*:

Table D.61: GroundZero_Feature_Selection_Identification_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Gender	0	0	1	1	1	1	0	0	0	0	0	**4**
Age of Onset	0	0	0	0	1	0	1	1	0	0	0	**3**
Optic Pathways	0	1	1	0	0	0	1	0	1	0	1	**5**
Brainstem-Cerebellum	0	0	0	0	0	1	0	0	0	0	0	1
Spinal Cord	0	0	1	1	1	1	1	0	0	0	0	**5**
Progression From Onset	0	0	0	0	0	0	0	0	1	0	0	1
Age of Diagnosis	0	0	1	1	1	0	0	1	0	0	0	**4**
Years from Onset to Diagnosis	1	0	1	1	1	0	0	1	0	0	0	**5**
MRI	0	0	0	0	0	0	1	0	0	0	0	1
Evoked Potentials	0	0	0	0	0	1	0	0	0	0	0	1
CSF	0	0	0	0	0	1	0	0	0	0	0	1
Age at SP Diagnosis	1	1	1	1	1	0	1	1	1	1	1	**10**
Years from Diagnosis to SP	0	1	1	1	1	0	0	0	1	1	1	**7**
Ms Course	0	1	1	1	1	1	1	0	1	1	1	**9**

Selected features: Gender, Age of Onset, Optic Pathways, Spinal Cord, Age of Diagnosis, Years from Onset to Diagnosis, Age at SP Diagnosis, MS Course.

Table D.62: GroundZero_Feature_Selection_Visits_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Relapse Age	0	0	1	1	1	0	0	0	0	0	0	**3**
Routine	0	0	0	0	0	0	1	0	0	0	0	1
Suspected Relapse	0	0	0	0	0	0	1	0	0	0	0	1
EDSS	1	1	1	1	1	0	0	1	0	1	1	**8**

Selected features: Relapse Age, EDSS.

Table D.63: GroundZero_Feature_Selection_Relapses_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Relapse Age	0	0	0	1	1	0	0	1	0	0	0	**3**
Time since onset	0	1	0	0	1	0	1	1	0	0	1	**5**
CNS Brain Stem	0	0	0	0	0	0	1	1	0	0	0	**2**
CNS Neuropsycho Functions	0	0	0	0	0	0	0	0	1	0	0	1
CNS Cerebellum	0	0	0	0	0	0	1	0	0	0	0	1
CNS Visual Functions	0	0	0	1	0	0	0	0	0	0	0	1
CNS Sensory Functions	0	0	0	0	0	1	0	0	0	0	0	1
Hospital	0	0	0	0	0	1	1	0	0	0	0	**2**
Ambulatory	0	0	0	1	0	0	0	0	0	0	0	1
Corticosteroids	0	0	0	0	0	1	0	0	0	0	0	1
Duration Days	0	0	0	0	0	0	0	1	0	0	0	1

Selected features: Relapse Age, Time since onset, CNS Brain Stem, Hospital.

For label *highestEDSS* (0/1 - (< 3)/(≥ 3)):

Final features: Optic pathways, MS Course, EDSS

Table D.64: GroundZero_Standard_Traditional_PCA_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.76	0.70	0.69	0.61	0.67	0.62	0.65	0.71	0.70	0.70	0.70
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
100.00	**60.00**	**80.00**	**60.00**	**60.00**	**60.00**	**60.00**	**80.00**	**60.00**	**60.00**	**60.00**
62.50	**75.00**	**62.50**	**62.50**	**62.50**	**62.50**	**75.00**	**62.50**	**75.00**	**75.00**	**75.00**
100.00	**75.00**	**83.33**	**71.43**	**71.43**	**71.43**	**75.00**	**83.33**	**75.00**	**75.00**	**75.00**
62.50	**60.00**	**57.14**	**50.00**	**50.00**	**50.00**	**60.00**	**57.14**	**60.00**	**60.00**	**60.00**
76.92	**69.23**	**69.23**	**61.54**	**61.54**	**61.54**	**69.23**	**69.23**	**69.23**	**69.23**	**69.23**
Confusion Matrix										
5 3 0 5	6 2 2 3	5 3 1 4	5 3 2 3	5 3 2 3	5 3 2 3	6 2 2 3	5 3 1 4	6 2 2 3	6 2 2 3	6 2 2 3

Table D.65: GroundZero_Standard_Traditional_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.60	NA	0.60	0.48	0.56	0.63	NA	0.59	0.60	0.60
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
100.00	100.00	NA	80.00	80.00	100.00	80.00	NA	100.00	100.00	100.00
12.50	25.00	NA	25.00	12.50	12.50	37.50	NA	22.22	25.00	25.00
100.00	100.00	NA	66.67	50.00	100.00	75.00	NA	100.00	100.00	100.00
41.67	45.45	NA	40.00	36.36	41.67	44.44	NA	41.67	45.45	45.45
46.15	53.85	NA	46.15	38.46	46.15	53.85	NA	50.00	53.85	53.85
Confusion Matrix										
1 7 0 5	2 6 0 5	NA NA	2 6 1 4	1 7 1 4	1 7 0 5	3 5 1 4	NA NA	1 7 0 5	2 6 0 5	2 6 0 5

Table D.66: GroundZero_Standard_kFold_PCA_highestEDSS< 3

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.58	0.58	0.62	0.52	0.58	0.56	0.51	0.60	0.58	0.58	0.57
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
64.71	**64.71**	**76.47**	**58.82**	**70.59**	**64.71**	**52.94**	**64.71**	**64.71**	**64.71**	**64.71**
70.00	**75.00**	**70.00**	**70.00**	**65.00**	**60.00**	**65.00**	**75.00**	**75.00**	**80.00**	**75.00**
70.00	**71.43**	**77.78**	**66.67**	**72.22**	**66.67**	**61.90**	**71.43**	**71.43**	**72.73**	**71.43**
64.71	**68.75**	**68.42**	**62.50**	**63.16**	**57.89**	**56.25**	**68.75**	**68.75**	**73.33**	**68.75**
67.57	**70.27**	**72.97**	**64.86**	**67.57**	**62.16**	**59.46**	**70.27**	**70.27**	**72.97**	**70.27**
Confusion Matrix										
14 6 6 11	15 5 6 11	14 6 4 13	14 6 7 10	13 7 5 12	12 8 6 11	13 7 8 9	15 5 6 11	15 5 6 11	16 4 6 11	15 5 6 11

Table D.67: GroundZero_Standard_kFold_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.60	0.67	NA	0.67	0.64	0.74	0.69	NA	NA	0.58	0.66
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
64.71	**70.59**	NA	**70.59**	**88.24**	**88.24**	**76.47**	NA	NA	**58.82**	**76.47**
80.00	**90.00**	NA	**85.00**	**65.00**	**85.00**	**85.00**	NA	NA	**90.00**	**90.00**
72.73	**78.26**	NA	**77.27**	**86.67**	**89.47**	**80.95**	NA	NA	**72.00**	**81.82**
73.33	**85.71**	NA	**80.00**	**68.18**	**83.33**	**81.25**	NA	NA	**83.33**	**86.67**
72.97	**81.08**	NA	**78.38**	**75.68**	**86.49**	**81.08**	NA	NA	**75.68**	**83.78**
Confusion Matrix										
16 4	18 2	NA	17 3	13 7	17 3	17 3	NA	NA	18 2	18 2
6 11	5 12	NA	5 12	2 15	2 15	4 13	NA	NA	7 10	4 13

Table D.68: GroundZero_Standard_LOO_PCA_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.65	0.65	0.60	0.62	0.73	0.68	0.59	0.67	0.65	0.67	0.67
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
58.82	**58.82**	**64.71**	**64.71**	**76.47**	**70.59**	**52.94**	**64.71**	**58.82**	**58.82**	**64.71**
70.00	**70.00**	**55.00**	**60.00**	**70.00**	**65.00**	**65.00**	**70.00**	**70.00**	**75.00**	**70.00**
66.67	**66.67**	**64.71**	**66.67**	**77.78**	**72.22**	**61.90**	**70.00**	**66.67**	**68.18**	**70.00**
62.50	**62.50**	**55.00**	**57.89**	**68.42**	**63.16**	**56.25**	**64.71**	**62.50**	**66.67**	**64.71**
64.86	**64.86**	**59.46**	**62.16**	**72.97**	**67.57**	**59.46**	**67.57**	**64.86**	**67.57**	**67.57**
Confusion Matrix										
14 6	14 6	11 9	12 8	14 6	13 7	13 7	14 6	14 6	15 5	14 6
7 10	7 10	6 11	6 11	4 13	5 12	8 9	6 11	7 10	7 10	6 11

Table D.69: GroundZero_Standard_LOO_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.00	0.00	NA	0.00	0.00	0.00	0.00	NA	0.00	0.59	0.67
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
0.00	0.00	NA	0.00	0.00	0.00	0.00	NA	0.00	41.1765	**58.82**
100.00	100.00	NA	100.00	100.00	100.00	100.00	NA	100.00	75.00	**75.00**
54.05	54.05	NA	54.05	54.05	54.05	54.05	NA	54.05	60.00	**68.18**
NaN	NaN	NA	NaN	NaN	NaN	NaN	NA	NaN	58.33	**66.67**
54.05	54.05	NA	54.05	54.05	54.05	54.05	NA	54.05	59.46	**67.57**
Confusion Matrix										
20 0 17 0	20 0 17 0	NA NA	20 0 17 0	20 0 17 0	20 0 17 0	20 0 17 0	NA NA	20 0 17 0	15 5 10 7	15 5 7 10

For label *highestEDSS* (0/1 - $(< 5)/(\geq 5)$**):**

The via pattern recognition study was not performed since the number of patients with *highestEDSS*≥ 5 was minimal.

For label *first2EDSS* (0/1 - $(< 3)/(\geq 3)$**):**

Final features: EDSS

Table D.70: GroundZero_Standard_Traditional_PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.61	0.77	0.61	0.75	0.70	0.72	0.68	0.69	NA	0.79	0.76
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
66.67	100.00	66.67	100.00	100.00	100.00	100.00	100.00	NA	100.00	66.67
45.00	65.00	55.00	60.00	55.00	55.00	45.00	45.00	NA	70.00	70.00
90.00	100.00	91.67	100.00	100.00	100.00	100.00	100.00	NA	100.00	93.33
15.38	30.00	18.18	27.27	25.00	25.00	21.43	21.43	NA	33.33	25.00
47.83	69.57	56.52	65.22	60.87	60.87	52.17	52.17	NA	73.91	69.57
Confusion Matrix										
9 11 1 2	13 7 0 3	11 9 1 2	12 8 0 3	11 9 0 3	11 9 0 3	9 11 0 3	9 11 0 3	NA NA	14 6 0 3	14 6 1 2

Table D.71: GroundZero_Standard_Traditional_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.51	0.50	0.51	0.64	0.52	0.52	0.50	0.51	0.51	0.51
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
5.00	0.00	0.00	0.00	40.00	5.00	5.00	0.00	0.00	0.00	0.00
100.00	NaN	NaN	NaN	100.00	100.00	100.00	NaN	NaN	NaN	NaN
13.64	13.04	13.04	13.04	20.00	13.64	13.64	13.04	13.04	13.04	13.04
17.39	13.04	13.04	13.04	47.83	17.39	17.39	13.04	13.04	13.04	13.04
Confusion Matrix										
1 19 0 3	0 20 0 3	0 20 0 3	0 20 0 3	8 12 0 3	1 19 0 3	1 19 0 3	0 20 0 3	0 20 0 3	0 20 0 3	0 20 0 3

Table D.72: GroundZero_Standard_kFold_PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.60	0.60	0.55	0.36	0.46	0.50	0.49	0.45	0.60	0.54	0.58
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
80.00	**80.00**	**70.00**	40.00	**50.00**	**60.00**	**60.00**	**60.00**	**80.00**	**70.00**	**80.00**
88.89	**92.59**	**88.89**	96.30	**92.59**	**92.59**	**88.89**	**100.00**	**92.59**	**85.19**	**92.59**
92.31	**92.59**	**88.89**	81.25	**83.33**	**86.21**	**85.71**	**87.10**	**92.59**	**88.46**	**92.59**
72.73	**80.00**	**70.00**	80.00	**71.43**	**75.00**	**66.67**	**100.00**	**80.00**	**63.64**	**80.00**
86.49	**89.19**	**83.78**	81.08	**81.08**	**83.78**	**81.08**	**89.19**	**89.19**	**81.08**	**89.19**
Confusion Matrix										
24 3 2 8	25 2 2 8	24 3 3 7	26 1 6 4	25 2 5 5	25 2 4 6	24 3 4 6	27 0 4 6	25 2 2 8	23 4 3 7	25 2 2 8

Table D.73: GroundZero_Standard_kFold_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.60	0.60	0.55	0.36	0.46	0.50	0.49	0.45	0.60	0.54	0.58
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
80.00	**80.00**	**70.00**	40.00	**50.00**	**60.00**	**60.00**	**60.00**	**80.00**	**70.00**	**80.00**
88.89	**92.59**	**88.89**	96.30	**92.59**	**92.59**	**88.89**	**100.00**	**92.59**	**85.19**	**92.59**
92.31	**92.59**	**88.89**	81.25	**83.33**	**86.21**	**85.71**	**87.10**	**92.59**	**88.46**	**92.59**
72.73	**80.00**	**70.00**	80.00	**71.43**	**75.00**	**66.67**	**100.00**	**80.00**	**63.64**	**80.00**
86.49	**89.19**	**83.78**	81.08	**81.08**	**83.78**	**81.08**	**89.19**	**89.19**	**81.08**	**89.19**
Confusion Matrix										
24 3 2 8	25 2 2 8	24 3 3 7	26 1 6 4	25 2 5 5	25 2 4 6	24 3 4 6	27 0 4 6	25 2 2 8	23 4 3 7	25 2 2 8

Table D.74: GroundZero_Standard_LOO_PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.42	0.45	0.52	0.46	0.42	0.41	0.39	0.46	0.45	0.50	0.45
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
20.00	20.00	30.00	10.00	10.00	10.00	10.00	10.00	20.00	30.00	20.00
62.96	70.37	74.07	85.19	77.78	74.07	70.37	85.19	70.37	70.37	70.37
68.00	70.37	74.07	71.88	70.00	68.97	67.86	71.88	70.37	73.08	70.37
16.67	20.00	30.00	20.00	14.29	12.50	11.11	20.00	20.00	27.27	20.00
51.35	56.76	62.16	64.86	59.46	56.76	54.05	64.86	56.76	59.46	56.76
Confusion Matrix										
17 10 8 2	19 8 8 2	20 7 7 3	23 4 9 1	21 6 9 1	20 7 9 1	19 8 9 1	23 4 9 1	19 8 8 2	19 8 7 3	19 8 8 2

Table D.75: GroundZero_Standard_LOO_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.49	0.50	0.50	0.51	0.49	0.50	0.50	0.49	0.44	0.44
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
30.00	20.00	30.00	30.00	20.00	20.00	30.00	30.00	20.00	20.00	20.00
70.37	77.78	70.37	70.37	81.48	77.78	70.37	70.37	77.78	66.67	66.67
73.08	72.41	73.08	73.08	73.33	72.41	73.08	73.08	72.41	69.23	69.23
27.27	25.00	27.27	27.27	28.57	25.00	27.27	27.27	25.00	18.18	18.18
59.46	62.16	59.46	59.46	64.86	62.16	59.46	59.46	62.16	54.05	54.05
Confusion Matrix										
19 8	21 6	19 8	19 8	22 5	21 6	19 8	19 8	21 6	18 9	18 9
7 3	8 2	7 3	7 3	8 2	8 2	7 3	7 3	8 2	8 2	8 2

For label *first2EDSS* (0/1 - (< 5)/(≥ 5)):

The via pattern recognition study was not performed since the number of patients with *first2EDSS*≥ 5 was minimal.

First feature selection process for *mediumEDSS*:

Table D.76: GroundZero_Feature_Selection_Identification_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Gender	0	0	1	1	1	1	1	1	0	0	0	**6**
Age of Onset	0	0	0	0	0	0	0	1	0	0	0	1
Supratentorial	0	0	1	0	0	0	1	0	0	0	0	**2**
Optic Pathways	0	0	1	0	0	0	0	0	0	0	0	1
Brainstem-Cerebellum	0	0	0	0	0	1	1	0	0	0	0	**2**
Spinal Cord	0	1	1	1	0	1	1	0	1	0	1	**7**
Progression From Onset	0	0	0	0	0	0	0	0	1	0	0	1
MRI	0	0	0	0	0	0	1	0	0	0	0	1
Evoked Potentials	0	0	0	0	0	1	0	0	0	0	0	1
CSF	0	1	1	1	1	1	1	0	1	0	1	**8**
Age at SP Diagnosis	0	1	1	1	1	0	1	1	1	1	1	**9**
Years from Diagnosis to SP	1	1	0	1	1	0	1	0	1	0	1	**7**
Ms Course	0	1	1	1	1	1	1	0	1	0	1	**8**

Selectd features: Gender, Supratentorial, Brainstem-Cerebellum, Spinal Cord, CSF, Age at SP Diagnosis, Years from Diagnosis to SP, MS Course.

Table D.77: GroundZero_Feature_Selection_Visits_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Relapse Age	0	0	0	0	0	0	1	1	0	0	0	**2**
Routine	0	0	0	1	1	0	1	0	0	0	0	**3**
EDSS	1	1	1	1	1	0	1	1	1	1	1	**10**

Selected features: Relapse Age, Routine, EDSS.

Table D.78: GroundZero_Feature_Selection_Relapses_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Relapse Age	0	0	0	0	0	0	1	1	0	0	0	2
Time since onset	0	0	0	0	1	0	1	0	0	0	0	2
CNS Pyramidal Tract	0	1	1	1	1	1	1	1	1	0	1	**9**
CNS Brain Stem	0	0	0	0	0	0	1	0	0	0	0	1
CNS Bowel Bladder	0	0	1	0	0	0	0	0	0	0	0	1
CNS Neuropsycho Functions	0	0	0	0	0	0	0	0	1	0	0	1
CNS Cerebellum	0	0	0	0	0	0	1	0	0	0	0	1
CNS Visual Functions	0	0	0	0	0	1	1	0	0	0	0	2
CNS Sensory Functions	0	0	0	0	0	1	0	0	0	0	0	1
Hospital	0	1	1	1	1	1	1	0	1	0	1	**8**
Ambulatory	0	0	1	0	0	0	0	0	0	0	0	1
Corticosteroids	0	0	0	0	0	1	0	0	0	0	0	1

Selected features: CNS Pyramidal Tract, CNS Visual Functions, Hospital.

For label *mediumEDSS* (0/1 - $(< 3)/(\geq 3)$**):**

Final features: Spinal Cord, CNS Pyramidal Tract, Brainstem-Cerebellum, Time since onset.

Table D.79: GroundZero_Standard_Traditional_PCA_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.65	0.72	0.66	0.74	0.71	0.71	0.69	0.71	0.72	0.72	0.71
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
66.67	66.67	66.67	66.67	66.67	66.67	66.67	66.67	66.67	66.67	66.67
61.11	72.22	55.56	77.78	77.78	83.33	77.78	72.22	72.22	72.22	72.22
91.67	92.86	90.91	93.33	93.33	93.75	93.33	92.86	92.86	92.86	92.86
22.22	28.57	20.00	33.33	33.33	40.00	33.33	28.57	28.57	28.57	28.57
61.90	71.43	57.14	76.19	76.19	80.95	76.19	71.43	71.43	71.43	71.43
Confusion Matrix										
11 7 1 2	13 5 1 2	10 8 1 2	14 4 1 2	14 4 1 2	15 3 1 2	14 4 1 2	13 5 1 2	13 5 1 2	13 5 1 2	13 5 1 2

Table D.80: GroundZero_Standard_Traditional_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.62	0.60	NA	0.65	0.63	0.61	0.63	NA	NA	0.57	0.56
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
66.67	100.00	NA	66.67	33.33	66.67	66.67	NA	NA	100.00	100.00
72.22	27.78	NA	61.11	77.78	72.22	66.67	NA	NA	27.78	16.67
92.86	100.00	NA	91.67	87.50	92.86	92.31	NA	NA	100.00	100.00
28.57	18.75	NA	22.22	20.00	28.57	25.00	NA	NA	18.75	16.67
71.43	38.10	NA	61.90	71.43	71.43	66.67	NA	NA	38.10	28.57
Confusion Matrix										
13 5 1 2	5 13 0 3	NA NA	11 7 1 2	14 4 2 1	13 5 1 2	12 6 1 2	NA NA	NA NA	5 13 0 3	3 15 0 3

Table D.81: GroundZero_Standard_kFold_PCA_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.58	0.55	0.44	0.35	0.56	0.42	0.43	0.55	NA	0.55	0.55
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
63.64	**63.64**	45.45	36.36	**63.64**	45.45	45.45	**63.64**	NA	**63.64**	**63.64**
84.62	**92.31**	88.46	96.15	**88.46**	96.15	92.31	**84.62**	NA	**92.31**	**88.46**
84.62	**85.71**	79.31	78.13	**85.19**	80.65	80.00	**84.62**	NA	**85.71**	**85.19**
63.64	**77.78**	62.50	80.00	**70.00**	83.33	71.43	**63.64**	NA	**77.78**	**70.00**
78.38	**83.78**	75.68	78.38	**81.08**	81.08	78.38	**78.38**	NA	**83.78**	**81.08**
Confusion Matrix										
22 4 4 7	24 2 4 7	23 3 6 5	25 1 7 4	23 3 4 7	25 1 6 5	24 2 6 5	22 4 4 7	NA NA	24 2 4 7	23 3 4 7

Table D.82: GroundZero_Standard_kFold_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.44	0.47	NA	0.43	0.59	0.46	0.33	NA	NA	0.53	0.56
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
45.45	45.45	NA	45.45	**81.82**	54.55	27.27	NA	NA	**63.64**	**72.73**
76.92	88.46	NA	92.31	**65.38**	65.38	92.31	NA	NA	**76.92**	**84.62**
76.92	79.31	NA	80.00	**89.47**	77.27	75.00	NA	NA	**83.33**	**88.00**
45.45	62.50	NA	71.43	**50.00**	40.00	60.00	NA	NA	**53.85**	**66.67**
67.57	75.68	NA	78.38	**70.27**	62.16	72.97	NA	NA	**72.97**	**81.08**
Confusion Matrix										
20 6 6 5	23 3 6 5	NA NA	24 2 6 5	17 9 2 9	17 9 5 6	24 2 8 3	NA NA	NA NA	20 6 4 7	22 4 3 8

Table D.83: GroundZero_Standard_LOO_PCA_mediumEDSS< 3

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.68	0.67	0.71	0.79	0.64	0.72	0.72	0.68	0.67	0.52	0.50
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
54.55	45.45	45.45	36.36	45.45	36.36	36.36	**54.55**	45.45	27.27	27.27
80.77	84.62	88.46	96.15	80.77	92.31	92.31	**80.77**	84.62	76.92	73.08
80.77	78.57	79.31	78.13	77.78	77.42	77.42	**80.77**	78.57	71.43	70.37
54.55	55.56	62.50	80.00	50.00	66.67	66.67	**54.55**	55.56	33.33	30.00
72.97	72.97	75.68	78.38	70.27	75.68	75.68	**72.97**	72.97	62.16	59.46
Confusion Matrix										
21 5 5 6	22 4 6 5	23 3 6 5	25 1 7 4	21 5 6 5	24 2 7 4	24 2 7 4	21 5 5 6	22 4 6 5	20 6 8 3	19 7 8 3

Table D.84: GroundZero_Standard_LOO_mediumEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.43	0.60	0.52	0.58	0.43	0.51	0.62	0.57	0.60	0.49	0.47
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
18.18	36.36	27.27	27.27	36.36	45.45	27.27	36.36	36.36	36.36	36.36
69.23	80.77	76.92	84.62	46.15	57.69	88.46	76.92	80.77	61.54	57.69
66.67	75.00	71.43	73.33	63.16	71.43	74.19	74.07	75.00	69.57	68.18
20.00	44.44	33.33	42.86	22.22	31.25	50.00	40.00	44.44	28.57	26.67
54.05	67.57	62.16	67.57	43.24	54.05	70.27	64.86	67.57	54.05	51.35
Confusion Matrix										
18 8 9 2	21 5 7 4	20 6 8 3	22 4 8 3	12 14 7 4	15 11 6 5	23 3 8 3	20 6 7 4	21 5 7 4	16 10 7 4	15 11 7 4

For label *mediumEDSS* (0/1 - $(< 5)/(\geq 5)$):

The via pattern recognition study was not performed since the number of patients with *mediumEDSS*≥ 5 was minimal.

D.1.2.2 Investigation procedure

For label *msCourse* (0/1 - RR/SP):

Features before selection: Age of onset, Relapse age, CNS pyramidal tract, CNS sensory functions;

Excluded features: EDSS, Relapse Age, Time since onset, Hospital.

Final features: Age of onset, Relapse age.

Table D.85: GroundZero_Investigation_Traditional_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.60	0.55	0.53	0.54	0.54	0.53	0.55	0.60	0.59	0.60
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
66.67	66.67	33.33	33.33	33.33	33.33	33.33	33.33	66.67	66.67	66.67
50.00	66.67	61.11	72.22	72.22	83.33	88.89	66.67	66.67	61.11	61.11
90.00	92.31	84.62	86.67	86.67	88.24	88.89	85.71	92.31	91.67	91.67
18.18	25.00	12.50	16.67	16.67	25.00	33.33	14.29	25.00	22.22	22.22
52.38	66.67	57.14	66.67	66.67	76.19	80.95	61.90	66.67	61.90	61.90
Confusion Matrix										
9 9 1 2	12 6 1 2	11 7 1 2	13 5 2 1	13 5 2 1	15 3 2 1	16 2 2 1	12 6 2 1	12 6 1 2	11 7 1 2	11 7 1 2

Table D.86: GroundZero_Investigation_Traditional_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.64	0.50	0.51	0.61	0.58	0.60	0.59	0.51	0.50	0.50	0.50
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	66.67	66.67	66.67	100.00	100.00	100.00	100.00
33.33	0.00	0.00	38.89	33.33	44.44	38.89	0.00	0.00	0.00	0.00
100.00	NaN	NaN	100.00	85.71	88.89	87.50	NaN	NaN	NaN	NaN
20.00	14.29	14.29	21.43	14.29	16.67	15.38	14.29	14.29	14.29	14.29
42.86	14.29	14.29	47.62	38.10	47.62	42.86	14.29	14.29	14.29	14.29
Confusion Matrix										
6 12 0 3	0 18 0 3	0 18 0 3	7 11 0 3	6 12 1 2	8 10 1 2	7 11 1 2	0 18 0 3	0 18 0 3	0 18 0 3	0 18 0 3

Table D.87: GroundZero_Investigation_kFold_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.43	0.35	0.37	0.22	0.39	0.21	0.06	0.36	0.34	0.35	0.51
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
45.45	27.27	36.36	18.18	36.36	18.18	0.00	36.36	27.27	36.36	**63.64**
73.08	84.62	84.62	92.31	73.08	88.46	92.31	88.46	84.62	84.62	**61.54**
76.00	73.33	75.86	72.73	73.08	71.88	68.57	76.67	73.33	75.86	**80.00**
41.67	42.86	50.00	50.00	36.36	40.00	0.00	57.14	42.86	50.00	**41.18**
64.86	67.57	70.27	70.27	62.16	67.57	64.86	72.97	67.57	70.27	**62.16**
Confusion Matrix										
19 7 6 5	22 4 8 3	22 4 7 4	24 2 9 2	19 7 7 4	23 3 9 2	24 2 11 0	23 3 7 4	22 4 8 3	22 4 7 4	16 10 4 7

Table D.88: GroundZero_Investigation_kFold_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.43	0.42	0.31	0.48	0.38	0.40	0.52	NA	0.57	0.53
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
63.64	45.45	45.45	27.27	**54.55**	36.36	45.45	**54.55**	NA	72.73	**63.64**
80.77	96.15	96.15	92.31	**80.77**	92.31	92.31	**76.92**	NA	65.38	**84.62**
84.00	80.65	80.65	75.00	**80.77**	77.42	80.00	**80.00**	NA	85.00	**84.62**
58.33	83.33	83.33	60.00	**54.55**	66.67	71.43	**50.00**	NA	47.06	**63.64**
75.68	81.08	81.08	72.97	**72.97**	75.68	78.38	**70.27**	NA	67.57	**78.38**
Confusion Matrix										
21 5	25 1	25 1	24 2	21 5	24 2	24 2	20 6	NA	17 9	22 4
4 7	6 5	6 5	8 3	5 6	7 4	6 5	5 6	NA	3 8	4 7

Table D.89: GroundZero_Investigation_LOO_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.49	0.47	0.61	0.48	0.44	0.34	0.42	0.49	0.58	0.59
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
27.27	18.18	18.18	18.18	27.27	9.09	0.00	9.09	18.18	27.27	63.64
65.38	80.77	76.92	92.31	69.23	84.62	92.31	80.77	80.77	84.62	57.69
68.00	70.00	68.97	72.73	69.23	68.75	68.57	67.74	70.00	73.33	78.95
25.00	28.57	25.00	50.00	27.27	20.00	0.00	16.67	28.57	42.86	38.89
54.05	62.16	59.46	70.27	56.76	62.16	64.86	59.46	62.16	67.57	59.46
Confusion Matrix										
17 9 8 3	21 5 9 2	20 6 9 2	24 2 9 2	18 8 8 3	22 4 10 1	24 2 11 0	21 5 10 1	21 5 9 2	22 4 8 3	15 11 4 7

Table D.90: GroundZero_Investigation_LOO_msCourse

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.38	0.42	0.42	0.33	0.35	0.42	0.40	0.47	0.42	0.39	0.42
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
18.18	9.09	9.09	0.00	9.09	9.09	9.09	27.27	9.09	27.27	18.18
53.85	80.77	80.77	80.77	61.54	80.77	76.92	65.38	80.77	46.15	65.38
60.87	67.74	67.74	65.63	61.54	67.74	66.67	68.00	67.74	60.00	65.38
14.29	16.67	16.67	0.00	9.09	16.67	14.29	25.00	16.67	17.65	18.18
43.24	59.46	59.46	56.76	45.95	59.46	56.76	54.05	59.46	40.54	51.35
Confusion Matrix										
14 12 9 2	21 5 10 1	21 5 10 1	21 5 11 0	16 10 10 1	21 5 10 1	20 6 10 1	17 9 8 3	21 5 10 1	12 14 8 3	17 9 9 2

For label *highestEDSS* (0/1 - (< 3)/(≥ 3)):

Features before selection: Optic Pathways, Spinal Cord, Time since onset, CNS Brain Stem, Gender, Age of Onset, Relapse Age.

Excluded features: MS Course, EDSS, Relapse Age.

Final Features: Time since onset, Relapse age.

Table D.91: GroundZero_Investigation_Traditional_PCA_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.58	0.68	0.63	0.50	0.42	0.54	0.68	0.58	0.68	0.66	0.66
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
60.00	**80.00**	**80.00**	60.00	80.00	80.00	**80.00**	100.00	**80.00**	**60.00**	**60.00**
62.50	**62.50**	**50.00**	37.50	12.50	37.50	**50.00**	25.00	**62.50**	**62.50**	**62.50**
71.43	**83.33**	**80.00**	60.00	50.00	75.00	**80.00**	100.00	**83.33**	**71.43**	**71.43**
50.00	**57.14**	**50.00**	37.50	36.36	44.44	**50.00**	45.45	**57.14**	**50.00**	**50.00**
61.54	**69.23**	**61.54**	46.15	38.46	53.85	**61.54**	53.85	**69.23**	**61.54**	**61.54**
Confusion Matrix										
5 3 2 3	5 3 1 4	4 4 1 4	3 5 2 3	1 7 1 4	3 5 1 4	4 4 1 4	2 6 0 5	5 3 1 4	5 3 2 3	5 3 2 3

Table D.92: GroundZero_Investigation_Traditional_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.50	0.54	0.52	0.52	0.57	0.56	0.55	0.50	0.50	0.50
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
60.00	100.00	80.00	60.00	40.00	40.00	**50.00**	80.00	100.00	100.00	100.00
37.50	0.00	25.00	37.50	75.00	62.50	**62.50**	25.00	0.00	0.00	0.00
60.00	NaN	66.67	60.00	66.67	62.50	**62.50**	66.67	NaN	NaN	NaN
37.50	38.46	40.00	37.50	50.00	40.00	**50.00**	40.00	38.46	38.46	38.46
46.15	38.46	46.15	46.15	61.54	53.85	**57.14**	46.15	38.46	38.46	38.46
Confusion Matrix										
3 5 2 3	0 8 0 5	2 6 1 4	3 5 2 3	6 2 3 2	5 3 3 2	5 3 3 3	2 6 1 4	0 8 0 5	0 8 0 5	0 8 0 5

Table D.93: GroundZero_Investigation_kFold_PCA_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.55	0.47	0.59	0.60	0.52	0.61	0.27	0.55	0.61	0.56
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
70.59	**64.71**	**88.24**	**76.47**	**64.71**	**64.71**	**82.35**	100.00	**64.71**	**76.47**	**76.47**
75.00	**60.00**	**40.00**	**65.00**	**80.00**	**60.00**	**65.00**	20.00	**60.00**	**65.00**	**60.00**
75.00	**66.67**	**80.00**	**76.47**	**72.73**	**66.67**	**81.25**	100.00	**66.67**	**76.47**	**75.00**
70.59	**57.89**	**55.56**	**65.00**	**73.33**	**57.89**	**66.67**	51.52	**57.89**	**65.00**	**61.90**
72.97	**62.16**	**62.16**	**70.27**	**72.97**	**62.16**	**72.97**	56.76	**62.16**	**70.27**	**67.57**
Confusion Matrix										
15 5 5 12	12 8 6 11	8 12 2 15	13 7 4 13	16 4 6 11	12 8 6 11	13 7 3 14	4 16 0 17	12 8 6 11	13 7 4 13	12 8 4 13

Table D.94: GroundZero_Investigation_kFold_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.49	0.45	0.43	0.44	0.56	0.54	0.50	NA	0.48	0.50
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
64.71	47.06	41.18	41.18	47.06	**52.94**	**52.94**	41.18	NA	47.06	**52.94**
70.00	65.00	70.00	75.00	55.00	**75.00**	**75.00**	80.00	NA	85.00	**65.00**
70.00	59.09	58.33	60.00	55.00	**65.22**	**65.22**	61.54	NA	65.38	**61.90**
64.71	53.33	53.85	58.33	47.06	**64.29**	**64.29**	63.64	NA	72.73	**56.25**
67.57	56.76	56.76	59.46	51.35	**64.86**	**64.86**	62.16	NA	67.57	**59.46**
Confusion Matrix										
14 6	13 7	14 6	15 5	11 9	15 5	15 5	16 4	NA	17 3	13 7
6 11	9 8	10 7	10 7	9 8	8 9	8 9	10 7	NA	9 8	8 9

Table D.95: GroundZero_Investigation_LOO_PCA_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.54	0.44	0.52	0.39	0.46	0.44	0.46	0.54	0.46	0.44
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
41.18	**52.94**	58.82	64.71	29.41	47.06	52.94	47.06	**52.94**	52.94	52.94
50.00	**55.00**	30.00	40.00	50.00	45.00	35.00	45.00	**55.00**	40.00	35.00
50.00	**57.89**	46.15	57.14	45.45	50.00	46.67	50.00	**57.89**	50.00	46.67
41.18	**50.00**	41.67	47.83	33.33	42.11	40.91	42.11	**50.00**	42.86	40.91
45.95	**54.05**	43.24	51.35	40.54	45.95	43.24	45.95	**54.05**	45.95	43.24
Confusion Matrix										
10 10 10 7	11 9 8 9	6 14 7 10	8 12 6 11	10 10 12 5	9 11 9 8	7 13 8 9	9 11 9 8	11 9 8 9	8 12 8 9	7 13 8 9

Table D.96: GroundZero_Investigation_LOO_highestEDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.62	0.56	0.56	0.51	0.51	0.65	0.65	0.62	0.47	0.56
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
58.82	**52.94**	41.18	41.18	47.06	41.18	**52.94**	47.06	**52.94**	29.41	**52.94**
60.00	**70.00**	70.00	70.00	55.00	60.00	**75.00**	80.00	**70.00**	65.00	**60.00**
63.16	**63.64**	58.33	58.33	55.00	54.55	**65.22**	64.00	**63.64**	52.00	**60.00**
55.56	**60.00**	53.85	53.85	47.06	46.67	**64.29**	66.67	**60.00**	41.67	**52.94**
59.46	**62.16**	56.76	56.76	51.35	51.35	**64.86**	64.86	**62.16**	48.65	**56.76**
Confusion Matrix										
12 8 7 10	14 6 8 9	14 6 10 7	14 6 10 7	11 9 9 8	12 8 10 7	15 5 8 9	16 4 9 8	14 6 8 9	13 7 12 5	12 8 8 9

For label *highestEDSS* (0/1 - $(< 5)/(\geq 5)$**):**

The via pattern recognition study was not performed since the number of patients with *highestEDSS*≥ 5 was minimal.

For label *first2EDSS* (0/1 - $(< 3)/(\geq 3)$**):**

Features before selection: Gender, Time since onset, CNS Brain Stem, Supratentorial, Optic Pathways, Brainstem-Cerebellum, CNS Sensory Functions.

Excluded features: MS Course, EDSS.

Final features: Gender, Time since onset, CNS Brain Stem, Supratentorial, Optic Pathways, CNS Sensory Functions.

Table D.97: GroundZero_Investigation_Traditional_PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.61	NA	0.56	0.51	0.51	0.53	0.59	NA	0.63	0.62
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
66.67	66.67	NA	66.67	66.67	66.67	100.00	100.00	NA	66.67	66.67
45.00	55.00	NA	40.00	35.00	25.00	15.00	20.00	NA	55.00	55.00
90.00	91.67	NA	88.89	87.50	83.33	100.00	100.00	NA	91.67	91.67
15.38	18.18	NA	14.29	13.33	11.76	15.00	15.79	NA	18.18	18.18
47.83	56.52	NA	43.48	39.13	30.43	26.09	30.43	NA	56.52	56.52
Confusion Matrix										
9 11	11 9	NA	8 12	7 13	5 15	3 17	4 16	NA	11 9	11 9
1 2	1 2	NA	1 2	1 2	1 2	0 3	0 3	NA	1 2	1 2

Table D.98: GroundZero_Investigation_Traditional_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	NA	NA	0.53	0.52	0.52	0.51	NA	NA	0.52	0.56
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
66.67	NA	NA	33.33	33.33	33.33	33.33	NA	NA	33.33	33.33
50.00	NA	NA	75.00	80.00	70.00	65.00	NA	NA	70.00	85.00
90.91	NA	NA	88.24	88.89	87.50	86.67	NA	NA	87.50	89.47
16.67	NA	NA	16.67	20.00	14.29	12.50	NA	NA	14.29	25.00
52.17	NA	NA	69.57	73.91	65.22	60.87	NA	NA	65.22	78.26
Confusion Matrix										
10 10	NA	NA	15 5	16 4	14 6	13 7	NA	NA	14 6	17 3
1 2	NA	NA	2 1	2 1	2 1	2 1	NA	NA	2 1	2 1

Table D.99: GroundZero_Investigation_kFold_PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.43	0.38	NA	0.08	0.46	0.22	0.53	0.55	0.36	0.54	0.52
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
50.00	40.00	NA	0.00	50.00	10.00	**60.00**	**60.00**	40.00	70.00	80.00
77.78	88.89	NA	92.59	70.37	77.78	**81.48**	**77.78**	88.89	66.67	66.67
80.77	80.00	NA	71.43	79.17	70.00	**84.62**	**84.00**	80.00	85.71	90.00
45.45	57.14	NA	0.00	38.46	14.29	**54.55**	**50.00**	57.14	43.75	47.06
70.27	75.68	NA	67.57	64.86	59.46	**75.68**	**72.97**	75.68	67.57	70.27
Confusion Matrix										
21 6	24 3	NA	25 2	19 8	21 6	22 5	21 6	24 3	18 9	18 9
5 5	6 4	NA	10 0	5 5	9 1	4 6	4 6	6 4	3 7	2 8

Table D.100: GroundZero_Investigation_kFold_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.43	0.43	NA	0.29	0.49	0.44	0.50	NA	0.39	0.52	0.53
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
40.00	**50.00**	NA	30.00	60.00	50.00	**60.00**	NA	40.00	70.00	70.00
74.07	**85.19**	NA	92.59	62.96	59.26	**77.78**	NA	85.19	62.96	59.26
76.92	**82.14**	NA	78.13	80.95	76.19	**84.00**	NA	79.31	85.00	84.21
36.36	**55.56**	NA	60.00	37.50	31.25	**50.00**	NA	50.00	41.18	38.89
64.86	**75.68**	NA	75.68	62.16	56.76	**72.97**	NA	72.97	64.86	62.16
Confusion Matrix										
20 7	23 4	NA	25 2	17 10	16 11	21 6	NA	23 4	17 10	16 11
6 4	5 5	NA	7 3	4 6	5 5	4 6	NA	6 4	3 7	3 7

Table D.101: GroundZero_Investigation_LOO_PCA_first2EDSS< 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.60	NA	0.62	0.59	0.64	0.63	0.63	0.60	0.43	0.43
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
30.00	30.00	NA	10.00	50.00	30.00	50.00	60.00	30.00	30.00	30.00
74.07	85.19	NA	96.30	70.37	88.89	77.78	70.37	85.19	51.85	51.85
74.07	76.67	NA	74.29	79.17	77.42	80.77	82.61	76.67	66.67	66.67
30.00	42.86	NA	50.00	38.46	50.00	45.45	42.86	42.86	18.75	18.75
62.16	70.27	NA	72.97	64.86	72.97	70.27	67.57	70.27	45.95	45.95
Confusion Matrix										
20 7	23 4	NA	26 1	19 8	24 3	21 6	19 8	23 4	14 13	14 13
7 3	7 3	NA	9 1	5 5	7 3	5 5	4 6	7 3	7 3	7 3

Table D.102: GroundZero_Investigation_LOO_first2EDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.39	NA	0.46	0.54	0.48	0.49	NA	0.34	0.52	0.47
Stats (Specificity, Sensibility, PPV, NPV, Accuracy) %										
40.00	10.00	NA	10.00	50.00	40.00	30.00	NA	0.00	50.00	40.00
59.26	70.37	NA	85.19	59.26	55.56	66.67	NA	77.78	55.56	51.85
72.73	67.86	NA	71.88	76.19	71.43	72.00	NA	67.74	75.00	70.00
26.67	11.11	NA	20.00	31.25	25.00	25.00	NA	0.00	29.41	23.53
54.05	54.05	NA	64.86	56.76	51.35	56.76	NA	56.76	54.05	48.65
Confusion Matrix										
16 11	19 8	NA	23 4	16 11	15 12	18 9	NA	21 6	15 12	14 13
6 4	9 1	NA	9 1	5 5	6 4	7 3	NA	10 0	5 5	6 4

For label *first2EDSS* (0/1 - $(< 5)/(\geq 5)$):

The via pattern recognition study was not performed since the number of patients with *first2EDSS*≥ 5 was minimal.

For label *mediumEDSS* (0/1 - $(< 3)/(\geq 3)$):

Features before selection: Gender, Spinal Cord, CNS Pyramidal Tract, Supratentorial, Brainstem-Cerebellum, CSF, Relapse Age, Routine, Relapse Age, Time since onset, CNS Visual Functions.

Excluded features: MS Course.

Final features: Spinal Cord, CNS Pyramidal Tract, Brainstem-Cerebellum, Time since onset.

Table D.103: GroundZero_Investigation_Traditional_PCA_mediumEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.58	0.68	0.64	0.66	0.63	0.67	0.66	0.66	0.68	0.68	0.69
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.67	66.67	66.67	66.67	66.67	66.67	66.67	66.67	66.67	66.67	66.67
61.11	61.11	55.56	66.67	61.11	66.67	66.67	61.11	61.11	61.11	61.11
91.67	91.67	90.91	92.31	91.67	92.31	92.31	91.67	91.67	91.67	91.67
22.22	22.22	20.00	25.00	22.22	25.00	25.00	22.22	22.22	22.22	22.22
61.90	61.90	57.14	66.67	61.90	66.67	66.67	61.90	61.90	61.90	61.90
Confusion Matrix										
11 7 1 2	11 7 1 2	10 8 1 2	12 6 1 2	11 7 1 2	12 6 1 2	12 6 1 2	11 7 1 2	11 7 1 2	11 7 1 2	11 7 1 2

Table D.104: GroundZero_Investigation_Traditional_mediumEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.60	0.58	NA	0.65	0.62	0.60	0.62	NA	0.50	0.56	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.67	100.00	NA	66.67	33.33	33.33	66.67	NA	100.00	100.00	100.00
66.67	27.78	NA	61.11	77.78	72.22	72.22	NA	11.11	22.22	16.67
92.31	100.00	NA	91.67	87.50	86.67	92.86	NA	100.00	100.00	100.00
25.00	18.75	NA	22.22	20.00	16.67	28.57	NA	15.79	17.65	16.67
66.67	38.10	NA	61.90	71.43	66.67	71.43	NA	23.81	33.33	28.57
Confusion Matrix										
12 6 1 2	5 13 0 3	NA NA	11 7 1 2	14 4 2 1	13 5 2 1	13 5 1 2	NA NA	2 16 0 3	4 14 0 3	3 15 0 3

Table D.105: GroundZero_Investigation_kFold_PCA_mediumEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.49	0.47	0.26	0.45	0.44	0.46	0.46	0.49	0.52	0.54
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
54.55	**54.55**	45.45	27.27	45.45	45.45	45.45	45.45	**54.55**	**63.64**	**63.64**
73.08	**88.46**	73.08	96.15	84.62	88.46	80.77	92.31	**88.46**	**76.92**	**73.08**
79.17	**82.14**	76.00	75.76	78.57	79.31	77.78	80.00	**82.14**	**83.33**	**82.61**
46.15	**66.67**	41.67	75.00	55.56	62.50	50.00	71.43	**66.67**	**53.85**	**50.00**
67.57	**78.38**	64.86	75.68	72.97	75.68	70.27	78.38	**78.38**	**72.97**	**70.27**
Confusion Matrix										
19 7 5 6	23 3 5 6	19 7 6 5	25 1 8 3	22 4 6 5	23 3 6 5	21 5 6 5	24 2 6 5	23 3 5 6	20 6 4 7	19 7 4 7

Table D.106: GroundZero_Investigation_kFold_mediumEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.44	0.47	NA	0.44	0.60	0.48	0.33	NA	NA	0.52	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
45.45	**54.55**	NA	45.45	**81.82**	54.55	27.27	NA	NA	**66.67**	**72.73**
76.92	**88.46**	NA	92.31	**65.38**	65.38	92.31	NA	NA	**76.92**	**84.62**
76.92	**82.14**	NA	80.00	**89.47**	77.27	75.00	NA	NA	**83.33**	**88.00**
45.45	**66.67**	NA	71.43	**50.00**	40.00	60.00	NA	NA	**57.14**	**66.67**
67.57	**78.38**	NA	78.38	**70.27**	62.16	72.97	NA	NA	**73.68**	**81.08**
Confusion Matrix										
20 6 6 5	23 3 5 6	NA NA	24 2 6 5	17 9 2 9	17 9 5 6	24 2 8 3	NA NA	NA NA	20 6 4 8	22 4 3 8

Table D.107: GroundZero_Investigation_LOO_PCA_mediumEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.55	0.49	0.61	0.52	0.55	0.50	0.55	0.55	0.40	0.49
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
36.36	27.27	36.36	18.18	27.27	27.27	27.27	27.27	27.27	18.18	36.36
57.69	80.77	61.54	92.31	76.92	80.77	73.08	80.77	80.77	61.54	61.54
68.18	72.41	69.57	72.73	71.43	72.41	70.37	72.41	72.41	64.00	69.57
26.67	37.50	28.57	50.00	33.33	37.50	30.00	37.50	37.50	16.67	28.57
51.35	64.86	54.05	70.27	62.16	64.86	59.46	64.86	64.86	48.65	54.05
Confusion Matrix										
15 11 7 4	21 5 8 3	16 10 7 4	24 2 9 2	20 6 8 3	21 5 8 3	19 7 8 3	21 5 8 3	21 5 8 3	16 10 9 2	16 10 7 4

Table D.108: GroundZero_Investigation_LOO_mediumEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.60	0.60	0.58	0.54	0.57	0.62	0.57	0.60	0.61	0.59
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
27.27	36.36	36.36	27.27	54.55	54.55	27.27	36.36	36.36	54.55	54.55
73.08	80.77	80.77	84.62	53.85	61.54	88.46	76.92	80.77	69.23	65.38
70.37	75.00	75.00	73.33	73.68	76.19	74.19	74.07	75.00	78.26	77.27
30.00	44.44	44.44	42.86	33.33	37.50	50.00	40.00	44.44	42.86	40.00
59.46	67.57	67.57	67.57	54.05	59.46	70.27	64.86	67.57	64.86	62.16
Confusion Matrix										
19 7 8 3	21 5 7 4	21 5 7 4	22 4 8 3	14 12 5 6	16 10 5 6	23 3 8 3	20 6 7 4	21 5 7 4	18 8 5 6	17 9 5 6

For label *mediumEDSS* (0/1 - $(< 5)/(\geq 5)$):

The via pattern recognition study was not performed since the number of patients with *mediumEDSS*≥ 5 was minimal.

D.1.3 Momentaneous Set

D.1.3.1 Standard procedure

For label *msCourse* (0/1 - RR/SP):

Final features: Age Visit, Last EDSS, Last BrainStem, Last Duration.

Table D.109: Momentaneous_Standard_Traditional_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.66	0.73	0.69	0.69	0.63	0.65	0.66	0.71	0.73	0.70	0.72
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
71.43	85.71	85.71	85.71	71.43	85.71	85.71	85.71	85.71	71.43	85.71
56.82	61.36	54.55	50.00	50.00	50.00	47.73	52.27	61.36	63.64	61.36
92.59	96.43	96.00	95.65	91.67	95.65	95.45	95.83	96.43	93.33	96.43
20.83	26.09	23.08	21.43	18.52	21.43	20.69	22.22	26.09	23.81	26.09
58.82	64.71	58.82	54.90	52.94	54.90	52.94	56.86	64.71	64.71	64.71
Confusion Matrix										
25 19 2 5	27 17 1 6	24 20 1 6	22 22 1 6	22 22 2 5	22 22 1 6	21 23 1 6	23 21 1 6	27 17 1 6	28 16 2 5	27 17 1 6

Table D.110: Momentaneous_Standard_Traditional_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.53	NA	0.51	0.53	0.50	0.50	NA	0.53	0.51	0.53
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	NA	100.00	100.00	100.00	100.00	NA	100.00	100.00	100.00
6.82	6.82	NA	2.27	6.82	0.00	0.00	NA	6.82	2.27	6.82
100.00	100.00	NA	100.00	100.00	NaN	NaN	NA	100.00	100.00	100.00
14.58	14.58	NA	14.00	14.58	13.73	13.73	NA	14.58	14.00	14.58
19.61	19.61	NA	15.69	19.61	13.73	13.73	NA	19.61	15.69	19.61
Confusion Matrix										
3 41 0 7	3 41 0 7	NA NA	1 43 0 7	3 41 0 7	0 44 0 7	0 44 0 7	NA NA	3 41 0 7	1 43 0 7	3 41 0 7

Table D.111: Momentaneous_Standard_kFold_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.69	0.61	0.64	0.55	0.61	0.69	0.66	0.62	0.61	0.63	0.68
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
60.00	44.00	57.69	32.00	52.00	**56.00**	**52.00**	48.00	40.00	64.00	**76.00**
82.26	83.87	74.19	93.55	72.58	**83.87**	**82.26**	82.26	85.48	70.97	**69.35**
83.61	78.79	80.70	77.33	78.95	**82.54**	**80.95**	79.69	77.94	83.02	**87.76**
57.69	52.38	48.39	66.67	43.33	**58.33**	**54.17**	52.17	52.63	47.06	**50.00**
75.86	72.41	69.32	75.86	66.67	**75.86**	**73.56**	72.41	72.41	68.97	**71.26**
Confusion Matrix										
51 11 10 15	52 10 14 11	46 16 11 15	58 4 17 8	45 17 12 13	52 10 11 14	51 11 12 13	51 11 13 12	53 9 15 10	44 18 9 16	43 19 6 19

Table D.112: Momentaneous_Standard_kFold_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.73	0.77	NA	0.85	0.81	0.83	0.84	NA	0.77	0.78	0.81
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
64.00	**72.00**	NA	**80.00**	**76.00**	**84.00**	**84.00**	NA	**72.00**	**84.00**	**84.00**
88.71	**90.32**	NA	**93.65**	**91.94**	**90.32**	**91.94**	NA	**90.32**	**82.26**	**87.10**
85.94	**88.89**	NA	**92.19**	**90.48**	**93.33**	**93.44**	NA	**88.89**	**92.73**	**93.10**
69.57	**75.00**	NA	**83.33**	**79.17**	**77.78**	**80.77**	NA	**75.00**	**65.63**	**72.41**
81.61	**85.06**	NA	**89.77**	**87.36**	**88.51**	**89.66**	NA	**85.06**	**82.76**	**86.21**
Confusion Matrix										
55 7 9 16	56 6 7 18	NA NA	59 4 5 20	57 5 6 19	56 6 4 21	57 5 4 21	NA NA	56 6 7 18	51 11 4 21	54 8 4 21

Table D.113: Momentaneous_Standard_LOO_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.43	0.51	0.59	0.60	0.51	0.49	0.52	0.48	0.49	0.51	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
20.00	24.00	48.00	20.00	36.00	28.00	28.00	24.00	20.00	40.00	48.00
66.13	77.42	70.97	90.32	66.13	70.97	75.81	72.58	79.03	61.29	56.45
67.21	71.64	77.19	73.68	71.93	70.97	72.31	70.31	71.01	71.70	72.92
19.23	30.00	40.00	45.45	30.00	28.00	31.82	26.09	27.78	29.41	30.77
52.87	62.07	64.37	70.11	57.47	58.62	62.07	58.62	62.07	55.17	54.02
Confusion Matrix										
41 21 20 5	48 14 19 6	44 18 13 12	56 6 20 5	41 21 16 9	44 18 18 7	47 15 18 7	45 17 19 6	49 13 20 5	38 24 15 10	35 27 13 12

Table D.114: Momentaneous_Standard_LOO_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.47	NA	0.49	0.53	0.53	0.52	NA	0.47	0.43	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
24.00	24.00	NA	28.00	32.00	36.00	32.00	NA	24.00	24.00	24.00
67.74	70.97	NA	70.97	74.19	70.97	72.58	NA	70.97	61.29	62.90
68.85	69.84	NA	70.97	73.02	73.33	72.58	NA	69.84	66.67	67.24
23.08	25.00	NA	28.00	33.33	33.33	32.00	NA	25.00	20.00	20.69
55.17	57.47	NA	58.62	62.07	60.92	60.92	NA	57.47	50.57	51.72
Confusion Matrix										
42 20 19 6	44 18 19 6	NA NA	44 18 18 7	46 16 17 8	44 18 16 9	45 17 17 8	NA NA	44 18 19 6	38 24 19 6	39 23 19 6

For label *currentEDSS* (0/1 - $(<3)/(\geq 3)$):

Final features: Spinal Cord, MS Course, Age Visit, Years since onset, Last cerebrellum.

Table D.115: Momentaneous_Standard_Traditional_PCA_currentEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.75	0.78	0.77	0.74	0.67	0.65	0.65	0.75	0.78	0.77	0.76
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	**70.00**	**80.00**	**70.00**	80.00	80.00	80.00	80.00	**70.00**	**70.00**	**70.00**
74.07	**81.48**	**77.78**	**77.78**	55.56	51.85	51.85	66.67	**81.48**	**85.19**	**81.48**
90.91	**88.00**	**91.30**	**87.50**	88.24	87.50	87.50	90.00	**88.00**	**88.46**	**88.00**
53.33	**58.33**	**57.14**	**53.85**	40.00	38.10	38.10	47.06	**58.33**	**63.64**	**58.33**
75.68	**75.68**	**78.38**	**75.68**	62.16	59.46	59.46	70.27	**78.38**	**81.08**	**78.38**
Confusion Matrix										
20 7 2 8	20 7 2 8	21 6 2 8	21 6 3 7	15 12 2 8	14 13 2 8	14 13 2 8	18 9 2 8	22 5 3 7	23 4 3 7	22 5 3 7

Table D.116: Momentaneous_Standard_Traditional_currentEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.64	0.53	NA	0.56	0.71	0.70	0.71	NA	0.53	0.50	0.54
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	100.00	NA	100.00	**60.00**	80.00	90.00	NA	100.00	100.00	100.00
48.15	7.41	NA	14.81	**77.78**	62.96	55.56	NA	7.41	0.00	7.41
86.67	100.00	NA	100.00	**84.00**	89.47	93.75	NA	100.00	NaN	100.00
36.36	28.57	NA	30.30	**50.00**	44.44	42.86	NA	28.57	27.03	28.57
56.76	32.43	NA	37.84	**72.97**	67.57	64.86	NA	32.43	27.03	32.43
Confusion Matrix										
13 14	2 25	NA	4 23	21 6	17 10	15 12	NA	2 25	0 27	2 25
2 8	0 10	NA	0 10	4 6	2 8	1 9	NA	0 10	0 10	0 10

Table D.117: Momentaneous_Standard_kFold_PCA_currentEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.80	0.79	0.80	0.76	0.80	0.77	0.82	0.75	0.79	0.78	0.76
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
77.14	**62.86**	**85.71**	**58.33**	**77.14**	**74.29**	**77.14**	**65.71**	**62.86**	**65.71**	**65.71**
84.62	**92.31**	**76.92**	**90.38**	**84.62**	**79.25**	**86.54**	**84.62**	**92.31**	**88.46**	**84.62**
84.62	**78.69**	**88.89**	**75.81**	**84.62**	**82.35**	**84.91**	**78.57**	**78.69**	**79.31**	**78.57**
77.14	**84.62**	**71.43**	**80.77**	**77.14**	**70.27**	**79.41**	**74.19**	**84.62**	**79.31**	**74.19**
81.61	**80.46**	**80.46**	**77.27**	**81.61**	**77.27**	**82.76**	**77.01**	**80.46**	**79.31**	**77.01**
Confusion Matrix										
44 8	48 4	40 12	47 5	44 8	42 11	45 7	44 8	48 4	46 6	44 8
8 27	13 22	5 30	15 21	8 27	9 26	8 27	12 23	13 22	12 23	12 23

Table D.118: Momentaneous_Standard_kFold_currentEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.72	0.77	0.75	0.78	0.81	0.78	0.75	0.74	0.77	0.74	0.73
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
71.43	**62.86**	**65.71**	**71.43**	**74.29**	**68.57**	**65.71**	**62.86**	**62.86**	**62.86**	**62.86**
75.00	**90.38**	**82.69**	**86.54**	**88.46**	**88.46**	**86.54**	**84.62**	**90.38**	**86.54**	**84.62**
79.59	**78.33**	**78.18**	**81.82**	**83.64**	**80.70**	**78.95**	**77.19**	**78.33**	**77.59**	**77.19**
65.79	**81.48**	**71.88**	**78.13**	**81.25**	**80.00**	**76.67**	**73.33**	**81.48**	**75.86**	**73.33**
73.56	**79.31**	**75.86**	**80.46**	**82.76**	**80.46**	**78.16**	**75.86**	**79.31**	**77.01**	**75.86**
Confusion Matrix										
39 13	47 5	43 9	45 7	46 6	46 6	45 7	44 8	47 5	45 7	44 8
10 25	13 22	12 23	10 25	9 26	11 24	12 23	13 22	13 22	13 22	13 22

Table D.119: Momentaneous_Standard_LOO_PCA_currentEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.53	0.50	0.53	0.55	0.54	0.56	0.46	0.53	0.44	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
28.57	20.00	40.00	20.00	28.57	25.71	25.71	28.57	20.00	28.57	34.29
53.85	65.38	40.38	65.38	51.92	48.08	51.92	59.62	65.38	59.62	65.38
52.83	54.84	50.00	54.84	51.92	49.02	50.94	55.36	54.84	55.36	59.65
29.41	28.00	31.11	28.00	28.57	25.00	26.47	32.26	28.00	32.26	40.00
43.68	47.13	40.23	47.13	42.53	39.08	41.38	47.13	47.13	47.13	52.87
Confusion Matrix										
28 24	34 18	21 31	34 18	27 25	25 27	27 25	31 21	34 18	31 21	34 18
25 10	28 7	21 14	28 7	25 10	26 9	26 9	25 10	28 7	25 10	23 12

Table D.120: Momentaneous_Standard_LOO_currentEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.37	0.38	0.40	0.40	0.41	0.42	0.45	0.40	0.38	0.43	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
31.43	17.14	25.71	25.71	25.71	25.71	28.57	22.86	17.14	25.71	31.43
42.31	61.54	55.77	53.85	57.69	59.62	61.54	57.69	61.54	61.54	63.46
47.83	52.46	52.73	51.85	53.57	54.39	56.14	52.63	52.46	55.17	57.89
26.83	23.08	28.13	27.27	29.03	30.00	33.33	26.67	23.08	31.03	36.67
37.93	43.68	43.68	42.53	44.83	45.98	48.28	43.68	43.68	47.13	50.57
Confusion Matrix										
22 30	32 20	29 23	28 24	30 22	31 21	32 20	30 22	32 20	32 20	33 19
24 11	29 6	26 9	26 9	26 9	26 9	25 10	27 8	29 6	26 9	24 11

For label *currentEDSS* (0/1 - $(< 5)/(\geq 5)$):

Final features: Spinal Cord, MS Course, Age Visit, Years since onset, Last Sensory.

Table D.121: Momentaneous_Standard_Traditional_PCA_currentEDSS < 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.65	0.72	NA	0.64	0.60	0.60	0.61	0.67	NA	0.71	0.71
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	80.00	NA	60.00	80.00	80.00	80.00	80.00	NA	80.00	80.00
51.67	65.00	NA	61.67	40.00	38.33	41.67	48.33	NA	66.67	65.00
96.88	97.50	NA	94.87	96.00	95.83	96.15	96.67	NA	97.56	97.50
12.12	16.00	NA	11.54	10.00	9.76	10.26	11.43	NA	16.67	16.00
53.85	66.15	NA	61.54	43.08	41.54	44.62	50.77	NA	67.69	66.15
Confusion Matrix										
31 29	39 21	NA	37 23	24 36	23 37	25 35	29 31	NA	40 20	39 21
1 4	1 4	NA	2 3	1 4	1 4	1 4	1 4	NA	1 4	1 4

Table D.122: Momentaneous_Standard_Traditional_currentEDSS < 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.60	0.60	NA	0.57	0.60	0.61	0.67	NA	0.60	0.53	0.60
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	100.00	NA	80.00	60.00	80.00	80.00	NA	100.00	100.00	100.00
43.33	26.67	NA	26.67	51.67	41.67	46.67	NA	26.67	5.00	26.67
96.30	100.00	NA	94.12	93.94	96.15	96.55	NA	100.00	100.00	100.00
10.53	10.20	NA	8.33	9.38	10.26	11.11	NA	10.20	8.06	10.20
46.15	32.31	NA	30.77	52.31	44.62	49.23	NA	32.31	12.31	32.31
Confusion Matrix										
26 34 1 4	16 44 0 5	NA NA	16 44 1 4	31 29 2 3	25 35 1 4	28 32 1 4	NA NA	16 44 0 5	3 57 0 5	16 44 0 5

Table D.123: Momentaneous_Standard_kFold_PCA_currentEDSS < 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.55	NA	0.15	0.60	0.45	0.51	0.47	0.45	0.65	0.62
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
37.50	43.75	NA	0.00	56.25	31.25	37.50	31.25	31.25	68.75	62.50
87.32	90.14	NA	94.37	84.51	85.92	95.77	92.96	91.55	80.28	76.06
86.11	87.67	NA	80.72	89.55	84.72	87.18	85.71	85.53	91.94	90.00
40.00	50.00	NA	0.00	45.00	33.33	66.67	50.00	45.45	44.00	37.04
78.16	81.61	NA	77.01	79.31	75.86	85.06	81.61	80.46	78.16	73.56
Confusion Matrix										
62 9 10 6	64 7 9 7	NA NA	67 4 16 0	60 11 7 9	61 10 11 5	68 3 10 6	66 5 11 5	65 6 11 5	57 14 5 11	54 17 6 10

Table D.124: Momentaneous_Standard_kFold_currentEDSS < 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.51	0.45	0.30	0.71	0.53	0.33	0.55	0.39	0.64	0.59
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
31.25	37.50	31.25	18.75	**68.75**	37.50	18.75	43.75	25.00	68.75	56.25
90.14	90.14	87.32	97.18	**94.37**	88.73	94.37	85.92	91.55	77.46	77.46
85.33	86.49	84.93	84.15	**93.06**	86.30	83.75	87.14	84.42	91.67	88.71
41.67	46.15	35.71	60.00	**73.33**	42.86	42.86	41.18	40.00	40.74	36.00
79.31	80.46	77.01	82.76	**89.66**	79.31	80.46	78.16	79.31	75.86	73.56
Confusion Matrix										
64 7	64 7	62 9	69 2	67 4	63 8	67 4	61 10	65 6	55 16	55 16
11 5	10 6	11 5	13 3	5 11	10 6	13 3	9 7	12 4	5 11	7 9

Table D.125: Momentaneous_Standard_LOO_PCA_currentEDSS < 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.52	0.48	0.40	0.54	0.52	0.51	0.47	0.54	0.65	0.62
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
18.75	18.75	37.50	0.00	31.25	18.75	12.50	6.25	18.75	68.75	62.50
81.69	84.51	56.34	94.37	78.87	84.51	88.73	90.14	87.32	80.28	76.06
81.69	82.19	80.00	80.72	83.58	82.19	81.82	81.01	82.67	91.94	90.00
18.75	21.43	16.22	0.00	25.00	21.43	20.00	12.50	25.00	44.00	37.04
70.11	72.41	52.87	77.01	70.11	72.41	74.71	74.71	74.71	78.16	73.56
Confusion Matrix										
58 13	60 11	40 31	67 4	56 15	60 11	63 8	64 7	62 9	57 14	54 17
13 3	13 3	10 6	16 0	11 5	13 3	14 2	15 1	13 3	5 11	6 10

Table D.126: Momentaneous_Standard_LOO_currentEDSS < 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.40	0.53	0.57	0.40	0.43	0.47	0.56	0.50	0.57	0.50	0.48
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
0.00	18.75	25.00	0.00	6.25	12.50	12.50	18.75	18.75	31.25	25.00
85.92	85.92	87.32	92.96	78.87	81.69	92.96	80.28	90.14	69.01	70.42
79.22	82.43	83.78	80.49	78.87	80.56	82.50	81.43	83.12	81.67	80.65
0.00	23.08	30.77	0.00	6.25	13.33	28.57	17.65	30.00	18.52	16.00
70.11	73.56	75.86	75.86	65.52	68.97	78.16	68.97	77.01	62.07	62.07
Confusion Matrix										
61 10	61 10	62 9	66 5	56 15	58 13	66 5	57 14	64 7	49 22	50 21
16 0	13 3	12 4	16 0	15 1	14 2	14 2	13 3	13 3	11 5	12 4

First feature selection process for *nextEDSS*:

Table D.127: Momentaneous_Feature_Selection_Identification_nextEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Gender	0	0	0	0	0	1	1	0	0	0	0	2
Age of Onset	0	0	0	0	0	0	1	1	0	0	0	2
Optic Pathways	0	1	1	0	0	0	1	0	1	0	1	**5**
Brainstem-Cerebellum	0	0	0	0	0	1	0	0	0	0	0	1
Spinal Cord	0	1	0	1	0	1	0	1	1	0	1	**6**
Progression From Onset	0	0	0	0	0	0	0	0	1	0	0	1
Age of Diagnosis	0	1	1	1	1	0	1	0	0	1	1	**7**
Years from Onset to Diagnosis	0	1	1	1	1	0	1	1	0	1	1	**8**
MRI	0	0	0	0	0	0	1	0	0	0	0	1
CSF	0	0	0	0	0	1	0	0	0	0	0	1
Age at SP Diagnosis	0	1	1	1	1	0	0	1	1	1	1	**8**
Years from Diagnosis to SP	0	1	1	1	1	0	0	0	1	1	1	**7**
Years from Diagnosis to Onset	0	1	1	1	1	0	0	0	1	1	1	**7**
MS Course	0	1	1	1	1	1	0	0	1	1	1	**8**
Age Visit	0	1	1	1	1	0	1	0	0	1	1	**7**
Years since Onset	1	1	1	1	1	0	1	1	0	1	1	**9**

Selected features: Optic Pathways, Spinal Cord, Age of Diagnosis, Years from Onset to Diagnosis, Age at SP Diagnosis, Years from Diagnosis to SP, Years from Diagnosis to Onset, MS Course, Age Visit, Years since Onset.

Table D.128: Momentaneous_Feature_Selection_Visits_nextEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Last Suspected	0	0	0	0	0	0	1	1	0	0	0	2
Last EDSS	1	1	1	1	0	0	1	1	0	1	1	**8**
Last Sympton	0	0	0	0	0	0	0	0	1	0	0	1

Selected features: Last EDSS.

Table D.129: Momentaneous_Feature_Selection_Relapses_nextEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Last Pyramidal	0	1	0	0	0	1	0	0	1	0	1	**4**
Last BrainStem	0	0	0	0	0	0	1	1	0	0	0	2
Last Bowel	0	0	0	0	0	0	0	0	1	0	0	1
Last Neuropsycho	0	0	0	0	0	0	1	0	0	0	0	1
Last Cerebellum	0	0	0	0	0	0	1	0	0	0	0	1
Last Visual	0	0	0	0	0	0	1	0	0	0	0	1
Last Sensory	0	1	1	1	0	1	1	1	1	1	1	**9**
Last Hospital	0	0	0	0	0	1	1	0	0	0	0	2
Last ambulatory	0	0	0	0	0	1	1	0	0	0	0	2
Last Corticosteroid	0	0	0	0	0	0	1	0	0	0	0	1

Selected features: Last Pyramidal, Last Sensory.

For label *nextEDSS* (0/1 - $(< 3)/(\geq 3)$**):**

Final features: Age Visit, Years since onset, Last EDSS.

Table D.130: Momentaneous_Standard_Traditional_PCA_nextEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.80	0.86	0.83	0.81	0.73	0.78	0.81	0.83	0.86	0.83	0.85
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	**80.00**	**90.00**	**70.00**	80.00	90.00	**90.00**	**80.00**	**80.00**	**70.00**	**80.00**
79.31	**93.10**	**79.31**	**89.66**	62.07	65.52	**72.41**	**82.76**	**93.10**	**93.10**	**93.10**
92.00	**93.10**	**95.83**	**89.66**	90.00	95.00	**95.45**	**92.31**	**93.10**	**90.00**	**93.10**
57.14	**80.00**	**60.00**	**70.00**	42.11	47.37	**52.94**	**61.54**	**80.00**	**77.78**	**80.00**
79.49	**89.74**	**82.05**	**84.62**	66.67	71.79	**76.92**	**82.05**	**89.74**	**87.18**	**89.74**
Confusion Matrix										
23 6	27 2	23 6	26 3	18 11	19 10	21 8	24 5	27 2	27 2	27 2
2 8	2 8	1 9	3 7	2 8	1 9	1 9	2 8	2 8	3 7	2 8

Table D.131: Momentaneous_Standard_Traditional_nextEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN
25.64	25.64	25.64	25.64	25.64	25.64	25.64	25.64	25.64	25.64	25.64
25.64	25.64	25.64	25.64	25.64	25.64	25.64	25.64	25.64	25.64	25.64
Confusion Matrix										
0 29 0 10	0 29 0 10	0 29 0 10	0 29 0 10	0 29 0 10	0 29 0 10	0 29 0 10	0 29 0 10	0 29 0 10	0 29 0 10	0 29 0 10

Table D.132: Momentaneous_Standard_kFold_PCA_nextEDSS < 3

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.83	0.82	0.84	0.82	0.88	0.84	0.84	0.84	0.82	0.86	0.84
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
76.47	**67.65**	**70.59**	**67.65**	**88.24**	**79.41**	**76.47**	**70.59**	**67.65**	**70.59**	**67.65**
86.79	**96.23**	**96.23**	**96.23**	**92.45**	**90.57**	**92.45**	**96.23**	**96.23**	**96.23**	**96.23**
85.19	**82.26**	**83.61**	**82.26**	**92.45**	**87.27**	**85.96**	**83.61**	**82.26**	**83.61**	**82.26**
78.79	**92.00**	**92.31**	**92.00**	**88.24**	**84.38**	**86.67**	**92.31**	**92.00**	**92.31**	**92.00**
82.76	**85.06**	**86.21**	**85.06**	**90.80**	**86.21**	**86.21**	**86.21**	**85.06**	**86.21**	**85.06**
Confusion Matrix										
46 7 8 26	51 2 11 23	51 2 10 24	51 2 11 23	49 4 4 30	48 5 7 27	49 4 8 26	51 2 10 24	51 2 11 23	51 2 10 24	51 2 11 23

Table D.133: Momentaneous_Standard_kFold_nextEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.91	0.95	0.90	0.94	0.87	0.91	0.91	0.91	NA	0.90	0.93
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.29	**88.24**	**91.18**	**91.18**	**85.29**	**85.29**	**85.29**	**91.18**	NA	**91.18**	**88.24**
94.34	**98.11**	**90.57**	**96.23**	**88.68**	**96.23**	**96.23**	**92.45**	NA	**92.45**	**98.11**
90.91	**92.86**	**94.12**	**94.44**	**90.38**	**91.07**	**91.07**	**94.23**	NA	**94.23**	**92.86**
90.63	**96.77**	**86.11**	**93.94**	**82.86**	**93.55**	**93.55**	**88.57**	NA	**88.57**	**96.77**
90.80	**94.25**	**90.80**	**94.25**	**87.36**	**91.95**	**91.95**	**91.95**	NA	**91.95**	**94.25**
Confusion Matrix										
50 3 5 29	52 1 4 30	48 5 3 31	51 2 3 31	47 6 5 29	51 2 5 29	51 2 5 29	49 4 3 31	NA NA	49 4 3 31	52 1 4 30

Table D.134: Momentaneous_Standard_LOO_PCA_nextEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.51	0.50	0.51	0.52	0.50	0.52	0.50	0.51	0.58	0.56
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
38.24	29.41	29.41	29.41	41.18	38.24	38.24	29.41	29.41	38.24	35.29
62.26	71.70	69.81	71.70	62.26	62.26	66.04	69.81	71.70	75.47	75.47
61.11	61.29	60.66	61.29	62.26	61.11	62.50	60.66	61.29	65.57	64.52
39.39	40.00	38.46	40.00	41.18	39.39	41.94	38.46	40.00	50.00	48.00
52.87	55.17	54.02	55.17	54.02	52.87	55.17	54.02	55.17	60.92	59.77
Confusion Matrix										
33 20	38 15	37 16	38 15	33 20	33 20	35 18	37 16	38 15	40 13	40 13
21 13	24 10	24 10	24 10	20 14	21 13	21 13	24 10	24 10	21 13	22 12

Table D.135: Momentaneous_Standard_LOO_nextEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.47	0.49	0.48	0.41	0.45	0.47	0.51	0.47	0.46	0.45
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
38.24	32.35	41.18	35.29	29.41	29.41	32.35	41.18	32.35	35.29	29.41
64.15	62.26	56.60	60.38	52.83	60.38	62.26	60.38	62.26	56.60	60.38
61.82	58.93	60.00	59.26	53.85	57.14	58.93	61.54	58.93	57.69	57.14
40.63	35.48	37.84	36.36	28.57	32.26	35.48	40.00	35.48	34.29	32.26
54.02	50.57	50.57	50.57	43.68	48.28	50.57	52.87	50.57	48.28	48.28
Confusion Matrix										
34 19	33 20	30 23	32 21	28 25	32 21	33 20	32 21	33 20	30 23	32 21
21 13	23 11	20 14	22 12	24 10	24 10	23 11	20 14	23 11	22 12	24 10

For label *nextEDSS* (0/1 - $(< 5)/(\geq 5)$):

Table D.136: Momentaneous_Standard_Traditional_PCA_nextEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.70	0.77	0.73	0.67	0.57	0.65	0.73	0.76	0.77	0.77	0.77
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
83.33	83.33	66.67	83.33	66.67	66.67	66.67	83.33	83.33	83.33	83.33
54.55	72.73	70.91	54.55	47.27	63.64	72.73	74.55	72.73	72.73	72.73
96.77	97.56	95.12	96.77	92.86	94.59	95.24	97.62	97.56	97.56	97.56
16.67	25.00	20.00	16.67	12.12	16.67	21.05	26.32	25.00	25.00	25.00
57.38	73.77	70.49	57.38	49.18	63.93	72.13	75.41	73.77	73.77	73.77
Confusion Matrix										
30 25	40 15	39 16	30 25	26 29	35 20	40 15	41 14	40 15	40 15	40 15
1 5	1 5	2 4	1 5	2 4	2 4	2 4	1 5	1 5	1 5	1 5

Table D.137: Momentaneous_Standard_Traditional_nextEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.63	0.50	0.51	0.62	0.70	0.77	0.69	0.51	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	83.33	100.00	100.00	100.00	100.00	100.00	100.00
25.45	0.00	1.82	23.64	58.18	54.55	38.18	1.82	1.82	0.00	0.00
100.00	NaN	100.00	100.00	96.97	100.00	100.00	100.00	100.00	NaN	NaN
12.77	9.84	10.00	12.50	17.86	19.35	15.00	10.00	10.00	9.84	9.84
32.79	9.84	11.48	31.15	60.66	59.02	44.26	11.48	11.48	9.84	9.84
Confusion Matrix										
14 41	0 55	1 54	13 42	32 23	30 25	21 34	1 54	1 54	0 55	0 55
0 6	0 6	0 6	0 6	1 5	0 6	0 6	0 6	0 6	0 6	0 6

Table D.138: Momentaneous_Standard_kFold_PCA_nextEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	0.62	0.56	0.24	0.74	0.43	0.37	0.54	0.58	0.69	0.67
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
42.11	**52.63**	47.37	10.53	**68.42**	26.32	21.05	42.11	42.11	**73.68**	**68.42**
89.71	**88.24**	82.35	95.59	**94.12**	94.12	94.12	88.24	89.71	**80.88**	**82.35**
84.72	**86.96**	84.85	79.27	**91.43**	82.05	81.01	84.51	84.72	**91.67**	**90.32**
53.33	**55.56**	42.86	40.00	**76.47**	55.56	50.00	50.00	53.33	**51.85**	**52.00**
79.31	**80.46**	74.71	77.01	**88.51**	79.31	78.16	78.16	79.31	**79.31**	**79.31**
Confusion Matrix										
61 7	60 8	56 12	65 3	64 4	64 4	64 4	60 8	61 7	55 13	56 12
11 8	9 10	10 9	17 2	6 13	14 5	15 4	11 8	11 8	5 14	6 13

Table D.139: Momentaneous_Standard_kFold_nextEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.80	0.80	0.80	0.80	0.76	0.80	0.80	0.80	0.80	0.77	0.77
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
84.21	**84.21**	**84.21**	**84.21**	**78.95**	**84.21**	**84.21**	**84.21**	**84.21**	**84.21**	**84.21**
98.53	**98.53**	**98.53**	**98.53**	**98.53**	**98.53**	**98.53**	**98.53**	**98.53**	**91.18**	**91.18**
95.71	**95.71**	**95.71**	**95.71**	**94.37**	**95.71**	**95.71**	**95.71**	**95.71**	**95.38**	**95.38**
94.12	**94.12**	**94.12**	**94.12**	**93.75**	**94.12**	**94.12**	**94.12**	**94.12**	**72.73**	**72.73**
95.40	**95.40**	**95.40**	**95.40**	**94.25**	**95.40**	**95.40**	**95.40**	**95.40**	**89.66**	**89.66**
Confusion Matrix										
67 1	67 1	67 1	67 1	67 1	67 1	67 1	67 1	67 1	62 6	62 6
3 16	3 16	3 16	3 16	4 15	3 16	3 16	3 16	3 16	3 16	3 16

Table D.140: Momentaneous_Standard_LOO_PCA_nextEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.47	0.46	0.38	0.54	0.50	0.52	0.41	0.44	0.58	0.61
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
21.05	15.79	15.79	0.00	26.32	10.53	10.53	5.26	10.53	47.37	47.37
85.29	77.94	75.00	92.65	80.88	89.71	91.18	79.41	79.41	73.53	77.94
79.45	76.81	76.12	76.83	79.71	78.21	78.48	75.00	76.06	83.33	84.13
28.57	16.67	15.00	0.00	27.78	22.22	25.00	6.67	12.50	33.33	37.50
71.26	64.37	62.07	72.41	68.97	72.41	73.56	63.22	64.37	67.82	71.26
Confusion Matrix										
58 10	53 15	51 17	63 5	55 13	61 7	62 6	54 14	54 14	50 18	53 15
15 4	16 3	16 3	19 0	14 5	17 2	17 2	18 1	17 2	10 9	10 9

Table D.141: Momentaneous_Standard_LOO_nextEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.58	0.58	0.58	0.58	0.60	0.58	0.58	0.58	0.58	0.43	0.43
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
31.58	31.58	31.58	31.58	31.58	31.58	31.58	31.58	31.58	15.79	15.79
83.82	83.82	83.82	83.82	85.29	83.82	83.82	83.82	83.82	67.65	67.65
81.43	81.43	81.43	81.43	81.69	81.43	81.43	81.43	81.43	74.19	74.19
35.29	35.29	35.29	35.29	37.50	35.29	35.29	35.29	35.29	12.00	12.00
72.41	72.41	72.41	72.41	73.56	72.41	72.41	72.41	72.41	56.32	56.32
Confusion Matrix										
57 11	57 11	57 11	57 11	58 10	57 11	57 11	57 11	57 11	46 22	46 22
13 6	13 6	13 6	13 6	13 6	13 6	13 6	13 6	13 6	16 3	16 3

First feature selection process for *highestEDSS*:

Table D.142: Momentaneous_Feature_Selection_Identification_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Gender	0	0	0	0	0	1	1	1	0	0	0	3
Age of Onset	0	0	0	0	0	0	1	1	0	0	0	2
Optic Pathways	0	1	1	0	0	0	1	0	1	1	1	**6**
Brainstem-Cerebellum	0	0	0	0	0	1	1	0	0	0	0	2
Spinal Cord	0	1	1	1	0	1	1	1	1	0	1	**8**
Progression From Onset	0	0	0	0	0	0	0	0	1	0	0	1
Age of Diagnosis	0	0	0	0	0	0	1	1	0	1	0	3
Years from Onset to Diagnosis	0	1	1	1	1	0	1	1	0	1	1	**8**
MRI	0	0	0	0	0	0	1	0	0	0	0	1
Evoked Potentials	0	0	0	0	0	0	1	0	0	0	0	1
CSF	0	0	0	0	0	1	1	0	0	0	0	2
Age at SP Diagnosis	0	1	1	1	1	0	1	1	1	1	1	**9**
Years from Diagnosis to SP	0	1	1	1	1	0	1	0	1	1	1	**8**
Years from Diagnosis to Onset	0	1	1	1	1	0	0	0	1	1	1	**7**
MS Course	0	1	1	1	1	1	0	0	1	1	1	**8**
Family History	0	0	0	0	0	0	1	0	0	0	0	1
Active	0	0	0	0	0	0	1	0	0	0	0	1
Age Visit	0	1	1	1	1	0	0	1	0	1	1	**7**
Years since Onset	1	1	1	0	1	0	1	0	0	1	1	**7**

Feature selection: Optic Pathways, Spinal-Cord, Age of Diagnosis, Years from

Onset to Onset to Diagnosis, Age at SP Diagnosis, Years from Diagnosis to Onset, MS Course, Age Visit, Years since Onset.

Table D.143: Momentaneous_Feature_Selection_Visits_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
ID	0	0	0	0	0	0	0	0	0	0	0	0
Last Routine	0	0	0	0	0	0	0	1	0	0	0	1
Last Suspected	0	0	0	0	0	0	0	0	0	0	0	0
Last EDSS	1	1	1	1	1	0	1	1	0	1	1	**9**
Last Weakness	0	0	0	0	0	0	0	0	0	0	0	0
Last Sympton	0	0	0	0	0	0	0	0	1	0	0	1

Feature selection: Last EDSS.

Table D.144: Momentaneous_Feature_Selection_Relapses_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Last Pyramidal	0	0	0	0	0	1	0	1	0	0	0	2
Last BrainStem	0	0	0	0	0	0	1	1	0	0	0	2
Last Bowel	0	0	0	0	0	0	0	0	1	0	0	1
Last Neuropsycho	0	0	0	0	0	0	1	0	0	0	0	1
Last Cerebellum	0	0	0	0	0	0	1	1	0	0	0	2
Last Visual	0	0	0	0	0	0	1	0	0	0	0	1
Last Sensory	0	1	1	1	0	1	1	1	1	1	1	**9**
Last Hospital	0	0	0	0	0	1	1	1	0	0	0	3
Last ambulatory	0	0	0	0	0	1	0	0	0	0	0	1
Last Corticosteroid	0	0	0	0	0	0	1	0	0	0	0	1
Last Treatment	0	0	0	0	0	0	1	0	1	0	0	2
Last Duration	0	0	0	0	0	0	1	1	0	0	0	2

Feature selection: Last Pyramidal, Last Sensory.

For label *highestEDSS* (0/1 - (< 3)/(≥ 3)):

Final Features: Years since Onset, Last EDSS.

Table D.145: Momentaneous_Standard_Traditional_PCA_highestEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.78	0.77	0.75	0.63	0.65	0.73	0.73	0.76	0.77	0.77	0.76
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
92.86	**71.43**	**71.43**	**50.00**	**64.29**	**71.43**	**64.29**	**71.43**	**71.43**	**71.43**	**71.43**
63.64	**81.82**	**81.82**	**72.73**	**63.64**	**72.73**	**81.82**	**81.82**	**81.82**	**81.82**	**81.82**
87.50	**69.23**	**69.23**	**53.33**	**58.33**	**66.67**	**64.29**	**69.23**	**69.23**	**69.23**	**69.23**
76.47	**83.33**	**83.33**	**70.00**	**69.23**	**76.92**	**81.82**	**83.33**	**83.33**	**83.33**	**83.33**
80.00	**76.00**	**76.00**	**60.00**	**64.00**	**72.00**	**72.00**	**76.00**	**76.00**	**76.00**	**76.00**
Confusion Matrix										
7 4 1 13	9 2 4 10	9 2 4 10	8 3 7 7	7 4 5 9	8 3 4 10	9 2 5 9	9 2 4 10	9 2 4 10	9 2 4 10	9 2 4 10

Table D.146: Momentaneous_Standard_Traditional_highestEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.71	0.50	0.50	0.50	0.50	0.53	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	92.86	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
0.00	0.00	45.45	0.00	0.00	0.00	0.00	9.09	0.00	0.00	0.00
NaN	NaN	83.33	NaN	NaN	NaN	NaN	100.00	NaN	NaN	NaN
56.00	56.00	68.42	56.00	56.00	56.00	56.00	58.33	56.00	56.00	56.00
56.00	56.00	72.00	56.00	56.00	56.00	56.00	60.00	56.00	56.00	56.00
Confusion Matrix										
0 11 0 14	0 11 0 14	5 6 1 13	0 11 0 14	0 11 0 14	0 11 0 14	0 11 0 14	1 10 0 14	0 11 0 14	0 11 0 14	0 11 0 14

Table D.147: Momentaneous_Standard_kFold_PCA_highestEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.80	0.78	0.77	0.76	0.81	0.75	0.77	0.78	0.78	0.77	0.77
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	**73.33**	**80.00**	**80.00**	**86.67**	**75.56**	**77.78**	**84.44**	**73.33**	**68.89**	**68.89**
78.57	**80.95**	**71.43**	**69.05**	**76.19**	**73.81**	**76.19**	**71.43**	**80.95**	**83.33**	**83.33**
78.57	**73.91**	**76.92**	**76.32**	**84.21**	**73.81**	**76.19**	**81.08**	**73.91**	**71.43**	**71.43**
80.00	**80.49**	**75.00**	**73.47**	**79.59**	**75.56**	**77.78**	**76.00**	**80.49**	**81.58**	**81.58**
79.31	**77.01**	**75.86**	**74.71**	**81.61**	**74.71**	**77.01**	**78.16**	**77.01**	**75.86**	**75.86**
Confusion Matrix										
33 9 9 36	34 8 12 33	30 12 9 36	29 13 9 36	32 10 6 39	31 11 11 34	32 10 10 35	30 12 7 38	34 8 12 33	35 7 14 31	35 7 14 31

Table D.148: Momentaneous_Standard_kFold_highestEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.87	0.86	0.84	0.91	0.87	0.88	0.89	0.82	0.86	0.81	0.85
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
88.89	**75.56**	**77.78**	**91.11**	**88.89**	**86.67**	**91.11**	**73.33**	**75.56**	**71.11**	**75.56**
88.10	**95.24**	**90.48**	**90.48**	**85.71**	**90.48**	**90.48**	**90.48**	**95.24**	**90.48**	**95.24**
88.10	**78.43**	**79.17**	**90.48**	**87.80**	**86.36**	**90.48**	**76.00**	**78.43**	**74.51**	**78.43**
88.89	**94.44**	**89.74**	**91.11**	**86.96**	**90.70**	**91.11**	**89.19**	**94.44**	**88.89**	**94.44**
88.51	**85.06**	**83.91**	**90.80**	**87.36**	**88.51**	**90.80**	**81.61**	**85.06**	**80.46**	**85.06**
Confusion Matrix										
37 5 5 40	40 2 11 34	38 4 10 35	38 4 4 41	36 6 5 40	38 4 6 39	38 4 4 41	38 4 12 33	40 2 11 34	38 4 13 32	40 2 11 34

Table D.149: Momentaneous_Standard_LOO_PCA_highestEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.48	0.52	0.53	0.53	0.52	0.49	0.47	0.48	0.60	0.61
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
57.78	42.22	57.78	**55.56**	57.78	**53.33**	51.11	55.56	42.22	**51.11**	**53.33**
47.62	54.76	45.24	**50.00**	47.62	**50.00**	47.62	38.10	54.76	**69.05**	**69.05**
51.28	46.94	50.00	**51.22**	51.28	**50.00**	47.62	44.44	46.94	**56.86**	**58.00**
54.17	50.00	53.06	**54.35**	54.17	**53.33**	51.11	49.02	50.00	**63.89**	**64.86**
52.87	48.28	51.72	**52.87**	52.87	**51.72**	49.43	47.13	48.28	**59.77**	**60.92**
Confusion Matrix										
20 22	23 19	19 23	21 21	20 22	21 21	20 22	16 26	23 19	29 13	29 13
19 26	26 19	19 26	20 25	19 26	21 24	22 23	20 25	26 19	22 23	21 24

Table D.150: Momentaneous_Standard_LOO_highestEDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.51	0.52	0.49	0.46	0.49	0.49	0.54	0.51	0.56	0.53
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
53.33	42.22	46.67	51.11	48.89	48.89	51.11	46.67	42.22	46.67	44.44
47.62	59.52	57.14	47.62	42.86	50.00	47.62	61.90	59.52	64.29	61.90
48.78	49.02	50.00	47.62	43.90	47.73	47.62	52.00	49.02	52.94	50.98
52.17	52.78	53.85	51.11	47.83	51.16	51.11	56.76	52.78	58.33	55.56
50.57	50.57	51.72	49.43	45.98	49.43	49.43	54.02	50.57	55.17	52.87
Confusion Matrix										
20 22	25 17	24 18	20 22	18 24	21 21	20 22	26 16	25 17	27 15	26 16
21 24	26 19	24 21	22 23	23 22	23 22	22 23	24 21	26 19	24 21	25 20

For label *highestEDSS* (0/1 - $(< 5)/(\geq 5)$):

Final features: MS Course, Years since onset, Last EDSS, Gender.

Table D.151: Momentaneous_Standard_Traditional_PCA_highestEDSS < 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.76	0.84	0.79	0.80	0.70	0.76	0.78	0.84	0.84	0.84	0.85
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	85.71	85.71	85.71	71.43	85.71	85.71	85.71	85.71	85.71	100.00
60.87	78.26	76.09	80.43	67.39	71.74	73.91	78.26	78.26	78.26	78.26
96.55	97.30	97.22	97.37	93.94	97.06	97.14	97.30	97.30	97.30	100.00
25.00	37.50	35.29	40.00	25.00	31.58	33.33	37.50	37.50	37.50	41.18
64.15	79.25	77.36	81.13	67.92	73.58	75.47	79.25	79.25	79.25	81.13
Confusion Matrix										
28 18	36 10	35 11	37 9	31 15	33 13	34 12	36 10	36 10	36 10	36 10
1 6	1 6	1 6	1 6	2 5	1 6	1 6	1 6	1 6	1 6	0 7

Table D.152: Momentaneous_Standard_Traditional_highestEDSS < 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.58	0.56	NA	0.74	0.65	0.69	0.68	NA	0.56	0.51	0.56
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	NA	100.00	85.71	85.71	85.71	NA	100.00	100.00	100.00
23.91	13.04	NA	54.35	47.83	54.35	47.83	NA	13.04	2.17	13.04
100.00	100.00	NA	100.00	95.65	96.15	95.65	NA	100.00	100.00	100.00
16.67	14.89	NA	25.00	20.00	22.22	20.00	NA	14.89	13.46	14.89
33.96	24.53	NA	60.38	52.83	58.49	52.83	NA	24.53	15.09	24.53
Confusion Matrix										
11 35 0 7	6 40 0 7	NA NA	25 21 0 7	22 24 1 6	25 21 1 6	22 24 1 6	NA NA	6 40 0 7	1 45 0 7	6 40 0 7

Table D.153: Momentaneous_Standard_kFold_PCA_highestEDSS < 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.76	0.77	0.75	0.65	0.76	0.73	0.68	0.75	0.77	0.76	0.77
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
75.00	**75.00**	**70.83**	**54.17**	**75.00**	**66.67**	**58.33**	**70.83**	**75.00**	**79.17**	**79.17**
90.48	**88.89**	**90.48**	**92.06**	**88.89**	**88.89**	**88.89**	**88.89**	**88.89**	**87.30**	**88.89**
90.48	**90.32**	**89.06**	**84.06**	**90.32**	**87.50**	**84.85**	**88.89**	**90.32**	**91.67**	**91.80**
75.00	**72.00**	**73.91**	**72.22**	**72.00**	**69.57**	**66.67**	**70.83**	**72.00**	**70.37**	**73.08**
86.21	**85.06**	**85.06**	**81.61**	**85.06**	**82.76**	**80.46**	**83.91**	**85.06**	**85.06**	**86.21**
Confusion Matrix										
57 6	56 7	57 6	58 5	56 7	56 7	56 7	56 7	56 7	55 8	56 7
6 18	6 18	7 17	11 13	6 18	8 16	10 14	7 17	6 18	5 19	5 19

Table D.154: Momentaneous_Standard_kFold_highestEDSS < 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.83	0.82	0.88	0.86	0.84	0.85	0.82	0.82	0.82	0.80	0.83
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
87.50	**83.33**	**95.83**	**87.50**	**87.50**	**87.50**	**79.17**	**87.50**	**83.33**	**75.00**	**87.50**
90.48	**92.06**	**93.65**	**95.24**	**93.65**	**95.24**	**95.24**	**90.48**	**92.06**	**88.89**	**90.48**
95.00	**93.55**	**98.33**	**95.24**	**95.16**	**95.24**	**92.31**	**95.00**	**93.55**	**90.32**	**95.00**
77.78	**80.00**	**85.19**	**87.50**	**84.00**	**87.50**	**86.36**	**77.78**	**80.00**	**72.00**	**77.78**
89.66	**89.66**	**94.25**	**93.10**	**91.95**	**93.10**	**90.80**	**89.66**	**89.66**	**85.06**	**89.66**
Confusion Matrix										
57 6 3 21	58 5 4 20	59 4 1 23	60 3 3 21	59 4 3 21	60 3 3 21	60 3 5 19	57 6 3 21	58 5 4 20	56 7 6 18	57 6 3 21

Table D.155: Momentaneous_Standard_LOO_PCA_highestEDSS < 5

Classifier								
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**
AUC								
0.60	0.56	0.57	0.56	0.56	0.57	0.59	0.57	0.56
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %								
37.50	37.50	37.50	25.00	37.50	37.50	37.50	37.50	37.50
80.95	74.60	76.19	84.13	74.60	76.19	79.37	76.19	74.60
77.27	75.81	76.19	74.65	75.81	76.19	76.92	76.19	75.81
42.86	36.00	37.50	37.50	36.00	37.50	40.91	37.50	36.00
68.97	64.37	65.52	67.82	64.37	65.52	67.82	65.52	64.37
Confusion Matrix								
51 12 15 9	47 16 15 9	48 15 15 9	53 10 18 6	47 16 15 9	48 15 15 9	50 13 15 9	48 15 15 9	47 16 15 9

Table D.156: Momentaneous_Standard_LOO_highestEDSS < 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.50	0.46	0.47	0.47	0.48	0.44	0.52	0.50	0.47	0.49
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
25.00	29.17	25.00	25.00	25.00	25.00	25.00	33.33	29.17	25.00	29.17
68.25	71.43	66.67	69.84	69.84	71.43	71.43	71.43	71.43	69.84	68.25
70.49	72.58	70.00	70.97	70.97	71.43	71.43	73.77	72.58	70.97	71.67
23.08	28.00	22.22	24.00	24.00	25.00	25.00	30.77	28.00	24.00	25.93
56.32	59.77	55.17	57.47	57.47	58.62	58.62	60.92	59.77	57.47	57.47
Confusion Matrix										
43 20 18 6	45 18 17 7	42 21 18 6	44 19 18 6	44 19 18 6	45 18 18 6	45 18 20 4	45 18 16 8	45 18 17 7	44 19 18 6	43 20 17 7

For label *first2EDSS* (0/1 - $(< 3)/(\geq 3)$):

Final features: Supratentorial, Spinal Cord, Years since Onset, Last EDSS.

Table D.157: Momentaneous_Standard_Traditional_PCA_first2EDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.81	0.82	0.79	0.82	0.79	0.81	0.79	0.78	0.82	0.83	0.83
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	85.71	85.71	85.71	85.71	85.71	85.71	85.71	85.71	100.00	100.00
72.00	72.00	72.00	72.00	70.00	72.00	68.00	64.00	72.00	72.00	72.00
97.30	97.30	97.30	97.30	97.22	97.30	97.14	96.97	97.30	100.00	100.00
30.00	30.00	30.00	30.00	28.57	30.00	27.27	25.00	30.00	33.33	33.33
73.68	73.68	73.68	73.68	71.93	73.68	70.18	66.67	73.68	75.44	75.44
Confusion Matrix										
36 14 1 6	36 14 1 6	36 14 1 6	36 14 1 6	35 15 1 6	36 14 1 6	34 16 1 6	32 18 1 6	36 14 1 6	36 14 0 7	36 14 0 7

Table D.158: Momentaneous_Standard_Traditional_first2EDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.57	NA	0.56	0.64	0.58	0.58	NA	0.57	0.60	0.58
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	NA	100.00	85.71	100.00	100.00	NA	100.00	100.00	100.00
20.00	14.00	NA	12.00	40.00	22.00	18.00	NA	14.00	20.00	16.00
100.00	100.00	NA	100.00	95.24	100.00	100.00	NA	100.00	100.00	100.00
14.89	14.00	NA	13.73	16.67	15.22	14.58	NA	14.00	14.89	14.29
29.82	24.56	NA	22.81	45.61	31.58	28.07	NA	24.56	29.82	26.32
Confusion Matrix										
10 40 0 7	7 43 0 7	NA NA	6 44 0 7	20 30 1 6	11 39 0 7	9 41 0 7	NA NA	7 43 0 7	10 40 0 7	8 42 0 7

Table D.159: Momentaneous_Standard_kFold_PCA_first2EDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.78	0.81	0.76	0.77	0.82	0.78	0.77	0.76	0.80	0.79	0.79
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
72.73	**77.27**	**63.64**	**68.18**	**81.82**	**68.18**	**63.64**	**63.64**	**72.73**	**90.91**	**86.36**
93.85	**92.31**	**95.38**	**98.46**	**93.85**	**95.38**	**96.92**	**95.38**	**93.85**	**84.62**	**83.08**
91.04	**92.31**	**88.57**	**90.14**	**93.85**	**89.86**	**88.73**	**88.57**	**91.04**	**96.49**	**94.74**
80.00	**77.27**	**82.35**	**93.75**	**81.82**	**83.33**	**87.50**	**82.35**	**80.00**	**66.67**	**63.33**
88.51	**88.51**	**87.36**	**90.80**	**90.80**	**88.51**	**88.51**	**87.36**	**88.51**	**86.21**	**83.91**
Confusion Matrix										
61 4 6 16	60 5 5 17	62 3 8 14	64 1 7 15	61 4 4 18	62 3 7 15	63 2 8 14	62 3 8 14	61 4 6 16	55 10 2 20	54 11 3 19

Table D.160: Momentaneous_Standard_kFold_first2EDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.85	0.83	NA	0.75	0.87	0.82	0.73	NA	0.83	0.74	0.80
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
90.91	86.36	NA	63.64	95.45	86.36	63.64	NA	86.36	77.27	86.36
93.85	90.77	NA	95.45	95.38	90.77	95.38	NA	90.77	84.62	87.69
96.83	95.16	NA	88.73	98.41	95.16	88.57	NA	95.16	91.67	95.00
83.33	76.00	NA	82.35	87.50	76.00	82.35	NA	76.00	62.96	70.37
93.10	89.66	NA	87.50	95.40	89.66	87.36	NA	89.66	82.76	87.36
Confusion Matrix										
61 4	59 6	NA	63 3	62 3	59 6	62 3	NA	59 6	55 10	57 8
2 20	3 19	NA	8 14	1 21	3 19	8 14	NA	3 19	5 17	3 19

Table D.161: Momentaneous_Standard_LOO_PCA_first2EDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.53	0.46	0.50	0.51	0.54	0.55	0.45	0.53	0.55	0.54
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
27.27	27.27	13.64	18.18	27.27	27.27	22.73	13.64	27.27	45.45	40.91
78.46	78.46	80.00	81.54	75.38	80.00	84.62	78.46	78.46	67.69	67.69
76.12	76.12	73.24	74.65	75.38	76.47	76.39	72.86	76.12	78.57	77.19
30.00	30.00	18.75	25.00	27.27	31.58	33.33	17.65	30.00	32.26	30.00
65.52	65.52	63.22	65.52	63.22	66.67	68.97	62.07	65.52	62.07	60.92
Confusion Matrix										
51 14	51 14	52 13	53 12	49 16	52 13	55 10	51 14	51 14	44 21	44 21
16 6	16 6	19 3	18 4	16 6	16 6	17 5	19 3	16 6	12 10	13 9

Table D.162: Momentaneous_Standard_LOO_PCA_first2EDSS < 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.56	0.46	NA	0.50	0.53	0.50	0.53	NA	0.46	0.59	0.53
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.91	22.73	NA	18.18	31.82	31.82	22.73	NA	22.73	45.45	36.36
72.31	69.23	NA	81.54	73.85	69.23	81.54	NA	69.23	73.85	70.77
78.33	72.58	NA	74.65	76.19	75.00	75.71	NA	72.58	80.00	76.67
33.33	20.00	NA	25.00	29.17	25.93	29.41	NA	20.00	37.04	29.63
64.37	57.47	NA	65.52	63.22	59.77	66.67	NA	57.47	66.67	62.07
Confusion Matrix										
47 18	45 20	NA	53 12	48 17	45 20	53 12	NA	45 20	48 17	46 19
13 9	17 5	NA	18 4	15 7	15 7	17 5	NA	17 5	12 10	14 8

For label *first2EDSS* (0/1 - (< 5)/(≥ 5)):

The via pattern recognition study was not performed since the number of patients with *first2EDSS*≥ 5 was minimal.

For label *tendencyEDSS* (0/1 - (Down/Equal & Up)):

Final features: MS Course, Age Visit, Years since Onset, Last EDSS;

Table D.163: Momentaneous_Standard_Traditional_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.45	0.45	0.47	0.47	0.45	0.46	0.45	0.45	0.44	0.43
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.00	40.00	40.00	40.00	40.00	40.00	40.00	20.00	40.00	40.00	40.00
58.33	48.33	55.00	48.33	55.00	51.67	53.33	65.00	48.33	48.33	46.67
92.11	90.63	91.67	90.63	91.67	91.18	91.43	90.70	90.63	90.63	90.32
7.41	6.06	6.90	6.06	6.90	6.45	6.67	4.55	6.06	6.06	5.88
56.92	47.69	53.85	47.69	53.85	50.77	52.31	61.54	47.69	47.69	46.15
Confusion Matrix										
35 25 3 2	29 31 3 2	33 27 3 2	29 31 3 2	33 27 3 2	31 29 3 2	32 28 3 2	39 21 4 1	29 31 3 2	29 31 3 2	28 32 3 2

Table D.164: Momentaneous_Standard_Traditional_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.48	NA	0.51	0.52	0.50	0.47	NA	0.48	0.50	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.00	60.00	NA	60.00	40.00	40.00	40.00	NA	60.00	60.00	60.00
58.33	38.33	NA	45.00	58.33	51.67	51.67	NA	38.33	31.67	40.00
92.11	92.00	NA	93.10	92.11	91.18	91.18	NA	92.00	90.48	92.31
7.41	7.50	NA	8.33	7.41	6.45	6.45	NA	7.50	6.82	7.69
56.92	40.00	NA	46.15	56.92	50.77	50.77	NA	40.00	33.85	41.54
Confusion Matrix										
35 25 3 2	23 37 2 3	NA NA	27 33 2 3	35 25 3 2	31 29 3 2	31 29 3 2	NA NA	23 37 2 3	19 41 2 3	24 36 2 3

Table D.165: Momentaneous_Standard_kFold_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.34	0.01	0.10	0.07	0.39	0.22	0.06	0.03	0.00	0.42	0.43
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
6.25	0.00	0.00	0.00	18.75	0.00	0.00	0.00	0.00	25.00	25.00
81.69	100.00	94.37	97.18	85.92	90.14	98.59	98.59	100.00	54.93	50.70
79.45	81.61	80.72	81.18	82.43	80.00	81.40	81.40	81.61	76.47	75.00
7.14	NaN	0.00	0.00	23.08	0.00	0.00	0.00	NaN	11.11	10.26
67.82	81.61	77.01	79.31	73.56	73.56	80.46	80.46	81.61	49.43	45.98
Confusion Matrix										
58 13 15 1	71 0 16 0	67 4 16 0	69 2 16 0	61 10 13 3	64 7 16 0	70 1 16 0	70 1 16 0	71 0 16 0	39 32 12 4	36 35 12 4

Table D.166: Momentaneous_Standard_kFold_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.35	0.01	0.27	0.01	0.48	0.22	0.14	0.24	0.00	0.49	0.45
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
12.50	0.00	12.50	0.00	25.00	0.00	0.00	12.50	0.00	31.25	31.25
83.10	100.00	94.37	100.00	81.69	88.89	94.37	95.77	100.00	71.83	54.93
80.82	81.61	82.72	81.61	82.86	80.00	80.72	82.93	81.61	82.26	78.00
14.29	NaN	33.33	NaN	23.53	0.00	0.00	40.00	NaN	20.00	13.51
70.11	81.61	79.31	81.61	71.26	72.73	77.01	80.46	81.61	64.37	50.57
Confusion Matrix										
59 12 14 2	71 0 16 0	67 4 14 2	71 0 16 0	58 13 12 4	64 8 16 0	67 4 16 0	68 3 14 2	71 0 16 0	51 20 11 5	39 32 11 5

Table D.167: Momentaneous_Standard_LOO_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.00	0.40	0.41	0.53	0.40	0.41	0.41	0.00	0.56	0.53
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
18.75	0.00	0.00	0.00	18.75	0.00	0.00	0.00	0.00	56.25	56.25
81.69	100.00	95.77	97.18	85.92	90.14	97.18	98.59	100.00	61.97	52.11
81.69	81.61	80.95	81.18	82.43	80.00	81.18	81.40	81.61	86.27	84.09
18.75	NaN	0.00	0.00	23.08	0.00	0.00	0.00	NaN	25.00	20.93
70.11	81.61	78.16	79.31	73.56	73.56	79.31	80.46	81.61	60.92	52.87
Confusion Matrix										
58 13 13 3	71 0 16 0	68 3 16 0	69 2 16 0	61 10 13 3	64 7 16 0	69 2 16 0	70 1 16 0	71 0 16 0	44 27 7 9	37 34 7 9

Table D.168: Momentaneous_Standard_LOO_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.00	0.49	0.00	0.45	0.56	0.61	0.40	0.00	0.51	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
18.75	0.00	6.25	0.00	12.50	12.50	12.50	0.00	0.00	31.25	31.25
84.51	100.00	92.96	100.00	77.46	92.96	95.77	94.37	100.00	71.83	57.75
82.19	81.61	81.48	81.61	79.71	82.50	82.93	80.72	81.61	82.26	78.85
21.43	NaN	16.67	NaN	11.11	28.57	40.00	0.00	NaN	20.00	14.29
72.41	81.61	77.01	81.61	65.52	78.16	80.46	77.01	81.61	64.37	52.87
Confusion Matrix										
60 11 13 3	71 0 16 0	66 5 15 1	71 0 16 0	55 16 14 2	66 5 14 2	68 3 14 2	67 4 16 0	71 0 16 0	51 20 11 5	41 30 11 5

First feature selection process for *mediumEDSS*:

Table D.169: Momentaneous_Feature_Selection_Identification_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Gender	0	0	0	0	0	1	1	0	0	0	0	2
Age of Onset	0	0	0	0	0	0	1	0	0	0	0	1
Supratentorial	0	0	0	0	0	0	1	0	0	0	0	1
Optic Pathways	0	1	0	0	0	0	1	0	1	0	1	**4**
Brainstem-Cerebellum	0	0	0	1	0	1	1	0	0	0	0	**3**
Spinal Cord	0	0	0	0	0	1	1	0	0	0	0	2
Progression From Onset	0	0	0	0	0	0	0	0	1	0	0	1
Age of Diagnosis	1	1	1	1	1	0	1	0	0	1	1	**8**
Years from Onset to Diagnosis	0	1	1	1	1	0	1	1	1	1	1	**9**
MRI	0	0	0	0	0	0	1	0	0	0	0	1
Evoked Potentials	0	0	0	0	0	1	1	0	0	0	0	2
CSF	0	0	0	0	0	1	1	0	0	0	0	2
Age at SP Diagnosis	0	1	1	1	1	0	1	1	1	1	1	**9**
Years from Diagnosis to SP	0	1	1	1	1	0	1	0	1	1	1	**8**
Years from Diagnosis to Onset	0	1	1	1	1	0	1	0	1	1	1	**8**
MS Course	0	1	1	1	1	1	1	0	1	1	1	**9**
Active	0	1	0	0	0	0	0	0	1	0	1	3
Age Visit	1	1	1	1	1	0	1	0	0	1	1	**8**
Years since Onset	1	1	1	1	1	0	1	0	0	1	1	**8**

Selected features: Optic Pathways, Spinal Cord, Age of Diagnosis, Years from Onset to Diagnosis, Age at SP Diagnosis, Years from Diagnosis to SP, Years from Diagnosis to Onset, MS Course, Age Visit, Years since Onset.

Table D.170: Momentaneous_Feature_Selection_Visits_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Last Suspected	0	0	0	0	0	0	1	0	0	0	0	1
Last EDSS	1	1	1	1	1	0	1	1	0	1	1	**9**
Last Weakness	0	1	0	0	0	0	0	0	1	0	0	2
Last Sympton	0	0	0	0	0	0	0	0	1	0	0	1

Selected features: Last EDSS.

Table D.171: Momentaneous_Feature_Selection_Relapses_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Last Pyramidal	0	1	1	1	0	1	0	1	1	0	1	**7**
Last BrainStem	0	1	0	1	0	0	1	1	1	0	1	**6**
Last Bowel	0	0	0	0	0	0	0	0	0	0	0	0
Last Neuropsycho	0	0	0	0	0	0	1	0	0	0	0	1
Last Cerebellum	0	0	0	0	0	0	1	1	0	0	0	2
Last Visual	0	0	0	0	0	0	1	1	0	0	0	2
Last Sensory	0	1	1	1	0	1	1	1	1	1	1	**9**
Last Hospital	0	0	0	0	0	1	1	0	0	0	0	2
Last ambulatory	0	0	0	0	0	1	1	1	0	0	0	3
Last Corticosteroid	0	0	0	0	0	0	1	0	0	0	0	1
Last Treatment	0	0	0	0	0	0	0	0	1	0	0	1
Last Duration	0	0	0	0	0	0	0	1	1	0	0	2

Selected features: Last Pyramidal, BrainStem, Last Sensory.

For label *mediumEDSS* (0/1 - $(<3)/(\geq 3)$):

Final features: Age of Diagnosis, Years from Onset to Diagnosis, Years since Onset, Last EDSS.

Table D.172: Momentaneous_Standard_Traditional_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.81	0.87	0.86	0.80	0.80	0.79	0.78	0.91	NA	0.87	0.87
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
90.00	**80.00**	**90.00**	**90.00**	**90.00**	90.00	90.00	**90.00**	NA	**80.00**	**80.00**
74.07	**92.59**	**77.78**	**70.37**	**66.67**	62.96	62.96	**92.59**	NA	**92.59**	**92.59**
95.24	**92.59**	**95.45**	**95.00**	**94.74**	94.44	94.44	**96.15**	NA	**92.59**	**92.59**
56.25	**80.00**	**60.00**	**52.94**	**50.00**	47.37	47.37	**81.82**	NA	**80.00**	**80.00**
78.38	**89.19**	**81.08**	**75.68**	**72.97**	70.27	70.27	**91.89**	NA	**89.19**	**89.19**
Confusion Matrix										
20 7 1 9	25 2 2 8	21 6 1 9	19 8 1 9	18 9 1 9	17 10 1 9	17 10 1 9	25 2 1 9	NA NA	25 2 2 8	25 2 2 8

Table D.173: Momentaneous_Standard_Traditional_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.67	NA	0.52	0.59	0.58	0.58	NA	NA	0.56	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	NA	100.00	100.00	100.00	100.00	NA	NA	100.00	100.00
3.70	37.04	NA	3.70	18.52	14.81	14.81	NA	NA	11.11	11.11
100.00	100.00	NA	100.00	100.00	100.00	100.00	NA	NA	100.00	100.00
27.78	37.04	NA	27.78	31.25	30.30	30.30	NA	NA	29.41	29.41
29.73	54.05	NA	29.73	40.54	37.84	37.84	NA	NA	35.14	35.14
Confusion Matrix										
1 26 0 10	10 17 0 10	NA NA	1 26 0 10	5 22 0 10	4 23 0 10	4 23 0 10	NA NA	NA NA	3 24 0 10	3 24 0 10

Table D.174: Momentaneous_Standard_kFold_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.91	0.86	0.89	0.91	0.90	0.92	0.92	0.89	0.86	0.87	0.88
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
88.57	**71.43**	**80.00**	**82.86**	**88.57**	**91.43**	**88.57**	**80.00**	**71.43**	**77.14**	**80.00**
94.23	**96.15**	**96.15**	**96.15**	**92.31**	**94.23**	**94.23**	**96.15**	**96.15**	**94.23**	**94.23**
92.45	**83.33**	**87.72**	**89.29**	**92.31**	**94.23**	**92.45**	**87.72**	**83.33**	**85.96**	**87.50**
91.18	**92.59**	**93.33**	**93.55**	**88.57**	**91.43**	**91.18**	**93.33**	**92.59**	**90.00**	**90.32**
91.95	**86.21**	**89.66**	**90.80**	**90.80**	**93.10**	**91.95**	**89.66**	**86.21**	**87.36**	**88.51**
Confusion Matrix										
49 3	50 2	50 2	50 2	48 4	49 3	49 3	50 2	50 2	49 3	49 3
4 31	10 25	7 28	6 29	4 31	3 32	4 31	7 28	10 25	8 27	7 28

Table D.175: Momentaneous_Standard_kFold_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.90	0.85	0.88	0.90	0.89	0.92	0.91	0.88	0.85	0.86	0.87
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
88.57	**71.43**	**80.00**	**82.86**	**88.57**	**91.43**	**88.57**	**80.00**	**71.43**	**77.14**	**80.00**
94.23	**96.15**	**96.15**	**96.15**	**90.38**	**94.23**	**94.23**	**96.15**	**96.15**	**94.23**	**94.23**
92.45	**83.33**	**87.72**	**89.29**	**92.16**	**94.23**	**92.45**	**87.72**	**83.33**	**85.96**	**87.50**
91.18	**92.59**	**93.33**	**93.55**	**86.11**	**91.43**	**91.18**	**93.33**	**92.59**	**90.00**	**90.32**
91.95	**86.21**	**89.66**	**90.80**	**89.66**	**93.10**	**91.95**	**89.66**	**86.21**	**87.36**	**88.51**
Confusion Matrix										
49 3	50 2	50 2	50 2	47 5	49 3	49 3	50 2	50 2	49 3	49 3
4 31	10 25	7 28	6 29	4 31	3 32	4 31	7 28	10 25	8 27	7 28

Table D.176: Momentaneous_Standard_LOO_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.50	0.47	0.50	0.50	0.47	0.47	0.47	0.50	0.47	0.46
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.00	31.43	31.43	37.14	40.00	37.14	37.14	31.43	31.43	31.43	31.43
63.46	69.23	63.46	63.46	59.62	57.69	57.69	63.46	69.23	63.46	61.54
61.11	60.00	57.89	60.00	59.62	57.69	57.69	57.89	60.00	57.89	57.14
42.42	40.74	36.67	40.63	40.00	37.14	37.14	36.67	40.74	36.67	35.48
54.02	54.02	50.57	52.87	51.72	49.43	49.43	50.57	54.02	50.57	49.43
Confusion Matrix										
33 19	36 16	33 19	33 19	31 21	30 22	30 22	33 19	36 16	33 19	32 20
21 14	24 11	24 11	22 13	21 14	22 13	22 13	24 11	24 11	24 11	24 11

Table D.177: Momentaneous_Standard_LOO_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.40	0.45	0.42	0.38	0.40	0.38	0.38	0.42	0.45	0.42	0.41
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
25.71	25.71	25.71	22.86	28.57	25.71	25.71	25.71	25.71	25.71	25.71
53.85	65.38	59.62	53.85	51.92	50.00	50.00	59.62	65.38	59.62	57.69
51.85	56.67	54.39	50.91	51.92	50.00	50.00	54.39	56.67	54.39	53.57
27.27	33.33	30.00	25.00	28.57	25.71	25.71	30.00	33.33	30.00	29.03
42.53	49.43	45.98	41.38	42.53	40.23	40.23	45.98	49.43	45.98	44.83
Confusion Matrix										
28 24	34 18	31 21	28 24	27 25	26 26	26 26	31 21	34 18	31 21	30 22
26 9	26 9	26 9	27 8	25 10	26 9	26 9	26 9	26 9	26 9	26 9

For label *nextEDSS* (0/1 - $(< 3)/(\geq 3)$):

The via pattern recognition study was not performed since the number of patients with *currentEDSS*≥ 5 was minimal.

D.1.3.2 Investigation procedure

For label *msCourse* (0/1 - (RR/SP):

It was not performed since the features used in standard procedure were not considered obvious.

For label *currentEDSS* (0/1 - (< 3)/(≥ 3)):

It was not performed since the features used in standard procedure were not considered obvious.

For label *currentEDSS* (0/1 - (< 5)/(≥ 5)):

The via pattern recognition study was not performed since the number of patients with *currentEDSS*≥ 5 was minimal.

For label *nextEDSS* (0/1 - (< 3)/(≥ 3)):

Features before selection: Optic Pathways, Spinal Cord, MS Course, Age Visit, Years since Onset, Last EDSS, Last Pyramidal, Last Sensory.

Excluded features: Last EDSS.

Final features: Optic Pathways, MS Course, Age Visit, Years since Onset, Years since Onset.

Table D.178: Momentaneous_Investigation_Traditional_PCA_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.78	0.82	0.80	0.79	0.70	0.72	0.78	0.82	0.82	0.83	0.83
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	**70.00**	**80.00**	**70.00**	70.00	80.00	**80.00**	**80.00**	**70.00**	**70.00**	**80.00**
75.86	**89.66**	**75.86**	**89.66**	68.97	68.97	**72.41**	**82.76**	**89.66**	**89.66**	**89.66**
91.67	**89.66**	**91.67**	**89.66**	86.96	90.91	**91.30**	**92.31**	**89.66**	**89.66**	**92.86**
53.33	**70.00**	**53.33**	**70.00**	43.75	47.06	**50.00**	**61.54**	**70.00**	**70.00**	**72.73**
76.92	**84.62**	**76.92**	**84.62**	69.23	71.79	**74.36**	**82.05**	**84.62**	**84.62**	**87.18**
Confusion Matrix										
22 7 2 8	26 3 3 7	22 7 2 8	26 3 3 7	20 9 3 7	20 9 2 8	21 8 2 8	24 5 2 8	26 3 3 7	26 3 3 7	26 3 2 8

Table D.179: Momentaneous_Investigation_Traditional_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.71	NA	0.54	0.58	0.61	0.58	NA	0.71	0.66	0.70
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
90.00	100.00	NA	100.00	80.00	100.00	100.00	NA	100.00	100.00	100.00
24.14	41.38	NA	10.34	31.03	24.14	17.24	NA	41.38	31.03	37.93
87.50	100.00	NA	100.00	81.82	100.00	100.00	NA	100.00	100.00	100.00
29.03	37.04	NA	27.78	28.57	31.25	29.41	NA	37.04	33.33	35.71
41.03	56.41	NA	33.33	43.59	43.59	38.46	NA	56.41	48.72	53.85
Confusion Matrix										
7 22 1 9	12 17 0 10	NA NA	3 26 0 10	9 20 2 8	7 22 0 10	5 24 0 10	NA NA	12 17 0 10	9 20 0 10	11 18 0 10

Table D.180: Momentaneous_Investigation_kFold_PCA_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.79	0.83	0.85	0.82	0.85	0.84	0.84	0.85	0.83	0.84	0.83
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
73.53	**67.65**	**70.59**	**67.65**	**85.29**	**82.35**	**82.35**	**70.59**	**67.65**	**70.59**	**67.65**
84.91	**96.23**	**96.23**	**96.23**	**86.79**	**86.79**	**86.79**	**96.23**	**96.23**	**96.23**	**96.23**
83.33	**82.26**	**83.61**	**82.26**	**90.20**	**88.46**	**88.46**	**83.61**	**82.26**	**83.61**	**82.26**
75.76	**92.00**	**92.31**	**92.00**	**80.56**	**80.00**	**80.00**	**92.31**	**92.00**	**92.31**	**92.00**
80.46	**85.06**	**86.21**	**85.06**	**86.21**	**85.06**	**85.06**	**86.21**	**85.06**	**86.21**	**85.06**
Confusion Matrix										
45 8 9 25	51 2 11 23	51 2 10 24	51 2 11 23	46 7 5 29	46 7 6 28	46 7 6 28	51 2 10 24	51 2 11 23	51 2 10 24	51 2 11 23

Table D.181: Momentaneous_Investigation_kFold_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.81	0.83	NA	0.79	0.86	0.89	0.82	NA	0.83	0.83	0.81
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
82.35	**67.65**	NA	**70.59**	**82.35**	**91.18**	**85.29**	NA	**67.65**	**67.65**	**70.59**
83.02	**94.34**	NA	**88.68**	**88.68**	**88.68**	**83.02**	NA	**94.34**	**96.23**	**90.57**
88.00	**81.97**	NA	**82.46**	**88.68**	**94.00**	**89.80**	NA	**81.97**	**82.26**	**82.76**
75.68	**88.46**	NA	**80.00**	**82.35**	**83.78**	**76.32**	NA	**88.46**	**92.00**	**82.76**
82.76	**83.91**	NA	**81.61**	**86.21**	**89.66**	**83.91**	NA	**83.91**	**85.06**	**82.76**
Confusion Matrix										
44 9 6 28	50 3 11 23	NA NA	47 6 10 24	47 6 6 28	47 6 3 31	44 9 5 29	NA NA	50 3 11 23	51 2 11 23	48 5 10 24

Table D.182: Momentaneous_Investigation_LOO_PCA_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.51	0.50	0.51	0.47	0.51	0.57	0.50	0.51	0.36	0.34
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
41.18	29.41	29.41	29.41	38.24	41.18	50.00	29.41	29.41	14.71	11.76
62.26	71.70	69.81	71.70	56.60	60.38	64.15	69.81	71.70	60.38	60.38
62.26	61.29	60.66	61.29	58.82	61.54	66.67	60.66	61.29	52.46	51.61
41.18	40.00	38.46	40.00	36.11	40.00	47.22	38.46	40.00	19.23	16.00
54.02	55.17	54.02	55.17	49.43	52.87	58.62	54.02	55.17	42.53	41.38
Confusion Matrix										
33 20	38 15	37 16	38 15	30 23	32 21	34 19	37 16	38 15	32 21	32 21
20 14	24 10	24 10	24 10	21 13	20 14	17 17	24 10	24 10	29 5	30 4

Table D.183: Momentaneous_Investigation_LOO_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.40	0.46	NA	0.48	0.39	0.42	0.49	NA	0.46	0.51	0.49
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
32.35	26.47	NA	32.35	26.47	32.35	44.12	NA	26.47	29.41	32.35
47.17	66.04	NA	64.15	50.94	50.94	52.83	NA	66.04	71.70	66.04
52.08	58.33	NA	59.65	51.92	54.00	59.57	NA	58.33	61.29	60.34
28.21	33.33	NA	36.67	25.71	29.73	37.50	NA	33.33	40.00	37.93
41.38	50.57	NA	51.72	41.38	43.68	49.43	NA	50.57	55.17	52.87
Confusion Matrix										
25 28	35 18	NA	34 19	27 26	27 26	28 25	NA	35 18	38 15	35 18
23 11	25 9	NA	23 11	25 9	23 11	19 15	NA	25 9	24 10	23 11

For label *nextEDSS* (0/1 - $(< 5)/(\geq 5)$):

Features before selection: Optic Pathways, Spinal Cord, MS Course, Age Visit, Years since Onset, Last EDSS, Last Pyramidal, Last Sensory.

Excluded features: Last EDSS.

Final features: Spinal Cord, MS Course, Age Visit.

Table D.184: Momentaneous_Investigation_Traditional_PCA_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.68	0.73	0.72	0.64	0.61	0.63	0.69	0.73	0.73	0.73	0.74
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
83.33	83.33	66.67	66.67	66.67	66.67	66.67	66.67	83.33	83.33	83.33
50.91	70.91	70.91	60.00	61.82	65.45	76.36	74.55	70.91	70.91	70.91
96.55	97.50	95.12	94.29	94.44	94.74	95.45	95.35	97.50	97.50	97.50
15.63	23.81	20.00	15.38	16.00	17.39	23.53	22.22	23.81	23.81	23.81
54.10	72.13	70.49	60.66	62.30	65.57	75.41	73.77	72.13	72.13	72.13
Confusion Matrix										
28 27	39 16	39 16	33 22	34 21	36 19	42 13	41 14	39 16	39 16	39 16
1 5	1 5	2 4	2 4	2 4	2 4	2 4	2 4	1 5	1 5	1 5

Table D.185: Momentaneous_Investigation_Traditional_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.63	0.53	NA	0.57	0.60	0.67	0.71	NA	0.53	0.50	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.67	100.00	NA	83.33	50.00	66.67	83.33	NA	100.00	100.00	100.00
60.00	7.27	NA	38.18	72.73	65.45	63.64	NA	7.27	0.00	9.09
94.29	100.00	NA	95.45	93.02	94.74	97.22	NA	100.00	NaN	100.00
15.38	10.53	NA	12.82	16.67	17.39	20.00	NA	10.53	9.84	10.71
60.66	16.39	NA	42.62	70.49	65.57	65.57	NA	16.39	9.84	18.03
Confusion Matrix										
33 22 2 4	4 51 0 6	NA NA	21 34 1 5	40 15 3 3	36 19 2 4	35 20 1 5	NA NA	4 51 0 6	0 55 0 6	5 50 0 6

Table D.186: Momentaneous_Investigation_kFold_PCA_nextEDSS > 5

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.57	0.60	0.50	0.30	0.65	0.55	0.42	0.52	0.55	0.68	0.66
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
42.11	47.37	36.84	10.53	**57.89**	36.84	26.32	36.84	36.84	**68.42**	63.16
88.24	88.24	80.88	95.59	**85.29**	85.29	95.59	89.71	91.18	**80.88**	80.88
84.51	85.71	82.09	79.27	**87.88**	82.86	82.28	83.56	83.78	**90.16**	88.71
50.00	52.94	35.00	40.00	**52.38**	41.18	62.50	50.00	53.85	**50.00**	48.00
78.16	79.31	71.26	77.01	**79.31**	74.71	80.46	78.16	79.31	**78.16**	77.01
Confusion Matrix										
60 8 11 8	60 8 10 9	55 13 12 7	65 3 17 2	58 10 8 11	58 10 12 7	65 3 14 5	61 7 12 7	62 6 12 7	55 13 6 13	55 13 7 12

Table D.187: Momentaneous_Investigation_kFold_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.60	0.65	0.31	0.57	0.62	0.34	0.64	0.52	0.66	0.64
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
47.37	47.37	**57.89**	15.79	42.11	47.37	15.79	**57.89**	36.84	68.42	63.16
86.76	89.71	**88.24**	94.12	85.29	92.65	92.65	**83.82**	91.18	77.94	80.88
85.51	85.92	**88.24**	80.00	84.06	86.30	79.75	**87.69**	83.78	89.83	88.71
50.00	56.25	**57.89**	42.86	44.44	64.29	37.50	**50.00**	53.85	46.43	48.00
78.16	80.46	**81.61**	77.01	75.86	82.76	75.86	**78.16**	79.31	75.86	77.01
Confusion Matrix										
59 9	61 7	60 8	64 4	58 10	63 5	63 5	57 11	62 6	53 15	55 13
10 9	10 9	8 11	16 3	11 8	10 9	16 3	8 11	12 7	6 13	7 12

Table D.188: Momentaneous_Investigation_LOO_PCA_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.39	0.40	0.43	0.45	0.42	0.39	0.38	0.42	0.41	0.48	0.49
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
5.26	5.26	10.53	5.26	10.53	5.26	0.00	5.26	5.26	26.32	26.32
72.06	76.47	75.00	89.71	72.06	73.53	88.24	82.35	80.88	69.12	72.06
73.13	74.29	75.00	77.22	74.24	73.53	75.95	75.68	75.34	77.05	77.78
5.00	5.88	10.53	12.50	9.52	5.26	0.00	7.69	7.14	19.23	20.83
57.47	60.92	60.92	71.26	58.62	58.62	68.97	65.52	64.37	59.77	62.07
Confusion Matrix										
49 19 18 1	52 16 18 1	51 17 17 2	61 7 18 1	49 19 17 2	50 18 18 1	60 8 19 0	56 12 18 1	55 13 18 1	47 21 14 5	49 19 14 5

Table D.189: Momentaneous_Investigation_LOO_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.47	0.46	0.47	0.54	0.52	0.50	0.54	0.53	0.52	0.53
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
21.05	15.79	15.79	5.26	26.32	21.05	10.53	31.58	15.79	31.58	31.58
79.41	77.94	76.47	92.65	80.88	82.35	89.71	76.47	88.24	72.06	75.00
78.26	76.81	76.47	77.78	79.71	78.87	78.21	80.00	78.95	79.03	79.69
22.22	16.67	15.79	16.67	27.78	25.00	22.22	27.27	27.27	24.00	26.09
66.67	64.37	63.22	73.56	68.97	68.97	72.41	66.67	72.41	63.22	65.52
Confusion Matrix										
54 14	53 15	52 16	63 5	55 13	56 12	61 7	52 16	60 8	49 19	51 17
15 4	16 3	16 3	18 1	14 5	15 4	17 2	13 6	16 3	13 6	13 6

For label *highestEDSS* (0/1 - (< 3)/(≥ 3)):

Features before selection: Optic Pathways, Spinal Cord, MS Course, Age Visit, Years since Onset, Last Sensory, Gender, Last Hospital.

Excluded features: Last EDSS.

Final features: Spinal Cord, Age Visit, Years Since Onset.

Table D.190: Momentaneous_Investigation_Traditional_PCA_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.76	0.76	0.76	0.59	0.61	0.71	0.71	0.75	0.76	0.74	0.74
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	**71.43**	**71.43**	42.86	**50.00**	**64.29**	**64.29**	**64.29**	**71.43**	**64.29**	**64.29**
63.64	**81.82**	**81.82**	72.73	**72.73**	**81.82**	**81.82**	**81.82**	**81.82**	**81.82**	**81.82**
77.78	**69.23**	**69.23**	50.00	**53.33**	**64.29**	**64.29**	**64.29**	**69.23**	**64.29**	**64.29**
75.00	**83.33**	**83.33**	66.67	**70.00**	**81.82**	**81.82**	**81.82**	**83.33**	**81.82**	**81.82**
76.00	**76.00**	**76.00**	56.00	**60.00**	**72.00**	**72.00**	**72.00**	**76.00**	**72.00**	**72.00**
Confusion Matrix										
7 4 2 12	9 2 4 10	9 2 4 10	8 3 8 6	8 3 7 7	9 2 5 9	9 2 5 9	9 2 5 9	9 2 4 10	9 2 5 9	9 2 5 9

Table D.191: Momentaneous_Investigation_Traditional_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.72	0.53	0.74	0.59	0.71	0.72	0.70	0.72	0.53	0.50	0.54
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	100.00	**78.57**	92.86	**78.57**	**71.43**	**78.57**	**92.86**	100.00	100.00	100.00
63.64	9.09	**72.73**	18.18	**63.64**	**72.73**	**63.64**	**54.55**	9.09	0.00	9.09
77.78	100.00	**72.73**	66.67	**70.00**	**66.67**	**70.00**	**85.71**	100.00	NaN	100.00
75.00	58.33	**78.57**	59.09	**73.33**	**76.92**	**73.33**	**72.22**	58.33	56.00	58.33
76.00	60.00	**76.00**	60.00	**72.00**	**72.00**	**72.00**	**76.00**	60.00	56.00	60.00
Confusion Matrix										
7 4 2 12	1 10 0 14	8 3 3 11	2 9 1 13	7 4 3 11	8 3 4 10	7 4 3 11	6 5 1 13	1 10 0 14	0 11 0 14	1 10 0 14

Table D.192: Momentaneous_Investigation_kFold_PCA_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.78	0.75	0.77	0.75	0.77	0.76	0.77	0.77	0.75	0.75	0.75
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	**68.89**	**80.00**	**77.78**	**75.56**	**77.78**	**80.00**	**80.00**	**68.89**	**66.67**	**66.67**
76.19	**78.57**	**71.43**	**69.05**	**76.19**	**73.81**	**73.81**	**71.43**	**78.57**	**83.33**	**80.95**
78.05	**70.21**	**76.92**	**74.36**	**74.42**	**75.61**	**77.50**	**76.92**	**70.21**	**70.00**	**69.39**
78.26	**77.50**	**75.00**	**72.92**	**77.27**	**76.09**	**76.60**	**75.00**	**77.50**	**81.08**	**78.95**
78.16	**73.56**	**75.86**	**73.56**	**75.86**	**75.86**	**77.01**	**75.86**	**73.56**	**74.71**	**73.56**
Confusion Matrix										
32 10 9 36	33 9 14 31	30 12 9 36	29 13 10 35	32 10 11 34	31 11 10 35	31 11 9 36	30 12 9 36	33 9 14 31	35 7 15 30	34 8 15 30

Table D.193: Momentaneous_Investigation_kFold_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.71	0.74	0.76	0.79	0.83	0.78	0.75	0.74	0.74	0.68	0.74
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
68.89	**68.89**	**73.33**	**77.78**	**84.44**	**80.00**	**71.11**	**69.57**	**68.89**	**51.11**	**68.89**
71.43	**78.57**	**78.57**	**80.95**	**80.95**	**73.81**	**76.19**	**78.57**	**78.57**	**83.33**	**78.57**
68.18	**70.21**	**73.33**	**77.27**	**82.93**	**77.50**	**71.11**	**70.21**	**70.21**	**61.40**	**70.21**
72.09	**77.50**	**78.57**	**81.40**	**82.61**	**76.60**	**76.19**	**78.05**	**77.50**	**76.67**	**77.50**
70.11	**73.56**	**75.86**	**79.31**	**82.76**	**77.01**	**73.56**	**73.86**	**73.56**	**66.67**	**73.56**
Confusion Matrix										
30 12 14 31	33 9 14 31	33 9 12 33	34 8 10 35	34 8 7 38	31 11 9 36	32 10 13 32	33 9 14 31	33 9 14 31	35 7 22 23	33 9 14 31

Table D.194: Momentaneous_Investigation_LOO_PCA_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.43	0.48	0.40	0.43	0.45	0.44	0.40	0.41	0.48	0.56	0.57
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
53.33	42.22	46.67	53.33	44.44	46.67	44.44	46.67	42.22	44.44	48.89
33.33	54.76	33.33	33.33	45.24	40.48	35.71	35.71	54.76	66.67	64.29
40.00	46.94	36.84	40.00	43.18	41.46	37.50	38.46	46.94	52.83	54.00
46.15	50.00	42.86	46.15	46.51	45.65	42.55	43.75	50.00	58.82	59.46
43.68	48.28	40.23	43.68	44.83	43.68	40.23	41.38	48.28	55.17	56.32
Confusion Matrix										
14 28	23 19	14 28	14 28	19 23	17 25	15 27	15 27	23 19	28 14	27 15
21 24	26 19	24 21	21 24	25 20	24 21	25 20	24 21	26 19	25 20	23 22

Table D.195: Momentaneous_Investigation_LOO_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.3915	0.4722	0.4945	0.4603	0.5167	0.4452	0.4715	0.4030	0.4722	0.5377	0.5192
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
35.56	44.44	48.89	44.44	**53.33**	51.11	46.67	35.56	44.44	37.78	46.67
42.86	50.00	50.00	47.62	**50.00**	38.10	47.62	45.24	50.00	69.05	57.14
38.30	45.65	47.73	44.44	**50.00**	42.11	45.45	39.58	45.65	50.88	50.00
40.00	48.78	51.16	47.62	**53.33**	46.94	48.84	41.03	48.78	56.67	53.85
39.08	47.13	49.43	45.98	**51.72**	44.83	47.13	40.23	47.13	52.87	51.72
Confusion Matrix										
18 24	21 21	21 21	20 22	21 21	16 26	20 22	19 23	21 21	29 13	24 18
29 16	25 20	23 22	25 20	21 24	22 23	24 21	29 16	25 20	28 17	24 21

For label *highestEDSS* (0/1 - $(< 5)/(\geq 5)$):

Features before selection: Optic Pathways, Spinal Cord, MS Course, Age Visit, Years since Onset, Last Sensory, Gender, Last Hospital.

Excluded features: Last EDSS.

Final features: Spinal Cord, MS Course, Age Visit, Gender.

Table D.196: Momentaneous_Investigation_Traditional_PCA_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.75	0.83	0.78	0.80	0.70	0.75	0.76	0.82	0.83	0.81	0.83
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	85.71	85.71	85.71	71.43	85.71	71.43	85.71	85.71	85.71	85.71
63.04	78.26	73.91	80.43	71.74	71.74	73.91	76.09	78.26	78.26	76.09
96.67	97.30	97.14	97.37	94.29	97.06	94.44	97.22	97.30	97.30	97.22
26.09	37.50	33.33	40.00	27.78	31.58	29.41	35.29	37.50	37.50	35.29
66.04	79.25	75.47	81.13	71.70	73.58	73.58	77.36	79.25	79.25	77.36
Confusion Matrix										
29 17	36 10	34 12	37 9	33 13	33 13	34 12	35 11	36 10	36 10	35 11
1 6	1 6	1 6	1 6	2 5	1 6	2 5	1 6	1 6	1 6	1 6

Table D.197: Momentaneous_Investigation_Traditional_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.72	0.53	NA	0.61	0.70	0.70	0.72	NA	0.53	0.51	0.54
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
71.43	100.00	NA	85.71	85.71	85.71	85.71	NA	100.00	100.00	100.00
67.39	8.70	NA	32.61	60.87	58.70	58.70	NA	8.70	2.17	8.70
93.94	100.00	NA	93.75	96.55	96.43	96.43	NA	100.00	100.00	100.00
25.00	14.29	NA	16.22	25.00	24.00	24.00	NA	14.29	13.46	14.29
67.92	20.75	NA	39.62	64.15	62.26	62.26	NA	20.75	15.09	20.75
Confusion Matrix										
31 15 2 5	4 42 0 7	NA NA	15 31 1 6	28 18 1 6	27 19 1 6	27 19 1 6	NA NA	4 42 0 7	1 45 0 7	4 42 0 7

Table D.198: Momentaneous_Investigation_kFold_PCA_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.77	0.78	0.76	0.66	0.75	0.76	0.69	0.75	0.78	0.77	0.78
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
75.00	**75.00**	**70.83**	**50.00**	**70.83**	**70.83**	**54.17**	**70.83**	**75.00**	**75.00**	**75.00**
88.89	**88.89**	**90.48**	**93.65**	**90.48**	**87.50**	**87.30**	**87.30**	**88.89**	**87.30**	**87.30**
90.32	**90.32**	**89.06**	**83.10**	**89.06**	**88.89**	**83.33**	**88.71**	**90.32**	**90.16**	**90.16**
72.00	**72.00**	**73.91**	**75.00**	**73.91**	**68.00**	**61.90**	**68.00**	**72.00**	**69.23**	**69.23**
85.06	**85.06**	**85.06**	**81.61**	**85.06**	**82.95**	**78.16**	**82.76**	**85.06**	**83.91**	**83.91**
Confusion Matrix										
56 7 6 18	56 7 6 18	57 6 7 17	59 4 12 12	57 6 7 17	56 7 7 17	55 8 11 13	55 8 7 17	56 7 6 18	55 8 6 18	55 8 6 18

Table D.199: Momentaneous_Investigation_kFold_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.74	0.77	0.74	0.76	0.82	0.78	0.70	0.77	0.77	0.77	0.77
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.67	**75.00**	**66.67**	**62.50**	**83.33**	**70.83**	**62.50**	**75.00**	**75.00**	**75.00**	**75.00**
88.89	**88.89**	**90.48**	**95.24**	**93.65**	**90.48**	**85.71**	**88.89**	**88.89**	**88.89**	**88.89**
87.50	**90.32**	**87.69**	**86.96**	**93.65**	**89.06**	**85.71**	**90.32**	**90.32**	**90.32**	**90.32**
69.57	**72.00**	**72.73**	**83.33**	**83.33**	**73.91**	**62.50**	**72.00**	**72.00**	**72.00**	**72.00**
82.76	**85.06**	**83.91**	**86.21**	**90.80**	**85.06**	**79.31**	**85.06**	**85.06**	**85.06**	**85.06**
Confusion Matrix										
56 7 8 16	56 7 6 18	57 6 8 16	60 3 9 15	59 4 4 20	57 6 7 17	54 9 9 15	56 7 6 18	56 7 6 18	56 7 6 18	56 7 6 18

Table D.200: Momentaneous_Investigation_LOO_PCA_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.42	0.45	0.41	0.45	0.46	0.39	0.43	0.45	0.45	0.52	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
16.67	20.83	12.50	12.50	20.83	12.50	16.67	20.83	20.83	33.33	33.33
66.67	68.25	69.84	79.37	71.43	65.08	69.84	68.25	68.25	71.43	71.43
67.74	69.35	67.69	70.42	70.31	66.13	68.75	69.35	69.35	73.77	73.77
16.00	20.00	13.64	18.75	21.74	12.00	17.39	20.00	20.00	30.77	30.77
52.87	55.17	54.02	60.92	57.47	50.57	55.17	55.17	55.17	60.92	60.92
Confusion Matrix										
42 21 20 4	43 20 19 5	44 19 21 3	50 13 21 3	45 18 19 5	41 22 21 3	44 19 20 4	43 20 19 5	43 20 19 5	45 18 16 8	45 18 16 8

Table D.201: Momentaneous_Investigation_LOO_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.50	0.50	0.49	0.54	0.54	0.47	0.50	0.50	0.45	0.45
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
25.00	29.17	25.00	20.83	33.33	33.33	25.00	29.17	29.17	20.83	20.83
73.02	71.43	74.60	77.78	74.60	74.60	69.84	71.43	71.43	68.25	68.25
71.88	72.58	72.31	72.06	74.60	74.60	70.97	72.58	72.58	69.35	69.35
26.09	28.00	27.27	26.32	33.33	33.33	24.00	28.00	28.00	20.00	20.00
59.77	59.77	60.92	62.07	63.22	63.22	57.47	59.77	59.77	55.17	55.17
Confusion Matrix										
46 17 18 6	45 18 17 7	47 16 18 6	49 14 19 5	47 16 16 8	47 16 16 8	44 19 18 6	45 18 17 7	45 18 17 7	43 20 19 5	43 20 19 5

For label *first2EDSS* (0/1 - $(< 3)/(\geq 3)$):

Features before selection: Supratentorial, Optic Pathways, Brainstem-Cerebellum, Spinal Cord, Evoked Potentials, MS Course, Years since Onset, Last Pyramidal, Last Sensory, Last Hospital.

Excluded features: Last EDSS.

Final features: Supratentorial, Spinal Cord, MS Course, Years Since Onset, Last Hospital.

Table D.202: Momentaneous_Investigation_Traditional_PCA_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.79	0.84	0.78	0.81	0.81	0.81	0.78	0.76	0.84	0.83	0.83
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	85.71	85.71	85.71	85.71	85.71	85.71	85.71	100.00	87.50	100.00
70.00	72.00	70.00	70.00	72.00	72.00	68.00	60.00	72.00	72.00	72.00
97.22	97.30	97.22	97.22	97.30	97.30	97.14	96.77	100.00	97.30	100.00
28.57	30.00	28.57	28.57	30.00	30.00	27.27	23.08	33.33	33.33	33.33
71.93	73.68	71.93	71.93	73.68	73.68	70.18	63.16	75.44	74.14	75.44
Confusion Matrix										
38 12 1 6	36 14 1 6	35 15 1 6	35 15 1 6	36 14 1 6	36 14 1 6	34 16 1 6	30 20 1 6	36 14 0 7	36 14 1 7	36 14 0 7

Table D.203: Momentaneous_Investigation_Traditional_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.77	NA	NA	0.60	0.78	0.76	0.74	NA	0.74	0.58	0.74
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	NA	NA	100.00	100.00	100.00	100.00	NA	100.00	100.00	100.00
72.00	NA	NA	20.00	60.00	56.00	50.00	NA	52.00	18.00	54.00
97.30	NA	NA	100.00	100.00	100.00	100.00	NA	100.00	100.00	100.00
30.00	NA	NA	14.89	25.93	24.14	21.88	NA	22.58	14.58	23.33
73.68	NA	NA	29.82	64.91	61.40	56.14	NA	57.89	28.07	59.65
Confusion Matrix										
36 14	NA	NA	10 40	30 20	28 22	25 25	NA	26 24	9 41	27 23
1 6	NA	NA	0 7	0 7	0 7	0 7	NA	0 7	0 7	0 7

Table D.204: Momentaneous_Investigation_kFold_PCA_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.74	0.77	0.73	0.73	0.77	0.78	0.72	0.68	0.77	0.78	0.78
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
68.18	**73.91**	**63.64**	**63.64**	**72.73**	**68.18**	**63.64**	**54.55**	**72.73**	**86.36**	**86.36**
90.77	**92.31**	**93.85**	**98.46**	**93.85**	**95.38**	**95.38**	**93.85**	**93.85**	**83.08**	**83.08**
89.39	**90.91**	**88.41**	**88.89**	**91.04**	**89.86**	**88.57**	**85.92**	**91.04**	**94.74**	**94.74**
71.43	**77.27**	**77.78**	**93.33**	**80.00**	**83.33**	**82.35**	**75.00**	**80.00**	**63.33**	**63.33**
85.06	**87.50**	**86.21**	**89.66**	**88.51**	**88.51**	**87.36**	**83.91**	**88.51**	**83.91**	**83.91**
Confusion Matrix										
59 6 7 15	60 5 6 17	61 4 8 14	64 1 8 14	61 4 6 16	62 3 7 15	62 3 8 14	61 4 10 12	61 4 6 16	54 11 3 19	54 11 3 19

Table D.205: Momentaneous_Investigation_kFold_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.71	0.77	NA	0.75	0.72	0.73	0.74	NA	0.77	0.78	0.83
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
68.18	**72.73**	NA	**68.18**	**68.18**	**68.18**	**72.73**	NA	**72.73**	**90.91**	**95.45**
89.23	**93.85**	NA	**93.85**	**87.69**	**90.77**	**90.77**	NA	**95.38**	**83.08**	**89.23**
89.23	**91.04**	NA	**89.71**	**89.06**	**89.39**	**90.77**	NA	**91.18**	**96.43**	**98.31**
68.18	**80.00**	NA	**78.95**	**65.22**	**71.43**	**72.73**	NA	**84.21**	**64.52**	**75.00**
83.91	**88.51**	NA	**87.36**	**82.76**	**85.06**	**86.21**	NA	**89.66**	**85.06**	**90.80**
Confusion Matrix										
58 7	61 4	NA	61 4	57 8	59 6	59 6	NA	62 3	54 11	58 7
7 15	6 16	NA	7 15	7 15	7 15	6 16	NA	6 16	2 20	1 21

Table D.206: Momentaneous_Investigation_LOO_PCA_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.40	0.47	0.41	0.39	0.43	0.47	0.42	0.43	0.47	0.50	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
9.09	18.18	9.09	4.55	13.64	18.18	9.09	9.09	18.18	36.36	45.45
72.31	75.38	75.38	80.00	73.85	76.92	78.46	80.00	75.38	64.62	67.69
70.15	73.13	71.01	71.23	71.64	73.53	71.83	72.22	73.13	75.00	78.57
10.00	20.00	11.11	7.14	15.00	21.05	12.50	13.33	20.00	25.81	32.26
56.32	60.92	58.62	60.92	58.62	62.07	60.92	62.07	60.92	57.47	62.07
Confusion Matrix										
47 18	49 16	49 16	52 13	48 17	50 15	51 14	52 13	49 16	42 23	44 21
20 2	18 4	20 2	21 1	19 3	18 4	20 2	20 2	18 4	14 8	12 10

Table D.207: Momentaneous_Investigation_LOO_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.52	NA	0.50	0.54	0.49	0.49	NA	0.52	0.55	0.57
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
27.27	22.73	NA	22.73	31.82	22.73	22.73	NA	22.73	45.45	45.45
73.85	80.00	NA	76.92	75.38	75.38	75.38	NA	80.00	66.15	70.77
75.00	75.36	NA	74.63	76.56	74.24	74.24	NA	75.36	78.18	79.31
26.09	27.78	NA	25.00	30.43	23.81	23.81	NA	27.78	31.25	34.48
62.07	65.52	NA	63.22	64.37	62.07	62.07	NA	65.52	60.92	64.37
Confusion Matrix										
48 17	52 13	NA	50 15	49 16	49 16	49 16	NA	52 13	43 22	46 19
16 6	17 5	NA	17 5	15 7	17 5	17 5	NA	17 5	12 10	12 10

For label *first2EDSS* (0/1 - (< 5)/(≥ 5)):

The via pattern recognition study was not performed since the number of patients with *first2EDSS*≥ 5 was minimal.

For label *tendencyEDSS* (0/1 - (Down/Equal & Up)):

It was not performed since the features used in standard procedure were not considered obvious.

For label mediumEDSS (0/1 - (< 3)/(≥ 3)):

Final features: Age of Diagnosis, MS Course, Years since Onset.

Table D.208: Momentaneous_Investigation_Traditional_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.57	0.58	0.57	0.57	0.57	0.55	0.59	0.54	0.59	0.41
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	90.00	90.00	90.00	90.00	100.00	100.00	100.00	100.00	25.71
22.22	14.81	22.22	25.93	22.22	18.52	11.11	22.22	11.11	22.22	57.69
100.00	100.00	85.71	87.50	85.71	83.33	100.00	100.00	100.00	100.00	53.57
32.26	30.30	30.00	31.03	30.00	29.03	29.41	32.26	29.41	32.26	29.03
43.24	37.84	40.54	43.24	40.54	37.84	35.14	43.24	35.14	43.24	44.83
Confusion Matrix										
6 21	4 23	6 21	7 20	6 21	5 22	3 24	6 21	3 24	6 21	30 22
0 10	0 10	1 9	1 9	1 9	1 9	0 10	0 10	0 10	0 10	26 9

Table D.209: Momentaneous_Investigation_Traditional_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.72	NA	0.55	0.62	0.58	0.56	NA	0.72	0.62	0.72	0.41
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
90.91	NA	100.00	90.00	100.00	100.00	NA	90.91	100.00	90.91	25.71
48.15	NA	11.11	29.63	18.52	11.11	NA	48.15	25.93	48.15	57.69
92.86	NA	100.00	88.89	100.00	100.00	NA	92.86	100.00	92.86	53.57
41.67	NA	29.41	32.14	31.25	29.41	NA	41.67	33.33	41.67	29.03
60.53	NA	35.14	45.95	40.54	35.14	NA	60.53	45.95	60.53	44.83
Confusion Matrix										
10 17	13 14	NA	3 24	8 19	5 22	3 24	NA	13 14	7 20	13 14
2 8	1 10	NA	0 10	1 9	0 10	0 10	NA	1 10	0 10	1 10

Table D.210: Momentaneous_Investigation_kFold_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.88	0.83	0.83	0.86	0.83	0.88	0.88	0.83	0.83	0.81	0.84
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
82.86	**71.43**	**71.43**	**74.29**	**77.14**	**85.71**	**82.86**	**71.43**	**71.43**	**71.43**	**74.29**
92.31	**94.23**	**94.23**	**96.15**	**88.46**	**92.31**	**94.23**	**94.23**	**94.23**	**90.38**	**94.23**
88.89	**83.05**	**83.05**	**84.75**	**85.19**	**90.57**	**89.09**	**83.05**	**83.05**	**82.46**	**84.48**
87.88	**89.29**	**89.29**	**92.86**	**81.82**	**88.24**	**90.63**	**89.29**	**89.29**	**83.33**	**89.66**
88.51	**85.06**	**85.06**	**87.36**	**83.91**	**89.66**	**89.66**	**85.06**	**85.06**	**82.76**	**86.21**
Confusion Matrix										
48 4	49 3	49 3	50 2	46 6	48 4	49 3	49 3	49 3	49 3	49 3
6 29	10 25	10 25	9 26	8 27	5 30	6 29	10 25	10 25	9 26	9 26

Table D.211: Momentaneous_Investigation_kFold_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.87	0.87	NA	0.86	0.90	0.88	0.91	NA	NA	0.83	0.87
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
91.43	**74.29**	NA	**80.00**	**88.89**	**82.86**	**82.86**	NA	NA	**71.43**	**80.00**
86.54	**96.15**	NA	**90.38**	**90.38**	**92.31**	**96.15**	NA	NA	**94.23**	**92.31**
93.75	**84.75**	NA	**87.04**	**92.16**	**88.89**	**89.29**	NA	NA	**83.05**	**87.27**
82.05	**92.86**	NA	**84.85**	**86.49**	**87.88**	**93.55**	NA	NA	**89.29**	**87.50**
88.51	**87.36**	NA	**86.21**	**89.77**	**88.51**	**90.80**	NA	NA	**85.06**	**87.36**
Confusion Matrix										
45 7	50 2	NA	47 5	47 5	48 4	50 2	NA	NA	49 3	48 4
3 32	9 26	NA	7 28	4 32	6 29	6 29	NA	NA	10 25	7 28

Table D.212: Momentaneous_Investigation_LOO_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.52	0.52	0.51	0.48	0.51	0.49	0.52	0.52	0.50	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
34.29	34.29	34.29	34.29	34.29	40.00	37.14	34.29	34.29	34.29	34.29
59.62	69.23	69.23	67.31	61.54	61.54	61.54	69.23	69.23	65.38	67.31
57.41	61.02	61.02	60.34	58.18	60.38	59.26	61.02	61.02	59.65	60.34
36.36	42.86	42.86	41.38	37.50	41.18	39.39	42.86	42.86	40.00	41.38
49.43	55.17	55.17	54.02	50.57	52.87	51.72	55.17	55.17	52.87	54.02
Confusion Matrix										
31 21	36 16	36 16	35 17	32 20	32 20	32 20	36 16	36 16	34 18	35 17
23 12	23 12	23 12	23 12	23 12	21 14	22 13	23 12	23 12	23 12	23 12

Table D.213: Momentaneous_Investigation_LOO_mediumEDSS ≥ 3

Classifier								
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**
AUC								
0.38	0.48	0.00	0.47	0.48	0.49	0.50	0.00	0.00
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %								
31.43	31.43	0.00	34.29	40.00	37.14	37.14	0.00	0.00
44.23	65.38	100.00	59.62	55.77	61.54	63.46	100.00	100.00
48.94	58.62	59.77	57.41	58.00	59.26	60.00	59.77	59.77
27.50	37.93	NaN	36.36	37.84	39.39	40.63	NaN	NaN
39.08	51.72	59.77	49.43	49.43	51.72	52.87	59.77	59.77
Confusion Matrix								
23 29	34 18	52 0	31 21	29 23	32 20	33 19	52 0	52 0
24 11	24 11	35 0	23 12	21 14	22 13	22 13	35 0	35 0

For label *nextEDSS* (0/1 - (< 3)/(≥ 3)):

The via pattern recognition study was not performed since the number of patients with *currentEDSS*≥ 5 was minimal.

D.1.4 Momentaneous with past Set

D.1.4.1 Standard procedure

For label *msCourse* (0/1 - RR/SP):

Final features: Age Visit, Years since Onset, EDSS Medium Value/Year, EDSS std/year, EDSS std of variance, Pyramidal 1st year.

Table D.214: Momentaneous_Past_Standard_Traditional_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.70	0.80	0.77	0.75	0.70	0.69	0.68	0.68	0.80	0.81	0.82
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	85.71	85.71	85.71	85.71	85.71	85.71	100.00	85.71	85.71	85.71
54.55	70.45	70.45	65.91	52.27	45.45	43.18	36.36	70.45	72.73	70.45
96.00	96.88	96.88	96.67	95.83	95.24	95.00	100.00	96.88	96.97	96.88
23.08	31.58	31.58	28.57	22.22	20.00	19.35	20.00	31.58	33.33	31.58
58.82	72.55	72.55	68.63	56.86	50.98	49.02	45.10	72.55	74.51	72.55
Confusion Matrix										
24 20 1 6	31 13 1 6	31 13 1 6	29 15 1 6	23 21 1 6	20 24 1 6	19 25 1 6	16 28 0 7	31 13 1 6	32 12 1 6	31 13 1 6

Table D.215: Momentaneous_Past_Standard_Traditional_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.56	0.52	NA	0.54	0.73	0.77	0.76	NA	0.52	0.50	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	NA	100.00	57.14	71.43	71.43	NA	100.00	100.00	100.00
13.64	4.55	NA	9.09	84.09	81.82	77.27	NA	4.55	0.00	2.27
100.00	100.00	NA	100.00	92.50	94.74	94.44	NA	100.00	NaN	100.00
15.56	14.29	NA	14.89	36.36	38.46	33.33	NA	14.29	13.73	14.00
25.49	17.65	NA	21.57	80.39	80.39	76.47	NA	17.65	13.73	15.69
Confusion Matrix										
6 38 0 7	2 42 0 7	NA NA	4 40 0 7	37 7 3 4	36 8 2 5	34 10 2 5	NA NA	2 42 0 7	0 44 0 7	1 43 0 7

Table D.216: Momentaneous_Past_Standard_kFold_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.67	0.70	0.75	0.57	0.69	0.67	0.63	0.73	0.70	0.71	0.78
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
56.00	**60.00**	**80.00**	32.00	**60.00**	**52.00**	44.00	**72.00**	**56.00**	**64.00**	**84.00**
83.87	**85.48**	**79.03**	95.16	**87.10**	**85.48**	88.71	**80.65**	**87.10**	**83.87**	**83.87**
82.54	**84.13**	**90.74**	77.63	**84.38**	**81.54**	79.71	**87.72**	**83.08**	**85.25**	**92.86**
58.33	**62.50**	**60.61**	72.73	**65.22**	**59.09**	61.11	**60.00**	**63.64**	**61.54**	**67.74**
75.86	**78.16**	**79.31**	77.01	**79.31**	**75.86**	75.86	**78.16**	**78.16**	**78.16**	**83.91**
Confusion Matrix										
52 10	53 9	49 13	59 3	54 8	53 9	55 7	50 12	54 8	52 10	52 10
11 14	10 15	5 20	17 8	10 15	12 13	14 11	7 18	11 14	9 16	4 21

Table D.217: Momentaneous_Past_Standard_kFold_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.74	0.77	0.77	0.79	0.80	0.76	0.74	0.78	0.77	0.75	0.82
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
68.00	**72.00**	**76.00**	**72.00**	**72.00**	**64.00**	**64.00**	**76.00**	**68.00**	**65.38**	**84.00**
87.10	**91.94**	**87.10**	**95.16**	**96.77**	**95.16**	**93.55**	**88.71**	**91.94**	**88.71**	**90.32**
87.10	**89.06**	**90.00**	**89.39**	**89.55**	**86.76**	**86.57**	**90.16**	**87.69**	**85.94**	**93.33**
68.00	**78.26**	**70.37**	**85.71**	**90.00**	**84.21**	**80.00**	**73.08**	**77.27**	**70.83**	**77.78**
81.61	**86.21**	**83.91**	**88.51**	**89.66**	**86.21**	**85.06**	**85.06**	**85.06**	**81.82**	**88.51**
Confusion Matrix										
54 8	57 5	54 8	59 3	60 2	59 3	58 4	55 7	57 5	55 7	56 6
8 17	7 18	6 19	7 18	7 18	9 16	9 16	6 19	8 17	9 17	4 21

Table D.218: Momentaneous_Past_Standard_LOO_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.45	0.49	0.49	0.48	0.52	0.48	0.48	0.45	0.53	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
12.00	28.00	48.00	12.00	12.00	28.00	16.00	32.00	28.00	36.00	32.00
66.13	74.19	66.13	87.10	67.74	75.81	80.65	64.52	74.19	70.97	61.29
65.08	71.88	75.93	71.05	65.63	72.31	70.42	70.18	71.88	73.33	69.09
12.50	30.43	36.36	27.27	13.04	31.82	25.00	26.67	30.43	33.33	25.00
50.57	60.92	60.92	65.52	51.72	62.07	62.07	55.17	60.92	60.92	52.87
Confusion Matrix										
41 21	46 16	41 21	54 8	42 20	47 15	50 12	40 22	46 16	44 18	38 24
22 3	18 7	13 12	22 3	22 3	18 7	21 4	17 8	18 7	16 9	17 8

Table D.219: Momentaneous_Past_Standard_LOO_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.52	0.53	0.50	0.51	0.49	0.51	0.49	0.52	0.56	0.56
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
36.00	28.00	36.00	24.00	24.00	20.00	24.00	28.00	28.00	36.00	40.00
70.97	75.81	70.97	75.81	77.42	79.03	77.42	69.35	75.81	75.81	72.58
73.33	72.31	73.33	71.21	71.64	71.01	71.64	70.49	72.31	74.60	75.00
33.33	31.82	33.33	28.57	30.00	27.78	30.00	26.92	31.82	37.50	37.04
60.92	62.07	60.92	60.92	62.07	62.07	62.07	57.47	62.07	64.37	63.22
Confusion Matrix										
44 18 16 9	47 15 18 7	44 18 16 9	47 15 19 6	48 14 19 6	49 13 20 5	48 14 19 6	43 19 18 7	47 15 18 7	47 15 16 9	45 17 15 10

For label *currentEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: Age visit, EDSS Medium Value/Year, EDSS increase first 2 years.

Table D.220: Momentaneous_Past_Standard_Traditional_PCA_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.73	0.85	0.80	0.82	0.75	0.76	0.75	0.81	0.85	0.83	0.84
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
90.00	**90.00**	**90.00**	**90.00**	**80.00**	**80.00**	**80.00**	**90.00**	**90.00**	**80.00**	**90.00**
55.56	**81.48**	**74.07**	**77.78**	**74.07**	**74.07**	**70.37**	**77.78**	**81.48**	**85.19**	**81.48**
93.75	**95.65**	**95.24**	**95.45**	**90.91**	**90.91**	**90.48**	**95.45**	**95.65**	**92.00**	**95.65**
42.86	**64.29**	**56.25**	**60.00**	**53.33**	**53.33**	**50.00**	**60.00**	**64.29**	**66.67**	**64.29**
64.86	**83.78**	**78.38**	**81.08**	**75.68**	**75.68**	**72.97**	**81.08**	**83.78**	**83.78**	**83.78**
Confusion Matrix										
15 12 1 9	22 5 1 9	20 7 1 9	21 6 1 9	20 7 2 8	20 7 2 8	19 8 2 8	21 6 1 9	22 5 1 9	23 4 2 8	22 5 1 9

Table D.221: Momentaneous_Past_Standard_Traditional_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.52	0.54	0.61	0.66	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
0.00	0.00	0.00	3.70	7.41	22.22	33.33	0.00	0.00	0.00	0.00
NaN	NaN	NaN	100.00	100.00	100.00	100.00	NaN	NaN	NaN	NaN
27.03	27.03	27.03	27.78	28.57	32.26	35.71	27.03	27.03	27.03	27.03
27.03	27.03	27.03	29.73	32.43	43.24	51.35	27.03	27.03	27.03	27.03
Confusion Matrix										
0 27 0 10	0 27 0 10	0 27 0 10	1 26 0 10	2 25 0 10	6 21 0 10	9 18 0 10	0 27 0 10	0 27 0 10	0 27 0 10	0 27 0 10

Table D.222: Momentaneous_Past_Standard_kFold_PCA_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.77	0.83	0.77	0.77	0.81	0.78	0.80	0.77	0.83	0.79	0.83
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
68.57	**71.43**	**74.29**	**62.86**	**74.29**	**65.71**	**68.57**	**60.00**	**71.43**	**65.71**	**80.00**
84.62	**92.31**	**78.85**	**86.54**	**88.46**	**90.38**	**90.38**	**90.38**	**92.31**	**90.38**	**88.46**
80.00	**82.76**	**82.00**	**77.59**	**83.64**	**79.66**	**81.03**	**77.05**	**82.76**	**79.66**	**86.79**
75.00	**86.21**	**70.27**	**75.86**	**81.25**	**82.14**	**82.76**	**80.77**	**86.21**	**82.14**	**82.35**
78.16	**83.91**	**77.01**	**77.01**	**82.76**	**80.46**	**81.61**	**78.16**	**83.91**	**80.46**	**85.06**
Confusion Matrix										
44 8	48 4	41 11	45 7	46 6	47 5	47 5	47 5	48 4	47 5	46 6
11 24	10 25	9 26	13 22	9 26	12 23	11 24	14 21	10 25	12 23	7 28

Table D.223: Momentaneous_Past_Standard_kFold_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.92	0.92	0.96	0.96	0.94	0.96	0.94	0.97	NA	0.91	0.94
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
97.14	**82.86**	**97.14**	**94.44**	**97.14**	**94.29**	**88.57**	**97.14**	NA	**85.71**	**85.71**
90.38	**100.00**	**96.15**	**96.15**	**94.23**	**96.15**	**98.08**	**98.08**	NA	**96.15**	**100.00**
97.92	**89.66**	**98.04**	**96.15**	**98.00**	**96.15**	**92.73**	**98.08**	NA	**90.91**	**91.23**
87.18	**100.00**	**94.44**	**94.44**	**91.89**	**94.29**	**96.88**	**97.14**	NA	**93.75**	**100.00**
93.10	**93.10**	**96.55**	**95.45**	**95.40**	**95.40**	**94.25**	**97.70**	NA	**91.95**	**94.25**
Confusion Matrix										
47 5	52 0	50 2	50 2	49 3	50 2	51 1	51 1	NA	50 2	52 0
1 34	6 29	1 34	2 34	1 34	2 33	4 31	1 34	NA	5 30	5 30

Table D.224: Momentaneous_Past_Standard_LOO_PCA_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.37	0.41	0.40	0.39	0.36	0.37	0.34	0.39	0.41	0.42	0.37
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
20.00	22.86	31.43	20.00	20.00	17.14	14.29	17.14	22.86	22.86	22.86
55.77	59.62	48.08	59.62	53.85	59.62	55.77	63.46	59.62	63.46	51.92
50.88	53.45	51.02	52.54	50.00	51.67	49.15	53.23	53.45	55.00	50.00
23.33	27.59	28.95	25.00	22.58	22.22	17.86	24.00	27.59	29.63	24.24
41.38	44.83	41.38	43.68	40.23	42.53	39.08	44.83	44.83	47.13	40.23
Confusion Matrix										
29 23	31 21	25 27	31 21	28 24	31 21	29 23	33 19	31 21	33 19	27 25
28 7	27 8	24 11	28 7	28 7	29 6	30 5	29 6	27 8	27 8	27 8

Table D.225: Momentaneous_Past_Standard_LOO_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.57	0.58	0.58	0.60	0.61	0.60	0.59	NA	0.50	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
54.29	40.00	**51.43**	**51.43**	**54.29**	**54.29**	48.57	**51.43**	NA	37.14	31.43
59.62	73.08	**65.38**	**65.38**	**65.38**	**67.31**	71.15	**67.31**	NA	63.46	63.46
65.96	64.41	**66.67**	**66.67**	**68.00**	**68.63**	67.27	**67.31**	NA	60.00	57.89
47.50	50.00	**50.00**	**50.00**	**51.35**	**52.78**	53.13	**51.43**	NA	40.63	36.67
57.47	59.77	**59.77**	**59.77**	**60.92**	**62.07**	62.07	**60.92**	NA	52.87	50.57
Confusion Matrix										
31 21	38 14	34 18	34 18	34 18	35 17	37 15	35 17	NA	33 19	33 19
16 19	21 14	17 18	17 18	16 19	16 19	18 17	17 18	NA	22 13	24 11

For label *currentEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: EDSS Medium Value/Year, Ratio nb EDSS increase, Visual ratio.

Table D.226: Momentaneous_Past_Standard_Traditional_PCA_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.64	0.79	0.66	0.73	0.68	0.62	0.67	0.75	0.79	0.75	0.79
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	80.00	60.00	80.00	80.00	80.00	80.00	100.00	80.00	80.00	100.00
43.33	68.33	78.33	65.00	55.00	46.67	51.67	58.33	68.33	68.33	68.33
96.30	97.62	95.92	97.50	97.06	96.55	96.88	100.00	97.62	97.62	100.00
10.53	17.39	18.75	16.00	12.90	11.11	12.12	16.67	17.39	17.39	20.83
46.15	69.23	76.92	66.15	56.92	49.23	53.85	61.54	69.23	69.23	70.77
Confusion Matrix										
26 34	41 19	47 13	39 21	33 27	28 32	31 29	35 25	41 19	41 19	41 19
1 4	1 4	2 3	1 4	1 4	1 4	1 4	0 5	1 4	1 4	0 5

Table D.227: Momentaneous_Past_Standard_Traditional_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.56	NA	NA	0.62	0.55	0.54	0.54	NA	0.51	0.53	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	NA	NA	100.00	80.00	100.00	100.00	NA	100.00	100.00	100.00
23.33	NA	NA	25.00	25.00	10.00	10.00	NA	1.69	8.33	1.67
93.33	NA	NA	100.00	93.75	100.00	100.00	NA	100.00	100.00	100.00
8.00	NA	NA	10.00	8.16	8.47	8.47	NA	7.94	8.33	7.81
27.69	NA	NA	30.77	29.23	16.92	16.92	NA	9.38	15.38	9.23
Confusion Matrix										
14 46	NA	NA	15 45	15 45	6 54	6 54	NA	1 58	5 55	1 59
1 4	NA	NA	0 5	1 4	0 5	0 5	NA	0 5	0 5	0 5

Table D.228: Momentaneous_Past_Standard_kFold_PCA_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.57	0.56	0.33	0.67	0.48	0.41	0.54	0.45	0.66	0.70
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
31.25	43.75	50.00	18.75	**68.75**	31.25	25.00	43.75	31.25	**68.75**	87.50
84.51	90.14	83.10	95.77	**92.96**	88.73	92.96	91.55	91.55	**84.51**	78.87
84.51	87.67	88.06	83.95	**92.96**	85.14	84.62	87.84	85.53	**92.31**	96.55
31.25	50.00	40.00	50.00	**68.75**	38.46	44.44	53.85	45.45	**50.00**	48.28
74.71	81.61	77.01	81.61	**88.51**	78.16	80.46	82.76	80.46	**81.61**	80.46
Confusion Matrix										
60 11 11 5	64 7 9 7	59 12 8 8	68 3 13 3	66 5 5 11	63 8 11 5	66 5 12 4	65 6 9 7	65 6 11 5	60 11 5 11	56 15 2 14

Table D.229: Momentaneous_Past_Standard_kFold_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.69	0.82	NA	0.76	0.79	0.77	0.73	NA	0.78	0.75	0.78
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
68.75	**93.75**	NA	**81.25**	**93.75**	**87.50**	**81.25**	NA	**81.25**	**93.75**	**100.00**
95.77	**95.77**	NA	**97.18**	**94.37**	**92.96**	**92.96**	NA	**97.18**	**87.32**	**90.14**
93.15	**98.55**	NA	**95.83**	**98.53**	**97.06**	**95.65**	NA	**95.83**	**98.41**	**100.00**
78.57	**83.33**	NA	**86.67**	**78.95**	**73.68**	**72.22**	NA	**86.67**	**62.50**	**69.57**
90.80	**95.40**	NA	**94.25**	**94.25**	**91.95**	**90.80**	NA	**94.25**	**88.51**	**91.95**
Confusion Matrix										
68 3	68 3	NA	69 2	67 4	66 5	66 5	NA	69 2	62 9	64 7
5 11	1 15	NA	3 13	1 15	2 14	3 13	NA	3 13	1 15	0 16

Table D.230: Momentaneous_Past_Standard_LOO_PCA_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	Mahalanobis
AUC										
0.49	0.47	0.41	0.40	0.39	0.39	0.40	0.44	0.45	0.47	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
25.00	12.50	6.25	0.00	0.00	0.00	0.00	6.25	6.25	18.75	18.75
71.83	81.69	73.24	88.73	78.87	78.87	87.32	83.10	85.92	73.24	63.38
80.95	80.56	77.61	79.75	77.78	77.78	79.49	79.73	80.26	80.00	77.59
16.67	13.33	5.00	0.00	0.00	0.00	0.00	7.69	9.09	13.64	10.34
63.22	68.97	60.92	72.41	64.37	64.37	71.26	68.97	71.26	63.22	55.17
Confusion Matrix										
51 20 12 4	58 13 14 2	52 19 15 1	63 8 16 0	56 15 16 0	56 15 16 0	62 9 16 0	59 12 15 1	61 10 15 1	52 19 13 3	45 26 13 3

Table D.231: Momentaneous_Past_Standard_LOO_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	NA	NA	0.46	0.48	0.48	0.49	NA	0.47	0.46	0.43
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
12.50	NA	NA	12.50	18.75	18.75	18.75	NA	12.50	18.75	12.50
81.69	NA	NA	80.28	77.46	76.06	78.87	NA	81.69	70.42	70.42
80.56	NA	NA	80.28	80.88	80.60	81.16	NA	80.56	79.37	78.13
13.33	NA	NA	12.50	15.79	15.00	16.67	NA	13.33	12.50	8.70
68.97	NA	NA	67.82	66.67	65.52	67.82	NA	68.97	60.92	59.77
Confusion Matrix										
58 13	NA	NA	57 14	55 16	54 17	56 15	NA	58 13	50 21	50 21
14 2	NA	NA	14 2	13 3	13 3	13 3	NA	14 2	13 3	14 2

First feature selection process for *nextEDSS*:

Table D.232: Momentaneous_Past_Feature_Selection_Identification_nextEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Gender	0	0	0	0	0	1	1	1	0	0	0	3
Age of Onset	0	0	0	0	0	0	1	0	0	0	0	1
Optic Pathways	0	1	1	0	0	0	1	0	1	0	1	**5**
Brainstem-Cerebellum	0	0	0	0	0	1	0	1	0	0	0	2
Spinal Cord	0	1	1	1	0	1	0	0	1	0	1	**6**
Progression From Onset	0	0	0	0	0	0	0	0	1	0	0	1
Age of Diagnosis	0	1	1	1	1	0	1	1	0	1	1	**8**
Years from Onset to Diagnosis	0	1	1	1	1	0	1	0	0	1	1	**7**
MRI	0	0	0	0	0	0	1	0	0	0	0	1
CSF	0	0	0	0	0	1	0	1	0	0	0	2
Age at SP Diagnosis	0	1	1	1	1	0	0	0	1	1	1	**7**
Years from Diagnosis to SP	0	1	1	1	1	0	0	0	1	1	1	**7**
Years from Diagnosis to Onset	0	1	1	1	1	0	0	0	1	1	1	**7**
MS Course	0	1	1	1	1	1	0	0	1	1	1	**8**
Age Visit	0	1	1	1	1	0	1	1	0	1	1	**8**
Years since Onset	1	1	1	1	1	0	1	0	0	1	1	**8**

Selected features: Optic Pathways, Spinal Cord, Age of Diagnosis, Years from Onset to Diagnosis, Age at SP Diagnosis, Years from Diagnosis to SP, Years from Diagnosis to Onset, MS Course, Age Visit, Years since Onset.

Table D.233: Momentaneous_Past_Feature_Selection_Visits_nextEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Nb of visits first 2 years	0	0	0	0	0	0	0	0	1	0	0	1
Suspected Relapses Ratio first 2 years	0	0	0	0	0	0	0	0	1	0	0	1
EDSS Medium Value/year	1	1	1	1	1	0	1	1	0	1	1	**9**
EDSS 1st year	0	1	1	1	1	0	1	0	0	1	1	**7**
EDSS first 2 years	1	1	1	1	1	0	1	0	0	1	1	**8**
EDSS std/year	0	1	1	1	1	0	0	0	1	1	1	**7**
EDSS 1st year std	0	0	0	0	0	0	1	0	0	0	0	1
EDSS first 2 years std	0	1	0	0	0	0	1	0	1	1	1	**5**
EDSS medium variation 1st year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS medium variation first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
EDSS std of variation 1st year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS std of variation first 2 years	0	0	0	0	0	0	1	0	1	1	0	3
EDSS Increase 1st Year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS Increase first 2 years	0	1	1	1	1	0	1	1	1	1	1	**9**
Ratio nb EDSS increase	0	1	1	1	1	0	1	0	1	1	1	**8**
Ratio nb EDSS decrease	0	0	0	0	0	0	1	0	0	0	0	1
Ratio nb EDSS decrease 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Ratio nb EDSS decrease first 2 years	0	0	0	0	0	0	1	0	1	1	0	3
Routine Visits Ratio 1st Year	0	0	0	0	0	1	0	0	0	0	0	1
Routine Visits first 2 years	0	0	0	0	0	1	1	0	0	0	0	2
No Years	0	1	1	1	1	0	0	0	0	0	1	**5**
Last Routine	0	0	0	0	0	1	0	0	0	0	0	1
Last Suspected	0	0	0	0	0	0	1	0	0	0	0	1
Last EDSS	1	1	1	1	1	0	1	1	0	1	1	**9**
Last Sympton	0	0	0	0	0	0	0	0	1	0	0	1

Selected features: Last EDSS.

Table D.234: Momentaneous_Past_Feature_Selection_Relapses_nextEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Relapses Per Year	0	1	1	0	0	0	0	1	0	1	1	**5**
Relapses 1st Year	0	0	0	0	0	0	1	0	0	0	0	1
Relapses first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Pyramidal ratio	0	1	1	1	1	0	0	0	0	1	1	**6**
Pyramidal 1st year	0	1	1	1	0	1	1	0	1	0	1	**7**
Pyramidal first 2 years	0	1	1	1	1	0	1	1	1	1	1	**9**
Brain Stem ratio	0	0	0	1	0	0	1	0	0	0	0	2
BrainStem 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Brain Stem first 2 years	0	1	0	1	0	0	1	1	0	0	1	**5**
Neuropsycho ratio	0	0	0	0	0	0	1	0	0	0	0	1
Neuropsycho 1st year	0	0	0	0	0	0	0	0	1	0	0	1
Neuropsycho first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Cerebellum 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Visual ratio	0	1	0	1	0	0	0	1	0	1	1	**5**
Visual 1st year	0	1	1	1	0	0	0	0	1	0	1	**5**
Visual first 2 years	0	1	1	1	0	0	1	0	1	1	1	**7**
Sensory ratio	0	1	1	1	0	0	1	1	1	1	1	**8**
Sensory 1st year	0	0	0	0	0	1	1	0	0	0	0	2
Sensory first 2 years	0	0	0	0	0	0	1	0	1	0	0	2
Corticosteroids Ratio	0	1	0	1	0	0	0	0	0	0	1	3
Corticosteroids/year	0	1	1	1	0	0	0	0	0	1	1	**5**
Corticosteroids 1st year	0	1	1	1	0	1	1	0	1	1	1	**8**
Corticosteroids first 2 years	0	0	0	0	0	0	1	1	0	0	0	2
Average Treatment Intensity	0	1	1	1	0	0	0	1	0	0	1	**5**
Average Treatment 1st year	0	1	1	1	0	0	0	0	1	0	1	**5**
Average Treatment 2 first years	0	1	0	1	0	0	1	0	0	1	1	**5**
Average Duration	0	1	1	1	0	0	1	0	0	0	1	**5**
Average Duration 1st year	0	1	1	1	0	0	1	0	1	1	1	**7**
Average Duration first 2 years	0	1	0	1	0	0	1	0	0	1	1	**5**
Last Pyramidal	0	1	0	0	0	1	0	0	1	0	1	**4**
Last BrainStem	0	0	0	0	0	0	1	0	0	0	0	1
Last Bowel	0	0	0	0	0	0	0	0	1	0	0	1
Last Sensory	0	1	1	1	0	1	0	0	1	1	1	**7**
Last Hospital	0	0	0	0	0	1	0	0	0	0	0	1
Last ambulatory	0	0	0	0	0	1	0	0	0	0	0	1
Last Corticosteroid	0	0	0	0	0	1	0	0	0	0	0	1
Last Treatment	0	0	0	0	0	0	1	0	0	0	0	1

Selected features: Last Pyramidal, Last Sensory.

For label *nextEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$:

Final features: Optic Pathways, EDSS Medium Value/year, EDSS first 2 years std, Relapses Per Year, Visual 1 ratio.

Table D.235: Momentaneous_Past_Standard_Traditional_PCA_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.80	0.90	0.87	0.84	0.75	0.75	0.76	0.88	0.90	0.88	0.89
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
90.00	**90.00**	**90.00**	**90.00**	80.00	80.00	**90.00**	**90.00**	**90.00**	**90.00**	**90.00**
68.97	**89.66**	**82.76**	**75.86**	68.97	65.52	**68.97**	**86.21**	**89.66**	**89.66**	**89.66**
95.24	**96.30**	**96.00**	**95.65**	90.91	90.48	**95.24**	**96.15**	**96.30**	**96.30**	**96.30**
50.00	**75.00**	**64.29**	**56.25**	47.06	44.44	**50.00**	**69.23**	**75.00**	**75.00**	**75.00**
74.36	**89.74**	**84.62**	**79.49**	71.79	69.23	**74.36**	**87.18**	**89.74**	**89.74**	**89.74**
Confusion Matrix										
20 9	26 3	24 5	22 7	20 9	19 10	20 9	25 4	26 3	26 3	26 3
1 9	1 9	1 9	1 9	2 8	2 8	1 9	1 9	1 9	1 9	1 9

Table D.236: Momentaneous_Past_Standard_Traditional_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.64	0.62	0.62	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	90.00	100.00	100.00	100.00	100.00	100.00	100.00
0.00	0.00	0.00	0.00	34.48	27.59	24.14	0.00	0.00	0.00	0.00
NaN	NaN	NaN	NaN	90.91	100.00	100.00	NaN	NaN	NaN	NaN
25.64	25.64	25.64	25.64	32.14	32.26	31.25	25.64	25.64	25.64	25.64
25.64	25.64	25.64	25.64	48.72	46.15	43.59	25.64	25.64	25.64	25.64
Confusion Matrix										
0 29	0 29	0 29	0 29	10 19	8 21	7 22	0 29	0 29	0 29	0 29
0 10	0 10	0 10	0 10	1 9	0 10	0 10	0 10	0 10	0 10	0 10

Table D.237: Momentaneous_Past_Standard_kFold_PCA_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.86	0.85	0.86	0.87	0.89	0.88	0.84	0.85	0.85	0.89	0.89
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
82.35	**73.53**	**79.41**	**76.47**	**88.24**	**85.29**	**76.47**	**73.53**	**73.53**	**79.41**	**82.35**
90.57	**94.34**	**92.45**	**94.34**	**92.45**	**90.57**	**92.45**	**94.34**	**94.34**	**96.23**	**94.34**
88.89	**84.75**	**87.50**	**86.21**	**92.45**	**90.57**	**85.96**	**84.75**	**84.75**	**87.93**	**89.29**
84.85	**89.29**	**87.10**	**89.66**	**88.24**	**85.29**	**86.67**	**89.29**	**89.29**	**93.10**	**90.32**
87.36	**86.21**	**87.36**	**87.36**	**90.80**	**88.51**	**86.21**	**86.21**	**86.21**	**89.66**	**89.66**
Confusion Matrix										
48 5	50 3	49 4	50 3	49 4	48 5	49 4	50 3	50 3	51 2	50 3
6 28	9 25	7 27	8 26	4 30	5 29	8 26	9 25	9 25	7 27	6 28

Table D.238: Momentaneous_Past_Standard_kFold_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.93	0.90	0.89	0.92	0.89	0.91	0.88	0.90	0.90	0.89	0.91
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
91.18	**82.35**	**91.18**	**88.24**	**85.29**	**85.29**	**79.41**	**91.18**	**82.35**	**79.41**	**85.29**
96.23	**98.11**	**90.57**	**96.23**	**92.45**	**96.23**	**96.23**	**92.45**	**98.11**	**98.11**	**96.23**
94.44	**89.66**	**94.12**	**92.73**	**90.74**	**91.07**	**87.93**	**94.23**	**89.66**	**88.14**	**91.07**
93.94	**96.55**	**86.11**	**93.75**	**87.88**	**93.55**	**93.10**	**88.57**	**96.55**	**96.43**	**93.55**
94.25	**91.95**	**90.80**	**93.10**	**89.66**	**91.95**	**89.66**	**91.95**	**91.95**	**90.80**	**91.95**
Confusion Matrix										
51 2 3 31	52 1 6 28	48 5 3 31	51 2 4 30	49 4 5 29	51 2 5 29	51 2 7 27	49 4 3 31	52 1 6 28	52 1 7 27	51 2 5 29

Table D.239: Momentaneous_Past_Standard_LOO_PCA_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.50	0.47	0.45	0.47	0.44	0.47	0.50	0.50	0.53	0.56
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
35.29	32.35	32.35	29.41	35.29	32.35	32.35	29.41	32.35	38.24	44.12
60.38	67.92	62.26	60.38	58.49	54.72	62.26	69.81	67.92	67.92	67.92
59.26	61.02	58.93	57.14	58.49	55.77	58.93	60.66	61.02	63.16	65.45
36.36	39.29	35.48	32.26	35.29	31.43	35.48	38.46	39.29	43.33	46.88
50.57	54.02	50.57	48.28	49.43	45.98	50.57	54.02	54.02	56.32	58.62
Confusion Matrix										
32 21 22 12	36 17 23 11	33 20 23 11	32 21 24 10	31 22 22 12	29 24 23 11	33 20 23 11	37 16 24 10	36 17 23 11	36 17 21 13	36 17 19 15

Table D.240: Momentaneous_Past_Standard_LOO_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.54	0.50	0.53	0.53	0.51	0.52	0.51	0.54	0.45	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
41.18	38.24	41.18	41.18	41.18	38.24	35.29	41.18	38.24	26.47	35.29
64.15	69.81	58.49	64.15	64.15	64.15	67.92	60.38	69.81	64.15	64.15
62.96	63.79	60.78	62.96	62.96	61.82	62.07	61.54	63.79	57.63	60.71
42.42	44.83	38.89	42.42	42.42	40.63	41.38	40.00	44.83	32.14	38.71
55.17	57.47	51.72	55.17	55.17	54.02	55.17	52.87	57.47	49.43	52.87
Confusion Matrix										
34 19 20 14	37 16 21 13	31 22 20 14	34 19 20 14	34 19 20 14	34 19 21 13	36 17 22 12	32 21 20 14	37 16 21 13	34 19 25 9	34 19 22 12

For label *nextEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: EDSS Medium Value/Year, EDSS first 2 years, EDSS std/year, Last EDSS.

Table D.241: Momentaneous_Past_Standard_Traditional_PCA_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.70	0.83	0.77	0.80	0.72	0.73	0.76	0.80	0.83	0.82	0.83
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
83.33	100.00	83.33	83.33	66.67	83.33	83.33	83.33	100.00	85.71	100.00
52.73	70.91	72.73	74.55	70.91	69.09	74.55	74.55	70.91	70.91	70.91
96.67	100.00	97.56	97.62	95.12	97.44	97.62	97.62	100.00	97.50	100.00
16.13	27.27	25.00	26.32	20.00	22.73	26.32	26.32	27.27	27.27	27.27
55.74	73.77	73.77	75.41	70.49	70.49	75.41	75.41	73.77	72.58	73.77
Confusion Matrix										
29 26 1 5	39 16 0 6	40 15 1 5	41 14 1 5	39 16 2 4	38 17 1 5	41 14 1 5	41 14 1 5	39 16 0 6	39 16 1 6	39 16 0 6

Table D.242: Momentaneous_Past_Standard_Traditional_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.62	0.50	0.65	0.68	0.68	0.74	0.79	0.51	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	66.67	83.33	83.33	100.00	100.00	100.00	100.00
23.64	0.00	34.55	40.00	70.91	67.27	67.27	1.82	0.00	0.00	0.00
100.00	NaN	100.00	100.00	95.12	97.37	97.37	100.00	NaN	NaN	NaN
12.50	9.84	14.29	15.38	20.00	21.74	21.74	10.00	9.84	9.84	9.84
31.15	9.84	40.98	45.90	70.49	68.85	68.85	11.48	9.84	9.84	9.84
Confusion Matrix										
13 42 0 6	0 55 0 6	19 36 0 6	22 33 0 6	39 16 2 4	37 18 1 5	37 18 1 5	1 54 0 6	0 55 0 6	0 55 0 6	0 55 0 6

Table D.243: Momentaneous_Past_Standard_kFold_PCA_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.63	0.58	0.66	0.50	0.83	0.73	0.40	0.68	0.54	0.71	0.74
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
52.63	47.37	**63.16**	36.84	**85.00**	**63.16**	26.32	**63.16**	36.84	**73.68**	**84.21**
89.71	89.71	**85.29**	98.53	**97.06**	**94.12**	97.06	**86.76**	91.18	**85.29**	**82.35**
87.14	85.92	**89.23**	84.81	**95.65**	**90.14**	82.50	**89.39**	83.78	**92.06**	**94.92**
58.82	56.25	**54.55**	87.50	**89.47**	**75.00**	71.43	**57.14**	53.85	**58.33**	**57.14**
81.61	80.46	**80.46**	85.06	**94.32**	**87.36**	81.61	**81.61**	79.31	**82.76**	**82.76**
Confusion Matrix										
61 7 9 10	61 7 10 9	58 10 7 12	67 1 12 7	66 2 3 17	64 4 7 12	66 2 14 5	59 9 7 12	62 6 12 7	58 10 5 14	56 12 3 16

Table D.244: Momentaneous_Past_Standard_kFold_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.81	0.80	0.79	0.79	0.78	0.79	0.79	0.79	0.81	0.81	0.79
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
84.21	**84.21**	**84.21**	**78.95**	**78.95**	**78.95**	**78.95**	**89.47**	**84.21**	**89.47**	**84.21**
97.06	**97.06**	**94.12**	**98.53**	**97.06**	**98.53**	**98.53**	**89.71**	**97.06**	**92.65**	**94.12**
95.65	**95.65**	**95.52**	**94.37**	**94.29**	**94.37**	**94.37**	**96.83**	**95.65**	**96.92**	**95.52**
88.89	**88.89**	**80.00**	**93.75**	**88.24**	**93.75**	**93.75**	**70.83**	**88.89**	**77.27**	**80.00**
94.25	**94.25**	**91.95**	**94.25**	**93.10**	**94.25**	**94.25**	**89.66**	**94.25**	**91.95**	**91.95**
Confusion Matrix										
66 2 3 16	66 2 3 16	64 4 3 16	67 1 4 15	66 2 4 15	67 1 4 15	67 1 4 15	61 7 2 17	66 2 3 16	63 5 2 17	64 4 3 16

Table D.245: Momentaneous_Past_Standard_LOO_PCA_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	0.48	0.50	0.38	0.53	0.47	0.47	0.54	0.46	0.49	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
26.32	15.79	26.32	0.00	26.32	15.79	5.26	31.58	10.53	26.32	26.32
82.35	80.88	73.53	88.24	79.41	77.94	92.65	77.94	83.82	70.59	66.18
80.00	77.46	78.13	75.95	79.41	76.81	77.78	80.30	77.03	77.42	76.27
29.41	18.75	21.74	0.00	26.32	16.67	16.67	28.57	15.38	20.00	17.86
70.11	66.67	63.22	68.97	67.82	64.37	73.56	67.82	67.82	60.92	57.47
Confusion Matrix										
56 12 14 5	55 13 16 3	50 18 14 5	60 8 19 0	54 14 14 5	53 15 16 3	63 5 18 1	53 15 13 6	57 11 17 2	48 20 14 5	45 23 14 5

Table D.246: Momentaneous_Past_Standard_LOO_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.47	0.46	0.48	0.51	0.48	0.48	0.46	0.47	0.45	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
21.05	15.79	15.79	15.79	21.05	15.79	15.79	21.05	15.79	15.79	15.79
79.41	77.94	75.00	80.88	80.88	80.88	80.88	70.59	77.94	72.06	77.94
78.26	76.81	76.12	77.46	78.57	77.46	77.46	76.19	76.81	75.38	76.81
22.22	16.67	15.00	18.75	23.53	18.75	18.75	16.67	16.67	13.64	16.67
66.67	64.37	62.07	66.67	67.82	66.67	66.67	59.77	64.37	59.77	64.37
Confusion Matrix										
54 14 15 4	53 15 16 3	51 17 16 3	55 13 16 3	55 13 15 4	55 13 16 3	55 13 16 3	48 20 15 4	53 15 16 3	49 19 16 3	53 15 16 3

First feature selection process for *highestEDSS*:

Table D.247: Momentaneous_Past_Feature_Selection_Identification_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Gender	0	0	0	0	0	1	1	1	0	0	0	3
Age of Onset	0	0	0	0	0	0	1	0	0	0	0	1
Optic Pathways	0	1	1	0	0	0	1	0	1	1	1	**6**
Brainstem-Cerebellum	0	0	0	0	0	1	1	1	0	0	0	3
Spinal Cord	0	1	1	1	0	1	1	0	1	0	1	**7**
Progression From Onset	0	0	0	0	0	0	0	1	1	0	0	2
Age of Diagnosis	0	0	0	0	0	0	1	1	0	1	0	3
Years from Onset to Diagnosis	0	0	1	1	1	0	1	0	0	1	1	**6**
MRI	0	0	0	0	0	0	1	0	0	0	0	1
Evoked Potentials	0	0	0	0	0	0	1	0	0	0	0	1
CSF	0	0	0	0	0	1	1	1	0	0	0	3
Age at SP Diagnosis	0	1	1	1	1	0	1	0	1	1	1	**8**
Years from Diagnosis to SP	0	1	1	1	1	0	1	0	1	1	1	**8**
Years from Diagnosis to Onset	0	1	1	1	1	0	1	0	1	1	1	**8**
MS Course	0	1	1	1	1	1	0	0	1	1	1	**8**
Family History	0	0	0	0	0	0	1	0	1	0	1	3
Active	0	0	0	0	0	0	0	1	0	0	0	1
Age Visit	0	1	1	1	1	0	1	0	0	1	1	**7**
Years since Onset	1	1	1	1	1	0	1	0	0	1	1	**8**

Selected features: Optic Pathways, Spinal Cord, Years from Onset to Diagnosis, Age at SP Diagnosis, Years from Diagnosis to SP, Years from Diagnosis to Onset, MS Course, Age Visit, Years since Onset.

Table D.248: Momentaneous_Past_Feature_Selection_Visits_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Nb of visits per Year	0	1	0	1	0	0	0	0	0	1	1	**4**
Nb of Visits 1st Year	0	0	0	0	0	0	0	0	0	0	1	1
Nb of visits first 2 years	0	0	0	0	0	0	1	0	0	0	1	2
Suspected Relapses Ratio per year	0	1	0	1	0	0	0	0	0	1	1	**4**
Suspected Relapses Ratio first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
EDSS Medium Value/year	1	1	1	1	1	0	1	1	0	1	1	**9**
EDSS 1st year	1	1	1	1	1	0	1	0	0	1	1	**8**
EDSS first 2 years	1	1	1	1	1	0	1	0	0	1	1	**8**
EDSS std/year	0	1	1	1	1	0	1	0	1	1	1	**8**
EDSS 1st year std	0	0	0	0	0	0	1	0	0	0	0	1
EDSS first 2 years std	0	0	0	0	0	0	1	0	1	1	0	3
EDSS medium variation/Year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS medium variation 1st year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS medium variation first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
EDSS std of variation/year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS std of variation 1st year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS std of variation first 2 years	0	0	0	0	0	0	1	0	1	1	0	3
EDSS Increase 1st Year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS Increase first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Ratio nb EDSS increase	0	1	1	1	1	0	1	0	0	1	1	**7**
Ratio nb EDSS decrease	0	0	0	0	0	0	1	0	1	0	0	2
Ratio nb EDSS decrease 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Ratio nb EDSS decrease first 2 years	0	0	0	0	0	0	1	0	1	0	0	2
Routine Visits Ratio 1st Year	0	1	1	1	0	1	1	0	0	0	1	**6**
Routine Visits first 2 years	0	0	0	0	0	1	1	0	0	0	0	2
No Years	0	0	1	0	0	0	0	0	0	0	0	1
Last Routine	0	0	0	0	0	1	0	1	0	0	0	2
Last EDSS	1	1	1	1	1	0	1	0	0	1	1	**8**
Last Weakness	0	0	0	0	0	0	1	0	0	0	0	1
Last Sympton	0	0	0	0	0	0	0	0	1	0	0	1

Selected features: Last EDSS.

Table D.249: Momentaneous_Past_Feature_Selection_Relapses_highestEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Relapses Per Year	0	0	0	0	0	0	1	0	0	0	0	1
Relapses 1st Year	0	0	0	0	0	0	1	0	0	0	0	1
Relapses first 2 years	0	0	0	0	0	0	1	1	0	0	0	2
Pyramidal ratio	0	1	1	1	1	0	1	0	0	1	1	**7**
Pyramidal 1st year	0	1	1	1	0	1	1	1	1	0	1	**8**
Pyramidal first 2 years	0	1	1	1	1	0	1	1	1	1	1	**9**
Brain Stem ratio	0	0	0	0	0	0	1	0	0	0	0	1
BrainStem 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Brain Stem first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Neuropsycho ratio	0	0	0	0	0	0	1	0	0	0	0	1
Neuropsycho 1st year	0	0	0	0	0	0	0	0	1	0	0	1
Neuropsycho first 2 years	0	0	0	1	0	0	1	0	0	0	0	2
Cerebellum ratio	0	1	1	0	0	0	1	1	1	0	1	**6**
Cerebellum 1st year	0	1	1	1	0	0	1	0	1	0	1	**6**
Cerebellum first 2 years	0	1	1	1	0	0	1	0	1	0	1	**6**
Visual ratio	0	1	1	1	0	0	0	0	1	1	1	**6**
Visual 1st year	0	1	1	1	0	0	0	0	1	1	1	**6**
Visual first 2 years	0	1	1	1	0	0	1	0	1	1	1	**7**
Sensory ratio	0	1	1	1	0	0	1	0	0	1	1	**6**
Sensory 1st year	0	0	0	0	0	1	1	0	0	0	0	2
Sensory first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Corticosteroids Ratio	0	1	1	1	0	0	0	0	0	1	1	**5**
Corticosteroids/year	0	1	1	1	0	0	0	0	0	1	1	**5**
Corticosteroids 1st year	0	1	1	1	0	1	1	0	1	1	1	**8**
Corticosteroids first 2 years	0	1	1	1	0	0	1	0	0	1	1	**6**
Average Treatment Intensity	0	1	1	1	0	0	0	0	0	1	1	**5**
Average Treatment 1st year	0	1	1	1	0	0	1	1	1	1	1	**8**
Average Treatment 2 first years	0	1	1	1	0	0	1	0	0	1	1	**6**
Average Duration	0	1	1	1	0	0	1	0	0	1	1	**6**
Average Duration 1st year	0	1	1	1	0	0	1	0	1	1	1	**7**
Average Duration first 2 years	0	1	1	1	0	0	1	0	0	1	1	**6**
Last Pyramidal	0	0	0	0	0	1	0	0	0	0	0	1
Last Bowel	0	0	0	0	0	0	0	0	1	0	0	1
Last Neuropsycho	0	0	0	0	0	0	1	0	0	0	0	1
Last Visual	0	0	0	0	0	0	0	1	0	0	0	1
Last Sensory	0	1	0	1	0	1	0	0	1	1	1	**6**
Last Hospital	0	0	0	0	0	1	0	0	0	0	0	1
Last ambulatory	0	0	0	0	0	1	0	0	0	0	0	1
Last Corticosteroid	0	0	0	0	0	1	0	0	0	0	0	1
Last Treatment	0	0	0	0	0	0	0	0	1	0	0	1

Selected features: Last Sensory.

For label *highestEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$:

Final features: Age Visit, EDSS Medium Value/Year, Average Treatment 2 first years.

Table D.250: Momentaneous_Past_Standard_Traditional_PCA_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.77	0.85	0.83	0.85	0.85	0.80	0.80	0.83	0.85	0.86	0.85
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
71.43	**85.71**	**78.57**	**78.57**	**78.57**	**78.57**	**78.57**	**85.71**	**85.71**	**85.71**	**85.71**
81.82	**81.82**	**81.82**	**90.91**	**90.91**	**81.82**	**81.82**	**81.82**	**81.82**	**81.82**	**81.82**
69.23	**81.82**	**75.00**	**76.92**	**76.92**	**75.00**	**75.00**	**81.82**	**81.82**	**81.82**	**81.82**
83.33	**85.71**	**84.62**	**91.67**	**91.67**	**84.62**	**84.62**	**85.71**	**85.71**	**85.71**	**85.71**
76.00	**84.00**	**80.00**	**84.00**	**84.00**	**80.00**	**80.00**	**84.00**	**84.00**	**84.00**	**84.00**
Confusion Matrix										
9 2 4 10	9 2 2 12	9 2 3 11	10 1 3 11	10 1 3 11	9 2 3 11	9 2 3 11	9 2 2 12	9 2 2 12	9 2 2 12	9 2 2 12

Table D.251: Momentaneous_Past_Standard_Traditional_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.74	0.80	0.75	0.53	0.48	0.50	0.55	0.74	0.59	0.73
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	**92.86**	**85.71**	**64.29**	50.00	50.00	50.00	100.00	**92.86**	100.00	**92.86**
0.00	**54.55**	**72.73**	**90.91**	54.55	45.45	54.55	9.09	**54.55**	18.18	**54.55**
NaN	**85.71**	**80.00**	**66.67**	46.15	41.67	46.15	100.00	**85.71**	100.00	**85.71**
56.00	**72.22**	**80.00**	**90.00**	58.33	53.85	58.33	58.33	**72.22**	60.87	**72.22**
56.00	**76.00**	**80.00**	**76.00**	52.00	48.00	52.00	60.00	**76.00**	64.00	**76.00**
Confusion Matrix										
0 11 0 14	6 5 1 13	8 3 2 12	10 1 5 9	6 5 7 7	5 6 7 7	6 5 7 7	1 10 0 14	6 5 1 13	2 9 0 14	6 5 1 13

Table D.252: Momentaneous_Past_Standard_kFold_PCA_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.85	0.84	0.80	0.84	0.87	0.79	0.78	0.81	0.84	0.87	0.84
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
86.67	**86.67**	**82.22**	**84.44**	**88.89**	**82.22**	**80.00**	**75.56**	**86.67**	**88.89**	**86.67**
85.71	**80.95**	**78.57**	**80.95**	**83.33**	**76.19**	**76.19**	**83.33**	**80.95**	**85.71**	**83.33**
85.71	**85.00**	**80.49**	**82.93**	**87.50**	**80.00**	**78.05**	**76.09**	**85.00**	**87.80**	**85.37**
86.67	**82.98**	**80.43**	**82.61**	**85.11**	**78.72**	**78.26**	**82.93**	**82.98**	**86.96**	**84.78**
86.21	**83.91**	**80.46**	**82.76**	**86.21**	**79.31**	**78.16**	**79.31**	**83.91**	**87.36**	**85.06**
Confusion Matrix										
36 6 6 39	34 8 6 39	33 9 8 37	34 8 7 38	35 7 5 40	32 10 8 37	32 10 9 36	35 7 11 34	34 8 6 39	36 6 5 40	35 7 6 39

Table D.253: Momentaneous_Past_Standard_kFold_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.90	0.92	0.95	0.97	0.97	0.93	0.94	0.93	0.92	0.69	0.92
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
93.33	**93.33**	**95.56**	**97.78**	**97.78**	**93.33**	**95.56**	**91.11**	**93.33**	**73.33**	**91.11**
85.71	**90.48**	**95.24**	**97.62**	**97.62**	**92.86**	**92.86**	**95.24**	**90.48**	**64.29**	**92.86**
92.31	**92.68**	**95.24**	**97.62**	**97.62**	**92.86**	**95.12**	**90.91**	**92.68**	**69.23**	**90.70**
87.50	**91.30**	**95.56**	**97.78**	**97.78**	**93.33**	**93.48**	**95.35**	**91.30**	**68.75**	**93.18**
89.66	**91.95**	**95.40**	**97.70**	**97.70**	**93.10**	**94.25**	**93.10**	**91.95**	**68.97**	**91.95**
Confusion Matrix										
36 6 3 42	38 4 3 42	40 2 2 43	41 1 1 44	41 1 1 44	39 3 3 42	39 3 2 43	40 2 4 41	38 4 3 42	27 15 12 33	39 3 4 41

Table D.254: Momentaneous_Past_Standard_LOO_PCA_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.41	0.45	0.45	0.52	0.48	0.52	0.49	0.44	0.45	0.52	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
44.44	48.89	46.67	55.56	51.11	55.56	53.33	40.00	48.89	55.56	55.56
38.10	40.48	42.86	47.62	45.24	47.62	45.24	47.62	40.48	47.62	47.62
39.02	42.50	42.86	50.00	46.34	50.00	47.50	42.55	42.50	50.00	50.00
43.48	46.81	46.67	53.19	50.00	53.19	51.06	45.00	46.81	53.19	53.19
41.38	44.83	44.83	51.72	48.28	51.72	49.43	43.68	44.83	51.72	51.72
Confusion Matrix										
16 26	17 25	18 24	20 22	19 23	20 22	19 23	20 22	17 25	20 22	20 22
25 20	23 22	24 21	20 25	22 23	20 25	21 24	27 18	23 22	20 25	20 25

Table D.255: Momentaneous_Past_Standard_LOO_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.40	0.42	0.40	0.40	0.42	0.42	0.41	0.41	0.42	0.55	0.59
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
46.67	46.67	42.22	42.22	44.44	44.44	44.44	42.22	46.67	**60.00**	**60.00**
33.33	38.10	38.10	38.10	40.48	40.48	38.10	40.48	38.10	**50.00**	**57.14**
36.84	40.00	38.10	38.10	40.48	40.48	39.02	39.53	40.00	**53.85**	**57.14**
42.86	44.68	42.22	42.22	44.44	44.44	43.48	43.18	44.68	**56.25**	**60.00**
40.23	42.53	40.23	40.23	42.53	42.53	41.38	41.38	42.53	**55.17**	**58.62**
Confusion Matrix										
14 28	16 26	16 26	16 26	17 25	17 25	16 26	17 25	16 26	21 21	24 18
24 21	24 21	26 19	26 19	25 20	25 20	25 20	26 19	24 21	18 27	18 27

For label *highestEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: Optic Pathways, EDSS Medium Value/Year, Pyramidal first 2 years, Cortiscosteroids 1st Year.

Table D.256: Momentaneous_Past_Standard_Traditional_PCA_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.73	0.88	0.86	0.84	0.82	0.79	0.80	0.82	0.88	0.87	0.87
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	85.71	85.71	85.71	85.71	85.71	100.00	100.00	100.00	100.00
52.17	78.26	84.78	78.26	78.26	71.74	69.57	67.39	78.26	78.26	76.09
100.00	100.00	97.50	97.30	97.30	97.06	96.97	100.00	100.00	100.00	100.00
24.14	41.18	46.15	37.50	37.50	31.58	30.00	31.82	41.18	41.18	38.89
58.49	81.13	84.91	79.25	79.25	73.58	71.70	71.70	81.13	81.13	79.25
Confusion Matrix										
24 22	36 10	39 7	36 10	36 10	33 13	32 14	31 15	36 10	36 10	35 11
0 7	0 7	1 6	1 6	1 6	1 6	1 6	0 7	0 7	0 7	0 7

Table D.257: Momentaneous_Past_Standard_Traditional_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	NA	NA	0.63	0.63	0.62	0.62	NA	NaN	0.67	0.66
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	NA	NA	85.71	85.71	85.71	100.00	NA	100.00	100.00	100.00
8.70	NA	NA	36.96	43.48	30.43	28.26	NA	35.56	34.78	36.96
100.00	NA	NA	94.44	95.24	93.33	100.00	NA	100.00	100.00	100.00
14.29	NA	NA	17.14	18.75	15.79	17.50	NA	19.44	18.92	19.44
20.75	NA	NA	43.40	49.06	37.74	37.74	NA	44.23	43.40	45.28
Confusion Matrix										
4 42	NA	NA	17 29	20 26	14 32	13 33	NA	16 29	16 30	17 29
0 7	NA	NA	1 6	1 6	1 6	0 7	NA	0 7	0 7	0 7

Table D.258: Momentaneous_Past_Standard_kFold_PCA_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.78	0.80	0.84	0.81	0.90	0.82	0.80	0.77	0.80	0.80	0.81
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
79.17	**75.00**	**83.33**	**75.00**	**95.83**	**83.33**	**75.00**	**70.83**	**75.00**	**79.17**	**84.00**
88.89	**92.06**	**93.65**	**95.24**	**95.24**	**88.89**	**92.06**	**92.06**	**92.06**	**90.48**	**88.89**
91.80	**90.63**	**93.65**	**90.91**	**98.36**	**93.33**	**90.63**	**89.23**	**90.63**	**91.94**	**93.33**
73.08	**78.26**	**83.33**	**85.71**	**88.46**	**74.07**	**78.26**	**77.27**	**78.26**	**76.00**	**75.00**
86.21	**87.36**	**90.80**	**89.66**	**95.40**	**87.36**	**87.36**	**86.21**	**87.36**	**87.36**	**87.50**
Confusion Matrix										
56 7	58 5	59 4	60 3	60 3	56 7	58 5	58 5	58 5	57 6	56 7
5 19	6 18	4 20	6 18	1 23	4 20	6 18	7 17	6 18	5 19	4 21

Table D.259: Momentaneous_Past_Standard_kFold_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.85	NA	NA	0.89	0.84	0.83	0.82	NA	0.76	0.81	0.82
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
87.50	NA	NA	**91.67**	**83.33**	**79.17**	**75.00**	NA	100.00	**66.67**	**87.50**
93.65	NA	NA	**95.24**	**92.06**	**93.65**	**93.65**	NA	34.09	**92.06**	**87.30**
95.16	NA	NA	**96.77**	**93.55**	**92.19**	**90.77**	NA	100.00	**87.88**	**94.83**
84.00	NA	NA	**88.00**	**80.00**	**82.61**	**81.82**	NA	17.14	**76.19**	**72.41**
91.95	NA	NA	**94.25**	**89.66**	**89.66**	**88.51**	NA	42.00	**85.06**	**87.36**
Confusion Matrix										
59 4	NA	NA	60 3	58 5	59 4	59 4	NA	15 29	58 5	55 8
3 21	NA	NA	2 22	4 20	5 19	6 18	NA	0 6	8 16	3 21

Table D.260: Momentaneous_Past_Standard_LOO_PCA_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.51	0.54	0.54	0.50	0.51	0.51	0.51	0.51	0.53	0.56
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
29.17	29.17	33.33	29.17	29.17	33.33	29.17	29.17	29.17	33.33	37.50
74.60	73.02	74.60	77.78	69.84	68.25	73.02	73.02	73.02	73.02	74.60
73.44	73.02	74.60	74.24	72.13	72.88	73.02	73.02	73.02	74.19	75.81
30.43	29.17	33.33	33.33	26.92	28.57	29.17	29.17	29.17	32.00	36.00
62.07	60.92	63.22	64.37	58.62	58.62	60.92	60.92	60.92	62.07	64.37
Confusion Matrix										
47 16 17 7	46 17 17 7	47 16 16 8	49 14 17 7	44 19 17 7	43 20 16 8	46 17 17 7	46 17 17 7	46 17 17 7	46 17 16 8	47 16 15 9

Table D.261: Momentaneous_Past_Standard_LOO_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.50	NA	0.47	0.50	0.52	0.46	NA	0.50	0.47	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
25.00	25.00	NA	25.00	29.17	29.17	20.83	NA	25.00	25.00	41.67
69.84	74.60	NA	68.25	71.43	74.60	71.43	NA	74.60	69.84	69.84
70.97	72.31	NA	70.49	72.58	73.44	70.31	NA	72.31	70.97	75.86
24.00	27.27	NA	23.08	28.00	30.43	21.74	NA	27.27	24.00	34.48
57.47	60.92	NA	56.32	59.77	62.07	57.47	NA	60.92	57.47	62.07
Confusion Matrix										
44 19	47 16	NA	43 20	45 18	47 16	45 18	NA	47 16	44 19	44 19
18 6	18 6	NA	18 6	17 7	17 7	19 5	NA	18 6	18 6	14 10

For label *first2EDSS* > 3 (0/1 - (< 3)/(≥ 3)):

Final features: EDSS Medium Value/Year, EDSS 1st year.

Table D.262: Momentaneous_Past_Standard_Traditional_PCA_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.75	0.80	0.73	0.78	0.68	0.69	0.64	0.71	0.80	0.78	0.80
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	85.71	71.43	85.71	85.71	85.71	85.71	100.00	85.71	85.71	85.71
64.00	72.00	72.00	66.00	50.00	50.00	38.00	44.00	72.00	72.00	70.59
96.97	97.30	94.74	97.06	96.15	96.15	95.00	100.00	97.30	97.30	97.30
25.00	30.00	26.32	26.09	19.35	19.35	16.22	20.00	30.00	30.00	28.57
66.67	73.68	71.93	68.42	54.39	54.39	43.86	50.88	73.68	73.68	72.41
Confusion Matrix										
32 18 1 6	36 14 1 6	36 14 2 5	33 17 1 6	25 25 1 6	25 25 1 6	19 31 1 6	22 28 0 7	36 14 1 6	36 14 1 6	36 15 1 6

Table D.263: Momentaneous_Past_Standard_Traditional_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
2.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
100.00	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN
12.50	12.28	12.28	12.28	12.28	12.28	12.28	12.28	12.28	12.28	12.28
14.04	12.28	12.28	12.28	12.28	12.28	12.28	12.28	12.28	12.28	12.28
Confusion Matrix										
1 49 0 7	0 50 0 7	0 50 0 7	0 50 0 7	0 50 0 7	0 50 0 7	0 50 0 7	0 50 0 7	0 50 0 7	0 50 0 7	0 50 0 7

Table D.264: Momentaneous_Past_Standard_kFold_PCA_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.74	0.73	0.72	0.74	0.72	0.76	0.75	0.69	0.73	0.78	0.78
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
72.73	**68.18**	**68.18**	**63.64**	**68.18**	**72.73**	**68.18**	**59.09**	**68.18**	**72.73**	**86.36**
86.15	**89.23**	**90.77**	**98.46**	**90.77**	**93.85**	**95.38**	**93.85**	**90.77**	**92.31**	**84.62**
90.32	**89.23**	**89.39**	**88.89**	**89.39**	**91.04**	**89.86**	**87.14**	**89.39**	**90.91**	**94.83**
64.00	**68.18**	**71.43**	**93.33**	**71.43**	**80.00**	**83.33**	**76.47**	**71.43**	**76.19**	**65.52**
82.76	**83.91**	**85.06**	**89.66**	**85.06**	**88.51**	**88.51**	**85.06**	**85.06**	**87.36**	**85.06**
Confusion Matrix										
56 9 6 16	58 7 7 15	59 6 7 15	64 1 8 14	59 6 7 15	61 4 6 16	62 3 7 15	61 4 9 13	59 6 7 15	60 5 6 16	55 10 3 19

Table D.265: Momentaneous_Past_Standard_kFold_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.91	0.88	0.91	0.91	0.93	0.93	0.92	0.88	NA	0.87	0.87
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
90.91	**86.36**	**90.91**	**90.91**	**100.00**	**100.00**	**95.45**	**95.45**	NA	**95.45**	**95.45**
100.00	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**93.85**	NA	**95.38**	**93.85**
97.01	**95.59**	**97.01**	**97.01**	**100.00**	**100.00**	**98.48**	**98.39**	NA	**98.41**	**98.39**
100.00	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**84.00**	NA	**87.50**	**84.00**
97.70	**96.55**	**97.70**	**97.70**	**100.00**	**100.00**	**98.85**	**94.25**	NA	**95.40**	**94.25**
Confusion Matrix										
65 0	65 0	65 0	65 0	65 0	65 0	65 0	61 4	NA	62 3	61 4
2 20	3 19	2 20	2 20	0 22	0 22	1 21	1 21	NA	1 21	1 21

Table D.266: Momentaneous_Past_Standard_LOO_PCA_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.48	0.49	0.54	0.52	0.53	0.54	0.53	0.48	0.47	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
31.82	22.73	22.73	22.73	27.27	27.27	27.27	22.73	22.73	18.18	27.27
69.23	73.85	75.38	83.08	76.92	78.46	80.00	81.54	73.85	75.38	66.15
75.00	73.85	74.24	76.06	75.76	76.12	76.47	75.71	73.85	73.13	72.88
25.93	22.73	23.81	31.25	28.57	30.00	31.58	29.41	22.73	20.00	21.43
59.77	60.92	62.07	67.82	64.37	65.52	66.67	66.67	60.92	60.92	56.32
Confusion Matrix										
45 20 15 7	48 17 17 5	49 16 17 5	54 11 17 5	50 15 16 6	51 14 16 6	52 13 16 6	53 12 17 5	48 17 17 5	49 16 18 4	43 22 16 6

Table D.267: Momentaneous_Past_Standard_LOO_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.48	0.49	0.54	0.52	0.53	0.54	0.53	0.48	0.47	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
31.82	22.73	22.73	22.73	27.27	27.27	27.27	22.73	22.73	18.18	27.27
69.23	73.85	75.38	83.08	76.92	78.46	80.00	81.54	73.85	75.38	66.15
75.00	73.85	74.24	76.06	75.76	76.12	76.47	75.71	73.85	73.13	72.88
25.93	22.73	23.81	31.25	28.57	30.00	31.58	29.41	22.73	20.00	21.43
59.77	60.92	62.07	67.82	64.37	65.52	66.67	66.67	60.92	60.92	56.32
Confusion Matrix										
45 20 15 7	48 17 17 5	49 16 17 5	54 11 17 5	50 15 16 6	51 14 16 6	52 13 16 6	53 12 17 5	48 17 17 5	49 16 18 4	43 22 16 6

For label *first2EDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: The via pattern recognition study was not performed since the number of patients with *first2EDSS*≥ 5 was minimal.

For label *tendencyEDSS* (0/1 - (Down or Equal)/Up):

Final features: EDSS medium variation/Year, Corticosteroids Ratio, Average Treatment 2 first years, Last ambulatory.

Table D.268: Momentaneous_Past_Standard_Traditional_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.63	0.61	0.57	0.56	0.57	0.56	0.62	0.63	0.63	0.61
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
75.00	75.00	75.00	50.00	50.00	50.00	50.00	75.00	75.00	75.00	75.00
52.46	54.10	54.10	59.02	59.02	60.66	59.02	59.02	54.10	54.10	50.82
96.97	97.06	97.06	94.74	94.74	94.87	94.74	97.30	97.06	97.06	96.88
9.38	9.68	9.68	7.41	7.41	7.69	7.41	10.71	9.68	9.68	9.09
53.85	55.38	55.38	58.46	58.46	60.00	58.46	60.00	55.38	55.38	52.31
Confusion Matrix										
32 29 1 3	33 28 1 3	33 28 1 3	36 25 2 2	36 25 2 2	37 24 2 2	36 25 2 2	36 25 1 3	33 28 1 3	33 28 1 3	31 30 1 3

Table D.269: Momentaneous_Past_Standard_Traditional_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.54	NA	0.56	0.58	0.59	0.56	NA	0.54	0.51	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
25.00	25.00	NA	25.00	50.00	50.00	50.00	NA	25.00	0.00	25.00
85.25	91.80	NA	83.61	70.49	60.66	57.38	NA	91.80	98.36	90.16
94.55	94.92	NA	94.44	95.56	94.87	94.59	NA	94.92	93.75	94.83
10.00	16.67	NA	9.09	10.00	7.69	7.14	NA	16.67	0.00	14.29
81.54	87.69	NA	80.00	69.23	60.00	56.92	NA	87.69	92.31	86.15
Confusion Matrix										
52 9	56 5	NA	51 10	43 18	37 24	35 26	NA	56 5	60 1	55 6
3 1	3 1	NA	3 1	2 2	2 2	2 2	NA	3 1	4 0	3 1

Table D.270: Momentaneous_Past_Standard_kFold_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.40	0.28	0.42	0.08	0.37	0.29	0.15	0.28	0.10	0.59	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
20.00	20.00	26.67	0.00	13.33	13.33	6.67	20.00	6.67	66.67	60.00
83.33	97.22	86.11	97.22	84.72	93.06	95.83	97.22	98.61	66.67	62.50
83.33	85.37	84.93	82.35	82.43	83.75	83.13	85.37	83.53	90.57	88.24
20.00	60.00	28.57	0.00	15.38	28.57	25.00	60.00	50.00	29.41	25.00
72.41	83.91	75.86	80.46	72.41	79.31	80.46	83.91	82.76	66.67	62.07
Confusion Matrix										
60 12 12 3	70 2 12 3	62 10 11 4	70 2 15 0	61 11 13 2	67 5 13 2	69 3 14 1	70 2 12 3	71 1 14 1	48 24 5 10	45 27 6 9

Table D.271: Momentaneous_Past_Standard_kFold_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.19	0.52	0.38	0.49	0.47	0.45	0.55	0.03	0.62	0.59
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.00	6.67	40.00	26.67	33.33	33.33	33.33	46.67	0.00	73.33	60.00
91.67	93.06	90.28	97.22	84.72	93.06	93.06	83.33	98.61	66.67	69.44
88.00	82.72	87.84	86.42	85.92	87.01	87.01	88.24	82.56	92.31	89.29
50.00	16.67	46.15	66.67	31.25	50.00	50.00	36.84	0.00	31.43	29.03
82.76	78.16	81.61	85.06	75.86	82.76	82.76	77.01	81.61	67.82	67.82
Confusion Matrix										
66 6	67 5	65 7	70 2	61 11	67 5	67 5	60 12	71 1	48 24	50 22
9 6	14 1	9 6	11 4	10 5	10 5	10 5	8 7	15 0	4 11	6 9

Table D.272: Momentaneous_Past_Standard_LOO_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.44	0.41	0.45	0.41	0.44	0.41	0.41	0.41	0.41	0.45	0.48
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
6.67	0.00	6.67	0.00	6.67	0.00	0.00	0.00	0.00	26.67	33.33
80.56	93.06	84.72	98.61	83.33	90.28	95.83	93.06	97.22	56.94	58.33
80.56	81.71	81.33	82.56	81.08	81.25	82.14	81.71	82.35	78.85	80.77
6.67	0.00	8.33	0.00	7.69	0.00	0.00	0.00	0.00	11.43	14.29
67.82	77.01	71.26	81.61	70.11	74.71	79.31	77.01	80.46	51.72	54.02
Confusion Matrix										
58 14	67 5	61 11	71 1	60 12	65 7	69 3	67 5	70 2	41 31	42 30
14 1	15 0	14 1	15 0	14 1	15 0	15 0	15 0	15 0	11 4	10 5

Table D.273: Momentaneous_Past_Standard_LOO_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.61	0.41	0.53	0.72	0.62	0.69	0.57	0.49	NA	0.55	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
26.67	0.00	20.00	26.67	40.00	33.33	20.00	20.00	NA	53.33	46.67
90.28	91.67	86.11	95.83	86.11	93.06	90.28	77.78	NA	62.50	68.06
85.53	81.48	83.78	86.25	87.32	87.01	84.42	82.35	NA	86.54	85.96
36.36	0.00	23.08	57.14	37.50	50.00	30.00	15.79	NA	22.85	23.33
79.31	75.86	74.71	83.91	78.16	82.76	78.16	67.82	NA	60.92	64.37
Confusion Matrix										
65 7	66 6	62 10	69 3	62 10	67 5	65 7	56 16	NA	45 27	49 23
11 4	15 0	12 3	11 4	9 6	10 5	12 3	12 3	NA	7 8	8 7

First feature selection process for *mediumEDSS*:

Table D.274: Momentaneous_Past_Feature_Selection_Identification_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Gender	0	0	0	0	0	1	0	0	0	0	0	1
Age of Onset	0	0	0	0	0	0	1	0	0	0	0	1
Optic Pathways	0	1	1	0	0	0	0	0	1	0	1	**4**
Brainstem-Cerebellum	0	0	0	1	0	1	0	0	0	0	0	2
Spinal Cord	0	0	0	0	0	1	1	0	0	0	0	2
Progression From Onset	0	0	0	0	0	0	0	1	1	0	0	2
Age of Diagnosis	1	1	1	1	1	0	1	1	0	1	1	**9**
Years from Onset to Diagnosis	1	1	1	1	1	0	1	0	1	1	1	**9**
Evoked Potentials	0	0	0	0	0	1	0	0	0	0	0	1
CSF	0	0	0	0	0	1	1	0	0	0	0	2
Age at SP Diagnosis	0	1	1	1	1	0	1	0	1	1	1	**8**
Years from Diagnosis to SP	0	1	1	1	1	0	1	0	1	1	1	**8**
Years from Diagnosis to Onset	0	1	1	1	1	0	1	0	1	1	1	**8**
MS Course	0	1	1	1	1	1	1	0	1	1	1	**9**
Family History	0	0	0	0	0	0	1	0	0	0	0	1
Active	0	1	0	0	0	0	0	0	1	0	0	2
Age Visit	1	1	1	1	1	0	1	0	0	1	1	**8**
Years since Onset	1	1	1	1	1	0	1	1	0	1	1	**9**

Selected features: Optic Pathways, Brainstem-Cerebellum, Age of Diagnosis, Years from Onset to Diagnosis, Age at SP Diagnosis, Years from Diagnosis to SP, Years from Diagnosis to Onset, MS Course, Age Visit, Years since Onset.

Table D.275: Momentaneous_Past_Feature_Selection_Visits_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Nb of Visits 1st Year	0	0	0	0	0	0	1	0	0	0	0	1
Nb of visits first 2 years	0	0	0	1	0	0	1	0	0	0	0	2
Suspected Relapses Ratio 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Suspected Relapses Ratio first 2 years	0	0	0	1	0	0	1	0	0	0	0	2
EDSS 1st year	1	1	1	1	1	0	1	0	0	1	1	**8**
EDSS first 2 years	1	1	1	1	1	0	1	0	0	1	1	**8**
EDSS std/year	0	1	1	1	1	0	0	0	1	1	1	**7**
EDSS 1st year std	0	0	0	0	0	0	1	0	0	0	0	1
EDSS first 2 years std	0	0	0	0	0	0	1	0	0	0	0	1
EDSS medium variation/Year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS medium variation 1st year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS medium variation first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
EDSS std of variation 1st year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS std of variation first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
EDSS Increase 1st Year	0	0	0	0	0	0	1	0	0	0	0	1
EDSS Increase first 2 years	0	0	1	0	0	0	1	0	1	0	0	3
Ratio nb EDSS increase	0	1	1	1	1	0	0	0	1	1	1	**7**
Ratio nb EDSS decrease	0	0	0	0	0	0	1	0	0	0	0	1
Ratio nb EDSS decrease 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Ratio nb EDSS decrease first 2 years	0	1	0	0	0	0	1	0	0	1	1	**4**
Routine Visits Ratio	0	0	0	0	0	0	0	1	0	0	0	1
Routine Visits Ratio 1st Year	0	0	0	0	0	1	1	0	0	0	0	2
Routine Visits first 2 years	0	1	0	0	0	1	1	0	1	1	1	**6**
No Years	0	0	1	0	0	0	0	0	0	0	0	1
Last Routine	0	0	0	0	0	1	0	0	0	0	0	1
Last EDSS	1	1	1	1	1	0	1	1	0	1	1	**9**
Last Weakness	0	1	0	0	0	0	1	0	1	0	1	**4**
Last Sympton	0	0	0	0	0	0	0	0	1	0	0	1

Selected features: Last EDSS.

Table D.276: Momentaneous_Past_Feature_Selection_Relapses_mediumEDSS

Feature Name	Test A	Test B	Test C	Test D	Test E	Test F	Test G	Test H	Test I	Test J	Test L	Overall Performance
Relapses Per Year	0	1	1	1	0	0	1	0	1	1	1	**7**
Relapses 1st Year	0	0	0	0	0	0	1	0	0	0	0	1
Relapses first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Pyramidal ratio	1	1	1	1	1	0	1	0	0	1	1	**8**
Pyramidal 1st year	0	1	1	1	1	1	1	0	1	1	1	**9**
Pyramidal first 2 years	0	1	1	1	1	0	1	1	1	1	1	**9**
Brain Stem ratio	0	1	1	1	0	0	1	0	0	1	1	**6**
BrainStem 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Brain Stem first 2 years	0	1	0	0	0	0	1	1	0	0	1	**4**
Bowel ratio	0	1	0	0	0	0	0	0	1	0	1	**3**
Bowel 1st year	0	1	0	0	0	0	0	0	1	0	1	**3**
Bowel first 2 years	0	1	0	0	0	0	0	0	1	0	1	**3**
Neuropsycho ratio	0	0	0	0	0	0	1	0	0	0	0	1
Neuropsycho 1st year	0	0	0	0	0	0	0	0	1	0	0	1
Neuropsycho first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Cerebellum ratio	0	0	0	0	0	0	1	0	0	0	0	1
Cerebellum 1st year	0	0	0	0	0	0	1	0	0	0	0	1
Cerebellum first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Visual ratio	0	1	0	0	0	0	1	1	0	0	1	**4**
Visual 1st year	0	1	1	1	0	0	0	0	1	0	1	**5**
Visual first 2 years	0	1	1	1	0	0	1	0	0	0	1	**5**
Sensory ratio	0	1	1	1	0	0	1	1	1	1	1	**8**
Sensory 1st year	0	0	0	0	0	1	1	0	0	0	0	2
Sensory first 2 years	0	0	0	0	0	0	1	0	1	0	0	2
Corticosteroids Ratio	0	1	1	1	0	0	0	0	0	1	1	**5**
Corticosteroids/year	1	1	1	1	0	0	0	1	0	1	1	**7**
Corticosteroids 1st year	0	1	1	1	0	1	0	0	1	1	1	**7**
Corticosteroids first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Average Treatment Intensity	1	1	1	1	0	0	0	0	0	0	1	**5**
Average Treatment 1st year	0	1	1	1	0	0	0	0	1	0	1	**5**
Average Treatment 2 first years	0	1	0	1	0	0	1	0	0	0	1	**4**
Average Duration	1	1	0	0	0	0	1	1	0	0	1	**5**
Average Duration 1st year	0	1	0	1	0	0	0	0	0	1	1	**4**
Average Duration first 2 years	0	0	0	0	0	0	1	0	0	0	0	1
Last Pyramidal	0	1	1	1	0	1	0	0	1	0	1	**6**
Last BrainStem	0	1	0	1	0	0	1	0	1	0	1	**5**
Last Bowel	0	0	0	0	0	0	0	0	1	0	0	1
Last Neuropsycho	0	0	0	0	0	0	1	0	0	0	0	1
Last Sensory	0	1	0	1	0	1	0	0	1	1	1	**6**
Last Hospital	0	0	0	0	0	1	0	0	0	0	0	1
Last ambulatory	0	0	0	0	0	1	0	0	0	0	0	1
Last Corticosteroid	0	0	0	0	0	1	0	0	0	0	0	1
Last Treatment	0	0	0	0	0	0	0	0	1	0	0	1
Last Duration	0	0	0	0	0	0	0	0	1	0	0	1

Selected Features: Last Pyramidal, Last BrainStem, Last Sensory.

For label *mediumEDSS* (0/1 - (< 3)/(≥ 3)):

Final features: Ratio nb EDSS increase, Last EDSS.

Table D.277: Momentaneous_Standard_Traditional_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.74	0.81	0.81	0.78	0.75	0.76	0.76	0.80	0.81	0.81	0.81
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
77.78	**88.89**	**88.89**	88.89	88.89	88.89	88.89	**77.78**	**88.89**	**77.78**	**88.89**
67.65	**79.41**	**76.47**	67.65	64.71	64.71	64.71	**82.35**	**79.41**	**79.41**	**79.41**
92.00	**96.43**	**96.30**	95.83	95.65	95.65	95.65	**93.33**	**96.43**	**93.10**	**96.43**
38.89	**53.33**	**50.00**	42.11	40.00	40.00	40.00	**53.85**	**53.33**	**50.00**	**53.33**
69.77	**81.40**	**79.07**	72.09	69.77	69.77	69.77	**81.40**	**81.40**	**79.07**	**81.40**
Confusion Matrix										
23 11 2 7	27 7 1 8	26 8 1 8	23 11 1 8	22 12 1 8	22 12 1 8	22 12 1 8	28 6 2 7	27 7 1 8	27 7 2 7	27 7 1 8

Table D.278: Momentaneous_Standard_Traditional_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	NA	NA	0.74	0.66	0.66	0.74	NA	NA	0.56	0.60
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	NA	NA	100.00	88.89	88.89	88.89	NA	NA	100.00	77.78
0.00	NA	NA	52.94	44.12	47.06	64.71	NA	NA	11.76	41.18
NaN	NA	NA	100.00	93.75	94.12	95.65	NA	NA	100.00	87.50
20.93	NA	NA	36.00	29.63	30.77	40.00	NA	NA	23.08	25.93
20.93	NA	NA	62.79	53.49	55.81	69.77	NA	NA	30.23	48.84
Confusion Matrix										
0 34 0 9	NA NA	NA NA	18 16 0 9	15 19 1 8	16 18 1 8	22 12 1 8	NA NA	NA NA	4 30 0 9	14 20 2 7

Table D.279: Momentaneous_Standard_kFold_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.75	0.78	0.79	0.72	0.80	0.80	0.76	0.79	0.78	0.79	0.79
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
67.74	**64.52**	**67.74**	**51.61**	**74.19**	**64.52**	**64.52**	**67.74**	**64.52**	**70.97**	**70.97**
85.71	**89.47**	**89.29**	**92.86**	**87.50**	**92.86**	**87.50**	**89.29**	**91.07**	**87.50**	**87.50**
82.76	**82.26**	**83.33**	**77.61**	**85.96**	**82.54**	**81.67**	**83.33**	**82.26**	**84.48**	**84.48**
72.41	**76.92**	**77.78**	**80.00**	**76.67**	**83.33**	**74.07**	**77.78**	**80.00**	**75.86**	**75.86**
79.31	**80.68**	**81.61**	**78.16**	**82.76**	**82.76**	**79.31**	**81.61**	**81.61**	**81.61**	**81.61**
Confusion Matrix										
48 8 10 21	51 6 11 20	50 6 10 21	52 4 15 16	49 7 8 23	52 4 11 20	49 7 11 20	50 6 10 21	51 5 11 20	49 7 9 22	49 7 9 22

Table D.280: Momentaneous_Standard_kFold_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.87	0.89	NA	0.87	0.84	0.82	0.78	NA	NA	0.78	0.87
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
83.87	**83.87**	NA	**77.42**	**77.42**	**67.74**	**61.29**	NA	NA	**70.97**	**83.87**
92.86	**94.64**	NA	**98.21**	**92.86**	**94.64**	**94.64**	NA	NA	**85.71**	**91.07**
91.23	**91.38**	NA	**88.71**	**88.14**	**84.13**	**81.54**	NA	NA	**84.21**	**91.07**
86.67	**89.66**	NA	**96.00**	**85.71**	**87.50**	**86.36**	NA	NA	**73.33**	**83.87**
89.66	**90.80**	NA	**90.80**	**87.36**	**85.06**	**82.76**	NA	NA	**80.46**	**88.51**
Confusion Matrix										
52 4	53 3	NA	55 1	52 4	53 3	53 3	NA	NA	48 8	51 5
5 26	5 26	NA	7 24	7 24	10 21	12 19	NA	NA	9 22	5 26

Table D.281: Momentaneous_Standard_LOO_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.45	0.49	0.52	0.47	0.45	0.49	0.48	0.52	0.50	0.52	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
22.58	29.03	35.48	19.35	29.03	25.81	29.03	35.48	29.03	35.48	35.48
67.86	69.64	67.86	76.79	60.71	73.21	67.86	67.86	71.43	67.86	67.86
61.29	63.93	65.52	63.24	60.71	64.06	63.33	65.52	64.52	65.52	65.52
28.00	34.62	37.93	31.58	29.03	34.78	33.33	37.93	36.00	37.93	37.93
51.72	55.17	56.32	56.32	49.43	56.32	54.02	56.32	56.32	56.32	56.32
Confusion Matrix										
38 18	39 17	38 18	43 13	34 22	41 15	38 18	38 18	40 16	38 18	38 18
24 7	22 9	20 11	25 6	22 9	23 8	22 9	20 11	22 9	20 11	20 11

Table D.282: Momentaneous_Standard_LOO_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.49	0.49	0.47	0.52	0.46	0.48	0.49	0.50	0.49	0.49
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
29.03	29.03	32.26	19.35	38.71	22.58	29.03	32.26	29.03	32.26	32.26
71.43	69.64	66.07	76.79	66.07	71.43	67.86	66.07	71.43	66.07	66.07
64.52	63.93	63.79	63.24	66.07	62.50	63.33	63.79	64.52	63.79	63.79
36.00	34.62	34.48	31.58	38.71	30.43	33.33	34.48	36.00	34.48	34.48
56.32	55.17	54.02	56.32	56.32	54.02	54.02	54.02	56.32	54.02	54.02
Confusion Matrix										
40 16	39 17	37 19	43 13	37 19	40 16	38 18	37 19	40 16	37 19	37 19
22 9	22 9	21 10	25 6	19 12	24 7	22 9	21 10	22 9	21 10	21 10

For label *nextEDSS* (0/1 - $(< 3)/(\geq 3)$):

The via pattern recognition study was not performed since the number of patients with *currentEDSS*≥ 5 was minimal.

D.1.4.2 Investigation procedure

For label *msCourse* (0/1 - RR/SP):

Features before selection: Optic Pathways, Brainstem-Cerebellum, Spinal Cord, Evoked Potentials, Age Visit, Years since Onset, Pyramidal 1 ratio, Pyramidal 1st year, Pyramidal first 2 years, Brain Stem 1 ratio, BrainStem 1st year, Brain Stem first 2 years, Visual 1 ratio, Visual first 2 years, Last Pyramidal, Last BrainStem.

Excluded features: EDSS Medium Value/year, EDSS 1st year, EDSS first 2 years, EDSS std/year, EDSS std of variation first 2 years, Last EDSS.

Final features: Spinal Cord, Age Visit, Years since Onset, Pyramidal 1 ratio, Visual 1 ratio.

Table D.283: Momentaneous_Past_Investigation_Traditional_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.71	0.77	0.74	0.70	0.69	0.66	0.65	0.65	0.77	0.75	0.76
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	85.71	71.43	71.43	85.71	85.71	85.71	100.00	85.71	85.71	85.71
52.27	63.64	75.00	70.45	50.00	43.18	38.64	31.82	63.64	68.18	65.91
95.83	96.55	94.29	93.94	95.65	95.00	94.44	100.00	96.55	96.77	96.67
22.22	27.27	31.25	27.78	21.43	19.35	18.18	18.92	27.27	30.00	28.57
56.86	66.67	74.51	70.59	54.90	49.02	45.10	41.18	66.67	70.59	68.63
Confusion Matrix										
23 21 1 6	28 16 1 6	33 11 2 5	31 13 2 5	22 22 1 6	19 25 1 6	17 27 1 6	14 30 0 7	28 16 1 6	30 14 1 6	29 15 1 6

Table D.284: Momentaneous_Past_Investigation_Traditional_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.56	0.52	NA	0.57	0.58	0.56	0.57	NA	0.52	0.50	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	NA	100.00	100.00	100.00	85.71	NA	100.00	100.00	100.00
15.91	4.55	NA	13.64	18.18	15.91	22.73	NA	4.55	0.00	4.55
100.00	100.00	NA	100.00	100.00	100.00	90.91	NA	100.00	NaN	100.00
15.91	14.29	NA	15.56	16.28	15.91	15.00	NA	14.29	13.73	14.29
27.45	17.65	NA	25.49	29.41	27.45	31.37	NA	17.65	13.73	17.65
Confusion Matrix										
7 37 0 7	2 42 0 7	NA NA	6 38 0 7	8 36 0 7	7 37 0 7	10 34 1 6	NA NA	2 42 0 7	0 44 0 7	2 42 0 7

Table D.285: Momentaneous_Past_Investigation_kFold_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.62	0.67	0.74	0.55	0.67	0.69	0.69	0.69	0.67	0.67	0.73
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
48.00	**52.00**	**80.00**	36.00	**56.00**	**60.00**	**60.00**	**72.00**	**52.00**	**60.00**	**84.00**
80.65	**88.71**	**79.03**	91.94	**83.87**	**85.48**	**80.65**	**74.19**	**90.32**	**80.65**	**69.35**
79.37	**82.09**	**90.74**	78.08	**82.54**	**84.13**	**83.33**	**86.79**	**82.35**	**83.33**	**91.49**
50.00	**65.00**	**60.61**	64.29	**58.33**	**62.50**	**55.56**	**52.94**	**68.42**	**55.56**	**52.50**
71.26	**78.16**	**79.31**	75.86	**75.86**	**78.16**	**74.71**	**73.56**	**79.31**	**74.71**	**73.56**
Confusion Matrix										
50 12 13 12	55 7 12 13	49 13 5 20	57 5 16 9	52 10 11 14	53 9 10 15	50 12 10 15	46 16 7 18	56 6 12 13	50 12 10 15	43 19 4 21

Table D.286: Momentaneous_Past_Investigation_kFold_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.72	0.76	NA	0.71	0.75	0.69	0.66	NA	0.76	0.69	0.76
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
60.00	**64.00**	NA	**52.00**	**68.00**	**56.00**	48.00	NA	**60.00**	**68.00**	**76.00**
90.32	**96.77**	NA	**98.39**	**88.71**	**88.71**	91.94	NA	**96.77**	**77.42**	**85.48**
84.85	**86.96**	NA	**83.56**	**87.30**	**83.33**	81.43	NA	**85.71**	**85.71**	**89.83**
71.43	**88.89**	NA	**92.86**	**70.83**	**66.67**	70.59	NA	**88.24**	**54.84**	**67.86**
81.61	**87.36**	NA	**85.06**	**82.76**	**79.31**	79.31	NA	**86.21**	**74.71**	**82.76**
Confusion Matrix										
56 6	60 2	NA	61 1	55 7	55 7	57 5	NA	60 2	48 14	53 9
10 15	9 16	NA	12 13	8 17	11 14	13 12	NA	10 15	8 17	6 19

Table D.287: Momentaneous_Past_Investigation_LOO_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.53	0.59	0.53	0.54	0.48	0.47	0.52	0.48	0.46	0.48
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
24.00	28.00	52.00	20.00	32.00	24.00	28.00	44.00	20.00	24.00	44.00
74.19	77.42	67.74	83.87	75.81	72.58	66.13	61.29	77.42	67.74	51.61
70.77	72.73	77.78	72.22	73.44	70.31	69.49	73.08	70.59	68.85	69.57
27.27	33.33	39.39	33.33	34.78	26.09	25.00	31.43	26.32	23.08	26.83
59.77	63.22	63.22	65.52	63.22	58.62	55.17	56.32	60.92	55.17	49.43
Confusion Matrix										
46 16 19 6	48 14 18 7	42 20 12 13	52 10 20 5	47 15 17 8	45 17 19 6	41 21 18 7	38 24 14 11	48 14 20 5	42 20 19 6	32 30 14 11

Table D.288: Momentaneous_Past_Investigation_LOO_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.50	0.54	0.49	0.47	0.52	0.54	0.53	0.50	0.47	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
24.00	20.00	36.00	16.00	24.00	28.00	24.00	36.00	20.00	32.00	32.00
72.58	80.65	72.58	82.26	70.97	75.81	82.26	69.35	80.65	61.29	67.74
70.31	71.43	73.77	70.83	69.84	72.31	72.86	72.88	71.43	69.09	71.19
26.09	29.41	34.62	26.67	25.00	31.82	35.29	32.14	29.41	25.00	28.57
58.62	63.22	62.07	63.22	57.47	62.07	65.52	59.77	63.22	52.87	57.47
Confusion Matrix										
45 17 19 6	50 12 20 5	45 17 16 9	51 11 21 4	44 18 19 6	47 15 18 7	51 11 19 6	43 19 16 9	50 12 20 5	38 24 17 8	42 20 17 8

For label *currentEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Features before selection: Optic Pathways, Spinal Cord, Age at SP Diagnosis, Age Visit, Years since Onset, Number of years Years, Relapses Per Year, Pyramidal 1 ratio, Pyramidal 1st year, Pyramidal first 2 years, Brain Stem first 2 years, Visual 1 ratio, Visual 1st year, Visual first 2 years, Sensory 1 ratio, Corticosteroids 1st year, Last Pyramidal, Last Sensory.

Excluded features: EDSS Medium Value/year, EDSS 1st year, EDSS first 2 years, EDSS std/year, EDSS Increase first 2 years, Ratio nb EDSS increase.

Final features: Age at SP Diagnnosis, Number of years, Pyramidal ratio, Pyramidal first 2 years ratio.

Table D.289: Momentaneous_Past_Investigation_Tradition_PCA_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.70	0.81	0.76	0.80	0.68	0.72	0.73	0.78	0.81	0.80	0.81
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
90.00	**80.00**	**90.00**	**80.00**	70.00	70.00	**72.73**	**80.00**	**80.00**	**80.00**	**80.00**
48.15	**85.19**	**66.67**	**77.78**	70.37	74.07	**70.37**	**77.78**	**85.19**	**85.19**	**85.19**
92.86	**92.00**	**94.74**	**91.30**	86.36	86.96	**86.36**	**91.30**	**92.00**	**92.00**	**92.00**
39.13	**66.67**	**50.00**	**57.14**	46.67	50.00	**50.00**	**57.14**	**66.67**	**66.67**	**66.67**
59.46	**83.78**	**72.97**	**78.38**	70.27	72.97	**71.05**	**78.38**	**83.78**	**83.78**	**83.78**
Confusion Matrix										
13 14 1 9	23 4 2 8	18 9 1 9	21 6 2 8	19 8 3 7	20 7 3 7	19 8 3 8	21 6 2 8	23 4 2 8	23 4 2 8	23 4 2 8

Table D.290: Momentaneous_Past_Investigation_Tradition_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.52	NA	0.58	0.60	0.68	0.73	NA	0.52	0.50	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	NA	100.00	100.00	90.00	90.00	NA	100.00	100.00	100.00
7.41	7.41	NA	18.52	25.93	44.44	59.26	NA	7.41	0.00	3.70
100.00	100.00	NA	100.00	100.00	92.31	94.12	NA	100.00	NaN	100.00
28.57	28.57	NA	31.25	33.33	37.50	45.00	NA	28.57	27.03	27.78
32.43	32.43	NA	40.54	45.95	56.76	67.57	NA	32.43	27.03	29.73
Confusion Matrix										
2 25 0 10	2 25 0 10	NA	5 22 0 10	7 20 0 10	12 15 1 9	16 11 1 9	NA	2 25 0 10	0 27 0 10	1 26 0 10

Table D.291: Momentaneous_Past_Investigation_kFold_PCA_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.75	0.80	0.75	0.77	0.81	0.80	0.81	0.75	0.80	0.78	0.80
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
65.71	**65.71**	**71.43**	**65.71**	**71.43**	**65.71**	**68.57**	**60.00**	**65.71**	**65.71**	**71.43**
82.69	**92.31**	**78.85**	**88.46**	**88.46**	**90.38**	**90.38**	**90.38**	**92.31**	**90.38**	**88.46**
78.18	**80.00**	**80.39**	**79.31**	**82.14**	**79.66**	**81.03**	**77.05**	**80.00**	**79.66**	**82.14**
71.88	**85.19**	**69.44**	**79.31**	**80.65**	**82.14**	**82.76**	**80.77**	**85.19**	**82.14**	**80.65**
75.86	**81.61**	**75.86**	**79.31**	**81.61**	**80.46**	**81.61**	**78.16**	**81.61**	**80.46**	**81.61**
Confusion Matrix										
43 9 12 23	48 4 12 23	41 11 10 25	46 6 12 23	46 6 10 25	47 5 12 23	47 5 11 24	47 5 14 21	48 4 12 23	47 5 12 23	46 6 10 25

Table D.292: Momentaneous_Past_Investigation_kFold_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.81	0.77	NA	0.84	0.73	0.79	0.79	NA	NA	0.80	0.80
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
74.29	**57.14**	NA	**77.14**	**74.29**	**68.57**	**65.71**	NA	NA	**71.43**	**68.57**
88.46	**94.23**	NA	**90.38**	**71.15**	**86.54**	**88.46**	NA	NA	**90.38**	**92.31**
83.64	**76.56**	NA	**85.45**	**80.43**	**80.36**	**79.31**	NA	NA	**82.46**	**81.36**
81.25	**86.96**	NA	**84.38**	**63.41**	**77.42**	**79.31**	NA	NA	**83.33**	**85.71**
82.76	**79.31**	NA	**85.06**	**72.41**	**79.31**	**79.31**	NA	NA	**82.76**	**82.76**
Confusion Matrix										
46 6 9 26	49 3 15 20	NA	47 5 8 27	37 15 9 26	45 7 11 24	46 6 12 23	NA	NA	47 5 10 25	48 4 11 24

Table D.293: Momentaneous_Past_Investigation_LOO_PCA_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.56	0.53	0.51	0.46	0.47	0.52	0.51	0.57	0.53	0.43	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.00	34.29	42.86	31.43	31.43	34.29	34.29	37.14	34.29	22.86	34.29
71.15	71.15	59.62	61.54	63.46	69.23	67.31	75.00	71.15	65.38	65.38
63.79	61.67	60.78	57.14	57.89	61.02	60.34	63.93	61.67	55.74	59.65
48.28	44.44	41.67	35.48	36.67	42.86	41.38	50.00	44.44	30.77	40.00
58.62	56.32	52.87	49.43	50.57	55.17	54.02	59.77	56.32	48.28	52.87
Confusion Matrix										
37 15	37 15	31 21	32 20	33 19	36 16	35 17	39 13	37 15	34 18	34 18
21 14	23 12	20 15	24 11	24 11	23 12	23 12	22 13	23 12	27 8	23 12

Table D.294: Momentaneous_Past_Investigation_LOO_currentEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.50	0.48	0.45	0.49	0.47	0.47	0.50	0.50	0.55	0.57
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
28.57	25.71	37.14	31.43	48.57	31.43	31.43	37.14	25.71	40.00	40.00
63.46	75.00	59.62	59.62	50.00	63.46	63.46	63.46	75.00	69.23	73.08
56.90	60.00	58.49	56.36	59.09	57.89	57.89	60.00	60.00	63.16	64.41
34.48	40.91	38.24	34.38	39.53	36.67	36.67	40.63	40.91	46.67	50.00
49.43	55.17	50.57	48.28	49.43	50.57	50.57	52.87	55.17	57.47	59.77
Confusion Matrix										
33 19	39 13	31 21	31 21	26 26	33 19	33 19	33 19	39 13	36 16	38 14
25 10	26 9	22 13	24 11	18 17	24 11	24 11	22 13	26 9	21 14	21 14

For label *currentEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Features before selection: Optic Pathways, Spinal Cord, Age at SP Diagnosis, Age Visit, Years since Onset, Number of years Years, Relapses Per Year, Pyramidal 1 ratio, Pyramidal 1st year, Pyramidal first 2 years, Brain Stem first 2 years, Visual 1 ratio, Visual 1st year, Visual first 2 years, Sensory 1 ratio, Corticosteroids 1st year, Last Pyramidal, Last Sensory.

Excluded features: EDSS Medium Value/year, EDSS 1st year, EDSS first 2 years, EDSS std/year, EDSS Increase first 2 years, Ratio nb EDSS increase.

Final features: Age at SP Diagnnosis, Number of years, Relapses per Year, Pyramidal ratio.

Table D.295: Momentaneous_Past_Investigation_Traditional_PCA_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.62	0.75	0.60	0.68	0.63	0.61	0.63	0.70	0.75	0.73	0.76
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	80.00	40.00	80.00	60.00	80.00	80.00	80.00	80.00	80.00	80.00
45.00	68.33	81.67	63.33	56.67	48.33	50.00	60.00	68.33	68.33	68.33
96.43	97.62	94.23	97.44	94.44	96.67	96.77	97.30	97.62	97.62	97.62
10.81	17.39	15.38	15.38	10.34	11.43	11.76	14.29	17.39	17.39	17.39
47.69	69.23	78.46	64.62	56.92	50.77	52.31	61.54	69.23	69.23	69.23
Confusion Matrix										
27 33 1 4	41 19 1 4	49 11 3 2	38 22 1 4	34 26 2 3	29 31 1 4	30 30 1 4	36 24 1 4	41 19 1 4	41 19 1 4	41 19 1 4

Table D.296: Momentaneous_Past_Investigation_Traditional_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.50	NA	0.57	0.61	0.64	0.68	NA	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	NA	100.00	60.00	80.00	80.00	NA	100.00	100.00	100.00
11.67	0.00	NA	18.33	58.33	50.00	55.00	NA	0.00	0.00	0.00
100.00	NaN	NA	100.00	94.59	96.77	97.06	NA	NaN	NaN	NaN
8.62	7.69	NA	9.26	10.71	11.76	12.90	NA	7.69	7.69	7.69
18.46	7.69	NA	24.62	58.46	52.31	56.92	NA	7.69	7.69	7.69
Confusion Matrix										
7 53 0 5	0 60 0 5	NA NA	11 49 0 5	35 25 2 3	30 30 1 4	33 27 1 4	NA NA	0 60 0 5	0 60 0 5	0 60 0 5

Table D.297: Momentaneous_Past_Investigation_kFold_PCA_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.45	0.55	0.30	0.65	0.42	0.41	0.51	0.34	0.63	0.68
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
31.25	31.25	43.75	18.75	**56.25**	25.00	25.00	37.50	18.75	68.75	81.25
87.32	88.73	80.28	95.77	**92.96**	87.32	91.55	91.55	91.55	83.10	77.46
84.93	85.14	86.36	83.95	**90.41**	83.78	84.42	86.67	83.33	92.19	94.83
35.71	38.46	33.33	50.00	**64.29**	30.77	40.00	50.00	33.33	47.83	44.83
77.01	78.16	73.56	81.61	**86.21**	75.86	79.31	81.61	78.16	80.46	78.16
Confusion Matrix										
62 9 11 5	63 8 11 5	57 14 9 7	68 3 13 3	66 5 7 9	62 9 12 4	65 6 12 4	65 6 10 6	65 6 13 3	59 12 5 11	55 16 3 13

Table D.298: Momentaneous_Past_Investigation_kFold_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.67	0.63	0.60	0.47	0.64	0.41	0.32	0.67	0.63	0.63	0.72
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
68.75	**56.25**	**56.25**	31.25	**56.25**	25.00	12.50	**62.50**	**56.25**	**68.75**	**81.25**
90.14	**91.55**	**88.73**	95.77	**91.55**	95.77	92.96	**87.50**	**91.55**	**80.28**	**85.92**
92.75	**90.28**	**90.00**	86.08	**90.28**	85.00	82.50	**91.30**	**90.28**	**91.94**	**95.31**
61.11	**60.00**	**52.94**	62.50	**60.00**	57.14	28.57	**52.63**	**60.00**	**44.00**	**56.52**
86.21	**85.06**	**82.76**	83.91	**85.06**	82.76	78.16	**82.95**	**85.06**	**78.16**	**85.06**
Confusion Matrix										
64 7 5 11	65 6 7 9	63 8 7 9	68 3 11 5	65 6 7 9	68 3 12 4	66 5 14 2	63 9 6 10	65 6 7 9	57 14 5 11	61 10 3 13

Table D.299: Momentaneous_Past_Investigation_LOO_PCA_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.44	0.44	0.61	0.52	0.48	0.51	0.53	0.46	0.47	0.46
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
18.75	6.25	12.50	12.50	18.75	12.50	12.50	18.75	6.25	18.75	25.00
83.10	84.51	73.24	95.77	84.51	83.10	88.73	85.92	88.73	73.24	63.38
81.94	80.00	78.79	82.93	82.19	80.82	81.82	82.43	80.77	80.00	78.95
20.00	8.33	9.52	40.00	21.43	14.29	20.00	23.08	11.11	13.64	13.33
71.26	70.11	62.07	80.46	72.41	70.11	74.71	73.56	73.56	63.22	56.32
Confusion Matrix										
59 12 13 3	60 11 15 1	52 19 14 2	68 3 14 2	60 11 13 3	59 12 14 2	63 8 14 2	61 10 13 3	63 8 15 1	52 19 13 3	45 26 12 4

Table D.300: Momentaneous_Past_Investigation_LOO_currentEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.47	0.50	0.47	0.50	0.58	0.54	0.48	0.47	0.46	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
18.75	12.50	18.75	6.25	18.75	12.50	12.50	18.75	12.50	18.75	31.25
80.28	81.69	81.69	90.14	81.69	94.37	91.55	77.46	81.69	69.01	73.24
81.43	80.56	81.69	81.01	81.69	82.72	82.28	80.88	80.56	79.03	82.54
17.65	13.33	18.75	12.50	18.75	33.33	25.00	15.79	13.33	12.00	20.83
68.97	68.97	70.11	74.71	70.11	79.31	77.01	66.67	68.97	59.77	65.52
Confusion Matrix										
57 14	58 13	58 13	64 7	58 13	67 4	65 6	55 16	58 13	49 22	52 19
13 3	14 2	13 3	15 1	13 3	14 2	14 2	13 3	14 2	13 3	11 5

For label *nextEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Features before selection: Optic Pathways, Spinal Cord, MS Course, Family History, Years since Onset, Number of Years, Relapses Per Year, Pyramidal 1 ratio, Pyramidal 1st year, Pyramidal first 2 years, Brain Stem first 2 years, Visual 1 ratio,

Visual 1st year, Visual first 2 years, Sensory 1 ratio, Corticosteroids/year, Corticosteroids 1st year, Average Treatment Intensity, Average Treatment 2 first years, Average Duration, Average Duration first 2 years, Last Pyramidal, Last Sensory.

Final features: MS Course, Number of Years, Pyramidal first 2 years, Visual 1 ratio, Average Duration.

Table D.301: Momentaneous_Past_Investigation_Traditional_PCA_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.76	0.87	0.84	0.85	0.74	0.74	0.75	0.84	0.87	0.87	0.87
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
90.00	**90.00**	**90.00**	**90.00**	80.00	80.00	80.00	**80.00**	**90.00**	**80.00**	**90.00**
65.52	**86.21**	**75.86**	**79.31**	68.97	68.97	68.97	**82.76**	**86.21**	**89.66**	**86.21**
95.00	**96.15**	**95.65**	**95.83**	90.91	90.91	90.91	**92.31**	**96.15**	**92.86**	**96.15**
47.37	**69.23**	**56.25**	**60.00**	47.06	47.06	47.06	**61.54**	**69.23**	**72.73**	**69.23**
71.79	**87.18**	**79.49**	**82.05**	71.79	71.79	71.79	**82.05**	**87.18**	**87.18**	**87.18**
Confusion Matrix										
19 10 1 9	25 4 1 9	22 7 1 9	23 6 1 9	20 9 2 8	20 9 2 8	20 9 2 8	24 5 2 8	25 4 1 9	26 3 2 8	25 4 1 9

Table D.302: Momentaneous_Past_Investigation_Traditional_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.64	0.65	NA	0.84	0.81	0.84	0.84	NA	0.65	0.71	0.64
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	100.00	NA	**80.00**	**80.00**	**80.00**	**70.00**	NA	100.00	90.00	100.00
48.28	31.03	NA	**82.76**	**79.31**	**93.10**	**93.10**	NA	31.03	48.28	27.59
87.50	100.00	NA	**92.31**	**92.00**	**93.10**	**90.00**	NA	100.00	93.33	100.00
34.78	33.33	NA	**61.54**	**57.14**	**80.00**	**77.78**	NA	33.33	37.50	32.26
56.41	48.72	NA	**82.05**	**79.49**	**89.74**	**87.18**	NA	48.72	58.97	46.15
Confusion Matrix										
14 15 2 8	9 20 0 10	NA NA	24 5 2 8	23 6 2 8	27 2 2 8	27 2 3 7	NA NA	9 20 0 10	14 15 1 9	8 21 0 10

Table D.303: Momentaneous_Past_Investigation_kFold_PCA_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.81	0.84	0.85	0.85	0.89	0.84	0.82	0.84	0.84	0.85	0.84
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
76.47	**70.59**	**79.41**	**73.53**	**88.24**	**82.35**	**73.53**	**70.59**	**70.59**	**73.53**	**73.53**
86.79	**94.34**	**90.57**	**94.34**	**90.57**	**88.68**	**88.68**	**94.34**	**94.34**	**94.34**	**94.34**
85.19	**83.33**	**87.27**	**84.75**	**92.31**	**88.68**	**83.93**	**83.33**	**83.33**	**84.75**	**84.75**
78.79	**88.89**	**84.38**	**89.29**	**85.71**	**82.35**	**80.65**	**88.89**	**88.89**	**89.29**	**89.29**
82.76	**85.06**	**86.21**	**86.21**	**89.66**	**86.21**	**82.76**	**85.06**	**85.06**	**86.21**	**86.21**
Confusion Matrix										
46 7 8 26	50 3 10 24	48 5 7 27	50 3 9 25	48 5 4 30	47 6 6 28	47 6 9 25	50 3 10 24	50 3 10 24	50 3 9 25	50 3 9 25

Table D.304: Momentaneous_Past_Investigation_kFold_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.87	0.83	NA	0.92	0.92	0.92	0.86	NA	NA	0.86	0.82
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.29	**64.71**	NA	**97.06**	**100.00**	**94.29**	**82.35**	NA	NA	**76.47**	**67.65**
88.68	**96.23**	NA	**88.68**	**88.68**	**90.57**	**92.45**	NA	NA	**94.34**	**96.23**
90.38	**80.95**	NA	**97.92**	**100.00**	**96.00**	**89.09**	NA	NA	**86.21**	**82.26**
82.86	**91.67**	NA	**84.62**	**85.00**	**86.84**	**87.50**	NA	NA	**89.66**	**92.00**
87.36	**83.91**	NA	**91.95**	**93.10**	**92.05**	**88.51**	NA	NA	**87.36**	**85.06**
Confusion Matrix										
47 6	51 2	NA	47 6	47 6	48 5	49 4	NA	NA	50 3	51 2
5 29	12 22	NA	1 33	0 34	2 33	6 28	NA	NA	8 26	11 23

Table D.305: Momentaneous_Past_Investigation_LOO_PCA_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.49	0.47	0.49	0.50	0.40	0.44	0.49	0.49	0.42	0.48
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
35.29	29.41	32.35	32.35	41.18	26.47	29.41	29.41	29.41	23.53	29.41
64.15	67.92	62.26	66.04	58.49	52.83	58.49	67.92	67.92	62.26	66.04
60.71	60.00	58.93	60.34	60.78	52.83	56.36	60.00	60.00	55.93	59.32
38.71	37.04	35.48	37.93	38.89	26.47	31.25	37.04	37.04	28.57	35.71
52.87	52.87	50.57	52.87	51.72	42.53	47.13	52.87	52.87	47.13	51.72
Confusion Matrix										
34 19	36 17	33 20	35 18	31 22	28 25	31 22	36 17	36 17	33 20	35 18
22 12	24 10	23 11	23 11	20 14	25 9	24 10	24 10	24 10	26 8	24 10

Table D.306: Momentaneous_Past_Investigation_LOO_nextEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.41	0.42	0.50	0.49	0.49	0.49	0.54	0.50	0.42	0.44	0.45
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
29.41	17.65	38.24	44.12	44.12	44.12	41.18	38.24	17.65	26.47	23.53
52.83	69.81	62.26	52.83	52.83	54.72	66.04	62.26	69.81	62.26	67.92
53.85	56.92	61.11	59.57	59.57	60.42	63.64	61.11	56.92	56.90	58.06
28.57	27.27	39.39	37.50	37.50	38.46	43.75	39.39	27.27	31.03	32.00
43.68	49.43	52.87	49.43	49.43	50.57	56.32	52.87	49.43	48.28	50.57
Confusion Matrix										
28 25	37 16	33 20	28 25	28 25	29 24	35 18	33 20	37 16	33 20	36 17
24 10	28 6	21 13	19 15	19 15	19 15	20 14	21 13	28 6	25 9	26 8

For label *nextEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Features before selection: Optic Pathways, Spinal Cord, MS Course, Family History, Years since Onset, Number of Years, Relapses Per Year, Pyramidal 1 ratio, Pyramidal 1st year, Pyramidal first 2 years, Brain Stem first 2 years, Visual 1 ratio,

Visual 1st year, Visual first 2 years, Sensory 1 ratio, Corticosteroids/year, Corticosteroids 1st year, Average Treatment Intensity, Average Treatment 2 first years, Average Duration, Average Duration first 2 years, Last Pyramidal, Last Sensory.

Excluded features: EDSS Medium Value/year, EDSS 1st year, EDSS first 2 years, EDSS std/year, EDSS first 2 years std, EDSS Increase first 2 years, Ratio nb EDSS increase, Last EDSS.

Final features: Optic Pathways, Number of Years, Pyramidal first 2 years, Sensory 1 ratio, Average Duration.

Table D.307: Momentaneous_Past_Investigation_Traditional_PCA_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.66	0.79	0.76	0.79	0.72	0.70	0.74	0.77	0.79	0.78	0.79
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
83.33	83.33	83.33	83.33	66.67	66.67	66.67	83.33	83.33	83.33	83.33
56.36	70.91	70.91	74.55	70.91	69.09	74.55	72.73	70.91	72.73	70.91
96.88	97.50	97.50	97.62	95.12	95.00	95.35	97.56	97.50	97.56	97.50
17.24	23.81	23.81	26.32	20.00	19.05	22.22	25.00	23.81	25.00	23.81
59.02	72.13	72.13	75.41	70.49	68.85	73.77	73.77	72.13	73.77	72.13
Confusion Matrix										
31 24 1 5	39 16 1 5	39 16 1 5	41 14 1 5	39 16 2 4	38 17 2 4	41 14 2 4	40 15 1 5	39 16 1 5	40 15 1 5	39 16 1 5

Table D.308: Momentaneous_Past_Investigation_Traditional_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	NA	NA	0.65	0.55	0.64	0.66	NA	NA	0.71	0.68
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.67	NA	NA	50.00	33.33	50.00	50.00	NA	NA	83.33	100.00
40.00	NA	NA	76.36	81.82	80.00	76.36	NA	NA	60.00	41.82
91.67	NA	NA	93.33	91.84	93.62	93.33	NA	NA	97.06	100.00
10.81	NA	NA	18.75	16.67	21.43	18.75	NA	NA	18.52	15.79
42.62	NA	NA	73.77	77.05	77.05	73.77	NA	NA	62.30	47.54
Confusion Matrix										
22 33 2 4	NA NA	NA NA	42 13 3 3	45 10 4 2	44 11 3 3	42 13 3 3	NA NA	NA NA	33 22 1 5	23 32 0 6

Table D.309: Momentaneous_Past_Investigation_kFold_PCA_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.56	0.67	0.48	0.80	0.66	0.43	0.65	0.50	0.67	0.72
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
36.84	42.11	**57.89**	**57.89**	**78.95**	**52.63**	26.32	**57.89**	31.58	**68.42**	**78.95**
91.18	88.24	**85.29**	**85.29**	**95.59**	**94.12**	95.59	**83.82**	91.18	**83.82**	**80.88**
83.78	84.51	**87.88**	**87.88**	**94.20**	**87.67**	82.28	**87.69**	82.67	**90.48**	**93.22**
53.85	50.00	**52.38**	**52.38**	**83.33**	**71.43**	62.50	**50.00**	50.00	**54.17**	**53.57**
79.31	78.16	**79.31**	**79.31**	**91.95**	**85.06**	80.46	**78.16**	78.16	**80.46**	**80.46**
Confusion Matrix										
62 6 12 7	60 8 11 8	58 10 8 11	67 1 13 6	65 3 4 15	64 4 9 10	65 3 14 5	57 11 8 11	62 6 13 6	57 11 6 13	55 13 4 15

Table D.310: Momentaneous_Past_Investigation_kFold_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.64	NA	0.41	0.69	0.67	0.64	NA	0.57	0.74	0.73
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
47.37	**52.63**	NA	26.32	**63.16**	**57.89**	**52.63**	NA	42.11	**78.95**	**75.00**
89.71	**89.71**	NA	97.06	**89.71**	**92.65**	**92.65**	NA	91.18	**82.35**	**83.82**
85.92	**87.14**	NA	82.50	**89.71**	**88.73**	**87.50**	NA	84.93	**93.33**	**91.94**
56.25	**58.82**	NA	71.43	**63.16**	**68.75**	**66.67**	NA	57.14	**55.56**	**57.69**
80.46	**81.61**	NA	81.61	**83.91**	**85.06**	**83.91**	NA	80.46	**81.61**	**81.82**
Confusion Matrix										
61 7 10 9	61 7 9 10	NA NA	66 2 14 5	61 7 7 12	63 5 8 11	63 5 9 10	NA NA	62 6 11 8	56 12 4 15	57 11 5 15

Table D.311: Momentaneous_Past_Investigation_LOO_PCA_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.49	0.47	0.45	0.39	0.45	0.46	0.45	0.53	0.55	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
10.53	15.79	21.05	5.26	5.26	10.53	5.26	15.79	15.79	36.84	36.84
86.76	82.35	72.06	89.71	73.53	80.88	91.18	73.53	88.24	75.00	69.12
77.63	77.78	76.56	77.22	73.53	76.39	77.50	75.76	78.95	80.95	79.66
18.18	20.00	17.39	12.50	5.26	13.33	14.29	14.29	27.27	29.17	25.00
70.11	67.82	60.92	71.26	58.62	65.52	72.41	60.92	72.41	66.67	62.07
Confusion Matrix										
59 9 17 2	56 12 16 3	49 19 15 4	61 7 18 1	50 18 18 1	55 13 17 2	62 6 18 1	50 18 16 3	60 8 16 3	51 17 12 7	47 21 12 7

Table D.312: Momentaneous_Past_Investigation_LOO_nextEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.50	Na	0.38	0.50	0.44	0.41	NA	0.46	0.44	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
15.79	21.05	NA	0.00	21.05	10.53	5.26	NA	10.53	21.05	15.79
80.88	77.94	NA	91.18	77.94	79.41	79.41	NA	83.82	64.71	69.12
77.46	77.94	NA	76.54	77.94	76.06	75.00	NA	77.03	74.58	74.60
18.75	21.05	NA	0.00	21.05	12.50	6.67	NA	15.38	14.29	12.50
66.67	65.52	NA	71.26	65.52	64.37	63.22	NA	67.82	55.17	57.47
Confusion Matrix										
55 13	53 15	NA	62 6	53 15	54 14	54 14	NA	57 11	44 24	47 21
16 3	15 4	NA	19 0	15 4	17 2	18 1	NA	17 2	15 4	16 3

For label *highestEDSS* > 3 (0/1 - (< 3)/(≥ 3):

Features before selection: Optic Pathways, Spinal Cord, MS Course, Age Visit, Years since Onset, Nb of visits per Year, Suspected Relapses Ratio 1st year, Routine Visits Ratio 1st Year, Pyramidal 1 ratio, Pyramidal 1st year, Pyramidal first 2 years, Cerebellum 1 ratio, Cerebellum 1st year, Cerebellum first 2 years, Visual ratio, Visual 1st year, Visual first 2 years, Sensory 1 ratio, Corticosteroids Ratio, Corticosteroids 1st year, Corticosteroids first 2 years, Average Treatment Intensity, Average Treatment 2 first years, Average Duration, Average Duration first 2 years, Last Sensory.

Excluded features: EDSS Medium Value/year, EDSS 1st year, EDSS first 2 years, EDSS std/year, Ratio nb EDSS increase, Last EDSS.

Final features: Spinal Cord, Age Visit, Years since Onset, Nb of visits per Year, Sensory ratio, Corticosteroids Ratio.

Table D.313: Momentaneous_Past_Investigation_Traditional_PCA_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.77	0.83	0.82	0.83	0.84	0.78	0.77	0.82	0.83	0.83	0.83
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
78.57	**85.71**	**78.57**	**78.57**	**78.57**	**78.57**	**78.57**	**85.71**	**85.71**	**85.71**	**78.57**
81.82	**81.82**	**81.82**	**81.82**	**81.82**	**81.82**	**72.73**	**81.82**	**81.82**	**81.82**	**81.82**
75.00	**81.82**	**75.00**	**75.00**	**75.00**	**75.00**	**72.73**	**81.82**	**81.82**	**81.82**	**75.00**
84.62	**85.71**	**84.62**	**84.62**	**84.62**	**84.62**	**78.57**	**85.71**	**85.71**	**85.71**	**84.62**
80.00	**84.00**	**80.00**	**80.00**	**80.00**	**80.00**	**76.00**	**84.00**	**84.00**	**84.00**	**80.00**
Confusion Matrix										
9 2	9 2	9 2	9 2	9 2	9 2	8 3	9 2	9 2	9 2	9 2
3 11	2 12	3 11	3 11	3 11	3 11	3 11	2 12	2 12	2 12	3 11

Table D.314: Momentaneous_Past_Investigation_Traditional_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.70	0.61	0.65	0.73	0.64	0.63	0.63	0.75	0.61	0.77	0.63
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
57.14	28.57	42.86	**64.29**	42.86	35.71	35.71	**64.29**	28.57	**71.43**	35.71
81.82	90.91	90.91	**81.82**	81.82	90.91	90.91	**81.82**	90.91	**81.82**	90.91
60.00	50.00	55.56	**64.29**	52.94	52.63	52.63	**64.29**	50.00	**69.23**	52.63
80.00	80.00	85.71	**81.82**	75.00	83.33	83.33	**81.82**	80.00	**83.33**	83.33
68.00	56.00	64.00	**72.00**	60.00	60.00	60.00	**72.00**	56.00	**76.00**	60.00
Confusion Matrix										
9 2 6 8	10 1 10 4	10 1 8 6	9 2 5 9	9 2 8 6	10 1 9 5	10 1 9 5	9 2 5 9	10 1 10 4	9 2 4 10	10 1 9 5

Table D.315: Momentaneous_Past_Investigation_kFold_PCA_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.84	0.81	0.79	0.80	0.86	0.78	0.77	0.79	0.81	0.86	0.82
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
82.22	**82.22**	**80.00**	**82.22**	**88.89**	**82.22**	**77.78**	**75.56**	**82.22**	**88.89**	**80.00**
85.71	**80.95**	**76.19**	**78.57**	**83.33**	**76.19**	**73.81**	**83.33**	**80.95**	**83.33**	**80.95**
81.82	**80.95**	**78.05**	**80.49**	**87.50**	**80.00**	**75.61**	**76.09**	**80.95**	**87.50**	**79.07**
86.05	**82.22**	**78.26**	**80.43**	**85.11**	**78.72**	**76.09**	**82.93**	**82.22**	**85.11**	**81.82**
83.91	**81.61**	**78.16**	**80.46**	**86.21**	**79.31**	**75.86**	**79.31**	**81.61**	**86.21**	**80.46**
Confusion Matrix										
36 6 8 37	34 8 8 37	32 10 9 36	33 9 8 37	35 7 5 40	32 10 8 37	31 11 10 35	35 7 11 34	34 8 8 37	35 7 5 40	34 8 9 36

Table D.316: Momentaneous_Past_Investigation_kFold_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.87	0.80	0.78	0.87	0.86	0.78	0.77	0.80	0.80	0.77	0.81
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
84.44	**84.44**	**82.22**	**88.89**	**88.89**	**80.00**	**82.22**	**84.44**	**84.44**	**77.78**	**84.44**
88.10	**76.19**	**76.19**	**83.33**	**83.33**	**73.81**	**69.05**	**76.19**	**76.19**	**76.19**	**76.19**
84.09	**82.05**	**80.00**	**87.50**	**87.50**	**77.50**	**78.38**	**82.05**	**82.05**	**76.19**	**82.05**
88.37	**79.17**	**78.72**	**85.11**	**85.11**	**76.60**	**74.00**	**79.17**	**79.17**	**77.78**	**79.17**
86.21	**80.46**	**79.31**	**86.21**	**86.21**	**77.01**	**75.86**	**80.46**	**80.46**	**77.01**	**80.46**
Confusion Matrix										
37 5 7 38	32 10 7 38	32 10 8 37	35 7 5 40	35 7 5 40	31 11 9 36	29 13 8 37	32 10 7 38	32 10 7 38	32 10 10 35	32 10 7 38

Table D.317: Momentaneous_Past_Investigation_LOO_PCA_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	0.46	0.48	0.50	0.50	0.52	0.50	0.46	0.46	0.50	0.49
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
53.33	46.67	51.11	53.33	53.33	55.56	53.33	42.22	46.67	55.56	48.89
57.14	45.24	45.24	47.62	47.62	47.62	47.62	50.00	45.24	45.24	50.00
53.33	44.19	46.34	48.78	48.78	50.00	48.78	44.68	44.19	48.72	47.73
57.14	47.73	50.00	52.17	52.17	53.19	52.17	47.50	47.73	52.08	51.16
55.17	45.98	48.28	50.57	50.57	51.72	50.57	45.98	45.98	50.57	49.43
Confusion Matrix										
24 18	19 23	19 23	20 22	20 22	20 22	20 22	21 21	19 23	19 23	21 21
21 24	24 21	22 23	21 24	21 24	20 25	21 24	26 19	24 21	20 25	23 22

Table D.318: Momentaneous_Past_Investigation_LOO_highestEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.87	0.80	0.78	0.87	0.86	0.78	0.77	0.80	0.80	0.55	0.54
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
84.44	**84.44**	**82.22**	**88.89**	**88.89**	**80.00**	**82.22**	**84.44**	**84.44**	**57.78**	**60.00**
88.10	**76.19**	**76.19**	**83.33**	**83.33**	**73.81**	**69.05**	**76.19**	**76.19**	**52.38**	**47.62**
84.09	**82.05**	**80.00**	**87.50**	**87.50**	**77.50**	**78.38**	**82.05**	**82.05**	**53.66**	**52.63**
88.37	**79.17**	**78.72**	**85.11**	**85.11**	**76.60**	**74.00**	**79.17**	**79.17**	**56.52**	**55.10**
86.21	**80.46**	**79.31**	**86.21**	**86.21**	**77.01**	**75.86**	**80.46**	**80.46**	**55.17**	**54.02**
Confusion Matrix										
37 5	32 10	32 10	35 7	35 7	31 11	29 13	32 10	32 10	16 26	16 26
7 38	7 38	8 37	5 40	5 40	9 36	8 37	7 38	7 38	25 20	22 23

For label *highestEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Features before selection: Optic Pathways, Spinal Cord, MS Course, Age Visit, Years since Onset, Nb of visits per Year, Suspected Relapses Ratio 1st year, Routine Visits Ratio 1st Year, Pyramidal 1 ratio, Pyramidal 1st year, Pyramidal first 2 years, Cerebellum 1 ratio, Cerebellum 1st year, Cerebellum first 2 years, Visual ratio, Visual 1st year, Visual first 2 years, Sensory 1 ratio, Corticosteroids Ratio, Corticosteroids 1st year, Corticosteroids first 2 years, Average Treatment Intensity, Average Treatment 2 first years, Average Duration, Average Duration first 2 years, Last Sensory.

Excluded features: EDSS Medium Value/year, EDSS 1st year, EDSS first 2 years, EDSS std/year, EDSS first 2 years std, EDSS Increase first 2 years, Ratio nb EDSS increase, Last EDSS.

Final features: Optic Pathways, Pyramidal first 2 years, Corticosteroids 1st year.

Table D.319: Momentaneous_Past_Investigation_Traditional_PCA_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.72	0.84	0.85	0.83	0.85	0.79	0.79	0.80	0.84	0.84	0.84
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	87.50	85.71	85.71	85.71	85.71	85.71	100.00	100.00	85.71	85.71
47.83	76.09	82.61	78.26	80.43	69.57	67.39	63.04	76.09	76.09	76.09
100.00	97.22	97.44	97.30	97.37	96.97	96.88	100.00	100.00	97.22	97.22
22.58	38.89	42.86	37.50	40.00	30.00	28.57	29.17	38.89	35.29	35.29
54.72	77.78	83.02	79.25	81.13	71.70	69.81	67.92	79.25	77.36	77.36
Confusion Matrix										
22 24 0 7	35 11 1 7	38 8 1 6	36 10 1 6	37 9 1 6	32 14 1 6	31 15 1 6	29 17 0 7	35 11 0 7	35 11 1 6	35 11 1 6

Table D.320: Momentaneous_Past_Investigation_Traditional_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	NA	NA	0.70	0.59	0.62	0.61	NA	NA	0.75	0.75
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	NA	NA	85.71	71.43	85.71	85.71	NA	NA	85.71	85.71
10.87	NA	NA	47.83	50.00	36.96	32.61	NA	NA	58.70	58.70
100.00	NA	NA	95.65	92.00	94.44	93.75	NA	NA	96.43	96.43
14.58	NA	NA	20.00	17.86	17.14	16.22	NA	NA	24.00	24.00
22.64	NA	NA	52.83	52.83	43.40	39.62	NA	NA	62.26	62.26
Confusion Matrix										
5 41 0 7	NA NA	NA NA	22 24 1 6	23 23 2 5	17 29 1 6	15 31 1 6	NA NA	NA NA	27 19 1 6	27 19 1 6

Table D.321: Momentaneous_Past_Investigation_kFold_PCA_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.78	0.78	0.82	0.81	0.90	0.80	0.75	0.80	0.78	0.81	0.78
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
79.17	**70.83**	**79.17**	**75.00**	**95.83**	**83.33**	**66.67**	**75.00**	**70.83**	**79.17**	**79.17**
85.71	**92.06**	**93.65**	**96.83**	**95.24**	**87.30**	**88.89**	**93.65**	**92.06**	**92.06**	**87.30**
91.53	**89.23**	**92.19**	**91.04**	**98.36**	**93.22**	**87.50**	**90.77**	**89.23**	**92.06**	**91.67**
67.86	**77.27**	**82.61**	**90.00**	**88.46**	**71.43**	**69.57**	**81.82**	**77.27**	**79.17**	**70.37**
83.91	**86.21**	**89.66**	**90.80**	**95.40**	**86.21**	**82.76**	**88.51**	**86.21**	**88.51**	**85.06**
Confusion Matrix										
54 9 5 19	58 5 7 17	59 4 5 19	61 2 6 18	60 3 1 23	55 8 4 20	56 7 8 16	59 4 6 18	58 5 7 17	58 5 5 19	55 8 5 19

Table D.322: Momentaneous_Past_Investigation_kFold_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.85	0.80	NA	0.79	0.87	0.82	0.79	NA	0.80	0.82	0.80
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
83.33	**79.17**	NA	**75.00**	**87.50**	**87.50**	**75.00**	NA	**79.17**	**79.17**	**79.17**
95.24	**92.06**	NA	**93.65**	**95.24**	**88.89**	**93.65**	NA	**92.06**	**92.06**	**88.89**
93.75	**92.06**	NA	**90.77**	**95.24**	**94.92**	**90.77**	NA	**92.06**	**92.06**	**91.80**
86.96	**79.17**	NA	**81.82**	**87.50**	**75.00**	**81.82**	NA	**79.17**	**79.17**	**73.08**
91.95	**88.51**	NA	**88.51**	**93.10**	**88.51**	**88.51**	NA	**88.51**	**88.51**	**86.21**
Confusion Matrix										
60 3	58 5	NA	59 4	60 3	56 7	59 4	NA	58 5	58 5	56 7
4 20	5 19	NA	6 18	3 21	3 21	6 18	NA	5 19	5 19	5 19

Table D.323: Momentaneous_Past_Investigation_LOO_PCA_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.58	0.56	0.58	0.52	0.52	0.53	0.51	0.58	0.56	0.48	0.46
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
45.83	33.33	37.50	25.00	33.33	37.50	29.17	37.50	33.33	25.00	25.00
71.43	77.78	77.78	77.78	71.43	68.25	73.02	77.78	77.78	71.43	66.67
77.59	75.38	76.56	73.13	73.77	74.14	73.02	76.56	75.38	71.43	70.00
37.93	36.36	39.13	30.00	30.77	31.03	29.17	39.13	36.36	25.00	22.22
64.37	65.52	66.67	63.22	60.92	59.77	60.92	66.67	65.52	58.62	55.17
Confusion Matrix										
45 18	49 14	49 14	49 14	45 18	43 20	46 17	49 14	49 14	45 18	42 21
13 11	16 8	15 9	18 6	16 8	15 9	17 7	15 9	16 8	18 6	18 6

Table D.324: Momentaneous_Past_Investigation_LOO_highestEDSS > 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.48	NA	0.50	0.51	0.51	0.49	NA	0.48	0.45	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
25.00	25.00	NA	25.00	29.17	33.33	25.00	NA	25.00	20.83	20.83
71.43	71.43	NA	74.60	73.02	69.84	73.02	NA	71.43	69.84	66.67
71.43	71.43	NA	72.31	73.02	73.33	71.88	NA	71.43	69.84	68.85
25.00	25.00	NA	27.27	29.17	29.63	26.09	NA	25.00	20.83	19.23
58.62	58.62	NA	60.92	60.92	59.77	59.77	NA	58.62	56.32	54.02
Confusion Matrix										
45 18	45 18	NA	47 16	46 17	44 19	46 17	NA	45 18	44 19	42 21
18 6	18 6	NA	18 6	17 7	16 8	18 6	NA	18 6	19 5	19 5

For label *first2EDSS* > 3 (0/1 - $(< 3)/(\geq 3)$:

Features before selection: Gender, Age of Onset, Supratentorial, Optic Pathways, Spinal Cord, Age at SP Diagnosis, Relapses Per Year, Pyramidal ratio, Pyramidal 1st year, Pyramidal first 2 years, BrainStem 1st year, Brain Stem first 2 years,

Bowel 1 ratio, Bowel 1st year, Visual 1 ratio, Visual 1st year, Visual first 2 years, Corticosteroids 1st year, Average Duration, Last Sensory.

Excluded features: Years since Onset, EDSS Medium Value/year, EDSS 1st year, EDSS std/year, EDSS first 2 years std, EDSS std of variation first 2 years, EDSS Increase first 2 years, Ratio nb EDSS increase, Last EDSS.

Final features: Age of Onset, Supratentorial, Spinal Cord, Years since Onset, Pyramidal 1 ratio.

Table D.325: Momentaneous_Past_Investigation_Traditional_PCA_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.74	0.80	0.72	0.74	0.65	0.66	0.62	0.67	0.80	0.77	0.78
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	85.71	71.43	85.71	85.71	85.71	85.71	100.00	85.71	85.71	85.71
64.00	72.00	70.00	58.00	44.00	44.00	32.00	36.00	72.00	74.00	70.00
96.97	97.30	94.59	96.67	95.65	95.65	94.12	100.00	97.30	97.37	97.22
25.00	30.00	25.00	22.22	17.65	17.65	15.00	17.95	30.00	31.58	28.57
66.67	73.68	70.18	61.40	49.12	49.12	38.60	43.86	73.68	75.44	71.93
Confusion Matrix										
32 18 1 6	36 14 1 6	35 15 2 5	29 21 1 6	22 28 1 6	22 28 1 6	16 34 1 6	18 32 0 7	36 14 1 6	37 13 1 6	35 15 1 6

Table D.326: Momentaneous_Past_Investigation_Traditional_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.72	NA	NA	0.71	0.69	0.72	0.68	NA	0.66	0.64	0.66
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	NA	NA	85.71	85.71	85.71	85.71	NA	100.00	100.00	100.00
66.00	NA	NA	50.00	58.00	54.00	44.00	NA	36.00	28.00	36.00
97.06	NA	NA	96.15	96.67	96.43	95.65	NA	100.00	100.00	100.00
26.09	NA	NA	19.35	22.22	20.69	17.65	NA	17.95	16.28	17.95
68.42	NA	NA	54.39	61.40	57.89	49.12	NA	43.86	36.84	43.86
Confusion Matrix										
33 17 1 6	NA NA	NA NA	25 25 1 6	29 21 1 6	27 23 1 6	22 28 1 6	NA NA	18 32 0 7	14 36 0 7	18 32 0 7

Table D.327: Momentaneous_Past_Investigation_KFold_PCA_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.70	0.71	0.72	0.71	0.74	0.77	0.72	0.70	0.71	0.74	0.74
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
63.64	**68.18**	**63.64**	**54.55**	**68.18**	**72.73**	**63.64**	**59.09**	**63.64**	**72.73**	**77.27**
87.69	**89.23**	**89.23**	**96.92**	**89.23**	**92.31**	**93.85**	**95.38**	**90.77**	**90.77**	**86.15**
87.69	**89.23**	**87.88**	**86.30**	**89.23**	**90.91**	**88.41**	**87.32**	**88.06**	**90.77**	**91.80**
63.64	**68.18**	**66.67**	**85.71**	**68.18**	**76.19**	**77.78**	**81.25**	**70.00**	**72.73**	**65.38**
81.61	**83.91**	**82.76**	**86.21**	**83.91**	**87.36**	**86.21**	**86.21**	**83.91**	**86.21**	**83.91**
Confusion Matrix										
57 8	58 7	58 7	63 2	58 7	60 5	61 4	62 3	59 6	59 6	56 9
8 14	7 15	8 14	10 12	7 15	6 16	8 14	9 13	8 14	6 16	5 17

Table D.328: Momentaneous_Past_Investigation_KFold_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.80	0.74	NA	0.71	0.72	0.68	0.68	NA	0.75	0.76	0.74
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
72.73	**68.18**	NA	**54.55**	**68.18**	**54.55**	**54.55**	NA	**63.64**	**77.27**	**77.27**
96.92	**89.23**	NA	**98.46**	**84.62**	**93.85**	**98.46**	NA	**90.77**	**84.62**	**83.08**
91.30	**89.23**	NA	**86.49**	**88.71**	**85.92**	**86.49**	NA	**88.06**	**91.67**	**91.53**
88.89	**68.18**	NA	**92.31**	**60.00**	**75.00**	**92.31**	NA	**70.00**	**62.96**	**60.71**
90.80	**83.91**	NA	**87.36**	**80.46**	**83.91**	**87.36**	NA	**83.91**	**82.76**	**81.61**
Confusion Matrix										
63 2	58 7	NA	64 1	55 10	61 4	64 1	NA	59 6	55 10	54 11
6 16	7 15	NA	10 12	7 15	10 12	10 12	NA	8 14	5 17	5 17

Table D.329: Momentaneous_Past_Investigation_LOO_PCA_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	0.48	0.51	0.59	0.51	0.52	0.52	0.50	0.47	0.45	0.46
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
31.82	22.73	27.27	27.27	27.27	27.27	22.73	18.18	18.18	18.18	22.73
78.46	72.31	73.85	86.15	75.38	76.92	80.00	81.54	76.92	70.77	67.69
77.27	73.44	75.00	77.78	75.38	75.76	75.36	74.65	73.53	71.88	72.13
33.33	21.74	26.09	40.00	27.27	28.57	27.78	25.00	21.05	17.39	19.23
66.67	59.77	62.07	71.26	63.22	64.37	65.52	65.52	62.07	57.47	56.32
Confusion Matrix										
51 14	47 18	48 17	56 9	49 16	50 15	52 13	53 12	50 15	46 19	44 21
15 7	17 5	16 6	16 6	16 6	16 6	17 5	18 4	18 4	18 4	17 5

Table D.330: Momentaneous_Past_Investigation_LOO_first2EDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.54	NA	0.56	0.49	0.50	0.53	NA	0.52	0.56	0.58
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
18.18	31.82	NA	22.73	27.27	18.18	18.18	NA	27.27	40.91	45.45
76.92	76.92	NA	86.15	70.77	81.54	86.15	NA	76.92	72.31	72.31
73.53	76.92	NA	76.71	74.19	74.65	75.68	NA	75.76	78.33	79.66
21.05	31.82	NA	35.71	24.00	25.00	30.77	NA	28.57	33.33	35.71
62.07	65.52	NA	70.11	59.77	65.52	68.97	NA	64.37	64.37	65.52
Confusion Matrix										
50 15 18 4	50 15 15 7	NA NA	56 9 17 5	46 19 16 6	53 12 18 4	56 9 18 4	NA NA	50 15 16 6	47 18 13 9	47 18 12 10

For label *first2EDSS* (0/1 - (< 5)/(≥ 5)):

The via pattern recognition study was not performed since the number of patients with *first2EDSS*≥ 5 was minimal.

For label *tendencyEDSS* (0/1 - (Down or Equal)/(Up)):

Features before selection: Nb of visits per Year, Cerebellum 1st year, Corticosteroids Ratio, Corticosteroids 1st year, Average Treatment Intensity, Average Treatment 2 first years, Average Duration, Last ambulatory, Last Treatment, Clinical Findings, MS Course, Years since Onset, Routine Visits Ratio, Average Duration first 2 years.

Excluded features: EDSS medium variation/Year, EDSS std of variation/year, EDSS medium variation first 2 years.

Selected features: Nb of visits per Year, Average Treatment Intensity, Years since Onset.

Table D.331: Momentaneous_Past_Investigation_Traditional_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.63	0.62	0.58	0.54	0.58	0.58	0.63	0.63	0.65	0.64
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
75.00	75.00	75.00	50.00	50.00	50.00	50.00	75.00	75.00	75.00	75.00
50.82	52.46	54.10	57.38	62.30	63.93	60.66	62.30	52.46	54.10	51.61
96.88	96.97	97.06	94.59	95.00	95.12	94.87	97.44	96.97	97.06	96.97
9.09	9.38	9.68	7.14	8.00	8.33	7.69	11.54	9.38	9.68	9.09
52.31	53.85	55.38	56.92	61.54	63.08	60.00	63.08	53.85	55.38	53.03
Confusion Matrix										
31 30 1 3	32 29 1 3	33 28 1 3	35 26 2 2	38 23 2 2	39 22 2 2	37 24 2 2	38 23 1 3	32 29 1 3	33 28 1 3	32 30 1 3

Table D.332: Momentaneous_Past_Investigation_Traditional_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.51	0.55	0.54	0.56	0.53	0.53	0.55	0.51	0.51	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
25.00	0.00	25.00	25.00	50.00	50.00	25.00	0.00	0.00	0.00	0.00
83.61	98.36	91.80	75.41	63.93	67.21	73.77	96.72	98.36	100.00	98.36
94.44	93.75	94.92	93.88	95.12	95.35	93.75	93.65	93.75	93.85	93.75
9.09	0.00	16.67	6.25	8.33	9.09	5.88	0.00	0.00	NaN	0.00
80.00	92.31	87.69	72.31	63.08	66.15	70.77	90.77	92.31	93.85	92.31
Confusion Matrix										
51 10 3 1	60 1 4 0	56 5 3 1	46 15 3 1	39 22 2 2	41 20 2 2	45 16 3 1	59 2 4 0	60 1 4 0	61 0 4 0	60 1 4 0

Table D.333: Momentaneous_Past_Investigation_kFold_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.40	0.29	0.43	0.08	0.36	0.27	0.17	0.28	0.08	0.60	0.56
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
20.00	13.33	26.67	0.00	13.33	13.33	6.67	18.75	0.00	66.67	60.00
84.72	95.83	86.11	97.22	84.72	94.44	94.44	97.22	98.61	66.67	62.50
83.56	84.15	84.93	82.35	82.43	83.95	82.93	84.34	82.56	90.57	88.24
21.43	40.00	28.57	0.00	15.38	33.33	20.00	60.00	0.00	29.41	25.00
73.56	81.61	75.86	80.46	72.41	80.46	79.31	82.95	81.61	66.67	62.07
Confusion Matrix										
61 11 12 3	69 3 13 2	62 10 11 4	70 2 15 0	61 11 13 2	68 4 13 2	68 4 14 1	70 2 13 2	71 1 15 0	48 24 5 10	45 27 6 9

Table D.334: Momentaneous_Past_Investigation_kFold_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.43	0.34	0.40	0.08	0.50	0.36	0.20	0.34	0.03	0.61	0.60
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
26.67	20.00	26.67	0.00	40.00	20.00	6.67	20.00	0.00	73.33	66.67
84.72	94.44	91.67	97.22	84.72	90.28	93.06	94.44	98.61	68.06	69.44
84.72	85.00	85.71	82.35	87.14	84.42	82.72	85.00	82.56	92.45	90.91
26.67	42.86	40.00	0.00	35.29	30.00	16.67	42.86	0.00	32.35	31.25
74.71	81.61	80.46	80.46	77.01	78.16	78.16	81.61	81.61	68.97	68.97
Confusion Matrix										
61 11 11 4	68 4 12 3	66 6 11 4	70 2 15 0	61 11 9 6	65 7 12 3	67 5 14 1	68 4 12 3	71 1 15 0	49 23 4 11	50 22 5 10

Table D.335: Momentaneous_Past_Investigation_LOO_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.51	0.50	0.41	0.53	0.50	0.41	0.51	0.41	0.50	0.54
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
13.33	6.67	13.33	0.00	20.00	6.67	0.00	6.67	0.00	40.00	53.33
87.50	94.44	86.11	97.22	86.11	93.06	94.44	94.44	98.61	59.72	61.11
82.89	82.93	82.67	82.35	83.78	82.72	81.93	82.93	82.56	82.69	86.27
18.18	20.00	16.67	0.00	23.08	16.67	0.00	20.00	0.00	17.14	22.22
74.71	79.31	73.56	80.46	74.71	78.16	78.16	79.31	81.61	56.32	59.77
Confusion Matrix										
63 9	68 4	62 10	70 2	62 10	67 5	68 4	68 4	71 1	43 29	44 28
13 2	14 1	13 2	15 0	12 3	14 1	15 0	14 1	15 0	9 6	7 8

Table D.336: Momentaneous_Past_Investigation_LOO_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.51	0.41	0.47	0.47	0.50	0.54	0.00	0.55	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
20.00	6.67	13.33	0.00	13.33	6.67	6.67	13.33	0.00	53.33	40.00
81.94	93.06	87.50	97.22	79.17	88.89	93.06	91.67	100.00	63.89	65.28
83.10	82.72	82.89	82.35	81.43	82.05	82.72	83.54	82.76	86.79	83.93
18.75	16.67	18.18	0.00	11.76	11.11	16.67	25.00	NaN	23.53	19.35
71.26	78.16	74.71	80.46	67.82	74.71	78.16	78.16	82.76	62.07	60.92
Confusion Matrix										
59 13	67 5	63 9	70 2	57 15	64 8	67 5	66 6	72 0	46 26	47 25
12 3	14 1	13 2	15 0	13 2	14 1	14 1	13 2	15 0	7 8	9 6

For label *mediumEDSS* (0/1 - $(<3)/(\geq 3)$):

Final features: Spinal Cord, MS Course, No Years, Pyramidal 1 ratio, Pyramidal first 2 years.

Table D.337: Momentaneous_Past_Investigation_Traditional_PCA_mediumEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.62	0.50	NA	0.64	0.54	0.57	0.60	NA	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
88.89	100.00	NA	88.89	66.67	77.78	77.78	NA	100.00	100.00	100.00
41.18	0.00	NA	41.18	44.12	38.24	38.24	NA	0.00	0.00	0.00
93.33	NaN	NA	93.33	83.33	86.67	86.67	NA	NaN	NaN	NaN
28.57	20.93	NA	28.57	24.00	25.00	25.00	NA	20.93	20.93	20.93
51.16	20.93	NA	51.16	48.84	46.51	46.51	NA	20.93	20.93	20.93
Confusion Matrix										
14 20	0 34	NA	14 20	15 19	13 21	13 21	NA	0 34	0 34	0 34
1 8	0 9	NA	1 8	3 6	2 7	2 7	NA	0 9	0 9	0 9

Table D.338: Momentaneous_Past_Investigation_Traditional_mediumEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.66	0.50	0.00	0.76	0.59	0.69	0.76	0.00	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
77.78	100.00	**88.89**	**77.78**	77.78	77.78	**77.78**	88.89	100.00	100.00	100.00
52.94	2.94	**76.47**	**79.41**	41.18	61.76	**79.41**	70.59	2.94	0.00	2.94
90.00	100.00	**96.30**	**93.10**	87.50	91.30	**93.10**	96.00	100.00	NaN	100.00
30.43	21.43	**50.00**	**50.00**	25.93	35.00	**50.00**	44.44	21.43	20.93	21.43
58.14	23.26	**79.07**	**79.07**	48.84	65.12	**79.07**	74.42	23.26	20.93	23.26
Confusion Matrix										
18 16 2 7	1 33 0 9	26 8 1 8	27 7 2 7	14 20 2 7	21 13 2 7	27 7 2 7	24 10 1 8	1 33 0 9	0 34 0 9	1 33 0 9

Table D.339: Momentaneous_Past_Investigation_kFold_PCA_mediumEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.75	0.79	0.84	0.83	0.86	0.76	0.73	0.82	0.79	0.77	0.77
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
64.52	**61.29**	**80.65**	**70.97**	**80.65**	**67.74**	**54.84**	**77.42**	**61.29**	**67.74**	**64.52**
83.93	**94.64**	**87.50**	**94.64**	**91.07**	**85.71**	**92.86**	**89.29**	**94.64**	**87.50**	**89.29**
81.03	**81.54**	**89.09**	**85.48**	**89.47**	**82.76**	**78.79**	**87.72**	**81.54**	**83.05**	**81.97**
68.97	**86.36**	**78.13**	**88.00**	**83.33**	**72.41**	**80.95**	**80.00**	**86.36**	**75.00**	**76.92**
77.01	**82.76**	**85.06**	**86.21**	**87.36**	**79.31**	**79.31**	**85.06**	**82.76**	**80.46**	**80.46**
Confusion Matrix										
47 9 11 20	53 3 12 19	49 7 6 25	53 3 9 22	51 5 6 25	48 8 10 21	52 4 14 17	50 6 7 24	53 3 12 19	49 7 10 21	50 6 11 20

Table D.340: Momentaneous_Past_Investigation_kFold_mediumEDSS > 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.73	0.78	0.83	0.83	0.85	0.76	0.73	0.81	0.78	0.77	0.77
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
64.52	**61.29**	**80.65**	**70.97**	**80.65**	**64.52**	**54.84**	**77.42**	**61.29**	**67.74**	**67.74**
83.93	**92.86**	**87.50**	**94.64**	**91.07**	**85.71**	**91.07**	**89.29**	**92.86**	**87.50**	**89.29**
81.03	**81.25**	**89.09**	**85.48**	**89.47**	**81.36**	**78.46**	**87.72**	**81.25**	**83.05**	**83.33**
68.97	**82.61**	**78.13**	**88.00**	**83.33**	**71.43**	**77.27**	**80.00**	**82.61**	**75.00**	**77.78**
77.01	**81.61**	**85.06**	**86.21**	**87.36**	**78.16**	**78.16**	**85.06**	**81.61**	**80.46**	**81.61**
Confusion Matrix										
47 9 11 20	52 4 12 19	49 7 6 25	53 3 9 22	51 5 6 25	48 8 11 20	51 5 14 17	50 6 7 24	52 4 12 19	49 7 10 21	50 6 10 21

Table D.341: Momentaneous_Past_Investigation_LOO_PCA_mediumEDSS > 3

Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.55	0.55	0.56	0.59	0.56	0.54	0.52	0.57	0.55	0.57	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
38.71	32.26	45.16	38.71	41.94	38.71	25.81	41.94	32.26	41.94	35.48
71.43	76.79	67.86	76.79	69.64	69.64	76.79	71.43	76.79	71.43	73.21
67.80	67.19	69.09	69.35	68.42	67.24	65.15	68.97	67.19	68.97	67.21
42.86	43.48	43.75	48.00	43.33	41.38	38.10	44.83	43.48	44.83	42.31
59.77	60.92	59.77	63.22	59.77	58.62	58.62	60.92	60.92	60.92	59.77
Confusion Matrix										
40 16 19 12	43 13 21 10	38 18 17 14	43 13 19 12	39 17 18 13	39 17 19 12	43 13 23 8	40 16 18 13	43 13 21 10	40 16 18 13	41 15 20 11

Table D.342: Momentaneous_Past_Investigation_LOO_mediumEDSS > 3

Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.42	0.52	0.54	0.56	0.48	0.49	0.61	0.54	0.52	0.59	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
22.58	29.03	41.94	35.48	32.26	32.26	35.48	38.71	29.03	45.16	35.48
62.50	75.00	66.07	75.00	64.29	66.07	82.14	69.64	75.00	73.21	73.21
59.32	65.63	67.27	67.74	63.16	63.79	69.70	67.24	65.63	70.69	67.21
25.00	39.13	40.63	44.00	33.33	34.48	52.38	41.38	39.13	48.28	42.31
48.28	58.62	57.47	60.92	52.87	54.02	65.52	58.62	58.62	63.22	59.77
Confusion Matrix										
35 21 24 7	42 14 22 9	37 19 18 13	42 14 20 11	36 20 21 10	37 19 21 10	46 10 20 11	39 17 19 12	42 14 22 9	41 15 17 14	41 15 20 11

For label *nextEDSS* (0/1 - $(< 3)/(\geq 3)$):

The via pattern recognition study was not performed since the number of patients with *currentEDSS*≥ 5 was minimal.

D.2 MRI Set

For label *msCourse* (0/1 - RR/SP):

Final features: 34_A1_NB_diff_FLAIR_bin_location_mean_std histogram, 29_A1_CSF_diff_DP_bin histogram, 87_A1_CSF_diff_DP_bin_location_median_std histogram, 92_A1_CSF_diff_DP_bin_location_ histogram.

Table D.343: MRI_Traditional_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.72	0.69	0.58	0.61	0.59	0.63	0.69	0.72	0.69	0.69
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
33.33	66.67	66.67	83.33	66.67	66.67	66.67	66.67	66.67	60.00	60.00
75.38	83.08	72.31	38.46	52.31	49.23	61.54	70.77	83.08	82.81	82.81
92.45	96.43	95.92	96.15	94.44	94.12	95.24	95.83	96.43	96.36	96.36
11.11	26.67	18.18	11.11	11.43	10.81	13.79	17.39	26.67	21.43	21.43
71.83	81.69	71.83	42.25	53.52	50.70	61.97	70.42	81.69	81.16	81.16
Confusion Matrix										
49 16 4 2	54 11 2 4	47 18 2 4	25 40 1 5	34 31 2 4	32 33 2 4	40 25 2 4	46 19 2 4	54 11 2 4	53 11 2 3	53 11 2 3

Table D.344: MRI_Traditional_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.60	0.71	NA	0.59	0.61	0.59	0.64	0.69	0.71	0.73	0.70
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
50.00	66.67	NA	66.67	66.67	66.67	66.67	66.67	66.67	60.00	60.00
67.69	80.00	NA	47.69	60.00	52.31	61.54	67.69	81.54	82.81	81.25
93.62	96.30	NA	93.94	95.12	94.44	95.24	95.65	96.36	96.36	96.30
12.50	23.53	NA	10.53	13.33	11.43	13.79	16.00	25.00	21.43	20.00
66.20	78.87	NA	49.30	60.56	53.52	61.97	67.61	80.28	81.16	79.71
Confusion Matrix										
44 21 3 3	52 13 2 4	NA NA	31 34 2 4	39 26 2 4	34 31 2 4	40 25 2 4	44 21 2 4	53 12 2 4	53 11 2 3	52 12 2 3

Table D.345: MRI_kFold_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.41	0.12	0.02	0.12	0.49	0.44	0.25	0.02	0.03	0.63	0.63
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
15.00	5.00	0.00	0.00	25.00	20.00	5.00	0.00	0.00	90.00	90.00
84.81	98.73	98.73	94.94	83.54	88.61	88.61	98.73	100.00	49.37	49.37
79.76	80.41	79.59	78.95	81.48	81.40	78.65	79.59	79.80	95.12	95.12
20.00	50.00	0.00	0.00	27.78	30.77	10.00	0.00	NaN	31.03	31.03
70.71	79.80	78.79	75.76	71.72	74.75	71.72	78.79	79.80	57.58	57.58
Confusion Matrix										
67 12 17 3	78 1 19 1	78 1 20 0	75 4 20 0	66 13 15 5	70 9 16 4	70 9 19 1	78 1 20 0	79 0 20 0	39 40 2 18	39 40 2 18

Table D.346: MRI_kFold_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.49	0.50	0.07	0.52	0.43	0.34	0.64	0.38	0.65	0.63
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
30.00	30.00	28.57	0.00	30.00	20.00	15.00	60.00	15.00	80.00	65.00
87.34	89.87	86.08	97.47	82.28	89.87	94.94	78.48	92.41	65.82	73.42
83.13	83.53	81.93	79.38	82.28	81.61	81.52	88.57	81.11	92.86	89.23
37.50	42.86	35.29	0.00	30.00	33.33	42.86	41.38	33.33	37.21	38.24
75.76	77.78	74.00	77.78	71.72	75.76	78.79	74.75	76.77	68.69	71.72
Confusion Matrix										
69 10	71 8	68 11	77 2	65 14	71 8	75 4	62 17	73 6	52 27	58 21
14 6	14 6	15 6	20 0	14 6	16 4	17 3	8 12	17 3	4 16	7 13

Table D.347: MRI_LOO_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	Mahalanobis
AUC										
0.59	0.40	0.00	0.74	0.55	0.56	0.61	0.43	0.51	0.55	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
30.00	0.00	0.00	10.00	25.00	20.00	20.00	0.00	0.00	70.00	70.00
86.08	97.47	100.00	98.73	83.54	88.61	92.41	100.00	100.00	44.30	44.30
82.93	79.38	79.80	81.25	81.48	81.40	82.02	79.80	79.80	85.37	85.37
35.29	0.00	NaN	66.67	27.78	30.77	40.00	NaN	NaN	24.14	24.14
74.75	77.78	79.80	80.81	71.72	74.75	77.78	79.80	79.80	49.49	49.49
Confusion Matrix										
68 11	77 2	79 0	78 1	66 13	70 9	73 6	79 0	79 0	35 44	35 44
14 6	20 0	20 0	18 2	15 5	16 4	16 4	20 0	20 0	6 14	6 14

Table D.348: MRI_LOO_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.43	0.47	0.55	0.40	0.46	0.44	0.48	0.43	0.51	0.49	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
5.00	10.00	20.00	0.00	15.00	5.00	5.00	15.00	10.00	40.00	35.00
86.08	84.81	87.34	98.73	77.22	87.34	93.67	67.09	91.14	55.70	68.35
78.16	78.82	81.18	79.59	78.21	78.41	79.57	75.71	80.00	78.57	80.60
8.33	14.29	28.57	0.00	14.29	9.09	16.67	10.34	22.22	18.60	21.88
69.70	69.70	73.74	78.79	64.65	70.71	75.76	56.57	74.75	52.53	61.62
Confusion Matrix										
68 11	67 12	69 10	78 1	61 18	69 10	74 5	53 26	72 7	44 35	54 25
19 1	18 2	16 4	20 0	17 3	19 1	19 1	17 3	18 2	12 8	13 7

For label *currentEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: 164_A1_CSF_ratio_T2_max_entropy, 22_A1_WM_diff_FLAIR_max_entropy, 22_A1_WM_ratio_FLAIR_max_entropy.

Table D.349: MRI_Traditional_PCA_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.44	0.50	0.50	0.48	0.45	0.48	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
75.00	100.00	100.00	75.00	75.00	91.67	100.00	100.00	NA	100.00	100.00
16.13	0.00	0.00	19.35	12.90	3.23	0.00	0.00	NA	0.00	0.00
62.50	NaN	NaN	66.67	57.14	50.00	NaN	NaN	NA	NaN	NaN
25.71	27.91	27.91	26.47	25.00	26.83	27.91	27.91	NA	27.91	27.91
32.56	27.91	27.91	34.88	30.23	27.91	27.91	27.91	NA	27.91	27.91
Confusion Matrix										
5 26	0 31	0 31	6 25	4 27	1 30	0 31	0 31	NA	0 31	0 31
3 9	0 12	0 12	3 9	3 9	1 11	0 12	0 12	NA	0 12	0 12

Table D.350: MRI_Traditional_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.50	0.50	0.50	0.50	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	NA	100.00	100.00
0.00	0.00	0.00	3.03	0.00	0.00	0.00	0.00	NA	0.00	0.00
NaN	NaN	NaN	100.00	NaN	NaN	NaN	NaN	NA	NaN	NaN
26.67	26.67	26.67	27.27	26.67	26.67	26.67	26.67	NA	26.67	26.67
26.67	26.67	26.67	28.89	26.67	26.67	26.67	26.67	NA	26.67	26.67
Confusion Matrix										
2 31	0 33	0 33	1 32	0 33	0 33	0 33	0 33	NA	0 33	0 33
0 12	0 12	0 12	0 12	0 12	0 12	0 12	0 12	NA	0 12	0 12

Table D.351: MRI_kFold_PCA_currentEDSS ≥ 3

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.56	0.63	0.63	0.41	0.58	0.56	0.56	0.63	NA	0.59	0.59
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
47.50	40.00	35.00	17.50	47.50	40.00	42.50	35.00	NA	**57.50**	**57.50**
64.41	84.75	89.83	76.27	66.10	71.19	67.80	89.83	NA	**61.02**	**61.02**
64.41	67.57	67.09	57.69	65.00	63.64	63.49	67.09	NA	**67.92**	**67.92**
47.50	64.00	70.00	33.33	48.72	48.48	47.22	70.00	NA	**50.00**	**50.00**
57.58	66.67	67.68	52.53	58.59	58.59	57.58	67.68	NA	**59.60**	**59.60**
Confusion Matrix										
38 21	50 9	53 6	45 14	39 20	42 17	40 19	53 6	NA	36 23	36 23
21 19	24 16	26 14	33 7	21 19	24 16	23 17	26 14	NA	17 23	17 23

Table D.352: MRI_kFold_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.63	0.67	0.66	0.63	0.58	0.69	0.70	0.72	NA	0.63	0.71
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
58.97	48.72	**51.28**	35.90	48.72	**58.97**	**53.85**	**58.97**	NA	**56.41**	**69.23**
66.67	83.33	**85.00**	85.00	66.67	**80.00**	**83.33**	**81.97**	NA	**68.33**	**73.33**
71.43	71.43	**72.86**	67.11	66.67	**75.00**	**73.53**	**75.76**	NA	**70.69**	**78.57**
53.49	65.52	**68.97**	60.87	48.72	**65.71**	**67.74**	**67.65**	NA	**53.66**	**62.79**
63.64	69.70	**71.72**	65.66	59.60	**71.72**	**71.72**	**73.00**	NA	**63.64**	**71.72**
Confusion Matrix										
40 20	50 10	51 9	51 9	40 20	48 12	50 10	50 11	NA	41 19	44 16
16 23	20 19	19 20	25 14	20 19	16 23	18 21	16 23	NA	17 22	12 27

Table D.353: MRI_LOO_PCA_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.52	0.50	0.56	0.56	0.59	0.52	0.50	NA	0.51	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
47.50	25.00	20.00	25.00	47.50	42.50	40.00	20.00	NA	47.50	47.50
57.63	77.97	79.66	83.05	64.41	74.58	64.41	79.66	NA	54.24	54.24
61.82	60.53	59.49	62.03	64.41	65.67	61.29	59.49	NA	60.38	60.38
43.18	43.48	40.00	50.00	47.50	53.13	43.24	40.00	NA	41.30	41.30
53.54	56.57	55.56	59.60	57.58	61.62	54.55	55.56	NA	51.52	51.52
Confusion Matrix										
34 25	46 13	47 12	49 10	38 21	44 15	38 21	47 12	NA	32 27	32 27
21 19	30 10	32 8	30 10	21 19	23 17	24 16	32 8	NA	21 19	21 19

Table D.354: MRI_LOO_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.41	0.38	0.48	0.45	0.39	0.42	0.38	NA	0.46	0.46
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
35.90	15.38	10.26	15.38	33.33	17.95	23.08	10.26	NA	41.03	41.03
56.67	71.67	73.33	81.67	56.67	63.33	61.67	73.33	NA	51.67	51.67
57.63	56.58	55.70	59.76	56.67	54.29	55.22	55.70	NA	57.41	57.41
35.00	26.09	20.00	35.29	33.33	24.14	28.13	20.00	NA	35.56	35.56
48.48	49.49	48.48	55.56	47.47	45.45	46.46	48.48	NA	47.47	47.47
Confusion Matrix										
34 26	43 17	44 16	49 11	34 26	38 22	37 23	44 16	NA	31 29	31 29
25 14	33 6	35 4	33 6	26 13	32 7	30 9	35 4	NA	23 16	23 16

For label *currentEDSS* > 5 **(0/1 -** $(< 5)/(\geq 5)$**:**

Final features: 102_A1_NB_ratio_T1_std_bin_location_mean histogram, 22_A1_WM_ratio_FLAIR_
histogram.

Table D.355: MRI_Traditional_PCA_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	NA	100.00	100.00
0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	NA	1.61	1.61
NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NA	100.00	100.00
10.14	10.14	10.14	10.14	10.14	10.14	10.14	10.14	NA	10.29	10.29
10.14	10.14	10.14	10.14	10.14	10.14	10.14	10.14	NA	11.59	11.59
Confusion Matrix										
0 62 0 7	0 62 0 7	0 62 0 7	0 62 0 7	0 62 0 7	0 62 0 7	0 62 0 7	0 62 0 7	NA NA	1 61 0 7	1 61 0 7

Table D.356: MRI_Traditional_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.50	0.50	0.50	0.50	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	100.00	100.00	100.00	71.43	100.00	100.00	100.00	NA	100.00	100.00
17.74	0.00	6.45	1.61	24.19	0.00	1.61	0.00	NA	0.00	0.00
91.67	NaN	100.00	100.00	88.24	NaN	100.00	NaN	NA	NaN	NaN
10.53	10.14	10.77	10.29	9.62	10.14	10.29	10.14	NA	10.14	10.14
24.64	10.14	15.94	11.59	28.99	10.14	11.59	10.14	NA	10.14	10.14
Confusion Matrix										
11 51 1 6	0 62 0 7	4 58 0 7	1 61 0 7	15 47 2 5	0 62 0 7	1 61 0 7	0 62 0 7	NA NA	0 62 0 7	0 62 0 7

Table D.357: MRI_kFold_PCA_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.46	0.49	0.11	0.53	0.54	0.59	0.49	0.45	0.64	0.64
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
36.36	27.27	27.27	0.00	36.36	31.82	36.36	27.27	22.73	**54.55**	**54.55**
80.52	94.81	94.81	96.10	76.62	87.01	92.21	94.81	94.81	**84.42**	**84.42**
81.58	82.02	82.02	77.08	80.82	81.71	83.53	82.02	81.11	**86.67**	**86.67**
34.78	60.00	60.00	0.00	30.77	41.18	57.14	60.00	55.56	**50.00**	**50.00**
70.71	79.80	79.80	74.75	67.68	74.75	79.80	79.80	78.79	**77.78**	**77.78**
Confusion Matrix										
62 15 14 8	73 4 16 6	73 4 16 6	74 3 22 0	59 18 14 8	67 10 15 7	71 6 14 8	73 4 16 6	73 4 17 5	65 12 10 12	65 12 10 12

Table D.358: MRI_kFold_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.46	0.61	0.24	0.56	0.55	0.60	0.63	NA	0.63	0.59
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
31.82	27.27	40.91	9.09	36.36	36.36	40.91	40.91	NA	**54.55**	45.45
81.82	97.40	94.81	96.10	80.52	89.61	92.21	94.81	NA	**84.42**	87.01
80.77	82.42	84.88	78.72	81.58	83.13	84.52	84.88	NA	**86.67**	84.81
33.33	75.00	69.23	40.00	34.78	50.00	60.00	69.23	NA	**50.00**	50.00
70.71	81.82	82.83	76.77	70.71	77.78	80.81	82.83	NA	**77.78**	77.78
Confusion Matrix										
63 14	75 2	73 4	74 3	62 15	69 8	71 6	73 4	NA	65 12	67 10
15 7	16 6	13 9	20 2	14 8	14 8	13 9	13 9	NA	10 12	12 10

Table D.359: MRI_LOO_PCA_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.49	0.49	0.56	0.42	0.50	0.45	0.49	0.50	0.44	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
18.18	9.09	9.09	4.55	13.64	18.18	9.09	9.09	9.09	13.64	13.64
72.73	89.61	89.61	97.40	68.83	81.82	84.42	89.61	90.91	72.73	72.73
75.68	77.53	77.53	78.13	73.61	77.78	76.47	77.53	77.78	74.67	74.67
16.00	20.00	20.00	33.33	11.11	22.22	14.29	20.00	22.22	12.50	12.50
60.61	71.72	71.72	76.77	56.57	67.68	67.68	71.72	72.73	59.60	59.60
Confusion Matrix										
56 21	69 8	69 8	75 2	53 24	63 14	65 12	69 8	70 7	56 21	56 21
18 4	20 2	20 2	21 1	19 3	18 4	20 2	20 2	20 2	19 3	19 3

Table D.360: MRI_LOO_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.44	0.44	0.46	0.47	0.47	0.48	0.45	0.46	NA	0.47	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
13.64	4.55	9.09	4.55	18.18	13.64	9.09	9.09	NA	18.18	18.18
75.32	89.61	85.71	93.51	75.32	83.12	84.42	85.71	NA	74.03	80.52
75.32	76.67	76.74	77.42	76.32	77.11	76.47	76.74	NA	76.00	77.50
13.64	11.11	15.38	16.67	17.39	18.75	14.29	15.38	NA	16.67	21.05
61.62	70.71	68.69	73.74	62.63	67.68	67.68	68.69	NA	61.62	66.67
Confusion Matrix										
58 19	69 8	66 11	72 5	58 19	64 13	65 12	66 11	NA	57 20	62 15
19 3	21 1	20 2	21 1	18 4	19 3	20 2	20 2	NA	18 4	18 4

For label *nextEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: 121_A1_BO_ratio_T2_raw_std_mean, 22_A1_WM_diff_FLAIR_max_entropy, 23_A1_WM_diff_FLAIR_max_entropy, 24_A1_WM_diff_FLAIR_max_entropy, 21_A1_WM_ratio_FLAIR

Table D.361: MRI_Traditional_PCA_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.49	0.51	0.51	0.48	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
83.33	100.00	91.67	75.00	83.33	100.00	100.00	100.00	NA	100.00	100.00
15.15	0.00	3.03	27.27	18.18	0.00	0.00	0.00	NA	0.00	0.00
71.43	NaN	50.00	75.00	75.00	NaN	NaN	NaN	NA	NaN	NaN
26.32	26.67	25.58	27.27	27.03	26.67	26.67	26.67	NA	26.67	26.67
33.33	26.67	26.67	40.00	35.56	26.67	26.67	26.67	NA	26.67	26.67
Confusion Matrix										
5 28	0 33	1 32	9 24	6 27	0 33	0 33	0 33	NA	0 33	0 33
2 10	0 12	1 11	3 9	2 10	0 12	0 12	0 12	NA	0 12	0 12

Table D.362: MRI_Traditional_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.50	0.48	0.52	0.52	0.51	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	83.33	100.00	100.00	100.00	100.00	NA	100.00	100.00
3.03	0.00	0.00	12.12	3.03	6.06	3.03	0.00	NA	0.00	0.00
100.00	NaN	NaN	66.67	100.00	100.00	100.00	NaN	NA	NaN	NaN
27.27	26.67	26.67	25.64	27.27	27.91	27.27	26.67	NA	26.67	26.67
28.89	26.67	26.67	31.11	28.89	31.11	28.89	26.67	NA	26.67	26.67
Confusion Matrix										
1 32	0 33	0 33	4 29	1 32	2 31	1 32	0 33	NA	0 33	0 33
0 12	0 12	0 12	2 10	0 12	0 12	0 12	0 12	NA	0 12	0 12

Table D.363: MRI_kFold_PCA_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.66	0.68	0.67	0.66	0.65	0.61	0.66	0.67	0.68	0.71	0.64
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
58.97	**56.41**	**58.97**	46.15	**58.97**	43.59	**53.85**	**53.85**	**56.41**	**76.92**	**64.10**
73.33	**78.33**	**75.00**	85.00	**71.67**	76.67	**78.33**	**78.33**	**78.33**	**65.00**	**66.67**
73.33	**73.44**	**73.77**	70.83	**72.88**	67.65	**72.31**	**72.31**	**73.44**	**81.25**	**74.07**
58.97	**62.86**	**60.53**	66.67	**57.50**	54.84	**61.76**	**61.76**	**62.86**	**58.82**	**55.56**
67.68	**69.70**	**68.69**	69.70	**66.67**	63.64	**68.69**	**68.69**	**69.70**	**69.70**	**65.66**
Confusion Matrix										
44 16	47 13	45 15	51 9	43 17	46 14	47 13	47 13	47 13	39 21	40 20
16 23	17 22	16 23	21 18	16 23	22 17	18 21	18 21	17 22	9 30	14 25

Table D.364: MRI_kFold_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.68	0.65	0.63	0.62	0.66	0.62	0.65	0.67	0.65	0.71	0.63
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
64.10	**51.28**	46.15	43.59	**61.54**	**53.85**	**53.85**	**61.54**	**51.28**	**76.92**	**58.97**
71.67	**78.33**	78.33	78.33	**73.33**	**71.67**	**75.00**	**75.00**	**78.33**	**66.67**	**66.67**
75.44	**71.21**	69.12	68.12	**74.58**	**70.49**	**71.43**	**75.00**	**71.21**	**81.63**	**71.43**
59.52	**60.61**	58.06	56.67	**60.00**	**55.26**	**58.33**	**61.54**	**60.61**	**60.00**	**53.49**
68.69	**67.68**	65.66	64.65	**68.69**	**64.65**	**66.67**	**69.70**	**67.68**	**70.71**	**63.64**
Confusion Matrix										
43 17	47 13	47 13	47 13	44 16	43 17	45 15	45 15	47 13	40 20	40 20
14 25	19 20	21 18	22 17	15 24	18 21	18 21	15 24	19 20	9 30	16 23

Table D.365: MRI_LOO_PCA_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.49	0.55	0.51	0.48	0.53	0.54	0.47	0.49	0.55	0.53
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
48.72	30.77	38.46	33.33	38.46	41.03	41.03	35.90	30.77	56.41	46.15
60.00	66.67	70.00	68.33	58.33	65.00	66.67	58.33	66.67	53.33	60.00
64.29	59.70	63.64	61.19	59.32	62.90	63.49	58.33	59.70	65.31	63.16
44.19	37.50	45.45	40.63	37.50	43.24	44.44	35.90	37.50	44.00	42.86
55.56	52.53	57.58	54.55	50.51	55.56	56.57	49.49	52.53	54.55	54.55
Confusion Matrix										
36 24	40 20	42 18	41 19	35 25	39 21	40 20	35 25	40 20	32 28	36 24
20 19	27 12	24 15	26 13	24 15	23 16	23 16	25 14	27 12	17 22	21 18

Table D.366: MRI_LOO_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.45	0.41	0.40	0.45	0.39	0.45	0.42	0.40	0.41	0.45	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
33.33	25.64	25.64	23.08	28.21	25.64	25.64	23.08	25.64	43.59	38.46
56.67	56.67	55.00	68.33	50.00	65.00	60.00	58.33	56.67	45.00	50.00
56.67	53.97	53.23	57.75	51.72	57.35	55.38	53.85	53.97	55.10	55.56
33.33	27.78	27.03	32.14	26.83	32.26	29.41	26.47	27.78	34.00	33.33
47.47	44.44	43.43	50.51	41.41	49.49	46.46	44.44	44.44	44.44	45.45
Confusion Matrix										
34 26	34 26	33 27	41 19	41 19	39 21	36 24	35 25	34 26	27 33	30 30
26 13	29 10	29 10	30 9	30 9	29 10	29 10	30 9	29 10	22 17	24 15

For label *nextEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: 81_A1_NB_diff_T1_std_bin_location_mean histogram, 34_A1_NB_ratio_T1_std_bin_ histogram.

Table D.367: MRI_Traditional_PCA_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.47	0.50	0.50	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	71.43	100.00	100.00	100.00	100.00	NA	100.00	100.00
0.00	0.00	0.00	17.74	0.00	0.00	0.00	0.00	NA	0.00	0.00
NaN	NaN	NaN	84.62	NaN	NaN	NaN	NaN	NA	NaN	NaN
10.14	10.14	10.14	8.93	10.14	10.14	10.14	10.14	NA	10.14	10.14
10.14	10.14	10.14	23.19	10.14	10.14	10.14	10.14	NA	10.14	10.14
Confusion Matrix										
0 62 0 7	0 62 0 7	0 62 0 7	11 51 2 5	0 62 0 7	0 62 0 7	0 62 0 7	0 62 0 7	NA NA	0 62 0 7	0 62 0 7

Table D.368: MRI_Traditional_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	NA	0.50	0.49
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
85.71	85.71	100.00	85.71	100.00	100.00	100.00	100.00	NA	100.00	100.00
17.74	8.06	1.61	11.29	0.00	0.00	0.00	0.00	NA	0.00	6.45
91.67	83.33	100.00	87.50	NaN	NaN	NaN	NaN	NA	NaN	100.00
10.53	9.52	10.29	9.84	10.14	10.14	10.14	10.14	NA	10.14	10.77
24.64	15.94	11.59	18.84	10.14	10.14	10.14	10.14	NA	10.14	15.94
Confusion Matrix										
11 51 1 6	5 57 1 6	1 61 0 7	7 55 1 6	0 62 0 7	0 62 0 7	0 62 0 7	0 62 0 7	NA NA	0 62 0 7	4 58 0 7

Table D.369: MRI_kFold_PCA_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.45	0.51	0.52	0.09	0.53	0.46	0.44	0.52	0.51	0.69	0.69
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
22.73	31.82	31.82	0.00	31.82	22.73	22.73	31.82	31.82	**63.64**	**63.64**
84.42	94.81	94.81	96.10	83.12	88.31	90.91	94.81	94.81	**85.71**	**85.71**
79.27	82.95	82.95	77.08	81.01	80.00	80.46	82.95	82.95	**89.19**	**89.19**
29.41	63.64	63.64	0.00	35.00	35.71	41.67	63.64	63.64	**56.00**	**56.00**
70.71	80.81	80.81	74.75	71.72	73.74	75.76	80.81	80.81	**80.81**	**80.81**
Confusion Matrix										
65 12 17 5	73 4 15 7	73 4 15 7	74 3 22 0	64 13 15 7	68 9 17 5	70 7 17 5	73 4 15 7	73 4 15 7	66 11 8 14	66 11 8 14

Table D.370: MRI_kFold_nextEDSS ≥ 5

Classifier								
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**
AUC								
0.55	0.51	0.53	0.10	0.52	0.46	0.44	0.59	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %								
36.36	31.82	31.82	0.00	31.82	22.73	22.73	40.91	31.82
90.91	94.81	94.81	96.10	80.52	88.31	90.91	92.21	96.10
83.33	82.95	82.95	77.08	80.52	80.00	80.46	84.52	83.15
53.33	63.64	63.64	0.00	31.82	35.71	41.67	60.00	70.00
78.79	80.81	80.81	74.75	69.70	73.74	75.76	80.81	81.82
Confusion Matrix								
70 7 14 8	73 4 15 7	73 4 15 7	74 3 22 0	62 15 15 7	68 9 17 5	70 7 17 5	71 6 13 9	74 3 15 7

Table D.371: MRI_LOO_PCA_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.48	0.48	0.64	0.52	0.54	0.47	0.48	0.48	0.38	0.38
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
27.27	9.09	9.09	4.55	22.73	18.18	9.09	9.09	9.09	4.55	4.55
84.42	88.31	88.31	98.70	80.52	87.01	87.01	88.31	88.31	68.83	68.83
80.25	77.27	77.27	78.35	78.48	78.82	77.01	77.27	77.27	71.62	71.62
33.33	18.18	18.18	50.00	25.00	28.57	16.67	18.18	18.18	4.00	4.00
71.72	70.71	70.71	77.78	67.68	71.72	69.70	70.71	70.71	54.55	54.55
Confusion Matrix										
65 12 16 6	68 9 20 2	68 9 20 2	76 1 21 1	62 15 17 5	67 10 18 4	67 10 20 2	68 9 20 2	68 9 20 2	53 24 21 1	53 24 21 1

Table D.372: MRI_LOO_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.58	0.56	0.39	0.53	0.54	0.56	0.53	0.58	0.49	0.54
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
18.18	18.18	18.18	0.00	27.27	18.18	18.18	18.18	18.18	31.82	31.82
87.01	90.91	89.61	96.10	79.22	87.01	89.61	85.71	90.91	76.62	66.23
78.82	79.55	79.31	77.08	79.22	78.82	79.31	78.57	79.55	79.73	77.27
28.57	36.36	33.33	0.00	27.27	28.57	33.33	26.67	36.36	28.00	21.21
71.72	74.75	73.74	74.75	67.68	71.72	73.74	70.71	74.75	66.67	58.59
Confusion Matrix										
67 10 18 4	70 7 18 4	69 8 18 4	74 3 22 0	61 16 16 6	67 10 18 4	69 8 18 4	66 11 18 4	70 7 18 4	59 18 15 7	51 26 15 7

For label *highestEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: 164_A1_CSF_ratio_T2_max_entropy, 22_A1_WM_diff_FLAIR_max_entropy.

Table D.373: MRI_Traditional_PCA_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.00	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	NaN	100.00	100.00
58.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	NaN	0.00	0.00
43.75	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN
54.55	55.56	55.56	55.56	55.56	55.56	55.56	55.56	NaN	55.56	55.56
48.15	55.56	55.56	55.56	55.56	55.56	55.56	55.56	NaN	55.56	55.56
Confusion Matrix										
7 5	0 12	0 12	0 12	0 12	0 12	0 12	0 12	0 12	0 12	0 12
9 6	0 15	0 15	0 15	0 15	0 15	0 15	0 15	0 15	0 15	0 15

Table D.374: MRI_Traditional_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.50	0.50	0.50	0.50	0.50	0.50	0.50	NA	0.50	0.00
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
86.67	100.00	100.00	100.00	100.00	100.00	100.00	100.00	NA	100.00	100.00
16.67	0.00	0.00	0.00	0.00	0.00	0.00	0.00	NA	0.00	0.00
50.00	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NA	NaN	NaN
56.52	55.56	55.56	55.56	55.56	55.56	55.56	55.56	NA	55.56	55.56
55.56	55.56	55.56	55.56	55.56	55.56	55.56	55.56	NA	55.56	55.56
Confusion Matrix										
2 10	0 12	0 12	0 12	0 12	0 12	0 12	0 12	NA	0 12	0 12
2 13	0 15	0 15	0 15	0 15	0 15	0 15	0 15	NA	0 15	0 15

Table D.375: MRI_kFold_PCA_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.67	0.71	0.75	0.67	0.69	0.68	0.70	0.73	0.71	0.65	0.71
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
72.55	**72.55**	**72.55**	**74.51**	**70.59**	**70.59**	**76.47**	**68.63**	**70.59**	**60.78**	**70.59**
62.50	**69.39**	**77.08**	**56.25**	**66.67**	**64.58**	**64.58**	**77.08**	**70.83**	**68.75**	**72.92**
68.18	**70.83**	**72.55**	**67.50**	**68.09**	**67.39**	**72.09**	**69.81**	**69.39**	**62.26**	**70.00**
67.27	**71.15**	**77.08**	**64.41**	**69.23**	**67.92**	**69.64**	**76.09**	**72.00**	**67.39**	**73.47**
67.68	**71.00**	**74.75**	**65.66**	**68.69**	**67.68**	**70.71**	**72.73**	**70.71**	**64.65**	**71.72**
Confusion Matrix										
30 18	34 15	37 11	27 21	32 16	31 17	31 17	37 11	34 14	33 15	35 13
14 37	14 37	14 37	13 38	15 36	15 36	12 39	16 35	15 36	20 31	15 36

Table D.376: MRI_kFold_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.67	0.71	0.76	0.67	0.69	0.68	0.70	0.73	0.71	0.65	0.71
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
70.59	**70.59**	**74.51**	**74.51**	**70.59**	**70.59**	**74.51**	**66.67**	**70.59**	**60.78**	**70.59**
62.50	**70.83**	**77.08**	**56.25**	**66.67**	**64.58**	**64.58**	**77.08**	**70.83**	**68.75**	**72.92**
66.67	**69.39**	**74.00**	**67.50**	**68.09**	**67.39**	**70.45**	**68.52**	**69.39**	**62.26**	**70.00**
66.67	**72.00**	**77.55**	**64.41**	**69.23**	**67.92**	**69.09**	**75.56**	**72.00**	**67.39**	**73.47**
66.67	**70.71**	**75.76**	**65.66**	**68.69**	**67.68**	**69.70**	**71.72**	**70.71**	**64.65**	**71.72**
Confusion Matrix										
30 18	34 14	37 11	27 21	32 16	31 17	31 17	37 11	34 14	33 15	35 13
15 36	15 36	13 38	13 38	15 36	15 36	13 38	17 34	15 36	20 31	15 36

Table D.377: MRI_LOO_PCA_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.53	0.57	0.56	0.59	0.58	0.58	0.57	0.53	0.55	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
64.71	**54.90**	**54.90**	**64.71**	**60.78**	**60.78**	**62.75**	**50.98**	**54.90**	**50.98**	**52.94**
52.08	**52.08**	**58.33**	**47.92**	**56.25**	**54.17**	**52.08**	**62.50**	**52.08**	**58.33**	**56.25**
58.14	**52.08**	**54.90**	**56.10**	**57.45**	**56.52**	**56.82**	**54.55**	**52.08**	**52.83**	**52.94**
58.93	**54.90**	**58.33**	**56.90**	**59.62**	**58.49**	**58.18**	**59.09**	**54.90**	**56.52**	**56.25**
58.59	**53.54**	**56.57**	**56.57**	**58.59**	**57.58**	**57.58**	**56.57**	**53.54**	**54.55**	**54.55**
Confusion Matrix										
25 23	25 23	28 20	23 25	27 21	26 22	25 23	30 18	25 23	28 20	27 21
18 33	23 28	23 28	18 33	20 31	20 31	19 32	25 26	23 28	25 26	24 27

Table D.378: MRI_LOO_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.56	0.49	0.44	0.48	0.51	0.51	0.49	0.56	0.53	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
58.82	**56.86**	47.06	52.94	50.98	54.90	56.86	43.14	**56.86**	49.02	**52.94**
45.83	**54.17**	50.00	35.42	45.83	47.92	45.83	54.17	**54.17**	56.25	**56.25**
51.16	**54.17**	47.06	41.46	46.81	50.00	50.00	47.27	**54.17**	50.94	**52.94**
53.57	**56.86**	50.00	46.55	50.00	52.83	52.73	50.00	**56.86**	54.35	**56.25**
52.53	**55.56**	48.48	44.44	48.48	51.52	51.52	48.48	**55.56**	52.53	**54.55**
Confusion Matrix										
22 26	26 22	24 24	17 31	22 26	23 25	22 26	26 22	26 22	27 21	27 21
21 30	22 29	27 24	24 27	25 26	23 28	22 29	29 22	22 29	26 25	24 27

For label *highestEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: 22_A1_WM_ratio_FLAIR_bin_location_median_median histogram.

Table D.379: MRI_Traditional_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.50	0.53	0.52	0.53	0.53	0.50	0.53	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
71.43	100.00	85.71	71.43	42.86	42.86	42.86	85.71	100.00	100.00	100.00
29.69	1.56	17.19	34.38	56.25	62.50	59.38	17.19	1.56	0.00	0.00
90.48	100.00	91.67	91.67	90.00	90.91	90.48	91.67	100.00	NaN	NaN
10.00	10.00	10.17	10.64	9.68	11.11	10.34	10.17	10.00	8.70	8.70
33.80	11.27	23.94	38.03	54.93	60.56	57.75	23.94	11.27	8.70	8.70
Confusion Matrix										
19 45 2 5	1 63 0 7	11 53 1 6	22 42 2 5	36 28 4 3	40 24 4 3	38 26 4 3	11 53 1 6	1 63 0 7	0 63 0 6	0 63 0 6

Table D.380: MRI_kFold_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.41	0.38	0.51	0.35	0.42	0.41	0.42	0.51	NA	0.51	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
23.81	23.81	33.33	19.05	23.81	23.81	23.81	33.33	NA	33.33	33.33
97.44	100.00	96.15	97.44	97.44	98.72	97.44	96.15	NA	96.15	96.15
82.61	82.98	84.27	81.72	82.61	82.80	82.61	84.27	NA	84.27	84.27
71.43	100.00	70.00	66.67	71.43	83.33	71.43	70.00	NA	70.00	70.00
81.82	83.84	82.83	80.81	81.82	82.83	81.82	82.83	NA	82.83	82.83
Confusion Matrix										
76 2 16 5	78 0 16 5	75 3 14 7	76 2 17 4	76 2 16 5	77 1 16 5	76 2 16 5	75 3 14 7	NA NA	75 3 14 7	75 3 14 7

Table D.381: MRI_LOO_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.56	0.60	0.55	0.49	0.54	0.56	0.52	0.55	NA	0.60	0.60
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
9.52	9.52	14.29	4.76	9.52	9.52	9.52	14.29	NA	19.05	19.05
94.87	96.15	91.03	94.87	93.59	94.87	92.31	91.03	NA	92.31	92.31
79.57	79.79	79.78	78.72	79.35	79.57	79.12	79.78	NA	80.90	80.90
33.33	40.00	30.00	20.00	28.57	33.33	25.00	30.00	NA	40.00	40.00
76.77	77.78	74.75	75.76	75.76	76.77	74.75	74.75	NA	76.77	76.77
Confusion Matrix										
74 4 19 2	75 3 19 2	71 7 18 3	74 4 20 1	73 5 19 2	74 4 19 2	72 6 19 2	71 7 18 3	NA NA	72 6 17 4	72 6 17 4

For label *first2EDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: 24_A1_WB_ratio_T1_gde_bin_location_mean_std histogram, raw_WM_brain_diff_F

Table D.382: MRI_Traditional_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.48	0.50	0.51	0.50	0.49	0.48	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.67	100.00	66.67	77.78	66.67	77.78	77.78	66.67	NA	100.00	100.00
27.08	0.00	31.25	25.00	35.42	27.08	20.83	31.25	NA	0.00	0.00
81.25	NaN	83.33	85.71	85.00	86.67	83.33	83.33	NA	NaN	NaN
14.63	15.79	15.38	16.28	16.22	16.67	15.56	15.38	NA	15.79	15.79
33.33	15.79	36.84	33.33	40.35	35.09	29.82	36.84	NA	15.79	15.79
Confusion Matrix										
13 35 3 6	0 48 0 9	15 33 3 6	12 36 2 7	17 31 3 6	13 35 2 7	10 38 2 7	15 33 3 6	NA NA	0 48 0 9	0 48 0 9

Table D.383: MRI_Traditional_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.51	0.49	0.49	0.50	0.47	0.49	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.67	66.67	100.00	66.67	66.67	66.67	66.67	66.67	NA	100.00	50.00
27.91	23.26	17.44	22.09	23.26	22.09	25.58	15.12	NA	7.06	29.41
96.00	95.24	100.00	95.00	95.24	95.00	95.65	92.86	NA	100.00	96.15
3.13	2.94	4.05	2.90	2.94	2.90	3.03	2.67	NA	2.47	1.64
29.21	24.72	20.22	23.60	24.72	23.60	26.97	16.85	NA	9.20	29.89
Confusion Matrix										
24 62 1 2	20 66 1 2	15 71 0 3	19 67 1 2	20 66 1 2	19 67 1 2	22 64 1 2	13 73 1 2	NA NA	6 79 0 2	25 60 1 1

Table D.384: MRI_kFold_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.41	0.44	0.36	0.45	0.45	0.45	0.44	0.39	0.56	0.56
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
26.67	16.67	20.00	13.33	23.33	20.00	20.00	20.00	16.67	36.67	36.67
76.81	95.65	95.65	91.30	71.01	76.81	89.86	95.65	95.65	81.16	81.16
70.67	72.53	73.33	70.79	68.06	68.83	72.09	73.33	72.53	74.67	74.67
33.33	62.50	66.67	40.00	25.93	27.27	46.15	66.67	62.50	45.83	45.83
61.62	71.72	72.73	67.68	56.57	59.60	68.69	72.73	71.72	67.68	67.68
Confusion Matrix										
53 16 22 8	66 3 25 5	66 3 24 6	63 6 26 4	63 6 26 4	53 16 24 6	62 7 24 6	66 3 24 6	66 3 25 5	56 13 19 11	56 13 19 11

Table D.385: MRI_kFold_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.24	0.13	0.24	0.00	0.30	0.08	0.00	0.35	0.00	0.50	0.57
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
25.00	0.00	12.50	0.00	12.50	0.00	0.00	25.00	0.00	50.00	75.00
97.80	95.60	93.41	100.00	91.21	97.80	100.00	93.41	100.00	82.42	73.63
93.68	91.58	92.39	91.92	92.22	91.75	91.92	93.41	91.92	94.94	97.10
50.00	0.00	14.29	NaN	11.11	0.00	NaN	25.00	NaN	20.00	20.00
91.92	87.88	86.87	91.92	84.85	89.90	91.92	87.88	91.92	79.80	73.74
Confusion Matrix										
89 2 6 2	87 4 8 0	85 6 7 1	91 0 8 0	83 8 7 1	89 2 8 0	91 0 8 0	85 6 6 2	91 0 8 0	75 16 4 4	67 24 2 6

Table D.386: MRI_LOO_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.52	0.52	0.54	0.50	0.53	0.47	0.52	0.52	0.44	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
20.00	10.00	10.00	10.00	26.67	26.67	10.00	10.00	10.00	16.67	16.67
75.36	91.30	91.30	92.75	72.46	78.26	86.96	91.30	91.30	72.46	72.46
68.42	70.00	70.00	70.33	69.44	71.05	68.97	70.00	70.00	66.67	66.67
26.09	33.33	33.33	37.50	29.63	34.78	25.00	33.33	33.33	20.83	20.83
58.59	66.67	66.67	67.68	58.59	62.63	63.64	66.67	66.67	55.56	55.56
Confusion Matrix										
52 17 24 6	63 6 27 3	63 6 27 3	64 5 27 3	50 19 22 8	54 15 22 8	60 9 27 3	63 6 27 3	63 6 27 3	50 19 25 5	50 19 25 5

Table D.387: MRI_LOO_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.46	0.46	0.00	0.46	0.46	0.00	0.46	0.00	0.48	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
12.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	12.50	37.50
96.70	96.70	92.31	100.00	90.11	97.80	100.00	91.21	100.00	79.12	70.33
92.63	91.67	91.30	91.92	91.11	91.75	91.92	91.21	91.92	91.14	92.75
25.00	0.00	0.00	NaN	0.00	0.00	NaN	0.00	NaN	5.00	10.00
89.90	88.89	84.85	91.92	82.83	89.90	91.92	83.84	91.92	73.74	67.68
Confusion Matrix										
88 3 7 1	88 3 8 0	84 7 8 0	91 0 8 0	82 9 8 0	89 2 8 0	91 0 8 0	83 8 8 0	91 0 8 0	72 19 7 1	64 27 5 3

For label *first2EDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: 24_A1_WB_ratio_T1_gde_bin_location_mean_std histogram, raw_WM_brain_diff_F

Table D.388: MRI_Traditional_PCA_first2EDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.48	0.50	0.51	0.50	0.49	0.48	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.67	100.00	66.67	77.78	66.67	77.78	77.78	66.67	NA	100.00	100.00
27.08	0.00	31.25	25.00	35.42	27.08	20.83	31.25	NA	0.00	0.00
81.25	NaN	83.33	85.71	85.00	86.67	83.33	83.33	NA	NaN	NaN
14.63	15.79	15.38	16.28	16.22	16.67	15.56	15.38	NA	15.79	15.79
33.33	15.79	36.84	33.33	40.35	35.09	29.82	36.84	NA	15.79	15.79
Confusion Matrix										
13 35 3 6	0 48 0 9	15 33 3 6	12 36 2 7	17 31 3 6	13 35 2 7	10 38 2 7	15 33 3 6	NA NA	0 48 0 9	0 48 0 9

Table D.389: MRI_Traditional_first2EDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.51	0.49	0.49	0.50	0.47	0.49	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.67	66.67	100.00	66.67	66.67	66.67	66.67	66.67	NA	100.00	50.00
27.91	23.26	17.44	22.09	23.26	22.09	25.58	15.12	NA	7.06	29.41
96.00	95.24	100.00	95.00	95.24	95.00	95.65	92.86	NA	100.00	96.15
3.13	2.94	4.05	2.90	2.94	2.90	3.03	2.67	NA	2.47	1.64
29.21	24.72	20.22	23.60	24.72	23.60	26.97	16.85	NA	9.20	29.89
Confusion Matrix										
24 62 1 2	20 66 1 2	15 71 0 3	19 67 1 2	20 66 1 2	19 67 1 2	22 64 1 2	13 73 1 2	NA NA	6 79 0 2	25 60 1 1

Table D.390: MRI_kFold_PCA_first2EDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.41	0.44	0.36	0.45	0.45	0.45	0.44	0.39	0.56	0.56
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
26.67	16.67	20.00	13.33	23.33	20.00	20.00	20.00	16.67	36.67	36.67
76.81	95.65	95.65	91.30	71.01	76.81	89.86	95.65	95.65	81.16	81.16
70.67	72.53	73.33	70.79	68.06	68.83	72.09	73.33	72.53	74.67	74.67
33.33	62.50	66.67	40.00	25.93	27.27	46.15	66.67	62.50	45.83	45.83
61.62	71.72	72.73	67.68	56.57	59.60	68.69	72.73	71.72	67.68	67.68
Confusion Matrix										
53 16 22 8	66 3 25 5	66 3 24 6	63 6 26 4	63 6 26 4	53 16 24 6	62 7 24 6	66 3 24 6	66 3 25 5	56 13 19 11	56 13 19 11

Table D.391: MRI_kFold_first2EDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.24	0.13	0.24	0.00	0.30	0.08	0.00	0.35	0.00	0.50	0.57
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
25.00	0.00	12.50	0.00	12.50	0.00	0.00	25.00	0.00	50.00	75.00
97.80	95.60	93.41	100.00	91.21	97.80	100.00	93.41	100.00	82.42	73.63
93.68	91.58	92.39	91.92	92.22	91.75	91.92	93.41	91.92	94.94	97.10
50.00	0.00	14.29	NaN	11.11	0.00	NaN	25.00	NaN	20.00	20.00
91.92	87.88	86.87	91.92	84.85	89.90	91.92	87.88	91.92	79.80	73.74
Confusion Matrix										
89 2 6 2	87 4 8 0	85 6 7 1	91 0 8 0	83 8 7 1	89 2 8 0	91 0 8 0	85 6 6 2	91 0 8 0	75 16 4 4	67 24 2 6

Table D.392: MRI_LOO_PCA_first2EDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.52	0.52	0.54	0.50	0.53	0.47	0.52	0.52	0.44	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
20.00	10.00	10.00	10.00	26.67	26.67	10.00	10.00	10.00	16.67	16.67
75.36	91.30	91.30	92.75	72.46	78.26	86.96	91.30	91.30	72.46	72.46
68.42	70.00	70.00	70.33	69.44	71.05	68.97	70.00	70.00	66.67	66.67
26.09	33.33	33.33	37.50	29.63	34.78	25.00	33.33	33.33	20.83	20.83
58.59	66.67	66.67	67.68	58.59	62.63	63.64	66.67	66.67	55.56	55.56
Confusion Matrix										
52 17 24 6	63 6 27 3	63 6 27 3	64 5 27 3	50 19 22 8	54 15 22 8	60 9 27 3	63 6 27 3	63 6 27 3	50 19 25 5	50 19 25 5

Table D.393: MRI_LOO_first2EDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.46	0.46	0.00	0.46	0.46	0.00	0.46	0.00	0.48	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
12.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	12.50	37.50
96.70	96.70	92.31	100.00	90.11	97.80	100.00	91.21	100.00	79.12	70.33
92.63	91.67	91.30	91.92	91.11	91.75	91.92	91.21	91.92	91.14	92.75
25.00	0.00	0.00	NaN	0.00	0.00	NaN	0.00	NaN	5.00	10.00
89.90	88.89	84.85	91.92	82.83	89.90	91.92	83.84	91.92	73.74	67.68
Confusion Matrix										
88 3 7 1	88 3 8 0	84 7 8 0	91 0 8 0	82 9 8 0	89 2 8 0	91 0 8 0	83 8 8 0	91 0 8 0	72 19 7 1	64 27 5 3

For label *tendencyEDSS* (0/1 - (Down or Equal)/Up:

Final features: 88_A1_WB_ratio_T1_bin_location_median_std histogram, T1_gde_GM_median_std
fft, T1_gde_WM_median_histogram_16, Anatomical_27_FLAIR_std_histogram_19, 24_A1_WM_ratio_F

Table D.394: MRI_Traditional_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.50	0.53	0.57	0.56	0.56	0.60	0.53	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
62.50	100.00	87.50	62.50	62.50	62.50	62.50	87.50	100.00	100.00	100.00
52.73	0.00	18.18	47.27	54.55	49.09	52.73	18.18	0.00	0.00	0.00
90.63	NaN	90.91	89.66	90.91	90.00	90.63	90.91	NaN	NaN	NaN
16.13	12.70	13.46	14.71	16.67	15.15	16.13	13.46	12.70	12.70	12.70
53.97	12.70	26.98	49.21	55.56	50.79	53.97	26.98	12.70	12.70	12.70
Confusion Matrix										
29 26 3 5	0 55 0 8	10 45 1 7	26 29 3 5	30 25 3 5	27 28 3 5	29 26 3 5	10 45 1 7	0 55 0 8	0 55 0 8	0 55 0 8

Table D.395: MRI_Traditional_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.53	0.56	0.54	0.53	0.53	0.53	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
87.50	100.00	87.50	12.50	12.50	12.50	0.00	75.00	100.00	100.00	100.00
14.55	0.00	23.64	100.00	96.36	100.00	100.00	27.27	0.00	0.00	0.00
88.89	NaN	92.86	88.71	88.33	88.71	87.30	88.24	NaN	NaN	NaN
12.96	12.70	14.29	100.00	33.33	100.00	NaN	13.04	12.70	12.70	12.70
23.81	12.70	31.75	88.89	85.71	88.89	87.30	33.33	12.70	12.70	12.70
Confusion Matrix										
8 47 1 7	0 55 0 8	13 42 1 7	55 0 7 1	53 2 7 1	55 0 7 1	55 0 8 0	15 40 2 6	0 55 0 8	0 55 0 8	0 55 0 8

Table D.396: MRI_kFold_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.37	0.43	0.09	0.53	0.44	0.45	0.43	0.37	0.47	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
26.92	19.23	23.08	0.00	34.62	19.23	23.08	23.08	19.23	26.92	26.92
82.19	98.63	98.63	95.89	75.34	86.30	93.15	98.63	98.63	95.89	95.89
75.95	77.42	78.26	72.92	76.39	75.00	77.27	78.26	77.42	78.65	78.65
35.00	83.33	85.71	0.00	33.33	33.33	54.55	85.71	83.33	70.00	70.00
67.68	77.78	78.79	70.71	64.65	68.69	74.75	78.79	77.78	77.78	77.78
Confusion Matrix										
60 13 19 7	72 1 21 5	72 1 20 6	70 3 26 0	55 18 17 9	63 10 21 5	68 5 20 6	72 1 20 6	72 1 21 5	70 3 19 7	70 3 19 7

Table D.397: MRI_kFold_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.77	0.78	0.79	0.53	0.58	0.50	0.77	NA	0.48	0.77
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
42.31	**61.54**	**69.23**	**66.67**	34.62	34.62	26.92	**69.23**	NA	26.92	**73.08**
83.56	**95.89**	**91.78**	**93.15**	76.71	91.78	93.15	**91.78**	NA	95.89	**87.67**
80.26	**87.50**	**89.33**	**88.31**	76.71	79.76	78.16	**89.33**	NA	78.65	**90.14**
47.83	**84.21**	**75.00**	**78.26**	34.62	60.00	58.33	**75.00**	NA	70.00	**67.86**
72.73	**86.87**	**85.86**	**86.00**	65.66	76.77	75.76	**85.86**	NA	77.78	**83.84**
Confusion Matrix										
61 12 15 11	70 3 10 16	67 6 8 18	68 5 9 18	56 17 17 9	67 6 17 9	68 5 19 7	67 6 8 18	NA NA	70 3 19 7	64 9 7 19

Table D.398: MRI_LOO_PCA_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.54	0.59	0.36	0.47	0.46	0.45	0.59	0.54	0.45	0.45
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
15.38	7.69	11.54	0.00	23.08	11.54	7.69	11.54	7.69	7.69	7.69
78.08	94.52	94.52	95.89	71.23	83.56	87.67	94.52	94.52	87.67	87.67
72.15	74.19	75.00	72.92	72.22	72.62	72.73	75.00	74.19	72.73	72.73
20.00	33.33	42.86	0.00	22.22	20.00	18.18	42.86	33.33	18.18	18.18
61.62	71.72	72.73	70.71	58.59	64.65	66.67	72.73	71.72	66.67	66.67
Confusion Matrix										
57 16 22 4	69 4 24 2	69 4 23 3	70 3 26 0	52 21 20 6	61 12 23 3	64 9 24 2	69 4 23 3	69 4 24 2	64 9 24 2	64 9 24 2

Table D.399: MRI_LOO_tendencyEDSS

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.46	0.44	0.44	0.53	0.38	0.45	0.44	NA	0.47	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
15.38	15.38	15.38	15.38	30.77	3.85	7.69	15.38	NA	7.69	23.08
78.08	78.08	72.60	73.97	75.34	80.82	86.30	73.97	NA	89.04	69.86
72.15	72.15	70.67	71.05	75.34	70.24	72.41	71.05	NA	73.03	71.83
20.00	20.00	16.67	17.39	30.77	6.67	16.67	17.39	NA	20.00	21.43
61.62	61.62	57.58	58.59	63.64	60.61	65.66	58.59	NA	67.68	57.58
Confusion Matrix										
57 16 22 4	57 16 22 4	53 20 22 4	54 19 22 4	55 18 18 8	59 14 25 1	63 10 24 2	54 19 22 4	NA NA	65 8 24 2	51 22 20 6

For label *mediumEDSS* > 3 **(0/1 -** $(< 3)/(\geq 3)$**:**

Final features: 66_A1_BO_ratio_T2_std_entropy, 121_A1_BO_ratio_T2_raw_std_mean, 48_A1_CSF_ratio_T2_std_energy_glcm, 92_A1_CSF_ratio_T2_mean_std histogram, 22_A1_WM_diff_FL 22_A1_WM_ratio_FLAIR_max_entropy, 85_A1_WM_ratio_FLAIR_max_entropy.

Table D.400: MRI_Traditional_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.50	0.48	0.48	0.43	0.50	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.67	100.00	91.67	66.67	66.67	100.00	100.00	100.00	NA	100.00	100.00
27.59	0.00	3.45	24.14	24.14	0.00	0.00	0.00	NA	0.00	0.00
66.67	NaN	50.00	63.64	63.64	NaN	NaN	NaN	NA	NaN	NaN
27.59	29.27	28.21	26.67	26.67	29.27	29.27	29.27	NA	29.27	29.27
39.02	29.27	29.27	36.59	36.59	29.27	29.27	29.27	NA	29.27	29.27
Confusion Matrix										
8 21 4 8	0 29 0 12	1 28 1 11	7 22 4 8	7 22 4 8	0 29 0 12	0 29 0 12	0 29 0 12	NA NA	0 29 0 12	0 29 0 12

Table D.401: MRI_Traditional_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.46	0.49	0.41	0.50	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
58.33	100.00	75.00	58.33	58.33	100.00	100.00	100.00	NA	100.00	100.00
41.38	0.00	13.79	37.93	24.14	0.00	0.00	0.00	NA	0.00	0.00
70.59	NaN	57.14	68.75	58.33	NaN	NaN	NaN	NA	NaN	NaN
29.17	29.27	26.47	28.00	24.14	29.27	29.27	29.27	NA	29.27	29.27
46.34	29.27	31.71	43.90	34.15	29.27	29.27	29.27	NA	29.27	29.27
Confusion Matrix										
12 17	0 29	4 25	11 18	7 22	0 29	0 29	0 29	NA	0 29	0 29
5 7	0 12	3 9	5 7	5 7	0 12	0 12	0 12	NA	0 12	0 12

Table D.402: MRI_kFold_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.65	0.66	0.69	0.60	0.63	0.66	0.70	0.69	0.66	0.71	0.67
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
58.54	**51.22**	**58.54**	43.90	**56.10**	**60.98**	**65.85**	**53.66**	**51.22**	**75.61**	**63.41**
68.97	**79.31**	**77.59**	74.14	**67.24**	**70.69**	**74.14**	**81.03**	**79.31**	**68.97**	**72.41**
70.18	**69.70**	**72.58**	65.15	**68.42**	**71.93**	**75.44**	**71.21**	**69.70**	**80.00**	**73.68**
57.14	**63.64**	**64.86**	54.55	**54.76**	**59.52**	**64.29**	**66.67**	**63.64**	**63.27**	**61.90**
64.65	**67.68**	**69.70**	61.62	**62.63**	**66.67**	**70.71**	**69.70**	**67.68**	**71.72**	**68.69**
Confusion Matrix										
40 18	46 12	45 13	43 15	39 19	41 17	43 15	47 11	46 12	40 18	42 16
17 24	20 21	17 24	23 18	18 23	16 25	14 27	19 22	20 21	10 31	15 26

Table D.403: MRI_kFold_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.70	0.69	0.68	0.72	0.71	0.70	0.72	0.71	0.69	0.72	0.70
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
63.41	**63.41**	**58.54**	**56.10**	**60.98**	**68.29**	**68.29**	**68.29**	**63.41**	**75.61**	**73.17**
74.58	**74.14**	**74.58**	**82.76**	**79.31**	**72.41**	**75.86**	**74.14**	**74.14**	**68.97**	**67.24**
74.58	**74.14**	**72.13**	**72.73**	**74.19**	**76.36**	**77.19**	**76.79**	**74.14**	**80.00**	**78.00**
63.41	**63.41**	**61.54**	**69.70**	**67.57**	**63.64**	**66.67**	**65.12**	**63.41**	**63.27**	**61.22**
70.00	**69.70**	**68.00**	**71.72**	**71.72**	**70.71**	**72.73**	**71.72**	**69.70**	**71.72**	**69.70**
Confusion Matrix										
44 15	43 15	44 15	48 10	46 12	42 16	44 14	43 15	43 15	40 18	39 19
15 26	15 26	17 24	18 23	16 25	13 28	13 28	13 28	15 26	10 31	11 30

Table D.404: MRI_LOO_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.43	0.48	0.52	0.50	0.40	0.40	0.42	0.43	0.39	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
39.02	26.83	36.59	34.15	41.46	29.27	31.71	24.39	26.83	36.59	34.15
60.34	60.34	60.34	68.97	58.62	50.00	48.28	62.07	60.34	41.38	53.45
58.33	53.85	57.38	59.70	58.62	50.00	50.00	53.73	53.85	48.00	53.45
41.03	32.35	39.47	43.75	41.46	29.27	30.23	31.25	32.35	30.61	34.15
51.52	46.46	50.51	54.55	51.52	41.41	41.41	46.46	46.46	39.39	45.45
Confusion Matrix										
35 23	35 23	35 23	40 18	34 24	29 29	28 30	36 22	35 23	24 34	31 27
25 16	30 11	26 15	27 14	24 17	29 12	28 13	31 10	30 11	26 15	27 14

Table D.405: MRI_LOO_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.57	0.51	0.51	0.48	0.53	0.48	0.57	0.57	0.47	0.53
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
46.34	**51.22**	39.02	34.15	34.15	48.78	41.46	53.66	**51.22**	46.34	53.66
60.34	**63.79**	62.07	67.24	62.07	56.90	55.17	60.34	**63.79**	48.28	51.72
61.40	**64.91**	59.02	59.09	57.14	61.11	57.14	64.81	**64.91**	56.00	61.22
45.24	**50.00**	42.11	42.42	38.89	44.44	39.53	48.89	**50.00**	38.78	44.00
54.55	**58.59**	52.53	53.54	50.51	53.54	49.49	57.58	**58.59**	47.47	52.53
Confusion Matrix										
35 23	37 21	36 22	39 19	36 22	33 25	32 26	35 23	37 21	28 30	30 28
22 19	20 21	25 16	27 14	27 14	21 20	24 17	19 22	20 21	22 19	19 22

For label *mediumEDSS* > 5 **(0/1 -** $(< 5)/(\geq 5)$**:**

Final features: 48_A1_BO_diff_T2_raw_std_mean, 48_A1_BO_ratio_T2_raw_mean_mean, 48_A1_BO_ratio_T2_raw_std_mean, 61_A1_BO_ratio_T2_raw_std_mean, Anatomical_31_DP_mean_hist
Anatomical_31_DP_std_histogram_18.

Table D.406: MRI_Traditional_PCA_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.49	0.48	0.49	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	75.00	100.00	100.00	100.00	NA	100.00	100.00
2.74	1.37	2.74	4.11	12.33	4.11	1.37	4.11	NA	1.37	1.37
100.00	100.00	100.00	100.00	90.00	100.00	100.00	100.00	NA	100.00	100.00
5.33	5.26	5.33	5.41	4.48	5.41	5.26	5.41	NA	5.26	5.26
7.79	6.49	7.79	9.09	15.58	9.09	6.49	9.09	NA	6.49	6.49
Confusion Matrix										
2 71	1 72	2 71	3 70	9 64	3 70	1 72	3 70	NA	1 72	1 72
0 4	0 4	0 4	0 4	1 3	0 4	0 4	0 4	NA	0 4	0 4

Table D.407: MRI_Traditional_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	NA	NA	0.49	0.45	0.50	0.50	NA	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	NA	NA	100.00	75.00	100.00	100.00	NA	NA	100.00	100.00
8.22	NA	NA	5.48	17.81	1.37	1.37	NA	NA	0.00	10.96
100.00	NA	NA	100.00	92.86	100.00	100.00	NA	NA	NaN	100.00
5.63	NA	NA	5.48	4.76	5.26	5.26	NA	NA	5.19	5.80
12.99	NA	NA	10.39	20.78	6.49	6.49	NA	NA	5.19	15.58
Confusion Matrix										
6 67	NA	NA	4 69	13 60	1 72	1 72	NA	NA	0 73	8 65
0 4	NA	NA	0 4	1 3	0 4	0 4	NA	NA	0 4	0 4

Table D.408: MRI_kFold_PCA_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.43	0.41	0.35	0.18	0.45	0.42	0.45	0.40	0.24	0.66	0.63
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
26.67	26.67	20.00	13.33	26.67	26.67	33.33	26.67	13.33	73.33	73.33
90.48	95.24	94.05	100.00	89.29	91.67	95.24	95.24	97.62	82.14	82.14
87.36	87.91	86.81	86.60	87.21	87.50	88.89	87.91	86.32	94.52	94.52
33.33	50.00	37.50	100.00	30.77	36.36	55.56	50.00	50.00	42.31	42.31
80.81	84.85	82.83	86.87	79.80	81.82	85.86	84.85	84.85	80.81	80.81
Confusion Matrix										
76 8	80 4	79 5	84 0	75 9	77 7	80 4	80 4	82 2	69 15	69 15
11 4	11 4	12 3	13 2	11 4	11 4	10 5	11 4	13 2	4 11	4 11

Table D.409: MRI_kFold_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	NA	NA	0.23	0.45	0.44	0.45	NA	NA	0.65	0.66
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
53.33	NA	NA	13.33	26.67	26.67	33.33	NA	NA	73.33	**66.67**
91.67	NA	NA	97.62	88.10	91.67	95.24	NA	NA	82.14	**88.10**
91.67	NA	NA	86.32	87.06	87.50	88.89	NA	NA	94.52	**93.67**
53.33	NA	NA	50.00	28.57	36.36	55.56	NA	NA	42.31	**50.00**
85.86	NA	NA	84.85	78.79	81.82	85.86	NA	NA	80.81	**84.85**
Confusion Matrix										
77 7	NA	NA	82 2	74 10	77 7	80 4	NA	NA	69 15	74 10
7 8	NA	NA	13 2	11 4	11 4	10 5	NA	NA	4 11	5 10

Table D.410: MRI_LOO_PCA_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.45	0.48	0.49	0.42	0.41	0.41	0.42	0.48	0.42	0.48	0.46
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
6.67	6.67	6.67	0.00	0.00	0.00	0.00	6.67	0.00	20.00	13.33
84.52	90.48	91.67	97.62	84.52	86.90	89.29	90.48	95.24	72.62	73.81
83.53	84.44	84.62	84.54	82.56	82.95	83.33	84.44	84.21	83.56	82.67
7.14	11.11	12.50	0.00	0.00	0.00	0.00	11.11	0.00	11.54	8.33
72.73	77.78	78.79	82.83	71.72	73.74	75.76	77.78	80.81	64.65	64.65
Confusion Matrix										
71 13	76 8	77 7	82 2	71 13	73 11	75 9	76 8	80 4	61 23	62 22
14 1	14 1	14 1	15 0	15 0	15 0	15 0	14 1	15 0	12 3	13 2

Table D.411: MRI_LOO_PCA_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	NA	NA	0.23	0.45	0.44	0.45	NA	NA	0.65	0.66
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
20.00	NA	NA	6.67	26.67	13.33	6.67	NA	NA	20.00	20.00
84.52	NA	NA	96.43	88.10	89.29	90.48	NA	NA	72.62	82.14
85.54	NA	NA	85.26	87.06	85.23	84.44	NA	NA	83.56	85.19
18.75	NA	NA	25.00	28.57	18.18	11.11	NA	NA	11.54	16.67
74.75	NA	NA	82.83	78.79	77.78	77.78	NA	NA	64.65	72.73
Confusion Matrix										
71 13	NA	NA	81 3	74 10	75 9	76 8	NA	NA	61 23	69 15
12 3	NA	NA	14 1	11 4	13 2	14 1	NA	NA	12 3	12 3

D.3 Lesion Set

D.3.1 One sample, one lesion Set

D.3.1.1 Standard procedure

For label *msCourse* (0/1 - RR/SP):

Final features: Mean Pixel Intensity/slice_meanPixel, Max Pixel Intensity/slice_meanPixel, T2_Median Pixel Intensity/slice_meanPixel, T1_Mean Pixel Intensity/slice_meanPixel, T1_Max Pixel Intensity/slice_meanPixel, T1_Min Pixel Intensity/slice_meanPixel, T1_gdeMean Pixel Intensity/slice_meanPixel, T1_gdeMax Pixel Intensity/slice_meanPixel, T1_gdeMin Pixel Intensity/slice_meanPixel, DP_Mean Pixel Intensity/slice_meanPixel, DP_Max Pixel Intensity/slice_meanPixel, DP_Min Pixel Intensity/slice_meanPixel.

Table D.412: One_sample_One_Lesion_Traditional_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.62	0.54	0.49	0.47	0.47	0.47	0.50	0.62	0.53	0.62
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
39.67	88.23	89.49	1.99	28.62	33.82	40.22	100.00	88.23	97.83	88.23
62.41	34.94	19.19	95.87	64.61	59.27	53.27	0.14	34.94	8.61	34.94
84.47	93.98	90.57	83.72	82.64	82.45	82.41	100.00	93.98	95.42	93.98
16.72	20.51	17.40	8.40	13.33	13.66	14.07	16.00	20.51	16.92	20.51
58.77	43.46	30.43	80.86	58.86	55.20	51.19	16.10	43.46	22.87	43.46
Confusion Matrix										
1811 1091	1014 1888	557 2345	2782 120	1875 1027	1720 1182	1546 1356	4 2898	1014 1888	250 2652	1014 1888
333 219	65 487	58 494	541 11	394 158	366 187	330 222	0 552	65 487	12 540	65 487

Table D.413: One_sample_One_Lesion_Traditional_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.61	0.54	0.49	0.47	0.47	0.47	0.50	NA	0.53	0.61
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
39.31	87.50	90.04	1.45	27.17	30.80	38.04	99.82	NA	97.28	87.50
63.09	35.29	18.30	96.55	66.27	62.34	55.93	0.62	NA	9.20	35.29
84.53	93.69	90.61	83.74	82.71	82.57	82.60	94.74	NA	94.68	93.69
16.85	20.46	17.33	7.41	13.29	13.46	14.10	16.04	NA	16.93	20.46
59.29	43.63	29.76	81.36	60.02	57.30	53.07	16.47	NA	23.28	43.63
Confusion Matrix										
1831 1071	1024 1878	531 2371	2802 100	1923 979	1809 1093	1623 1279	18 2884	NA	267 2635	1024 1878
335 217	69 483	55 497	544 8	402 150	382 170	342 210	1 551	NA	15 537	69 483

For label *currentEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: T1_Var Pixel Intensity/slice_meanPixel, Median Pixel Intensity/slice_meanPixel, T2_Var Pixel Intensity/slice_meanPixel, Max Pixel Intensity/slice_meanPixel, T1_gdeVar Pixel Intensity/slice_meanPixel, DP_Var Pixel Intensity/slice_meanPixel,

Var Pixel Intensity/slice_meanPixel, T2_Max Pixel Intensity/slice_meanPixel, Eccentricity.

Table D.414: One_sample_One_Lesion_Traditional_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.58	0.54	0.52	0.50	0.51	0.52	0.50	0.58	0.50	0.58
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
61.74	42.52	66.50	76.19	50.85	66.33	72.28	99.66	42.52	100.00	42.52
36.50	72.55	41.91	27.15	49.22	35.94	30.90	0.63	72.55	0.00	72.55
81.39	85.27	85.15	83.95	82.12	83.03	83.64	89.47	85.27	NaN	85.27
17.49	25.25	19.98	18.57	17.93	18.42	18.58	17.95	25.25	17.91	25.25
41.02	67.17	46.32	35.93	49.51	41.38	38.31	18.36	67.17	17.91	67.17
Confusion Matrix										
984 1712	1956 740	1130 1566	732 1964	1327 1369	969 1727	833 1863	17 2679	1956 740	0 2696	1956 740
225 363	338 250	197 391	140 448	289 299	198 390	163 425	2 586	338 250	0 588	338 250

Table D.415: One_sample_One_Lesion_Traditional_PCA_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.50	0.51	0.51	0.49	0.49	0.49	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
37.69	100.00	76.19	92.35	32.31	38.61	44.39	100.00	100.00	100.00	100.00
59.90	0.00	26.56	10.61	65.73	59.72	53.95	0.00	0.00	0.00	0.00
81.48	NaN	83.65	86.41	81.66	81.68	81.65	NaN	NaN	NaN	NaN
17.04	17.91	18.45	18.39	17.06	17.29	17.37	17.91	17.91	17.91	17.91
55.92	17.91	35.45	25.24	59.74	55.94	52.24	17.91	17.91	17.91	17.91
Confusion Matrix										
1615 1081	0 2696	716 1980	286 2410	1772 924	1610 1086	1455 1242	0 2696	0 2696	0 2696	0 2696
367 222	0 588	140 448	45 543	398 190	361 227	327 261	0 588	0 588	0 588	0 588

For label *currentEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$:

Final features: RefSpace, Mean Pixel Intensity/slice_meanPixel, T2_Min Pixel Intensity/slice_meanPixel, T1_Mean Pixel Intensity/slice_meanPixel, T1_Max Pixel Intensity/slice_meanPixel, T1_Min Pixel Intensity/slice_meanPixel, T1_gdeMean Pixel Intensity/slice_meanPixel, T1_gdeMax Pixel Intensity/slice_meanPixel, T1_gdeMin Pixel Intensity/slice_meanPixel, DP_Mean Pixel Intensity/slice_meanPixel, DP_Max Pixel Intensity/slice_meanPixel, DP_Min Pixel Intensity/slice_meanPixel.

Table D.416: One_sample_One_Lesion_Traditional_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.51	0.50	0.50	0.49	0.48	0.48	0.50	0.51	0.50	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
24.21	2.40	0.74	1.85	52.87	52.87	55.82	0.00	2.40	0.00	2.40
74.72	99.43	99.70	98.48	44.85	42.52	39.89	100.00	99.43	100.00	99.43
84.38	84.80	84.62	84.60	83.90	83.17	83.18	84.56	84.80	84.56	84.80
14.89	43.33	30.77	18.18	14.90	14.38	14.50	NaN	43.33	NaN	43.33
66.92	84.45	84.42	83.56	46.09	44.12	42.35	84.56	84.45	84.56	84.45
Confusion Matrix										
2214 749	2946 17	2954 9	2918 45	1329 1634	1260 1703	1182 1781	2963 0	2946 17	2963 0	2946 17
410 131	528 13	537 4	531 10	255 286	255 286	239 302	541 0	528 13	541 0	528 13

Table D.417: One_sample_One_Lesion_Traditional_PCA_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.50	0.50	0.50	0.48	0.47	0.46	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.48	0.55	0.00	1.11	54.34	54.53	56.01	0.00	0.55	0.00	0.55
52.68	99.73	99.97	99.70	40.90	38.58	36.96	100.00	99.73	100.00	99.73
82.90	84.60	84.56	84.67	83.07	82.29	82.15	84.56	84.60	84.56	84.60
13.51	27.27	0.00	40.00	14.38	13.95	13.96	NaN	27.27	NaN	27.27
50.80	84.42	84.53	84.48	42.98	41.04	39.90	84.56	84.42	84.56	84.42
Confusion Matrix										
1561 1402	2955 8	2962 1	2954 9	1212 1751	1143 1820	1095 1868	2963 0	2955 8	2963 0	2955 8
322 219	538 3	541 0	535 6	247 294	246 295	238 303	541 0	538 3	541 0	538 3

For label *nextEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: T1_gdeVar Pixel Intensity/slice_meanPixel.

Table D.418: One_sample_One_Lesion_Traditional_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.50	0.50	0.51	0.52	0.52	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
55.72	99.89	12.10	78.51	51.62	55.40	57.13	12.10	99.89	100.00	100.00
47.07	0.00	88.01	21.94	50.77	47.96	46.05	88.01	0.00	0.00	0.00
47.37	0.00	45.88	46.36	47.05	47.66	47.63	45.88	0.00	NaN	NaN
55.42	54.13	54.37	54.29	55.32	55.70	55.57	54.37	54.13	54.15	54.15
51.75	54.09	46.90	52.57	51.23	51.99	52.05	46.90	54.09	54.15	54.15
Confusion Matrix										
369 415	0 784	690 94	172 612	398 386	376 408	361 423	690 94	0 784	0 784	0 784
410 516	1 925	814 112	199 727	448 478	413 513	397 529	814 112	1 925	0 926	0 926

For label *nextEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: RefSpace, Mean Pixel Intensity/slice_meanPixel, Max Pixel Intensity/slice_meanPixel, T2_Mean Pixel Intensity/slice_meanPixel, T2_Min Pixel

Intensity/slice_meanPixel, T1_Mean Pixel Intensity/slice_meanPixel, T1_Min Pixel Intensity/slice_meanPixel, T1_gdeMax Pixel Intensity/slice_meanPixel, T1_gdeMin Pixel Intensity/slice_meanPixel, T1_gdeMedian Pixel Intensity/slice_meanPixel, DP_Mean Pixel Intensity/slice_meanPixel, DP_Max Pixel Intensity/slice_meanPixel.

Table D.419: One_sample_One_Lesion_Traditional_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.59	0.55	0.50	0.50	0.51	0.51	0.52	0.59	0.60	0.59
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
42.01	24.83	82.14	4.25	26.53	29.42	35.03	94.39	24.83	37.25	24.83
59.57	92.88	28.00	96.37	72.74	71.66	67.17	9.05	92.88	82.42	92.88
82.49	85.00	87.79	82.19	81.95	82.32	82.58	88.09	85.00	85.76	85.00
18.47	43.20	19.93	20.33	17.51	18.46	18.88	18.46	43.20	31.60	43.20
56.43	80.69	37.70	79.87	64.46	64.10	61.42	24.33	80.69	74.33	80.69
Confusion Matrix										
1606 1090 341 247	2504 192 442 146	755 1941 105 483	2598 98 563 25	1961 735 432 156	1932 764 415 173	1811 885 382 206	244 2452 33 555	2504 192 442 146	2222 474 369 219	2504 192 442 146

Table D.420: One_sample_One_Lesion_Traditional_PCA_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.63	0.52	0.51	0.50	0.51	0.51	0.51	0.63	0.60	0.63
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
59.18	68.54	94.56	5.61	29.25	35.03	40.99	98.81	68.54	39.97	68.54
43.58	58.23	10.09	96.29	71.07	66.28	60.83	2.45	58.23	79.94	58.23
83.04	89.46	89.47	82.39	82.16	82.39	82.54	90.41	89.46	85.93	89.46
18.62	26.36	18.66	24.81	18.07	18.48	18.58	18.09	26.36	30.28	26.36
46.38	60.08	25.21	80.06	63.58	60.69	57.28	19.70	60.08	72.79	60.08
Confusion Matrix										
1175 1521 240 348	1570 1126 185 403	272 2424 32 556	2596 100 555 33	1916 780 416 172	1787 909 382 206	1640 1056 347 241	66 2630 7 581	1570 1126 185 403	2156 541 353 235	1570 1126 185 403

For label *mediumEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$:

Final features: T2_Mean Pixel Intensity/slice_meanPixel, T2_Min Pixel Intensity/slice_meanPixel, T1_Mean Pixel Intensity/slice_meanPixel, T1_Min Pixel Intensity/slice_meanPixel, T1_gdeMean Pixel Intensity/slice_meanPixel, T1_gdeMin Pixel Intensity/slice_meanPixel, DP_Mean Pixel Intensity/slice_meanPixel.

Table D.421: One_sample_One_Lesion_Traditional_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.61	0.57	0.50	0.52	0.52	0.52	0.50	0.61	0.55	0.61
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
44.35	**58.32**	83.82	97.44	49.94	50.52	52.04	99.77	**58.32**	14.44	**58.32**
62.27	**63.57**	29.37	3.19	53.66	53.66	51.59	0.09	**63.57**	95.35	**63.57**
60.20	**67.34**	71.04	62.71	59.16	59.45	59.25	33.33	**67.34**	60.10	**67.34**
46.52	**54.22**	46.75	42.68	44.36	44.65	44.30	42.49	**54.22**	69.66	**54.22**
54.65	**61.34**	52.53	43.27	52.08	52.33	51.78	42.48	**61.34**	60.94	**61.34**
Confusion Matrix										
723 438	738 423	341 820	37 1124	623 538	623 538	599 562	1 1160	738 423	1107 54	738 423
478 381	358 501	139 720	22 837	430 429	425 434	412 447	2 857	358 501	735 124	358 501

Table D.422: One_sample_One_Lesion_Traditional_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.61	0.55	0.50	0.52	0.52	0.52	0.59	0.61	0.55	0.61
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.40	**55.06**	87.08	95.11	37.37	35.74	36.21	67.52	**55.06**	13.39	**55.06**
61.67	**66.15**	23.08	4.31	67.27	68.05	67.53	49.70	**66.15**	95.87	**66.15**
58.31	**66.55**	70.71	54.35	59.21	58.87	58.86	67.41	**66.55**	59.94	**66.55**
43.81	**54.62**	45.58	42.38	45.79	45.28	45.20	49.83	**54.62**	70.55	**54.62**
52.62	**61.44**	50.30	42.92	54.55	54.31	54.21	57.28	**61.44**	60.79	**61.44**
Confusion Matrix										
716 445	768 393	268 893	50 1111	781 380	790 371	784 377	577 584	768 393	1113 48	768 393
512 347	386 473	111 748	42 817	538 321	552 307	548 311	279 580	386 473	744 115	386 473

For label *mediumEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$:

Final features: Solidity, WM_mean tissue prob, T2_Mean Pixel Intensity/slice_meanPixel, T2_Min Pixel Intensity/slice_meanPixel, T1_Mean Pixel Intensity/slice_meanPixel, T1_Max Pixel Intensity/slice_meanPixel, T1_Min Pixel Intensity/slice_meanPixel, T1_Median Pixel Intensity/slice_meanPixel, T1_gdeMax Pixel Intensity/slice_meanPixel, T1_gdeMedian Pixel Intensity/slice_meanPixel, DP_Median Pixel Intensity/slice_meanPixel.

Table D.423: One_sample_One_Lesion_Traditional_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.54	0.53	0.53	0.51	0.50	0.49	0.50	NA	0.50	0.54
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
30.63	16.24	31.37	14.76	76.38	80.07	81.18	0.37	NA	0.00	16.24
67.29	91.55	75.30	90.44	26.48	19.04	16.41	99.49	NA	100.00	91.55
94.15	94.77	94.79	94.63	94.90	94.07	93.54	94.31	NA	94.32	94.77
5.34	10.38	7.11	8.51	5.89	5.62	5.53	4.17	NA	NaN	10.38
65.21	87.27	72.80	86.14	29.32	22.50	20.09	93.86	NA	94.32	87.27
Confusion Matrix										
3026 1471	4117 380	3386 1111	4067 430	1191 3306	856 3641	738 3759	4474 23	NA	4497 0	4117 380
188 83	227 44	186 85	231 40	64 207	54 217	51 220	270 1	NA	271 0	227 44

Table D.424: One_sample_One_Lesion_Traditional_PCA_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.52	0.51	0.49	0.48	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
44.28	0.37	3.32	7.75	70.11	71.96	73.06	5.90	0.37	0.00	0.37
56.44	99.69	96.13	95.89	32.58	26.60	23.68	93.66	99.69	100.00	99.69
94.39	94.32	94.29	94.52	94.76	94.03	93.59	94.29	94.32	94.32	94.32
5.77	6.67	4.92	10.19	5.90	5.58	5.45	5.32	6.67	NaN	6.67
55.75	94.04	90.86	90.88	34.71	29.17	26.49	88.67	94.04	94.32	94.04
Confusion Matrix										
2538 1959	4483 14	4323 174	4312 185	1465 3032	1196 3301	1065 3432	4212 285	4483 14	4497 0	4483 14
151 120	270 1	262 9	250 21	81 190	76 195	73 198	255 16	270 1	271 0	270 1

For label *highestEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: Orientation Var Pixel, Intensity/slice_meanPixel, WM_squares numbers lesion region 90%/total region with 90, T1_Var Pixel Intensity/slice_meanPixel, T1_gdeVar Pixel Intensity/slice_meanPixel.

Table D.425: One_sample_One_Lesion_Traditional_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.50	0.52	0.51	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
47.71	100.00	0.00	99.71	82.73	69.94	63.65	0.00	100.00	100.00	100.00
52.13	0.00	100.00	0.00	17.02	32.98	37.23	100.00	0.00	0.00	0.00
8.21	NaN	8.23	0.00	8.12	8.96	8.41	8.23	NaN	NaN	NaN
91.74	91.77	NaN	91.75	91.75	92.09	91.87	NaN	91.77	91.77	91.77
48.07	91.77	8.23	91.51	77.32	66.90	61.47	8.23	91.77	91.77	91.77
Confusion Matrix										
49 45	0 94	94 0	0 94	16 78	31 63	35 59	94 0	0 94	0 94	0 94
548 500	0 1048	1048 0	3 1045	181 867	315 733	381 667	1048 0	0 1048	0 1048	0 1048

Table D.426: One_sample_One_Lesion_Traditional_PCA_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
53.72	100.00	0.00	72.81	59.54	62.60	63.84	0.00	100.00	100.00	100.00
46.81	0.00	100.00	26.60	40.43	38.30	36.17	100.00	0.00	0.00	0.00
8.32	NaN	8.23	8.06	8.23	8.41	8.23	8.23	NaN	NaN	NaN
91.84	91.77	NaN	91.71	91.77	91.88	91.77	NaN	91.77	91.77	91.77
53.15	91.77	8.23	69.00	57.97	60.60	61.56	8.23	91.77	91.77	91.77
Confusion Matrix										
44 50	0 94	94 0	25 69	38 56	36 58	34 60	94 0	0 94	0 94	0 94
485 563	0 1048	1048 0	285 763	424 624	392 656	379 669	1048 0	0 1048	0 1048	0 1048

For label *highestEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: Solidity, Max Pixel Intensity/slice_meanPixel, T2_Mean Pixel Intensity/slice_meanPixel, T2_Min Pixel Intensity/slice_meanPixel, T1_gdeMean Pixel Intensity/slice_meanPixel, T1_gdeMax Pixel Intensity/slice_meanPixel, DP_Mean Pixel Intensity/slice_meanPixel, DP_Max Pixel Intensity/slice_meanPixel, DP_Min Pixel Intensity/slice_meanPixel.

Table D.427: One_sample_One_Lesion_Traditional_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.50	0.50	0.53	0.52	0.51	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
6.67	0.00	0.22	0.00	20.67	14.22	7.11	0.00	0.00	0.00	0.00
95.23	100.00	99.94	100.00	85.37	90.34	94.71	100.00	100.00	100.00	100.00
88.75	88.54	88.56	88.54	89.27	89.06	88.74	88.54	88.54	88.54	88.54
15.31	NaN	33.33	NaN	15.45	16.00	14.82	NaN	NaN	NaN	NaN
85.08	88.54	88.52	88.54	77.95	81.62	84.67	88.54	88.54	88.54	88.54
Confusion Matrix										
3312 166	3478 0	3476 2	3478 0	2969 509	3142 336	3294 184	3478 0	3478 0	3478 0	3478 0
420 30	450 0	449 1	450 0	357 93	386 64	418 32	450 0	450 0	450 0	450 0

Table D.428: One_sample_One_Lesion_Traditional_PCA_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.50	0.50	0.51	0.51	0.50	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
15.78	0.00	0.00	0.00	17.56	7.11	1.56	0.00	0.00	0.00	0.00
87.06	100.00	100.00	99.94	85.02	94.51	98.94	100.00	100.00	100.00	100.00
88.88	88.54	88.54	88.54	88.85	88.72	88.59	88.54	88.54	88.54	88.54
13.63	NaN	NaN	0.00	13.17	14.35	15.91	NaN	NaN	NaN	NaN
78.90	88.54	88.54	88.49	77.29	84.50	87.78	88.54	88.54	88.54	88.54
Confusion Matrix										
3028 450	3478 0	3478 0	3476 2	2957 521	3287 191	3441 37	3478 0	3478 0	3478 0	3478 0
379 71	450 0	450 0	450 0	371 79	418 32	443 7	450 0	450 0	450 0	450 0

For label *first2EDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: RefSpace, Mean Pixel Intensity/slice_meanPixel, Max Pixel Intensity/slice_meanPixel, T2_Min Pixel Intensity/slice_meanPixel, T2_Median Pixel Intensity/slice_meanPixel, T1_gdeMin Pixel Intensity/slice_meanPixel, T1_gdeMedian Pixel Intensity/slice_meanPixel, DP_Mean Pixel, Intensity/slice_meanPixel, DP_Max Pixel Intensity/slice_meanPixel.

Table D.429: One_sample_One_Lesion_Traditional_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.55	0.54	0.49	0.48	0.51	0.52	0.50	0.55	0.50	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
42.59	83.80	83.02	26.54	47.22	57.87	64.66	100.00	83.80	100.00	83.80
57.08	26.38	24.13	72.26	49.53	43.30	38.42	0.04	26.38	0.00	26.38
78.35	85.56	83.80	78.17	77.35	78.90	79.82	100.00	85.56	NaN	85.56
21.43	23.83	23.12	20.82	20.45	21.90	22.39	21.56	23.83	21.56	23.83
53.96	38.76	36.83	62.41	49.04	46.44	44.08	21.59	38.76	21.56	38.76
Confusion Matrix										
1346 1012	622 1736	569 1789	1704 654	1168 1190	1021 1337	906 1452	1 2357	622 1736	0 2358	622 1736
372 276	105 543	110 538	476 172	342 306	273 375	229 419	0 648	105 543	0 648	105 543

Table D.430: One_sample_One_Lesion_Traditional_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.53	0.52	0.50	0.50	0.49	0.51	0.50	0.53	0.50	0.53
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
35.96	91.98	86.88	55.56	32.72	35.80	45.83	100.00	91.98	100.00	91.98
64.84	13.53	17.94	44.49	67.01	62.77	55.22	0.04	13.53	0.00	13.53
78.65	85.98	83.27	78.46	78.37	78.06	78.77	100.00	85.98	NaN	85.98
21.94	22.62	22.54	21.57	21.41	20.90	21.95	21.56	22.62	21.56	22.62
58.62	30.44	32.80	46.87	59.61	56.95	53.19	21.59	30.44	21.56	30.44
Confusion Matrix										
1529 829	319 2039	423 1935	1049 1309	1580 778	1480 878	1302 1056	1 2357	319 2039	0 2358	319 2039
415 233	52 596	85 563	288 360	436 212	416 232	351 297	0 648	52 596	0 648	52 596

For label *first2EDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: WM_mean tissue prob, WM_min tissue prob, T2_Min Pixel Intensity/slice_meanPixel, T1_Mean Pixel Intensity/slice_meanPixel, T1_Min Pixel Intensity/slice_meanPixel, T1_gdeMean Pixel Intensity/slice_meanPixel, T1_gdeMax Pixel Intensity/slice_meanPixel, T1_gdeMin Pixel Intensity/slice_meanPixel.

Table D.431: One_sample_One_Lesion_Traditional_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.50	0.51	0.50	0.49	0.50	0.50	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
5.77	0.00	3.85	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
86.23	100.00	96.57	100.00	98.50	99.90	100.00	99.97	100.00	100.00	100.00
99.02	99.10	99.11	99.10	99.09	99.10	99.10	99.10	99.10	99.10	99.10
0.38	NaN	1.01	NaN	0.00	0.00	NaN	0.00	NaN	NaN	NaN
85.51	99.10	95.73	99.10	97.62	99.00	99.10	99.07	99.10	99.10	99.10
Confusion Matrix										
4948 790	5738 0	5541 197	5738 0	5652 86	5732 6	5738 0	5736 2	5738 0	5738 0	5738 0
49 3	52 0	50 2	52 0	52 0	52 0	52 0	52 0	52 0	52 0	52 0

Table D.432: One_sample_One_Lesion_Traditional_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
1.92	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
94.32	100.00	99.55	99.76	98.87	99.93	100.00	99.86	100.00	100.00	100.00
99.07	99.10	99.10	99.10	99.09	99.10	99.10	99.10	99.10	99.10	99.10
0.31	NaN	0.00	0.00	0.00	0.00	NaN	0.00	NaN	NaN	NaN
93.49	99.10	98.65	98.86	97.98	99.03	99.10	98.96	99.10	99.10	99.10
Confusion Matrix										
5412 326 51 1	5738 0 52 0	5712 26 52 0	5724 14 52 0	5673 65 52 0	5734 4 52 0	5738 0 52 0	5730 8 52 0	5738 0 52 0	5738 0 52 0	5738 0 52 0

D.3.1.2 Lesion result ensemble procedure

The features used are the ones selected in the standard procedure.

For label *msCourse* (0/1 - RR/SP):

Table D.433: One_sample_One_Lesion_Ensemble_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.62	0.52	0.50	0.45	0.44	0.44	0.50	NA	0.51	0.62
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
27.36	96.74	96.74	0.00	13.04	19.20	27.72	100.00	NA	99.64	96.74
74.40	26.67	7.34	99.24	77.53	69.43	60.13	0.03	NA	2.83	26.67
84.34	97.73	92.21	83.92	82.42	81.88	81.39	100.00	NA	97.62	97.73
16.89	20.06	16.57	0.00	9.94	10.67	11.68	15.99	NA	16.32	20.06
66.88	37.87	21.63	83.38	67.23	61.41	54.95	16.01	NA	18.30	37.87
Confusion Matrix										
2159 743 401 151	774 2128 18 534	213 2689 18 534	2880 22 552 0	2250 652 480 72	2015 887 446 106	1745 1157 399 153	1 2901 0 552	NA NA	82 2820 2 550	774 2128 18 534

Table D.434: One_sample_One_Lesion_Ensemble_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.51	0.55	0.50	0.46	0.44	0.43	0.50	NA	0.52	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
27.36	96.74	96.74	0.00	13.04	19.20	27.72	100.00	NA	99.64	96.74
74.40	26.67	7.34	99.24	77.53	69.43	60.13	0.03	NA	2.83	26.67
84.34	97.73	92.21	83.92	82.42	81.88	81.39	100.00	NA	97.62	97.73
16.89	20.06	16.57	0.00	9.94	10.67	11.68	15.99	NA	16.32	20.06
66.88	37.87	21.63	83.38	67.23	61.41	54.95	16.01	NA	18.30	37.87
Confusion Matrix										
1655 1247 345 207	100 2802 5 547	447 2455 27 525	2605 297 499 53	2420 482 499 53	2092 810 469 83	1802 1100 424 128	18 2884 0 552	NA NA	124 2778 4 548	100 2802 5 547

For label *mediumEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Table D.435: One_sample_One_Lesion_Ensemble_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.60	0.53	0.50	0.53	0.54	0.53	0.54	NA	0.50	0.60
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
42.28	75.00	92.44	97.38	54.32	69.44	74.38	42.13	NA	1.08	75.00
62.64	45.34	14.42	2.12	52.67	38.51	32.27	65.39	NA	99.75	45.34
79.79	86.84	87.40	74.63	80.75	82.10	82.09	80.44	NA	78.58	86.84
23.72	27.38	22.89	21.46	23.98	23.68	23.18	25.07	NA	53.85	27.38
58.25	51.73	31.24	22.65	53.03	45.18	41.35	60.38	NA	78.48	51.73
Confusion Matrix										
1477 881	1069 1289	340 2018	50 2309	1242 1116	908 1450	761 1597	1542 816	NA	2352 6	1069 1289
374 274	162 486	49 599	17 631	296 352	198 450	166 482	375 273	NA	641 7	162 486

Table D.436: One_sample_One_Lesion_Ensemble_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.52	0.53	0.50	0.53	0.52	0.53	0.53	NA	0.50	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
68.36	5.71	17.59	53.40	64.97	52.93	54.78	24.23	NA	0.46	5.71
33.50	98.69	88.21	46.40	41.82	50.85	50.42	81.89	NA	99.75	98.69
79.40	79.20	79.57	78.37	81.29	79.72	80.23	79.73	NA	78.48	79.20
22.03	54.41	29.08	21.49	23.48	22.84	23.29	26.88	NA	33.33	54.41
41.02	78.64	72.99	47.90	46.81	51.30	51.36	69.46	NA	78.34	78.64
Confusion Matrix										
790 1568	2327 31	2080 278	1094 1264	986 1372	1199 1159	1189 1169	1931 427	NA	2352 6	2327 31
205 443	611 37	534 114	302 346	227 421	305 343	293 355	491 157	NA	645 3	611 37

For label *mediumEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Table D.437: One_sample_One_Lesion_Ensemble_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.50	0.52	0.50	0.50	0.50	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
9.43	0.00	3.85	0.00	0.00	0.00	0.00	0.00	NA	0.00	0.00
87.75	100.00	99.60	99.46	99.48	100.00	100.00	100.00	NA	100.00	100.00
99.06	99.10	99.13	99.10	99.10	99.10	99.10	99.10	NA	99.10	99.10
0.71	NaN	8.00	0.00	0.00	NaN	NaN	NaN	NA	NaN	NaN
87.03	99.10	98.74	98.57	98.58	99.10	99.10	99.10	NA	99.10	99.10
Confusion Matrix										
3432 1065	4458 39	3932 565	4392 105	835 3662	617 3880	588 3909	4461 36	NA	4497 0	4458 39
211 60	256 15	216 55	256 15	40 231	40 231	50 221	270 1	NA	271 0	256 15

Table D.438: One_sample_One_Lesion_Ensemble_PCA_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.49	0.50	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
5.77	0.00	0.00	0.00	0	0.00	0.00	0.00	NA	0.00	0.00
96.83	100.00	100.00	100.00	97.21	100.00	100.00	100.00	NA	100.00	100.00
99.13	99.10	99.10	99.10	99.08	99.10	99.10	99.10	NA	99.10	99.10
1.62	NaN	NaN	NaN	0.00	NaN	NaN	NaN	NA	NaN	NaN
96.01	99.10	99.10	99.10	96.34	99.10	99.10	99.10	NA	99.10	99.10
Confusion Matrix										
5556 182	5738 0	5738 0	5682 56	5738 0	5738 0	5738 0	5738 0	NA	5738 0	5738 0
49 3	52 0	52 0	52 0	52 0	52 0	52 0	52 0	NA	52 0	52 0

For label *highestEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Table D.439: One_sample_One_Lesion_Ensemble_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.53	0.48	0.47	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.51	100.00	0.00	91.82	35.80	40.90	50.15	0.00	NA	100.00	100.00
35.28	0.00	100.00	7.51	69.97	55.73	44.74	100.00	NA	0.00	0.00
79.31	NaN	78.44	76.96	79.86	77.43	76.56	78.44	NA	NaN	NaN
22.02	21.56	NaN	21.43	24.68	20.24	19.96	NaN	NA	21.56	21.56
42.02	21.56	78.44	25.68	62.61	52.53	45.91	78.44	NA	21.56	21.56
Confusion Matrix										
832 1526	0 2358	0 2358	177 2181	1650 708	1314 1044	1055 1303	0 2358	NA	0 2358	0 2358
217 431	0 648	0 648	53 595	416 232	383 265	323 325	0 648	NA	0 648	0 648

Table D.440: One_sample_One_Lesion_Ensemble_PCA_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.58	0.57	0.57	0.57	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
61.93	100.00	0.00	91.51	70.80	79.01	81.39	0.00	NA	100.00	100.00
46.81	0.00	100.00	25.53	42.55	36.17	32.98	100.00	NA	0.00	0.00
9.93	NaN	8.23	21.24	11.56	13.39	13.72	8.23	NA	NaN	NaN
92.85	91.77	NaN	93.20	93.22	93.24	93.12	NaN	NA	91.77	91.77
60.68	91.77	8.23	86.08	68.48	75.48	77.41	8.23	NA	91.77	91.77
Confusion Matrix										
44 50	94 0	94 0	24 70	40 54	34 60	31 63	94 0	NA	94 0	94 0
399 649	1048 0	1048 0	89 959	306 742	220 828	195 853	1048 0	NA	1048 0	1048 0

For label *highestEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Table D.441: One_sample_One_Lesion_Ensemble_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.50	0.50	0.50	0.48	0.51	0.51	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
3.85	0.00	0.00	0.00	1.92	3.85	3.85	0.00	NA	0.00	0.00
92.07	100.00	100.00	100.00	92.92	98.19	99.58	100.00	NA	100.00	100.00
99.06	99.10	99.10	99.10	99.05	99.12	99.13	99.10	NA	99.10	99.10
0.44	NaN	NaN	NaN	0.25	1.89	7.69	NaN	NA	NaN	NaN
91.28	99.10	99.10	99.10	92.11	97.34	98.72	99.10	NA	99.10	99.10
Confusion Matrix										
5283 4555	5738 0	5738 0	5738 0	5332 406	5634 104	5714 24	5738 0	NA	5738 0	5738 0
50 2	52 0	52 0	52 0	51 1	50 2	50 2	52 0	NA	52 0	52 0

Table D.442: One_sample_One_Lesion_Ensemble_PCA_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.50	0.50	0.50	0.49	0.51	0.50	0.51	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
1.92	0.00	0.00	0.00	7.69	7.69	1.92	1.92	NA	0.00	0.00
94.53	100.00	100.00	99.01	90.36	95.29	98.92	99.91	NA	100.00	100.00
99.07	99.10	99.10	99.09	99.08	99.13	99.11	99.12	NA	99.10	99.10
0.32	NaN	NaN	0.00	0.72	1.46	1.59	16.67	NA	NaN	NaN
93.70	99.10	99.10	98.12	89.62	94.51	98.05	99.03	NA	99.10	99.10
Confusion Matrix										
5424 314	5738 0	5738 0	5681 57	5185 553	5468 270	5676 62	5733 5	NA	5738 0	5738 0
51 1	52 0	52 0	52 0	48 4	48 4	51 1	51 1	NA	52 0	52 0

For label *first2EDSS* > 3 (0/1 - $(< 3)/(\geq 3)$:

Table D.443: One_sample_One_Lesion_Ensemble_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.57	0.54	0.50	0.46	0.50	0.51	0.50	NA	0.50	0.57
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
33.33	90.90	92.75	26.39	46.60	57.72	65.74	100.00	NA	100.00	90.90
66.84	22.35	14.93	73.20	45.59	41.98	36.56	0.00	NA	0.00	22.35
78.49	89.93	88.22	78.35	75.65	78.32	79.52	NaN	NA	NaN	89.93
21.64	24.34	23.05	21.30	19.05	21.47	22.16	21.56	NA	21.56	24.34
59.61	37.13	31.70	63.11	45.81	45.38	42.85	21.56	NA	21.56	37.13
Confusion Matrix										
1576 782	527 1831	352 2006	1726 632	1075 1283	990 1368	862 1496	0 2358	NA	0 2358	527 1831
432 216	59 589	47 601	477 171	346 302	274 374	222 426	0 648	NA	0 648	59 589

Table D.444: One_sample_One_Lesion_Ensemble_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.52	0.52	0.50	0.49	0.48	0.50	0.50	NA	0.50	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
36.42	97.99	91.98	58.02	25.00	30.86	48.92	100.00	NA	100.00	97.99
64.55	5.26	11.96	41.94	73.41	64.97	50.47	0.08	NA	0.00	5.26
78.70	90.51	84.43	78.43	78.08	77.37	78.24	100.00	NA	NaN	90.51
22.01	22.13	22.31	21.55	20.53	19.49	21.35	21.57	NA	21.56	22.13
58.48	25.25	29.21	45.41	62.97	57.62	50.13	21.62	NA	21.56	25.25
Confusion Matrix										
1522 836	124 2234	282 2076	989 1369	1731 627	1532 826	1190 1168	2 2356	NA	0 2358	124 2234
412 236	13 635	52 596	272 376	486 162	448 200	331 317	0 648	NA	0 648	13 635

For label *first2EDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Table D.445: One_sample_One_Lesion_Ensemble_first2EDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.50	0.50	0.50	0.50	0.50	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
3.85	0.00	0.00	0.00	0.00	0.00	0.00	0.00	NA	0.00	0.00
85.52	100.00	99.98	100.00	100.00	100.00	100.00	100.00	NA	100.00	100.00
98.99	99.10	99.10	99.10	99.10	99.10	99.10	99.10	NA	99.10	99.10
0.24	NaN	0.00	NaN	NaN	NaN	NaN	NaN	NA	NaN	NaN
84.78	99.10	99.08	99.10	99.10	99.10	99.10	99.10	NA	99.10	99.10
Confusion Matrix										
4907 831	5738 0	5737 1	5738 0	5738 0	5738 0	5738 0	5738 0	NA	5738 0	5738 0
50 2	52 0	52 0	52 0	52 0	52 0	52 0	52 0	NA	52 0	52 0

Table D.446: One_sample_One_Lesion_Ensemble_PCA_first2EDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.50	0.50	0.50	0.50	0.50	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	NA	0.00	0.00
99.01	100.00	100.00	100.00	100.00	100.00	100.00	100.00	NA	100.00	100.00
99.09	99.10	99.10	99.10	99.10	99.10	99.10	99.10	NA	99.10	99.10
0.00	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NA	NaN	NaN
98.12	99.10	99.10	99.10	99.10	99.10	99.10	99.10	NA	99.10	99.10
Confusion Matrix										
5681 57	5681 57	5681 57	5681 57	5681 57	5681 57	5681 57	5681 57	NA	5681 57	5681 57
52 0	52 0	52 0	52 0	52 0	52 0	52 0	52 0	NA	52 0	52 0

For label *currentEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Table D.447: One_sample_One_Lesion_Ensemble_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.50	0.54	0.50	0.47	0.46	0.44	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
52.12	0.33	17.71	99.78	21.05	36.19	39.76	100.00	NA	100.00	0.33
40.47	100.00	90.78	0.21	73.83	56.46	47.46	0.00	NA	0.00	100.00
47.04	51.33	53.70	50.00	49.57	48.19	45.30	NaN	NA	NaN	51.33
45.44	100.00	64.63	48.75	43.35	44.16	41.85	48.75	NA	48.75	100.00
46.15	51.41	55.16	48.75	48.10	46.58	43.70	48.75	NA	48.75	51.41
Confusion Matrix										
382 562	944 0	857 87	2 942	697 247	533 411	448 496	0 944	NA	0 944	944 0
430 468	895 3	739 159	2 896	709 189	573 325	541 357	0 898	NA	0 898	895 3

Table D.448: One_sample_One_Lesion_Ensemble_PCA_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.50	0.50	0.50	0.44	0.41	0.41	0.50		0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
57.68	100.00	100.00	99.89	31.74	34.86	38.64	100.00	NA	100.00	100.00
34.11	0.00	0.00	0.00	55.51	47.35	42.90	0.00	NA	0.00	0.00
45.87	NaN	NaN	0.00	46.09	43.31	42.36	NaN	NA	NaN	NaN
45.44	48.75	48.75	48.72	40.43	38.64	39.16	48.75	NA	48.75	48.75
45.60	48.75	48.75	48.70	43.92	41.26	40.83	48.75	NA	48.75	48.75
Confusion Matrix										
322 622	0 944	0 944	0 944	524 420	447 497	405 539	0 944	NA	0 944	0 944
380 518	0 898	0 898	1 897	613 285	585 313	551 347	0 898	NA	0 898	0 898

For label *currentEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$:

Table D.449: One_sample_One_Lesion_Ensemble_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.45	0.44	0.46	0.50	0.00	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
13.68	0.00	0.00	0.18	52.50	57.67	62.85	0.00	NA	0.00	0.00
85.66	100.00	100.00	99.93	37.46	31.05	28.96	100.00	NA	100.00	100.00
84.46	84.56	84.56	84.58	81.20	80.07	81.02	84.56	NA	84.56	84.56
14.83	NaN	NaN	33.33	13.29	13.25	13.91	NaN	NA	NaN	NaN
74.54	84.56	84.56	84.53	39.78	35.16	34.19	84.56	NA	84.56	84.56
Confusion Matrix										
2538 425	2963 0	2963 0	2961 2	1110 1853	920 2043	858 2105	2963 0	NA	2963 0	2963 0
467 74	541 0	541 0	540 1	257 284	229 312	201 340	541 0	NA	541 0	541 0

Table D.450: One_sample_One_Lesion_Ensemble_PCA_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.50	0.50	0.50	0.46	0.43	0.43	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
34.01	0.00	0.00	0.37	56.93	54.34	57.67	0.00	NA	0.00	0.00
57.24	100.00	100.00	99.97	34.69	32.20	27.61	100.00	NA	100.00	100.00
82.61	84.56	84.56	84.60	81.52	79.43	78.13	84.56	NA	84.56	84.56
12.68	NaN	NaN	66.67	13.73	12.77	12.70	NaN	NA	NaN	NaN
53.65	84.56	84.56	84.59	38.13	35.62	32.25	84.56	NA	84.56	84.56
Confusion Matrix										
1696 1267	2963 0	2963 0	2962 1	1028 1935	954 2009	818 2145	2963 0	NA	2963 0	2963 0
357 184	541 0	541 0	539 2	233 308	247 294	229 312	541 0	NA	541 0	541 0

For label *nextEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Table D.451: One_sample_One_Lesion_Ensemble_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	0.50	0.53	0.54	0.56	0.55	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
54.54	100.00	14.90	93.74	54.54	**60.69**	61.88	14.90	NA	100.00	100.00
52.68	0.00	85.46	11.35	53.19	**51.53**	47.58	85.46	NA	0.00	0.00
49.52	NaN	45.95	60.54	49.76	**52.60**	51.38	45.95	NA	NaN	NaN
57.65	54.15	54.76	55.53	57.91	**59.66**	58.23	54.76	NA	54.15	54.15
53.68	54.15	47.25	55.96	53.92	**56.49**	55.32	47.25	NA	54.15	54.15
Confusion Matrix										
413 371	0 784	0 784	89 695	417 367	404 380	373 411	670 114	NA	0 784	0 784
421 505	0 926	0 926	58 868	421 505	364 562	353 573	788 138	NA	0 926	0 926

For label *nextEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Table D.452: One_sample_One_Lesion_Ensemble_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.52	0.50	0.50	0.50	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
55.10	100.00	19.05	91.34	56.63	60.88	56.97	19.05	NA	100.00	100.00
45.07	0.00	81.01	9.38	46.36	39.50	43.32	81.01	NA	0.00	0.00
82.15	NaN	82.11	83.22	83.06	82.24	82.20	82.11	NA	NaN	NaN
17.95	17.90	17.95	18.05	18.72	18.00	17.98	17.95	NA	17.90	17.90
46.86	17.90	69.91	24.08	48.20	43.33	45.77	69.91	NA	17.90	17.90
Confusion Matrix										
1215 1481	0 2696	2184 512	253 2443	1250 1446	1065 1631	1168 1528	2184 512	NA	0 2696	0 2696
264 324	0 588	476 112	51 538	255 333	230 358	253 335	476 112	NA	0 588	0 588

D.3.2 One sample, one study Set

For label *msCourse* (0/1 - RR/SP):

Final features: Mean_Anatomical_I_42_var pixel intensity, Var_Anatomical_I_42_lesion in the region, Mean_Anatomical_I_42_ratio on region affected by lesion, Mean_Anatomical_I_42_max pixel intensity, Max_Anatomical_I_21_ratio on region affected by lesion, Mean_T2_Var Pixel Intensity/slice_meanPixel, Var_Anatomical_I_42_max pixel intensity, Mean_Anatomical_I_42_me pixel intensity, Var_Var Pixel Intensity/slice_meanPixel.

Table D.453: One_sample_One_Study_Traditional_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.50	0.58	0.51	0.51	0.52	0.51	0.58	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
83.33	100.00	50.00	100.00	83.33	100.00	100.00	50.00	100.00	100.00	100.00
12.31	0.00	66.15	10.77	26.15	9.23	4.62	66.15	0.00	0.00	0.00
88.89	NaN	93.48	100.00	94.44	100.00	100.00	93.48	NaN	NaN	NaN
8.06	8.45	12.00	9.38	9.43	9.23	8.82	12.00	8.45	8.45	8.45
18.31	8.45	64.79	18.31	30.99	16.90	12.68	64.79	8.45	8.45	8.45
Confusion Matrix										
8 57 1 5	0 65 0 6	43 22 3 3	7 58 0 6	17 48 1 5	6 59 0 6	3 62 0 6	43 22 3 3	0 65 0 6	0 65 0 6	0 65 0 6

Table D.454: One_sample_One_Study_Traditional_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	NA	0.54	0.55	0.55	0.55	NA	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	NA	100.00	83.33	66.67	66.67	NA	100.00	100.00	100.00
6.15	4.62	NA	13.85	33.85	50.77	44.62	NA	4.62	0.00	4.62
100.00	100.00	NA	100.00	95.65	94.29	93.55	NA	100.00	NaN	100.00
8.96	8.82	NA	9.68	10.42	11.11	10.00	NA	8.82	8.45	8.82
14.09	12.68	NA	21.13	38.03	52.11	46.48	NA	12.68	8.45	12.68
Confusion Matrix										
4 61 0 6	3 62 0 6	NA NA	9 56 0 6	22 43 1 5	33 32 2 4	29 36 2 4	NA NA	3 62 0 6	0 65 0 6	3 62 0 6

Table D.455: One_sample_One_Study_kFold_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.55	0.54	0.08	0.54	0.50	0.46	0.54	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
30.00	35.00	35.00	0.00	35.00	30.00	25.00	35.00	NA	65.00	65.00
84.81	94.94	94.94	97.47	83.54	92.41	92.41	94.94	NA	78.48	78.48
82.72	85.23	85.23	79.38	83.54	83.91	82.96	85.23	NA	89.86	89.86
33.33	63.64	63.64	0.00	35.00	50.00	45.46	63.64	NA	43.33	43.33
73.74	82.83	82.83	77.78	73.74	79.80	78.79	82.83	NA	75.76	75.76
Confusion Matrix										
67 12 14 6	75 4 13 7	75 4 13 7	77 2 20 0	66 13 13 7	73 6 14 6	73 6 15 5	75 4 13 7	NA NA	62 17 7 13	62 17 7 13

Table D.456: One_sample_One_Study_kFold_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.54	0.40	0.19	0.55	0.50	0.50	0.62	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
35.00	35.00	20.00	**10.00**	35.00	30.00	30.00	50.00	NA	65.00	60.00
84.81	88.61	88.61	**97.47**	89.87	91.14	89.87	84.81	NA	78.48	82.28
83.75	84.34	81.40	**81.05**	84.52	83.72	83.53	87.01	NA	89.86	89.04
36.84	43.75	30.77	**50.00**	46.67	46.15	42.86	45.46	NA	43.33	46.15
74.75	77.78	74.75	**79.80**	78.79	78.79	77.78	77.78	NA	75.76	77.78
Confusion Matrix										
67 12 13 7	70 9 13 7	70 9 16 4	77 2 18 2	71 8 13 7	72 7 14 6	71 8 14 6	67 12 10 10	NA NA	62 17 7 13	65 14 8 12

Table D.457: One_sample_One_Study_LOO_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.49	0.49	0.40	0.50	0.57	0.49	0.49	0.55	0.47	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
15.00	10.00	10.00	0.00	20.00	20.00	10.00	10.00	10.00	25.00	25.00
79.75	88.61	88.61	97.47	79.75	89.87	88.61	88.61	93.67	68.35	68.35
78.75	79.55	79.55	79.38	79.75	81.61	79.55	79.55	80.44	78.26	78.26
15.79	18.18	18.18	0.00	20.00	33.33	18.18	18.18	28.57	16.67	16.67
66.67	72.73	72.73	77.78	67.68	75.76	72.73	72.73	76.77	59.60	59.60
Confusion Matrix										
63 16 17 3	70 9 18 2	70 9 18 2	77 2 20 0	77 2 20 0	71 8 16 4	70 9 18 2	70 9 18 2	74 5 18 2	54 25 15 5	54 25 15 5

Table D.458: One_sample_One_Study_LOO_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.49	0.55	0.40	0.50	0.47	0.47	0.40	0.47	0.43	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
15.00	15.00	25.00	0.00	15.00	10.00	10.00	5.00	10.00	15.00	25.00
77.22	83.54	83.54	97.47	84.81	86.08	84.81	73.42	86.08	65.82	74.68
78.21	79.52	81.48	79.38	79.76	79.07	78.82	75.33	79.07	75.36	79.73
14.29	18.75	27.78	0.00	20.00	15.39	14.29	4.55	15.39	10.00	20.00
64.65	69.70	71.72	77.78	70.71	70.71	69.70	59.60	70.71	55.56	64.65
Confusion Matrix										
61 18 17 3	66 13 17 3	66 13 15 5	77 2 20 0	67 12 17 3	68 11 18 2	67 12 18 2	58 21 19 1	68 11 18 2	52 27 17 3	59 20 15 5

For label *currentEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: Mean_Anatomical_II_408_ratio on region affected by lesion, Var_Anatomical_II_408 pixel intensity, Var_Anatomical_II_408_min pixel intensity, Max_Anatomical_II_408_mean pixel intensity

Table D.459: One_sample_One_Study_Traditional_PCA_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.63	0.50	0.50	0.53	0.55	0.55	0.50	0.65	0.58	0.58
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
50.00	41.67	50.00	100.00	50.00	66.67	41.67	50.00	33.33	66.67	66.67
58.06	83.87	48.39	0.00	58.06	41.94	70.97	48.39	96.77	48.39	48.39
75.00	78.79	71.43	NaN	75.00	76.47	75.86	71.43	78.95	78.95	78.95
31.58	50.00	27.27	27.91	31.58	30.77	35.71	27.27	80.00	33.33	33.33
55.81	72.09	48.84	27.91	55.81	48.84	62.79	48.84	79.07	53.49	53.49
Confusion Matrix										
18 13 6 6	26 5 7 5	15 16 6 6	0 31 0 12	18 13 6 6	13 18 4 8	22 9 7 5	15 16 6 6	30 1 8 4	15 16 4 8	15 16 4 8

Table D.460: One_sample_One_Study_Traditional_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.60	NA	0.53	0.54	0.53	0.51	NA	0.63	0.56	0.58
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
50.00	58.33	NA	8.33	8.33	8.33	0.00	NA	41.67	66.67	66.67
51.61	64.52	NA	100.00	100.00	100.00	100.00	NA	83.87	41.94	51.61
72.73	80.00	NA	73.81	73.81	73.81	72.09	NA	78.79	76.47	80.00
28.57	38.89	NA	100.00	100.00	100.00	NaN	NA	50.00	30.77	34.78
51.16	62.79	NA	74.42	74.42	74.42	72.09	NA	72.09	48.84	55.81
Confusion Matrix										
16 15 6 6	20 11 5 7	NA NA	31 0 11 1	31 0 11 1	31 0 11 1	31 0 12 0	NA NA	26 5 7 5	13 8 4 8	16 15 4 8

Table D.461: One_sample_One_Study_kFold_PCA_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.61	0.61	NA	0.64	0.59	0.64	0.64	NA	NA	0.64	0.62
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
30.00	30.00	NA	32.50	27.50	32.50	32.50	NA	NA	32.50	30.00
96.61	96.61	NA	96.61	96.61	96.61	96.61	NA	NA	96.61	96.61
67.06	67.06	NA	67.86	66.28	67.86	67.86	NA	NA	67.86	67.06
85.71	85.71	NA	86.67	84.62	86.67	86.67	NA	NA	86.67	85.71
69.70	69.70	NA	70.71	68.69	70.71	70.71	NA	NA	70.71	69.70
Confusion Matrix										
57 2 28 12	57 2 28 12	NA NA	57 2 27 13	57 2 29 11	57 2 27 13	57 2 27 13	NA NA	NA NA	57 2 27 13	57 2 28 12

Table D.462: One_sample_One_Study_kFold_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.60	0.60	NA	0.65	0.57	0.64	0.64	NA	NA	0.64	0.60
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
30.00	30.00	NA	32.50	27.50	32.50	32.50	NA	NA	32.50	30.00
96.61	96.61	NA	96.61	96.61	96.61	96.61	NA	NA	96.61	96.61
67.06	67.06	NA	67.86	66.28	67.86	67.86	NA	NA	67.86	67.06
85.71	85.71	NA	86.67	84.62	86.67	86.67	NA	NA	86.67	85.71
69.70	69.70	NA	70.71	68.69	70.71	70.71	NA	NA	70.71	69.70
Confusion Matrix										
57 2	57 2	NA	57 2	57 2	57 2	57 2	NA	NA	57 2	57 2
28 12	28 12	NA	27 13	29 11	27 13	27 13	NA	NA	27 13	28 12

Table D.463: One_sample_One_Study_LOO_PCA_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.47	NA	0.46	0.49	0.46	0.46	NA	NA	0.46	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
12.50	12.50	NA	12.50	12.50	12.50	12.50	NA	NA	12.50	12.50
84.75	84.75	NA	83.05	86.44	83.05	83.05	NA	NA	83.05	84.75
58.82	58.82	NA	58.33	59.30	58.33	58.33	NA	NA	58.33	58.82
35.71	35.71	NA	33.33	38.46	33.33	33.33	NA	NA	33.33	35.71
55.56	55.56	NA	54.55	56.57	54.55	54.55	NA	NA	54.55	55.56
Confusion Matrix										
50 9	50 9	NA	49 10	51 8	49 10	49 10	NA	NA	49 10	50 9
35 5	35 5	NA	35 5	35 5	35 5	35 5	NA	NA	35 5	35 5

Table D.464: One_sample_One_Study_LOO_currentEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.43	0.47	NA	0.46	0.40	0.46	0.46	NA	NA	0.46	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
10.00	12.50	NA	12.50	7.50	12.50	12.50	NA	NA	12.50	12.50
83.05	84.75	NA	83.05	83.05	83.05	83.05	NA	NA	83.05	84.75
57.65	58.82	NA	58.33	56.98	58.33	58.33	NA	NA	58.33	58.82
28.57	35.71	NA	33.33	23.08	33.33	33.33	NA	NA	33.33	35.71
53.54	55.56	NA	54.55	52.53	54.55	54.55	NA	NA	54.55	55.56
Confusion Matrix										
49 10	50 9	NA	49 10	49 10	49 10	49 10	NA	NA	49 10	49 10
36 4	35 5	NA	35 5	37 3	35 5	35 5	NA	NA	35 5	35 5

For label *currentEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$:

Final features: Var_Anatomical_I_122_median pixel intensity, Var_Solidity, Max_Anatomical_I_12
pixel intensity, Mean_Anatomical_I_122_lesion in the region, Mean_Anatomical_II_34_var

pixel intensity, Var_Anatomical_II_34_var pixel intensity, Var_Anatomical_I_122_ratio on region affected by lesion.

Table D.465: One_sample_One_Study_Traditional_PCA_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.54	0.53	0.50	0.51	0.51	0.50	0.53	0.54	0.54	0.54
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
57.14	100.00	28.57	71.43	57.14	57.14	57.14	28.57	100.00	100.00	100.00
46.77	11.29	72.58	29.03	41.94	43.55	45.16	72.58	11.29	11.29	11.29
90.63	100.00	90.00	90.00	89.66	90.00	90.32	90.00	100.00	100.00	100.00
10.81	11.29	10.53	10.20	10.00	10.26	10.53	10.53	11.29	11.29	11.29
47.83	20.29	68.12	33.33	43.48	44.93	46.38	68.12	20.29	20.29	20.29
Confusion Matrix										
29 33	7 55	45 17	18 44	26 36	27 25	28 24	45 17	7 55	7 55	7 55
3 4	0 7	5 2	2 5	3 4	3 4	3 4	5 2	0 7	0 7	0 7

Table D.466: One_sample_One_Study_Traditional_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.44	NA	0.51	0.49	0.51	0.51	NA	0.44	0.50	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
57.14	71.43	NA	42.86	42.86	42.86	42.86	NA	71.43	100.00	71.43
48.39	12.90	NA	58.06	50.00	59.68	58.06	NA	12.90	0.00	12.90
90.91	80.00	NA	90.00	88.57	90.24	90.00	NA	80.00	NaN	80.00
11.11	8.47	NA	10.34	8.82	10.71	10.34	NA	8.47	10.14	8.47
49.28	18.84	NA	56.52	49.28	57.97	56.52	NA	18.84	10.14	18.84
Confusion Matrix										
30 32	8 54	NA	36 26	31 31	37 25	36 26	NA	8 54	0 62	8 54
3 4	2 5	NA	4 3	4 3	4 3	4 3	NA	2 5	0 7	2 5

Table D.467: One_sample_One_Study_kFold_PCA_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.47	0.14	0.10	0.17	0.47	0.37	0.35	0.10	0.04	0.62	0.62
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
22.73	4.55	4.55	0.00	22.73	13.64	13.64	4.55	0.00	77.27	77.27
80.52	97.40	97.40	92.21	75.32	87.01	90.91	97.40	98.70	59.74	59.74
78.48	78.13	78.13	76.34	77.33	77.91	78.65	78.13	77.55	90.20	90.20
25.00	33.33	33.33	0.00	20.83	23.08	30.00	33.33	0.00	35.42	35.42
67.68	76.77	76.77	71.72	63.64	70.71	73.74	76.77	76.77	63.64	63.64
Confusion Matrix										
62 15	75 2	75 2	71 6	58 19	67 10	70 7	75 2	76 1	46 31	46 31
17 5	21 1	21 1	22 0	17 5	19 3	19 3	21 1	22 0	5 17	5 17

Table D.468: One_sample_One_Study_kFold_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.46	NA	0.16	0.50	0.47	0.26	NA	NA	0.63	0.62
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
45.45	27.27	NA	4.55	31.82	22.73	9.09	NA	NA	77.27	63.64
84.42	94.81	NA	97.40	74.03	89.61	93.51	NA	NA	59.74	70.13
84.42	82.02	NA	78.13	79.17	80.23	78.26	NA	NA	90.20	87.10
45.45	60.00	NA	33.33	25.93	38.46	28.57	NA	NA	35.42	37.84
75.76	79.80	NA	76.77	64.65	74.75	74.75	NA	NA	63.64	68.69
Confusion Matrix										
65 12	73 4	NA	75 2	57 20	69 8	72 5	NA	NA	46 31	54 23
12 10	16 6	NA	21 1	15 7	17 5	20 2	NA	NA	5 17	8 14

Table D.469: One_sample_One_Study_LOO_PCA_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.42	0.39	0.39	0.38	0.41	0.37	0.38	0.39	NA	0.41	0.41
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
9.09	0.00	0.00	0.00	9.09	0.00	0.00	0.00	NA	27.27	27.27
75.32	96.10	97.40	92.21	71.43	84.42	87.01	97.40	NA	45.45	45.45
74.36	77.08	77.32	76.34	73.33	74.71	75.28	77.32	NA	68.63	68.63
9.52	0.00	0.00	0.00	8.33	0.00	0.00	0.00	NA	12.50	12.50
60.61	74.75	75.76	71.72	57.58	65.66	67.68	75.76	NA	41.41	41.41
Confusion Matrix										
58 19	74 3	75 2	71 6	55 22	65 12	67 10	75 2	NA	35 42	35 42
20 2	22 0	22 0	22 0	20 2	22 0	22 0	22 0	NA	16 6	16 6

Table D.470: One_sample_One_Study_LOO_currentEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.45	0.47	0.56	0.49	0.58	0.61	0.48	NA	0.47	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
31.82	4.55	9.09	4.55	27.27	22.73	13.64	9.09	NA	40.91	31.82
76.62	90.91	87.01	97.40	71.43	88.31	94.81	88.31	NA	49.35	59.74
79.73	76.92	77.01	78.13	77.46	80.00	79.35	77.27	NA	74.51	75.41
28.00	12.50	16.67	33.33	21.43	35.71	42.86	18.18	NA	18.75	18.42
66.67	71.72	69.70	76.77	61.62	73.74	76.77	70.71	NA	47.47	53.54
Confusion Matrix										
59 18	70 7	67 10	75 2	55 22	68 9	73 4	68 9	NA	38 39	46 31
15 7	21 1	20 2	21 1	16 6	17 5	19 3	20 2	NA	13 9	15 7

For label *nextEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$:

Final features: Var_GM_min tissue prob, Max_GM_min tissue prob, Var_Anatomical_I_21_var pixel intensity, Mean_Anatomical_I_21_var pixel intensity, Max_Anatomical_I_29_ratio on region affected by lesion, Mean_Anatomical_I_29_var pixel intensity, Max_Anatomical_I_29_var

pixel intensity, Var_Anatomical_I_42_var pixel intensity, Var_Anatomical_I_21_ratio on region affected by lesion, Var_Var Pixel Intensity/slice_meanPixel.

Table D.471: One_sample_One_Study_Traditional_PCA_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.51	0.51	0.52	0.59	0.55	0.51	0.50	0.51	0.50	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
76.92	30.77	38.46	23.08	61.54	61.54	38.46	7.69	30.77	100.00	30.77
25.00	67.86	64.29	82.14	60.71	50.00	60.71	92.86	67.86	0.00	67.86
70.00	67.86	69.23	69.70	77.27	73.68	68.00	68.42	67.86	NaN	67.86
32.26	30.77	33.33	37.50	42.11	36.36	31.25	33.33	30.77	31.71	30.77
41.46	56.10	56.10	63.41	60.98	53.66	53.66	65.85	56.10	31.71	56.10
Confusion Matrix										
7 21	19 9	18 10	23 5	17 11	14 14	17 11	26 2	19 9	0 28	19 9
3 10	9 4	8 5	10 3	5 8	5 8	8 5	12.00	9 4	0 13	9 4

Table D.472: One_sample_One_Study_Traditional_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.53	0.59	0.56	0.51	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
69.23	38.46	46.15	23.08	69.23	61.54	46.15	7.69	38.46	100.00	38.46
28.57	64.29	53.57	85.71	53.57	50.00	57.14	89.29	64.29	0.00	64.29
66.67	69.23	68.18	70.59	78.95	73.68	69.57	67.57	69.23	NaN	69.23
31.03	33.33	31.58	42.86	40.91	36.36	33.33	25.00	33.33	31.71	33.33
41.46	56.10	51.22	65.85	58.54	53.66	53.66	63.42	56.10	31.71	56.10
Confusion Matrix										
8 20	18 10	15 13	24 4	15 13	14 14	16 12	25 3	18 10	0 28	18 10
4 9	8 5	7 6	10 3	4 9	5 8	7 6	12 1	8 5	0 13	8 5

Table D.473: One_sample_One_Study_KFold_PCA_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.67	0.66	0.71	0.55	0.61	0.58	0.66	NA	0.64	0.67
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
45.24	42.86	47.62	**54.76**	50.00	47.62	45.24	45.24	NA	47.62	**52.38**
61.40	87.72	82.46	**84.21**	59.65	73.68	71.93	85.96	NA	78.95	**78.95**
60.34	67.57	68.12	**71.64**	61.82	65.63	64.06	68.06	NA	67.16	**69.23**
46.34	72.00	66.67	**71.88**	47.73	57.14	54.29	70.37	NA	62.50	**64.71**
54.55	68.69	67.68	**71.72**	55.56	62.63	60.61	68.69	NA	65.66	**67.68**
Confusion Matrix										
35 22	50 7	47 10	48 9	34 23	42 15	41 16	49 8	NA	45 12	45 12
23 19	24 18	22 20	19 23	21 21	22 20	23 19	23 19	NA	22 20	20 22

Table D.474: One_sample_One_Study_KFold_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	0.66	0.66	0.71	0.54	0.60	0.60	0.66	NA	0.64	0.66
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
47.62	42.86	47.62	**54.76**	50.00	45.24	45.24	45.24	NA	**50.00**	**51.16**
61.40	87.72	82.46	**84.21**	57.90	71.93	71.93	85.97	NA	**78.95**	**78.95**
61.40	67.57	68.12	**71.64**	61.11	64.06	64.06	68.06	NA	**68.18**	**68.18**
47.62	72.00	66.67	**71.88**	46.67	54.29	54.29	70.37	NA	**63.64**	**64.71**
55.56	68.69	67.68	**71.72**	54.55	60.61	60.61	68.69	NA	**66.67**	**67.00**
Confusion Matrix										
35 22	50 7	47 10	48 9	33 24	41 16	41 16	49 8	NA	45 12	45 12
22 20	24 18	22 20	19 23	21 21	23 19	23 19	23 19	NA	21 21	21 22

Table D.475: One_sample_One_Study_LOO_PCA_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.42	0.42	0.43	0.46	0.41	0.39	0.39	0.50	0.37	0.39
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
38.10	16.67	21.43	23.81	40.48	26.19	23.81	16.67	0.00	19.05	23.81
57.89	71.93	64.91	63.16	50.88	57.89	56.14	66.67	100.00	57.89	56.14
55.93	53.95	52.86	52.94	53.70	51.56	50.00	52.05	57.58	49.25	50.00
40.00	30.43	31.03	32.26	37.78	31.43	28.57	26.92	NaN	25.00	28.57
49.49	48.48	46.46	46.46	46.46	44.44	42.42	45.45	57.58	41.41	42.42
Confusion Matrix										
33 24	41 16	37 20	36 21	29 28	33 24	32 25	38 19	57 0	33 24	32 25
26 16	35 7	33 9	32 10	25 17	31 11	32 10	35 7	42 0	34 8	32 10

Table D.476: One_sample_One_Study_LOO_nextEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.51	0.52	0.52	0.46	0.46	0.46	0.50	NA	0.58	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
45.24	23.81	30.95	33.33	40.48	30.95	30.95	26.19	NA	40.48	35.71
63.16	77.19	71.93	70.18	50.88	61.40	61.40	73.68	NA	73.68	64.91
61.02	57.89	58.57	58.82	53.70	54.69	54.69	57.53	NA	62.69	57.81
47.50	43.48	44.83	45.16	37.78	37.14	37.14	42.31	NA	53.13	42.86
55.56	54.55	54.55	54.55	46.46	48.48	48.48	53.54	NA	59.60	52.53
Confusion Matrix										
36 21	44 13	41 16	40 17	29 28	35 22	35 22	42 15	NA	42 15	37 20
23 19	32 10	29 13	28 14	25 17	29 13	29 13	31 11	NA	25 17	27 15

For label *nextEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: Median_T1_Var Pixel Intensity/slice_meanPixel, Var_GM_min tissue prob, Max_GM_min tissue prob, Max_Anatomical_I_21_var pixel intensity, Max_GM_mean tissue prob, Var_Anatomical_I_21_var pixel intensity, Var_Anatomical_I_29_ratio

on region affected by lesion, Mean_Anatomical_I_21_var pixel intensity, Var_Anatomical_I_29_var pixel intensity, Max_Anatomical_I_29_ratio on region affected by lesion, Mean_Anatomical_I_29_var pixel intensity, Mean_Anatomical_I_42_var pixel intensity, Mean_Anatomical_I_29_ratio on region affected by lesion, Var_Var Pixel Intensity/slice_meanPixel.

Table D.477: One_sample_One_Study_Traditional_PCA_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.50	0.58	0.50	0.51	0.50	0.49	0.58	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
61.54	100.00	46.15	69.23	61.54	69.23	69.23	46.15	100.00	100.00	100.00
35.71	0.00	71.43	32.14	39.29	32.14	28.57	71.43	0.00	0.00	0.00
66.67	NaN	74.07	69.23	68.75	69.23	66.67	74.07	NaN	NaN	NaN
30.77	31.71	42.86	32.14	32.00	32.14	31.03	42.86	31.71	31.71	31.71
43.90	31.71	63.41	43.90	46.34	43.90	41.46	63.41	31.71	31.71	31.71
Confusion Matrix										
10 18	0 28	20 8	9 19	11 17	9 19	8 20	20 8	0 28	0 28	0 28
5 8	0 13	7 6	4 8	5 8	4 8	4 8	7 6	0 13	0 13	0 13

Table D.478: One_sample_One_Study_Traditional_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.45	0.49	0.53	0.53	0.52	0.52	0.50	0.45	0.50	0.45
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
69.23	38.46	92.31	38.46	84.62	84.62	69.23	7.69	38.46	100.00	38.46
32.14	53.57	3.57	67.86	21.43	21.43	35.71	96.43	53.57	0.00	53.57
69.23	65.22	50.00	70.37	75.00	75.00	71.43	69.23	65.22	NaN	65.22
32.14	27.78	30.77	35.71	33.33	33.33	33.33	50.00	27.78	31.71	27.78
43.90	48.78	31.71	58.54	41.46	41.46	46.34	68.29	48.78	31.71	48.78
Confusion Matrix										
9 19	15 13	1 27	19 9	6 22	6 22	10 18	27 1	15 13	0 28	15 13
4 9	8 5	1 12	8 5	2 11	2 11	4 9	12 1	8 5	0 13	8 5

Table D.479: One_sample_One_Study_kFold_PCA_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	0.65	0.67	0.68	0.60	0.56	0.62	0.69	NA	0.65	0.66
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
47.62	42.86	**50.00**	**54.76**	45.24	40.48	45.24	**50.00**	NA	**52.38**	47.62
61.40	85.96	**82.46**	**77.19**	75.44	70.18	77.19	**85.96**	NA	**77.19**	84.21
61.40	67.12	**69.12**	**69.84**	65.15	61.54	65.67	**70.00**	NA	**68.75**	68.57
47.62	69.23	**67.74**	**63.89**	57.58	50.00	59.38	**72.41**	NA	**62.86**	68.97
55.56	67.68	**68.69**	**67.68**	62.63	57.58	63.64	**70.71**	NA	**66.67**	68.69
Confusion Matrix										
35 22	49 8	47 10	44 13	43 14	40 17	44 13	49 8	NA	44 13	48 9
22 20	24 18	21 21	19 23	23 19	25 17	23 19	21 21	NA	20 22	22 20

Table D.480: One_sample_One_Study_kFold_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.56	0.66	0.68	0.69	0.61	0.56	0.62	0.70	NA	0.66	0.66
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
50.00	42.86	**50.00**	**57.14**	45.24	40.48	45.24	**50.00**	NA	**52.38**	47.62
61.40	87.72	**82.46**	**78.95**	73.68	70.18	77.19	**85.96**	NA	**77.19**	84.21
62.50	67.57	**69.12**	**71.43**	64.62	61.54	65.67	**70.00**	NA	**68.75**	68.57
48.84	72.00	**67.74**	**66.67**	55.88	50.00	59.38	**72.41**	NA	**62.86**	68.97
56.57	68.69	**68.69**	**69.70**	61.62	57.58	63.64	**70.71**	NA	**66.67**	68.69
Confusion Matrix										
35 22	50 7	47 10	45 12	42 15	40 17	44 13	49 8	NA	44 13	48 9
21 21	24 18	21 21	18 24	23 19	25 17	23 19	21 21	NA	20 22	22 20

Table D.481: One_sample_One_Study_LOO_PCA_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.58	0.50	0.47	0.48	0.52	0.59	0.56	0.44	NA	0.54	0.45
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
59.52	23.81	26.19	33.33	35.71	45.24	38.10	23.81	NA	40.48	23.81
56.14	75.44	68.42	63.16	68.42	71.93	71.93	66.67	NA	66.67	68.42
65.31	57.33	55.71	56.25	59.09	64.06	61.19	54.29	NA	60.32	54.93
50.00	41.67	37.93	40.00	45.45	54.29	50.00	34.48	NA	47.22	35.71
57.58	53.54	50.51	50.51	54.55	60.61	57.58	48.48	NA	55.56	49.49
Confusion Matrix										
32 25	43 14	39 18	36 21	39 18	41 16	41 16	38 19	NA	38 19	39 18
17 25	32 10	31 11	28 14	27 15	23 19	26 16	32 10	NA	25 17	32 10

Table D.482: One_sample_One_Study_LOO_nextEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.50	0.49	0.48	0.45	0.46	0.44	0.49	NA	0.47	0.53
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
45.24	23.81	28.57	33.33	28.57	30.95	26.19	28.57	NA	33.33	30.95
45.61	75.44	70.18	63.16	63.16	61.40	63.16	70.18	NA	61.40	73.68
53.06	57.33	57.14	56.25	54.55	54.69	53.73	57.14	NA	55.56	59.15
38.00	41.67	41.38	40.00	36.36	37.14	34.38	41.38	NA	38.89	46.43
45.45	53.54	52.53	50.51	48.48	48.48	47.47	52.53	NA	49.49	55.56
Confusion Matrix										
26 31	43 14	40 17	36 21	36 21	35 22	36 21	40 17	NA	35 22	42 15
23 19	32 10	30 12	28 14	30 12	29 13	31 11	30 12	NA	28 14	29 13

For label *mediumEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$:

Final features: Var_Solidity, Mean_Anatomical_II_408_mean pixel intensity, Mean_Anatomical_II_
pixel intensity, Mean_Anatomical_II_408_min pixel intensity, Var_Anatomical_II_408_min

pixel intensity, Max_Anatomical_II_408_mean pixel intensity, Max_Anatomical_II_408_median pixel intensity, Mean_Anatomical_II_408_lesion in the region.

Table D.483: One_sample_One_Study_Traditional_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.61	0.61	0.50	0.54	0.57	0.54	0.61	0.64	0.56	0.56
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
8.33	50.00	50.00	91.67	8.33	16.67	8.33	50.00	41.67	75.00	75.00
100.00	72.41	72.41	3.45	100.00	100.00	100.00	72.41	89.66	41.38	41.38
72.50	77.78	77.78	50.00	72.50	74.36	72.50	77.78	78.79	80.00	80.00
100.00	42.86	42.86	28.21	100.00	100.00	100.00	42.86	62.50	34.62	34.62
73.17	65.85	65.85	29.27	73.17	75.61	73.17	65.85	75.61	51.22	51.22
Confusion Matrix										
29 0	21 8	21 8	1 28	29 0	29 0	29 0	21 8	26 3	12 17	12 17
11 1	6 6	6 6	1 11	11 1	10 2	11 1	6 6	7 5	3 9	3 9

Table D.484: One_sample_One_Study_Traditional_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.56	NA	0.57	0.56	0.56	0.54		0.62	0.56	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
58.33	58.33	NA	16.67	16.67	16.67	8.33	NA	33.33	66.67	66.67
41.38	51.72	NA	96.55	96.55	100.00	100.00	NA	89.66	44.83	44.83
70.59	75.00	NA	73.68	73.68	74.36	72.50	NA	76.47	76.47	76.47
29.17	33.33	NA	66.67	66.67	100.00	100.00	NA	57.14	33.33	33.33
46.34	53.66	NA	73.17	73.17	75.61	73.17	NA	73.17	51.22	51.22
Confusion Matrix										
12 17	15 14	NA	28 1	28 1	29 0	29 0	NA	26 3	13 16	13 16
5 7	5 7	NA	10 2	10 2	10 2	11 1	NA	8 4	4 8	4 8

Table D.485: One_sample_One_Study_kFold_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.69	0.62	0.62	0.58	0.68	0.65	0.61	0.62	0.62	0.62	0.62
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
60.98	31.71	31.71	43.90	**63.42**	**56.10**	48.78	31.71	31.71	31.71	31.71
75.86	96.55	96.55	72.41	**72.41**	**72.41**	70.69	96.55	96.55	96.55	96.55
73.33	66.67	66.67	64.62	**73.68**	**70.00**	66.13	66.67	66.67	66.67	66.67
64.10	86.67	86.67	52.94	**61.91**	**58.97**	54.05	86.67	86.67	86.67	86.67
69.70	69.70	69.70	60.61	**68.69**	**65.66**	61.62	69.70	69.70	69.70	69.70
Confusion Matrix										
44 14	56 2	56 2	42 16	42 16	42 16	41 17	56 2	56 2	56 2	56 2
16 25	28 13	28 13	23 18	15 26	18 23	21 20	28 13	28 13	28 13	28 13

Table D.486: One_sample_One_Study_kFold_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.61	0.64	NA	0.64	0.58	0.64	0.64	NA	NA	0.61	0.61
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
29.27	31.71	NA	31.71	26.83	31.71	31.71	NA	NA	31.71	31.71
96.55	96.55	NA	96.55	96.55	96.55	96.55	NA	NA	96.55	96.55
65.88	66.67	NA	66.67	65.12	66.67	66.67	NA	NA	66.67	66.67
85.71	86.67	NA	86.67	84.62	86.67	86.67	NA	NA	86.67	86.67
68.69	69.70	NA	69.70	67.68	69.70	69.70	NA	NA	69.70	69.70
Confusion Matrix										
56 2	56 2	NA	56 2	56 2	56 2	56 2	NA	NA	56 2	56 2
29 12	28 13	NA	28 13	30 11	28 13	28 13	NA	NA	28 13	28 13

Table D.487: One_sample_One_Study_LOO_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.45	0.45	0.45	0.46	0.50	0.43	0.44	0.45	0.45	0.45	0.45
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
34.15	12.20	12.20	26.83	43.90	31.71	17.07	12.20	12.20	12.20	12.20
55.17	82.76	82.76	65.52	56.90	55.17	31.71	82.76	82.76	82.76	82.76
54.24	57.14	57.14	55.88	58.93	53.33	56.90	57.14	57.14	57.14	57.14
35.00	33.33	33.33	35.48	41.86	33.33	54.10	33.33	33.33	33.33	33.33
46.47	53.54	53.54	49.50	51.52	45.46	34.21	53.54	53.54	53.54	53.54
Confusion Matrix										
32 26	48 10	48 10	38 20	33 25	32 26	33 25	48 10	48 10	48 10	48 10
27 14	36 5	36 5	30 11	23 18	28 13	28 13	36 5	36 5	36 5	36 5

Table D.488: One_sample_One_Study_LOO_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.43	0.45	NA	0.45	0.44	0.45	0.45	NA	0.45	0.45	0.45
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
9.76	12.20	NA	12.20	9.76	12.20	12.20	NA	12.20	12.20	12.20
82.76	82.76	NA	82.76	84.48	82.76	82.76	NA	82.76	82.76	82.76
56.47	57.14	NA	57.14	56.98	57.14	57.14	NA	57.14	57.14	57.14
28.57	33.33	NA	33.33	30.77	33.33	33.33	NA	33.33	33.33	33.33
52.53	53.54	NA	53.54	53.54	53.54	53.54	NA	53.54	53.54	53.54
Confusion Matrix										
48 10	48 10	NA	48 10	49 9	48 10	48 10	NA	48 10	48 10	48 10
37 4	36 5	NA	36 5	37 4	36 5	36 5	NA	36 5	36 5	36 5

For label *mediumEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

The via pattern recognition study was not performed since the number of patients with *mediumEDSS*≥ 5 was minimal.

For label *highestEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: Var_Solidity, Mean_GM_min tissue prob, Var_GM_min tissue prob, Mean_Anatomical_I_162_lesion in the region, Max_Anatomical_I_162_ratio on region affected by lesion, Var_Anatomical_I_162_ratio on region affected by lesion, Mean_Anatomical_I_162_ratio on region affected by lesion, Var_Anatomical_I_162_median pixel intensity, Max_Anatomical_I_162_lesion in the region, Max_Anatomical_I_162_max pixel intensity.

Table D.489: One_sample_One_Study_Traditional_PCA_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.50	0.53	0.47	0.49	0.51	0.49	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
46.67	100.00	13.33	60.00	40.00	46.67	40.00	0.00	100.00	100.00	100.00
66.67	0.00	91.67	33.33	58.33	58.33	58.33	100.00	0.00	0.00	0.00
50.00	NaN	45.83	40.00	43.75	46.67	43.75	44.44	NaN	NaN	NaN
63.64	55.56	66.67	52.94	54.55	58.33	54.55	NaN	55.56	55.56	55.56
55.56	55.56	48.15	48.15	48.15	51.85	48.15	44.44	55.56	55.56	55.56
Confusion Matrix										
8 4	0 12	11 1	4 8	7 5	7 5	7 5	12 0	0 12	0 12	0 12
8 7	0 15	13 2	6 9	9 6	8 7	9 6	15 0	0 15	0 15	0 15

Table D.490: One_sample_One_Study_Traditional_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.49	NA	0.48	0.44	0.48	0.52	NA	0.49	0.50	0.49
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
46.67	100.00	NA	93.33	53.33	53.33	33.33	NA	100.00	100.00	100.00
58.33	0.00	NA	0.00	33.33	41.67	75.00	NA	0.00	0.00	0.00
46.67	NaN	NA	0.00	36.36	41.67	47.37	NA	NaN	NaN	NaN
58.33	55.56	NA	53.85	50.00	53.33	62.50	NA	55.56	55.56	55.56
51.85	55.56	NA	51.85	44.44	48.15	51.85	NA	55.56	55.56	55.56
Confusion Matrix										
7 5	0 12	NA	0 12	4 8	5 7	9 3	NA	0 12	0 12	0 12
8 7	0 15	NA	1 14	7 8	7 8	10 5	NA	0 15	0 15	0 15

Table D.491: One_sample_One_Study_kFold_PCA_highestEDSS ≥ 3

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.64	0.66	0.70	0.64	0.58	0.56	0.57	0.68	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
64.71	**60.78**	**60.78**	**62.75**	**58.82**	49.02	**56.86**	**56.86**	NA	**52.94**	**58.82**
62.50	**70.83**	**79.17**	**64.58**	**56.25**	62.50	**56.25**	**77.08**	NA	**75.00**	**72.92**
62.50	**62.96**	**65.52**	**62.00**	**56.25**	53.57	**55.10**	**62.71**	NA	**60.00**	**62.50**
64.71	**68.89**	**75.61**	**65.31**	**58.82**	58.14	**58.00**	**72.50**	NA	**69.23**	**69.77**
63.64	**65.66**	**69.70**	**63.64**	**57.58**	55.56	**56.57**	**66.67**	NA	**63.64**	**65.66**
Confusion Matrix										
30 18	34 14	38 10	31 17	27 21	30 18	27 21	37 11	NA	36 12	35 13
18 33	20 31	20 31	19 32	21 30	26 25	22 29	22 29	NA	24 27	21 30

Table D.492: One_sample_One_Study_kFold_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.65	0.66	0.70	0.64	0.58	0.56	0.57	0.68	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
64.71	**60.78**	**60.78**	**62.75**	**58.82**	49.02	**56.86**	**56.86**	NA	**52.94**	**58.82**
64.58	**68.75**	**79.17**	**62.50**	**56.25**	62.50	**56.25**	**77.08**	NA	**75.00**	**72.92**
63.27	**62.26**	**65.52**	**61.22**	**56.25**	53.57	**55.10**	**62.71**	NA	**60.00**	**62.50**
66.00	**67.39**	**75.61**	**64.00**	**58.82**	58.14	**58.00**	**72.50**	NA	**69.23**	**69.77**
64.65	**64.65**	**69.70**	**62.63**	**57.58**	55.56	**56.57**	**66.67**	NA	**63.64**	**65.66**
Confusion Matrix										
31 17	33 15	38 10	30 18	27 21	30 18	27 21	37 11	NA	36 12	35 13
18 33	20 31	20 31	19 32	21 30	26 25	22 29	22 29	NA	24 27	21 30

Table D.493: One_sample_One_Study_LOO_PCA_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.45	0.50	0.47	0.55	0.50	0.47	0.49	NA	0.50	0.41
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
56.86	41.18	39.22	47.06	**58.82**	41.18	49.02	37.26	NA	39.22	35.29
45.83	47.92	60.42	47.92	**52.08**	58.33	45.83	60.42	NA	60.42	47.92
50.00	43.40	48.33	46.00	**54.35**	48.28	45.83	47.54	NA	48.33	41.07
52.73	45.65	51.28	48.98	**56.60**	51.22	49.02	50.00	NA	51.28	41.86
51.52	44.44	49.50	47.48	**55.56**	49.50	47.48	48.49	NA	49.50	41.41
Confusion Matrix										
22 26	23 25	29 19	23 25	25 23	28 20	22 26	29 19	NA	29 19	23 25
22 29	30 21	31 20	27 24	21 30	30 21	26 25	32 19	NA	31 20	33 18

Table D.494: One_sample_One_Study_LOO_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.53	0.50	0.56	0.45	0.50	0.51	0.47	NA	0.50	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
54.90	49.02	39.22	**54.90**	49.02	41.18	**52.94**	35.29	NA	39.22	45.10
43.75	56.25	60.42	**56.25**	41.67	58.33	**50.00**	58.33	NA	60.42	58.33
47.73	50.94	48.33	**54.00**	43.48	48.28	**50.00**	45.90	NA	48.33	50.00
50.91	54.35	51.28	**57.14**	47.17	51.22	**52.94**	47.37	NA	51.28	53.49
49.50	52.53	49.50	**55.56**	45.46	49.50	**51.52**	46.47	NA	49.50	51.52
Confusion Matrix										
21 27	27 21	29 19	27 21	20 28	28 20	24 24	28 20	NA	29 19	28 20
23 28	26 25	31 20	23 28	26 25	30 21	24 27	33 18	NA	31 20	28 23

For label *highestEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: Var_Anatomical_II_39_mean pixel intensity, Var_Anatomical_I_122_median pixel intensity, Mean_Anatomical_II_39_lesion in the region.

Table D.495: One_sample_One_Study_Traditional_PCA_highestEDSS ≥ 5

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.51	0.59	0.51	0.52	0.51	0.52	0.51	0.51	0.63	0.55	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
50.00	100.00	16.67	66.67	50.00	50.00	50.00	16.67	100.00	100.00	100.00
52.38	19.05	88.89	41.27	55.56	50.79	47.62	88.89	26.98	11.11	11.11
91.67	100.00	91.80	92.86	92.11	91.43	90.91	91.80	100.00	100.00	100.00
9.09	10.53	12.50	9.76	9.68	8.82	8.33	12.50	11.54	9.68	9.68
52.17	26.09	82.61	43.48	55.07	50.73	47.83	82.61	33.33	18.84	18.84
Confusion Matrix										
33 30	12 51	56 7	26 37	35 28	32 31	30 33	56 7	17 46	7 56	7 56
3 3	0 6	5 1	2 4	3 3	3 3	3 3	5 1	0 6	0 6	0 6

Table D.496: One_sample_One_Study_Traditional_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.52	0.51	0.50	0.51	0.50	0.50	0.51	0.60	0.53	0.51
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
71.43	83.33	33.33	83.33	66.67	66.67	83.33	16.67	83.33	100.00	83.33
25.40	23.81	74.60	19.05	31.75	39.68	22.22	76.19	39.68	6.35	22.22
88.89	93.75	92.16	92.31	90.91	92.59	93.33	90.57	96.15	100.00	93.33
9.62	9.43	11.11	8.93	8.51	9.52	9.26	6.25	11.63	9.23	9.26
30.00	28.99	71.01	24.64	34.78	42.03	27.54	71.01	43.48	14.49	27.54
Confusion Matrix										
16 47	15 48	47 16	12 51	20 43	25 38	14 49	48 15	25 38	4 59	14 49
2 5	1 5	4 2	1 5	2 4	2 4	1 5	5 1	1 5	0 6	1 5

Table D.497: One_sample_One_Study_kFold_PCA_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.61	0.45	0.40	0.06	0.48	0.37	0.23	0.52	NA	0.67	0.67
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
42.86	23.81	19.05	4.76	23.81	18.18	4.76	33.33	NA	52.38	57.14
85.90	93.59	88.46	100.00	83.33	93.59	94.87	87.18	NA	75.64	74.36
84.81	82.02	80.23	79.59	80.25	80.22	78.72	82.93	NA	85.51	86.57
45.00	50.00	30.77	100.00	27.78	44.44	20.00	41.18	NA	36.67	37.50
76.77	78.79	73.74	79.80	70.71	77.00	75.76	75.76	NA	70.71	70.71
Confusion Matrix										
67 11	73 5	69 9	78 0	65 13	73 5	74 4	68 10	NA	59 19	58 20
12 9	16 5	17 4	20 1	16 5	18 4	20 1	14 7	NA	10 11	9 12

Table D.498: One_sample_One_Study_kFold_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.44	0.39	0.07	0.47	0.38	0.22	0.53	NA	0.63	0.73
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
42.86	23.81	19.05	0.00	23.81	19.05	4.76	33.33	NA	57.14	57.14
87.18	93.59	88.46	98.72	83.33	93.59	94.87	87.18	NA	75.64	74.36
85.00	82.02	80.23	78.57	80.25	81.11	78.72	82.93	NA	86.77	86.57
47.37	50.00	30.77	0.00	27.78	44.44	20.00	41.18	NA	38.71	37.50
77.78	78.79	73.74	77.78	70.71	77.78	75.76	75.76	NA	71.72	70.71
Confusion Matrix										
68 10	73 5	69 9	77 1	65 13	73 5	74 4	68 10	NA	59 19	58 20
12 9	16 5	17 4	21 0	16 5	17 4	20 1	14 7	NA	9 12	9 12

Table D.499: One_sample_One_Study_LOO_PCA_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.58	0.49	0.64	0.06	0.51	0.44	0.39	0.51	NA	0.49	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
33.33	9.52	23.81	0.00	19.05	4.76	0.00	19.05	NA	28.57	33.33
82.05	89.74	92.31	100.00	83.33	89.74	93.59	82.05	NA	69.23	67.95
82.05	78.65	81.82	78.79	79.27	77.78	77.66	79.01	NA	78.26	79.10
33.33	20.00	45.46	NaN	23.53	11.11	0.00	22.22	NA	20.00	21.88
71.72	72.73	77.78	78.79	69.70	71.72	73.74	68.69	NA	60.61	60.61
Confusion Matrix										
64 14	70 8	72 6	78 0	65 13	70 8	73 5	64 14	NA	54 24	53 25
14 7	19 2	16 5	21 0	17 4	20 1	21 0	17 4	NA	15 6	14 7

Table D.500: One_sample_One_Study_LOO_highestEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.38	0.43	0.07	0.62	0.44	0.49	0.40	NA	0.40	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
14.29	0.00	4.76	0.00	33.33	4.76	4.76	4.76	NA	9.52	19.05
76.92	87.18	87.18	100.00	87.18	89.74	94.87	78.21	NA	64.10	64.10
76.92	76.40	77.27	78.79	82.93	77.78	78.72	75.31	NA	72.46	74.63
14.29	0.00	9.09	NaN	41.18	11.11	20.00	5.56	NA	6.67	12.50
63.64	68.69	69.70	78.79	75.76	71.72	75.76	62.63	NA	52.53	54.55
Confusion Matrix										
60 18 18 3	68 10 21 0	68 10 20 1	78 0 21 0	68 10 14 7	70 8 20 1	74 4 20 1	61 17 20 1	NA NA	50 28 19 2	50 28 17 4

For label *first2EDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: Mean_Anatomical_II_38_mean pixel intensity, Mean_Anatomical_II_39_median pixel intensity, Var_Anatomical_II_70_lesion in the region, Mean_Anatomical_I_162_ratio on region affected by lesion, Max_Anatomical_I_162_ratio on region affected by lesion.

Table D.501: One_sample_One_Study_Traditional_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.53	0.53	0.52	0.53	0.49	0.53	0.55	0.50	0.53	0.53	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
55.56	88.89	40.00	66.67	66.67	66.67	55.56	33.33	77.78	88.89	88.89
47.92	20.83	64.58	35.42	31.25	41.67	52.08	68.75	24.49	12.50	12.50
85.19	90.91	83.78	85.00	83.33	86.96	86.21	84.62	85.71	85.71	85.71
16.67	17.39	19.05	16.22	15.39	17.65	17.86	16.67	15.91	16.00	16.00
49.12	31.58	60.35	40.35	36.84	45.61	52.63	63.16	32.76	24.56	24.56
Confusion Matrix										
23 25 4 5	10 38 1 8	31 17 6 4	17 31 3 6	15 33 3 6	20 28 3 6	25 23 4 5	33 15 6 3	12 37 2 7	6 42 1 8	6 42 1 8

Table D.502: One_sample_One_Study_Traditional_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.53	NA	0.55	0.51	0.53	0.52	NA	0.54	0.52	0.53
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
55.56	88.89	NA	33.33	22.22	33.33	22.22	NA	77.78	88.89	88.89
39.58	18.75	NA	79.17	79.17	72.92	81.25	NA	25.00	14.58	16.67
82.61	90.00	NA	86.36	84.44	85.37	84.78	NA	85.71	87.50	88.89
14.71	17.02	NA	23.08	16.67	18.75	18.18	NA	16.28	16.33	16.67
42.11	29.83	NA	71.93	70.18	66.67	71.93	NA	33.33	26.32	28.07
Confusion Matrix										
19 29 4 5	9 39 1 8	NA NA	38 10 6 3	38 10 7 2	35 13 6 3	39 9 7 2	NA NA	12 36 2 7	7 41 1 8	8 40 1 8

Table D.503: One_sample_One_Study_KFold_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.56	0.58	0.63	0.58	0.56	0.64	0.63	0.69	0.57	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
36.67	33.33	43.33	30.00	36.67	46.67	40.00	**50.00**	30.00	**50.00**	**56.67**
81.16	89.86	89.86	89.86	78.57	88.41	88.41	**88.41**	91.30	**86.96**	**75.36**
74.67	75.61	78.48	74.70	74.32	79.22	77.22	**80.26**	75.00	**80.00**	**80.00**
45.83	58.82	65.00	56.25	42.31	63.64	60.00	**65.22**	60.00	**62.50**	**50.00**
67.68	72.73	75.76	71.72	66.00	75.76	73.74	**76.77**	72.73	**75.76**	**69.70**
Confusion Matrix										
56 13	62 7	62 7	62 7	55 15	61 8	61 8	61 8	63 6	60 9	52 17
19 11	20 10	17 13	21 9	19 11	16 14	18 12	15 15	21 9	15 15	13 17

Table D.504: One_sample_One_Study_KFold_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.56	0.59	0.66	0.59	0.57	0.67	0.64	0.69	0.58	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
36.67	33.33	43.33	30.00	36.67	46.67	40.00	**50.00**	33.33	**50.00**	**60.00**
82.61	89.86	91.30	89.86	78.26	88.41	88.41	**88.41**	91.30	**86.96**	**75.36**
75.00	75.61	78.75	74.70	73.97	79.22	77.22	**80.26**	75.90	**80.00**	**81.25**
47.83	58.82	68.42	56.25	42.31	63.64	60.00	**65.22**	62.50	**62.50**	**51.43**
68.69	72.73	76.77	71.72	65.66	75.76	73.74	**76.77**	73.74	**75.76**	**70.71**
Confusion Matrix										
57 12	62 7	63 6	62 7	54 15	61 8	61 8	61 8	63 6	60 9	52 17
19 11	20 10	17 13	21 9	19 11	16 14	18 12	18 12	20 10	15 15	12 18

Table D.505: One_sample_One_Study_LOO_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.45	0.49	0.48	0.48	0.53	0.46	0.46	0.47	0.49	0.44	0.45
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
20.00	16.67	16.67	16.67	30.00	16.67	16.67	20.00	16.67	16.67	26.67
71.01	82.61	79.71	79.71	75.36	76.81	76.81	75.36	82.61	72.46	62.32
67.12	69.51	68.75	68.75	71.23	67.95	67.95	68.42	69.51	66.67	66.15
23.08	29.41	26.32	26.32	34.62	23.81	23.81	26.09	29.41	20.83	23.53
55.56	62.63	60.61	60.61	61.62	58.59	58.59	58.59	62.63	55.56	51.52
Confusion Matrix										
49 20	57 12	55 14	55 14	52 17	53 16	53 16	52 17	57 12	50 19	43 26
24 6	25 5	25 5	25 5	21 9	25 5	25 5	24 6	25 5	25 5	22 8

Table D.506: One_sample_One_Study_LOO_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.56	0.49	0.51	0.54	0.61	0.58	0.58	0.56	0.49	0.58	0.52
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
33.33	16.67	20.00	23.33	40.00	30.00	30.00	30.00	16.67	33.33	36.67
76.81	82.61	81.16	82.61	79.71	82.61	82.61	79.71	82.61	79.71	66.67
72.60	69.51	70.00	71.25	75.34	73.08	73.08	72.37	69.51	73.33	70.77
38.46	29.41	31.58	36.84	46.15	42.86	42.86	39.13	29.41	41.67	32.35
63.64	62.63	62.63	64.65	67.68	66.67	66.67	64.65	62.63	65.66	57.58
Confusion Matrix										
53 16 20 10	57 12 25 5	56 13 24 6	57 12 23 7	55 14 18 12	57 12 21 9	57 12 21 9	55 14 21 9	57 12 25 5	55 14 20 10	46 23 19 11

For label *first2EDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features:

The via pattern recognition study was not performed since the number of patients with first2EDSS≥ 5 was minimal.

D.3.3 One sample, one patient Set

For label *msCourse* (0/1 - RR/SP:

Final features: Max_Max_Anatomical_II_52_ratio on region affected by lesion, Mean_Mean_Anatomical_I_25_ratio on region affected by lesion, Min_Var_Anatomical_I_42_var pixel intensity, Min_Max_Anatomical_I_42_var pixel intensity, Mean_Var_Anatomical_II_52_ratio on region affected by lesion, Mean_Var_Anatomical_I_42_lesion in the region, Min_Mean_Anatomical_I_ pixel intensity, Min_Median_Eccentricity, Mean_Var_Anatomical_I_25_ratio on region affected by lesion.

Table D.507: One_sample_One_Patient_Traditional_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.51	0.50	0.50	0.50	0.52	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
0.00	0.00	0.00	0.00	0.00	0.00	0.00	5.26	0.00	0.00	0.00
NaN	NaN	NaN	NaN	NaN	NaN	NaN	100.00	NaN	NaN	NaN
13.64	13.64	13.64	13.64	13.64	13.64	13.64	14.29	13.64	13.64	13.64
13.64	13.64	13.64	13.64	13.64	13.64	13.64	18.18	13.64	13.64	13.64
Confusion Matrix										
0 19 0 3	0 19 0 3	0 19 0 3	0 19 0 3	0 19 0 3	0 19 0 3	0 19 0 3	1 18 0 3	0 19 0 3	0 19 0 3	0 19 0 3

Table D.508: One_sample_One_Patient_Traditional_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.51	0.50	0.50	0.50	0.50	0.51	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
0.00	0.00	5.26	5.26	0.00	0.00	0.00	5.26	0.00	0.00	0.00
NaN	NaN	100.00	100.00	NaN	NaN	NaN	100.00	NaN	NaN	NaN
13.64	13.64	14.29	14.29	13.64	13.64	13.64	14.29	13.64	13.64	13.64
13.64	13.64	18.18	18.18	13.64	13.64	13.64	18.18	13.64	13.64	13.64
Confusion Matrix										
0 19 0 3	0 19 0 3	1 18 0 3	1 18 0 3	0 19 0 3	0 19 0 3	0 19 0 3	1 18 0 3	0 19 0 3	0 19 0 3	0 19 0 3

Table D.509: One_sample_One_Patient_kFold_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.59	0.42	0.37	0.35	0.53	0.59	0.60	0.28	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
80.00	**50.00**	40.00	40.00	**70.00**	**80.00**	**80.00**	30.00	NA	**80.00**	**80.00**
84.62	**84.62**	88.46	92.31	**96.15**	**84.62**	**80.77**	92.31	NA	**84.62**	**84.62**
91.67	**81.48**	79.31	80.00	**89.29**	**91.67**	**91.30**	77.42	NA	**91.67**	**91.67**
66.67	**55.56**	57.14	66.67	**87.50**	**66.67**	**61.54**	60.00	NA	**66.67**	**66.67**
83.33	**75.00**	75.00	77.78	**88.89**	**83.33**	**80.56**	75.00	NA	**83.33**	**83.33**
Confusion Matrix										
22 4 2 8	22 4 5 5	23 3 6 4	24 2 6 4	25 1 3 7	22 4 2 8	21 5 2 8	24 2 7 3	NA NA	22 4 2 8	22 4 2 8

Table D.510: One_sample_One_Patient_kFold_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.49	0.44	NA	0.39	0.55	0.61	0.62	NA	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
60.00	**50.00**	NA	40.00	**70.00**	**80.00**	**80.00**	NA	NA	**80.00**	**60.00**
88.46	**84.62**	NA	80.77	**96.15**	**84.62**	**84.62**	NA	NA	**84.62**	**80.77**
85.19	**81.48**	NA	77.78	**89.29**	**91.67**	**91.67**	NA	NA	**91.67**	**84.00**
66.67	**55.56**	NA	44.44	**87.50**	**66.67**	**66.67**	NA	NA	**66.67**	**54.55**
80.56	**75.00**	NA	69.44	**88.89**	**83.33**	**83.33**	NA	NA	**83.33**	**75.00**
Confusion Matrix										
23 3 4 6	22 4 5 5	NA NA	21 5 6 4	25 1 3 7	22 4 2 8	22 4 2 8	NA NA	NA NA	22 4 2 8	21 5 4 6

Table D.511: One_sample_One_Patient_LOO_PCA_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.54	0.48	0.50	0.43	0.48	0.48	0.46	0.48	0.48	0.48	0.48
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.00	20.00	20.00	10.00	20.00	30.00	30.00	10.00	20.00	30.00	30.00
69.23	76.92	80.77	80.77	76.92	65.38	61.54	88.46	76.92	65.38	65.38
75.00	71.43	72.41	70.00	71.43	70.83	69.57	71.88	71.43	70.83	70.83
33.33	25.00	28.57	16.67	25.00	25.00	23.08	25.00	25.00	25.00	25.00
61.11	61.11	63.89	61.11	61.11	55.56	52.78	66.67	61.11	55.56	55.56
Confusion Matrix										
18 8 6 4	20 6 8 2	21 5 8 2	21 5 9 1	20 6 8 2	17 9 7 3	16 10 7 3	23 3 9 1	20 6 8 2	17 9 7 3	17 9 7 3

Table D.512: One_sample_One_Patient_LOO_msCourse

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.40	0.39	NA	0.39	0.40	0.48	0.46	NA	NA	0.42	0.43
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
10.00	10.00	NA	10.00	10.00	30.00	30.00	NA	NA	20.00	20.00
73.08	69.23	NA	69.23	73.08	65.38	61.54	NA	NA	61.54	65.38
67.86	66.67	NA	66.67	67.86	70.83	69.57	NA	NA	66.67	68.00
12.50	11.11	NA	11.11	12.50	25.00	23.08	NA	NA	16.67	18.18
55.56	52.78	NA	52.78	55.56	55.56	52.78	NA	NA	50.00	52.78
Confusion Matrix										
19 7 9 1	18 8 9 1	NA NA	18 8 9 1	19 7 9 1	17 9 7 3	16 10 7 3	NA NA	NA NA	16 10 8 2	17 9 8 2

For label *mediumEDSS* > 3 **(0/1 -** $(< 3)/(\geq 3)$**:**

Final features: Max_Mean_RefSpace Max_Median_RefSpace, Var_Var_Anatomical_I_31_var pixel intensity, Max_Mean_Anatomical_I_25_ratio on region affected by lesion, Mean_Var_Anatomical_I on region affected by lesion, Mean_Var_Anatomical_I_29_ratio on region affected by lesion, Max_Var_Anatomical_I_31_mean pixel intensity, Mean_Max_Anatomical_I_31_var pixel intensity.

Table D.513: One_sample_One_Patient_Traditional_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	LDA	QDA	SVM	KNN-1	KNN-3	KNN-5	Naive Bayes	GLM	Euclidean	Mahalanobis
AUC										
0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
0.00	0.00	0.00	8.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00
NaN	NaN	NaN	100.00	NaN	NaN	NaN	NaN	NaN	NaN	NaN
25.00	25.00	25.00	26.67	25.00	25.00	25.00	25.00	25.00	25.00	25.00
25.00	25.00	25.00	31.25	25.00	25.00	25.00	25.00	25.00	25.00	25.00
Confusion Matrix										
0 12 0 4	0 12 0 4	0 12 0 4	1 11 0 4	0 12 0 4	0 12 0 4	0 12 0 4	0 12 0 4	0 12 0 4	0 12 0 4	0 12 0 4

Table D.514: One_sample_One_Patient_Traditional_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.50	0.50	0.50	0.50	0.51	0.50	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
0.00	0.00	0.00	0.00	0.00	0.00	8.33	0.00	0.00	0.00	0.00
NaN	NaN	NaN	NaN	NaN	NaN	100.00	NaN	NaN	NaN	NaN
25.00	25.00	25.00	25.00	25.00	25.00	26.67	25.00	25.00	25.00	25.00
25.00	25.00	25.00	25.00	25.00	25.00	31.25	25.00	25.00	25.00	25.00
Confusion Matrix										
0 12 0 4	0 12 0 4	0 12 0 4	0 12 0 4	0 12 0 4	0 12 0 4	1 11 0 4	0 12 0 4	0 12 0 4	0 12 0 4	0 12 0 4

Table D.515: One_sample_One_Patient_kFold_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.51	0.58	0.53	0.62	0.55	0.58	0.58	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
57.14	**50.00**	**57.14**	**57.14**	**71.43**	**64.29**	**64.29**	**57.14**	NA	**71.43**	**71.43**
86.36	**90.91**	**86.96**	**86.36**	**90.91**	**72.73**	**81.82**	**86.96**	NA	**86.36**	**86.36**
76.00	**74.07**	**76.92**	**76.00**	**83.33**	**76.19**	**78.26**	**76.92**	NA	**82.61**	**82.61**
72.73	**77.78**	**72.73**	**72.73**	**83.33**	**60.00**	**69.23**	**72.73**	NA	**76.92**	**76.92**
75.00	**75.00**	**75.68**	**75.00**	**83.33**	**69.44**	**75.00**	**75.68**	NA	**80.56**	**80.56**
Confusion Matrix										
19 3 6 8	20 2 7 7	20 3 6 8	19 3 6 8	20 2 4 10	16 6 5 9	18 4 5 9	20 3 6 8	NA NA	19 3 4 10	19 3 4 10

Table D.516: One_sample_One_Patient_kFold_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.51	0.58	0.53	0.62	0.55	0.58	0.58	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
57.14	**50.00**	**57.14**	**57.14**	**71.43**	**64.29**	**64.29**	**57.14**	NA	**71.43**	**71.43**
86.36	**90.91**	**86.96**	**86.36**	**90.91**	**72.73**	**81.82**	**86.96**	NA	**86.36**	**86.36**
76.00	**74.07**	**76.92**	**76.00**	**83.33**	**76.19**	**78.26**	**76.92**	NA	**82.61**	**82.61**
72.73	**77.78**	**72.73**	**72.73**	**83.33**	**60.00**	**69.23**	**72.73**	NA	**76.92**	**76.92**
75.00	**75.00**	**75.68**	**75.00**	**83.33**	**69.44**	**75.00**	**75.68**	NA	**80.56**	**80.56**
Confusion Matrix										
19 3 6 8	20 2 7 7	20 3 6 8	19 3 6 8	20 2 4 10	16 6 5 9	18 4 5 9	20 3 6 8	NA NA	19 3 4 10	19 3 4 10

Table D.517: One_sample_One_Patient_LOO_PCA_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	0.31	0.42	0.55	0.58	0.45	0.47	0.42	0.31	0.44	0.44
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
35.71	7.14	21.43	35.71	42.86	35.71	35.71	21.43	7.14	28.57	28.57
72.73	63.64	63.64	72.73	72.73	54.55	59.09	63.64	63.64	59.09	59.09
64.00	51.85	56.00	64.00	66.67	57.14	59.09	56.00	51.85	56.52	56.52
45.46	11.11	27.27	45.46	50.00	33.33	35.71	27.27	11.11	30.77	30.77
58.33	41.67	47.22	58.33	61.11	47.22	50.00	47.22	41.67	47.22	47.22
Confusion Matrix										
16 6 9 5	14 8 13 1	14 8 11 3	16 6 9 5	16 6 8 6	12 10 9 5	13 9 9 5	14 8 11 3	14 8 13 1	13 9 10 4	13 9 10 4

Table D.518: One_sample_One_Patient_LOO_mediumEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.40	0.44	0.45	0.42	0.42	0.47	0.48	NA	0.56	0.40
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
42.86	21.43	28.57	35.71	21.43	28.57	35.71	28.57	NA	42.86	21.43
59.09	59.09	59.09	54.55	63.64	54.55	59.09	68.18	NA	68.18	59.09
61.91	54.17	56.52	57.14	56.00	54.55	59.09	60.00	NA	65.22	54.17
40.00	25.00	30.77	33.33	27.27	28.57	35.71	36.36	NA	46.15	25.00
52.78	44.44	47.22	47.22	47.22	44.44	50.00	52.78	NA	58.33	44.44
Confusion Matrix										
13 9 8 6	13 9 11 3	13 9 10 4	12 10 9 5	14 8 11 3	12 10 10 4	13 9 9 5	15 7 10 4	NA NA	15 7 8 6	13 9 11 3

For label *mediumEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

Final features: Max_Max_Anatomical_II_14_ratio on region affected by lesion, Max_Mean_Anatomical_I_43_lesion in the region, Max_Mean_Anatomical_I_43_max pixel intensity, Max_Var_Anatomical_I_43_mean pixel intensity, Max_Var_Anatomical_I_31_mean

pixel intensity, Max_Var_Anatomical_I_31_min pixel intensity, Max_Max_Anatomical_II_54_ratio on region affected by lesion, Max_Mean_Anatomical_I_43_mean pixel intensity.

Table D.519: One_sample_One_Patient_Traditional_PCA_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.50	0.53	0.53	0.52	0.56	0.56	0.56	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
0.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
100.00	0.00	37.04	44.44	22.22	51.85	37.04	51.85	0.00	0.00	0.00
96.43	NaN	100.00	100.00	100.00	100.00	100.00	100.00	NaN	NaN	NaN
NaN	3.57	5.56	6.25	4.55	7.14	5.56	7.14	3.57	3.57	3.57
96.43	3.57	39.29	46.43	25.00	53.57	39.29	53.57	3.57	3.57	3.57
Confusion Matrix										
27 0 1 0	0 27 0 1	10 17 0 1	12 15 0 1	6 21 0 1	14 13 0 1	10 17 0 1	14 13 0 1	0 27 0 1	0 27 0 1	0 27 0 1

Table D.520: One_sample_One_Patient_Traditional_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.49	NA	0.60	0.55	0.56	0.56	NA	0.49	0.50	0.49
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
0.00	100.00	NA	100.00	100.00	100.00	100.00	NA	100.00	100.00	100.00
100.00	25.93	NA	37.04	33.33	62.96	40.74	NA	25.93	0.00	25.93
96.43	100.00	NA	100.00	100.00	100.00	100.00	NA	100.00	NaN	100.00
NaN	4.76	NA	5.56	5.26	9.09	5.88	NA	4.76	3.57	4.76
96.43	28.57	NA	39.29	35.71	64.29	42.86	NA	28.57	3.57	28.57
Confusion Matrix										
27 0 1 0	7 20 0 1	NA NA	10 17 0 1	9 18 0 1	17 10 0 1	11 16 0 1	NA NA	7 20 0 1	0 27 0 1	7 20 0 1

Table D.521: One_sample_One_Patient_KFold_PCA_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.31	0.27	NA	0.06	0.27	0.21	0.24	NA	0.09	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.00	**60.00**	NA	0.00	40.00	40.00	40.00	NA	20.00	**100.00**	**100.00**
90.32	**96.77**	NA	96.77	90.32	96.77	96.77	NA	100.00	**87.10**	**83.87**
90.32	**93.75**	NA	85.71	90.32	90.91	90.91	NA	88.57	**100.00**	**100.00**
40.00	**75.00**	NA	0.00	40.00	66.67	66.67	NA	100.00	**55.56**	**50.00**
83.33	**91.67**	NA	83.33	83.33	88.89	88.89	NA	88.89	**88.89**	**86.11**
Confusion Matrix										
28 3 3 2	30 1 2 3	NA NA	30 1 5 0	28 3 3 2	30 1 3 2	30 1 3 2	NA NA	31 0 4 1	27 4 0 5	26 5 0 5

Table D.522: One_sample_One_Patient_KFold_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.33	0.23	NA	0.16	0.27	0.21	0.27	NA	0.12	0.50	0.59
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
20.00	40.00	NA	40.00	40.00	40.00	40.00	NA	20.00	**100.00**	80.00
74.19	93.55	NA	100.00	90.32	96.77	96.77	NA	96.77	**87.10**	80.65
85.19	90.63	NA	91.18	90.32	90.91	90.91	NA	88.24	**100.00**	96.15
11.11	50.00	NA	100.00	40.00	66.67	66.67	NA	50.00	**55.56**	40.00
66.67	86.11	NA	91.67	83.33	88.89	88.89	NA	86.11	**88.89**	80.56
Confusion Matrix										
23 8 4 1	29 2 3 2	NA NA	31 0 3 2	28 3 3 2	30 1 3 2	30 1 3 2	NA NA	30 1 4 1	27 4 0 5	25 6 1 4

Table D.523: One_sample_One_Patient_LOO_PCA_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.41	0.42	0.42	0.43	0.54	0.42	0.42	0.42	0.43	0.48	0.47
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
0.00	0.00	0.00	0.00	20.00	0.00	0.00	0.00	0.00	20.00	20.00
77.42	90.32	87.10	96.77	87.10	90.32	87.10	90.32	96.77	74.19	70.97
82.76	84.85	84.38	85.71	87.10	84.85	84.38	84.85	85.71	85.19	84.62
0.00	0.00	0.00	0.00	20.00	0.00	0.00	0.00	0.00	11.11	10.00
66.67	77.78	75.00	83.33	77.78	77.78	75.00	77.78	83.33	66.67	63.89
Confusion Matrix										
24 7 5 0	28 3 5 0	27 4 5 0	30 1 5 0	27 4 4 1	28 3 5 0	27 4 5 0	28 3 5 0	30 1 5 0	23 8 4 1	22 9 4 1

Table D.524: One_sample_One_Patient_LOO_mediumEDSS ≥ 5

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.65	0.42	0.50	0.43	0.54	0.42	0.42	0.50	0.43	0.48	0.40
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
60.00	0.00	0.00	0.00	20.00	0.00	0.00	0.00	0.00	20.00	0.00
83.87	90.32	100.00	93.55	87.10	90.32	87.10	100.00	93.55	74.19	64.52
92.86	84.85	86.11	85.29	87.10	84.85	84.38	86.11	85.29	85.19	80.00
37.50	0.00	NaN	0.00	20.00	0.00	0.00	NaN	0.00	11.11	0.00
80.56	77.78	86.11	80.56	77.78	77.78	75.00	86.11	80.56	66.67	55.56
Confusion Matrix										
26 5 2 3	28 3 5 0	31 0 5 0	29 2 5 0	27 4 4 1	28 3 5 0	27 4 5 0	31 0 5 0	29 2 5 0	23 8 4 1	20 11 5 0

For label *highestEDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: Max_Max_Anatomical_I_29_ratio on region affected by lesion, Mean_Var_Anatomical_II_40_var pixel intensity, Var_Max_Anatomical_II_40_var pixel

intensity, Mean_Mean_Anatomical_II_40_var pixel intensity, Var_Var_Anatomical_II_40_var pixel intensity.

Table D.525: One_sample_One_Patient_Traditional_PCA_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.58	0.51	0.50	0.51	0.51	0.51	0.51	0.60	0.55	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	100.00	100.00	80.00	100.00	100.00	100.00	100.00	100.00	100.00
11.11	11.11	11.11	0.00	11.11	0.00	0.00	11.11	22.22	11.11	11.11
100.00	100.00	100.00	NaN	50.00	NaN	NaN	100.00	100.00	100.00	100.00
38.46	38.46	38.46	35.71	33.33	35.71	35.71	38.46	41.67	38.46	38.46
42.86	42.86	42.86	35.71	35.71	35.71	35.71	42.86	50.00	42.86	42.86
Confusion Matrix										
1 8	1 8	1 8	0 9	1 8	0 9	0 9	1 8	2 7	1 8	1 8
0 5	0 5	0 5	0 5	1 4	0 5	0 5	0 5	0 5	0 5	0 5

Table D.526: One_sample_One_Patient_Traditional_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.50	0.56	NA	0.54	0.54	0.56	0.54	NA	0.59	0.57	0.56
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	NA	80.00	80.00	80.00	60.00	NA	100.00	100.00	100.00
0.00	11.11	NA	22.22	22.22	33.33	55.56	NA	22.22	11.11	11.11
NaN	100.00	NA	66.67	66.67	75.00	71.43	NA	100.00	100.00	100.00
35.71	38.46	NA	36.36	36.36	40.00	42.86	NA	41.67	38.46	38.46
35.71	42.86	NA	42.86	42.86	50.00	57.14	NA	50.00	42.86	42.86
Confusion Matrix										
0 9	1 8	NA	2 7	2 7	3 6	5 4	NA	2 7	1 8	1 8
0 5	0 5	NA	1 4	1 4	1 4	2 3	NA	0 5	0 5	0 5

Table D.527: One_sample_One_Patient_kFold_PCA_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.57	0.58	0.58	0.38	0.46	0.52	0.54	0.58	NA	0.61	0.61
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
68.75	**62.50**	**62.50**	37.50	43.75	**62.50**	**62.50**	**62.50**	NA	**68.75**	**68.75**
70.00	**85.00**	**85.00**	60.00	70.00	**60.00**	**70.00**	**85.00**	NA	**80.00**	**80.00**
73.68	**73.91**	**73.91**	54.55	60.87	**66.67**	**70.00**	**73.91**	NA	**76.19**	**76.19**
64.71	**76.92**	**76.92**	42.86	53.85	**55.56**	**62.50**	**76.92**	NA	**73.33**	**73.33**
69.44	**75.00**	**75.00**	50.00	58.33	**61.11**	**66.67**	**75.00**	NA	**75.00**	**75.00**
Confusion Matrix										
14 6	17 3	17 3	12 8	14 6	12 8	14 6	17 3	NA	16 4	16 4
5 11	6 10	6 10	10 6	9 7	6 10	6 10	6 10	NA	5 11	5 11

Table D.528: One_sample_One_Patient_kFold_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.55	0.60	0.43	0.52	0.47	0.53	0.55	0.49	NA	0.49	0.67
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
62.50	**56.25**	37.50	**50.00**	43.75	**62.50**	**62.50**	43.75	NA	**68.75**	**62.50**
75.00	**85.00**	95.00	**70.00**	75.00	**61.91**	**70.00**	90.00	NA	**80.00**	**80.00**
71.43	**70.83**	65.52	**63.64**	62.50	**68.42**	**70.00**	66.67	NA	**76.19**	**72.73**
66.67	**75.00**	85.71	**57.14**	58.33	**55.56**	**62.50**	77.78	NA	**73.33**	**71.43**
69.44	**72.22**	69.44	**61.11**	61.11	**62.16**	**66.67**	69.44	NA	**75.00**	**72.22**
Confusion Matrix										
15 5 6 10	17 3 7 9	19 1 10 6	14 6 8 8	15 5 9 7	13 8 6 10	14 6 6 10	18 2 9 7	NA NA	16 4 5 11	16 4 6 10

Table D.529: One_sample_One_Patient_LOO_PCA_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.64	0.72	0.75	0.51	0.63	0.61	0.66	0.75	0.72	0.69	0.69
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
62.50	**62.50**	**62.50**	37.50	**50.00**	**62.50**	**62.50**	**62.50**	**62.50**	**62.50**	**62.50**
65.00	**80.00**	**85.00**	65.00	**75.00**	**60.00**	**70.00**	**85.00**	**80.00**	**75.00**	**75.00**
68.42	**72.73**	**73.91**	56.52	**65.22**	**66.67**	**70.00**	**73.91**	**72.73**	**71.43**	**71.43**
58.82	**71.43**	**76.92**	46.15	**61.54**	**55.56**	**62.50**	**76.92**	**71.43**	**66.67**	**66.67**
63.89	**72.22**	**75.00**	52.78	**63.89**	**61.11**	**66.67**	**75.00**	**72.22**	**69.44**	**69.44**
Confusion Matrix										
13 7 6 10	16 4 6 10	17 3 6 10	13 7 10 6	15 5 8 8	12 8 6 10	14 6 6 10	17 3 6 10	16 4 6 10	15 5 6 10	15 5 6 10

Table D.530: One_sample_One_Patient_LOO_highestEDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.54	0.49	0.52	0.48	0.56	0.55	0.57	0.57	0.52	0.55
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
37.50	37.50	18.75	43.75	31.25	**56.25**	**50.00**	31.25	43.75	43.75	43.75
55.00	70.00	80.00	60.00	65.00	**55.00**	**60.00**	80.00	70.00	60.00	65.00
52.38	58.33	55.17	57.14	54.17	**61.11**	**60.00**	59.26	60.87	57.14	59.09
40.00	50.00	42.86	46.67	41.67	**50.00**	**50.00**	55.56	53.85	46.67	50.00
47.22	55.56	52.78	52.78	50.00	**55.56**	**55.56**	58.33	58.33	52.78	55.56
Confusion Matrix										
11 9 10 6	14 6 10 6	16 4 13 3	12 8 9 7	13 7 11 5	11 9 7 9	12 8 8 8	16 4 11 5	14 6 9 7	12 8 9 7	13 7 9 7

For label *highestEDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

The via pattern recognition study was not performed since the number of patients with *highestEDSS*≥ 5 was minimal.

For label *first2EDSS* > 3 (0/1 - $(< 3)/(\geq 3)$):

Final features: Max_Max_GM_squares numbers lesion region 90%/total region with 90, Max_Mean_Anatomical_II_58_lesion in the region, Max_Mean_WM_var tissue prob, Max_Var_Anatomical_II_39_var pixel intensity, Var_Mean_Anatomical_II_40_var pixel intensity, Max_Mean_T2_Var Pixel Intensity/slice_meanPixel, Var_Max_Anatomical_II_40_var pixel intensity, Max_Mean_Anatomical_II_45_max pixel intensity.

Table D.531: One_sample_One_Patient_Traditional_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.52	0.50	0.51	0.52	0.52	0.53	0.53	0.51	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
66.67	100.00	33.33	66.67	66.67	66.67	66.67	25.00	100.00	100.00	100.00
26.32	0.00	73.68	21.05	21.05	26.32	25.00	84.21	0.00	0.00	0.00
83.33	NaN	87.50	80.00	80.00	83.33	83.33	84.21	NaN	NaN	NaN
12.50	13.64	16.67	11.76	11.76	12.50	11.76	25.00	13.64	13.64	13.64
31.82	13.64	68.18	27.27	27.27	31.82	30.43	73.91	13.64	13.64	13.64
Confusion Matrix										
5 14 1 2	0 19 0 3	14 5 2 1	4 15 1 2	4 15 1 2	5 14 1 2	5 15 1 2	16 3 3 1	0 19 0 3	0 19 0 3	0 19 0 3

Table D.532: One_sample_One_Patient_Traditional_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.50	NA	0.54	0.51	0.51	0.51	NA	0.50	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
100.00	100.00	NA	66.67	33.33	33.33	33.33	NA	100.00	100.00	100.00
10.53	0.00	NA	42.11	57.89	84.21	73.68	NA	0.00	0.00	0.00
100.00	NaN	NA	88.89	84.62	88.89	87.50	NA	NaN	NaN	NaN
15.00	13.64	NA	15.38	11.11	25.00	16.67	NA	13.64	13.64	13.64
22.73	13.64	NA	45.45	54.55	77.27	68.18	NA	13.64	13.64	13.64
Confusion Matrix										
2 17 0 3	0 19 0 3	NA NA	8 11 1 2	11 8 2 1	16 3 2 1	14 5 2 1	NA NA	0 19 0 3	0 19 0 3	0 19 0 3

Table D.533: One_sample_One_Patient_kFold_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.51	0.38	0.37	0.15	0.34	0.46	0.48	0.40	0.36	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
70.00	40.00	40.00	0.00	30.00	**50.00**	**50.00**	40.00	40.00	**90.00**	**81.82**
92.31	92.31	88.46	84.62	80.77	**84.62**	**84.62**	88.46	92.31	**84.62**	**84.62**
88.89	80.00	79.31	68.75	75.00	**81.48**	**81.48**	79.31	80.00	**95.65**	**91.67**
77.78	66.67	57.14	0.00	37.50	**55.56**	**55.56**	57.14	66.67	**69.23**	**69.23**
86.11	77.78	75.00	61.11	66.67	**75.00**	**75.00**	75.00	77.78	**86.11**	**83.78**
Confusion Matrix										
24 2 3 7	24 2 6 4	23 3 6 4	22 4 10 0	21 5 7 3	22 4 5 5	22 4 5 5	23 3 6 4	24 2 6 4	22 4 1 9	22 4 2 9

Table D.534: One_sample_One_Patient_kFold_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.46	0.45	NA	0.48	0.48	0.43	0.50	NA	NA	0.50	0.50
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
50.00	**50.00**	NA	**50.00**	**60.00**	**50.00**	**60.00**	NA	NA	**90.00**	**80.00**
80.77	**84.62**	NA	**88.46**	**88.46**	**88.46**	**80.77**	NA	N	**84.62**	**84.62**
80.77	**81.48**	NA	**82.14**	**85.19**	**82.14**	**84.00**	NA	NA	**95.65**	**91.67**
50.00	**55.56**	NA	**62.50**	**66.67**	**62.50**	**54.55**	NA	NA	**69.23**	**66.67**
72.22	**75.00**	NA	**77.78**	**80.56**	**77.78**	**75.00**	NA	NA	**86.11**	**83.33**
Confusion Matrix										
21 5 5 5	22 4 5 5	NA NA	23 3 5 5	23 3 4 6	23 3 5 5	21 5 4 6	NA NA	NA NA	22 4 1 9	22 4 2 8

Table D.535: One_sample_One_Patient_LOO_PCA_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.48	0.53	0.42	0.45	0.56	0.46	0.46	0.42	0.53	0.46	0.46
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
20.00	20.00	10.00	10.00	30.00	20.00	20.00	10.00	20.00	30.00	30.00
76.92	84.62	76.92	84.62	80.77	73.08	73.08	76.92	84.62	61.54	61.54
71.43	73.33	68.97	70.97	75.00	70.37	70.37	68.97	73.33	69.57	69.57
25.00	33.33	14.29	20.00	37.50	22.22	22.22	14.29	33.33	23.08	23.08
61.11	66.67	58.33	63.89	66.67	58.33	58.33	58.33	66.67	52.78	52.78
Confusion Matrix										
20 6 8 2	22 4 8 2	20 6 9 1	22 4 9 1	21 5 7 3	19 7 8 2	19 7 8 2	20 6 9 1	22 4 8 2	16 10 7 3	16 10 7 3

Table D.536: One_sample_One_Patient_LOO_first2EDSS ≥ 3

Classifier										
Decision Tree	**LDA**	**QDA**	**SVM**	**KNN-1**	**KNN-3**	**KNN-5**	**Naive Bayes**	**GLM**	**Euclidean**	**Mahalanobis**
AUC										
0.56	0.46	0.43	0.52	0.39	0.32	0.30	0.46	NA	0.34	0.42
Stats (Sensibility, Specificity, PPV, NPV, Accuracy) %										
40.00	20.00	10.00	30.00	10.00	0.00	0.00	20.00	NA	10.00	20.00
73.08	73.08	80.77	73.08	69.23	69.23	57.69	73.08	NA	53.85	61.54
76.00	70.37	70.00	73.08	66.67	64.29	60.00	70.37	NA	60.87	66.67
36.36	22.22	16.67	30.00	11.11	0.00	0.00	22.22	NA	7.69	16.67
63.89	58.33	61.11	61.11	52.78	50.00	41.67	58.33	NA	41.67	50.00
Confusion Matrix										
19 7 6 4	19 7 8 2	21 5 9 1	19 7 7 3	18 8 9 1	18 8 10 0	15 11 10 0	19 7 8 2	NA NA	14 12 9 1	16 10 8 2

For label *first2EDSS* > 5 (0/1 - $(< 5)/(\geq 5)$):

The via pattern recognition study was not performed since the number of patients with *mediumEDSS*≥ 5 was minimal.

Chapter E

Appendix V - Results interpretation

Table E.1: The AUC performance method, regarding the attributed points according to the value of the lowest stat value.

Condition	Attributed points
AUC <0.70	0
AUC >0.69	1
AUC >0.79	2
AUC >0.89	3

Table E.2: The classification performance measures method, regarding the atributed points according to the value of the lowest stat value.

Condition	Attributed points
Lowest stat [0,0.49]	0
Lowest stat [50,0.59]	1
Lowest stat $[60, 0.69]$	2
Lowest stat $[70, 0.79]$	3
Lowest stat $[80, 0.89]$	4
Lowest stat $[90, 100]$	5

Table E.3: The partition method multiplication factor, used in the stats performance method and in the AUC performance method.

Partition Method	Multiplication factor
70-30 (Traditional)	1
k-Fold	2
LOO	3

E.1 Performance method results

E.1.1 AUC method

E.1.1.1 Image databases

Table E.4: Results for the *MRI Total Head* database using the AUC performance method.

Label	Score
msCourse	**12**
currentEDSS >3	6
currentEDSS >5	0
nextEDSS >3	4
nextEDSS >5	0
highestEDSS >3	**24**
highestEDSS >5	0
first2EDSS >3	0
first2EDSS >5	0
tendency >EDSS	10
mediumEDSS_ >3	**20**
mediumEDSS_ >5	0

Table E.5: Results for the *One sample one lesion* database using the AUC performance method.

Label	Score
msCourse	0
currentEDSS >3	0
currentEDSS >5	0
first2EDSS >3	0
first2EDSS >5	0
highestEDSS >3	0
highestEDSS >5	0
mediumEDSS>3	0
mediumEDSS>5	0
nextEDSS>3	0
nextEDSS>5	0

Table E.6: Results for the *One sample one lesion* database with lesion ensembling using the AUC performance method.

Label	Score
msCourse	0
currentEDSS >3	0
currentEDSS >5	0
first2EDSS >3	0
first2EDSS >5	0
highestEDSS >3	0
highestEDSS >5	0
mediumEDSS>3	0
mediumEDSS>5	0
nextEDSS>3	0
nextEDSS>5	0

Table E.7: Results for the *One sample one study* database using the AUC performance method.

Label	Score
msCourse	0
currentEDSS >3	0
currentEDSS >5	0
first2EDSS >3	0
first2EDSS >5	not performed
highestEDSS >3	**4**
highestEDSS >5	**2**
mediumEDSS>3	0
mediumEDSS>5	not performed
nextEDSS>3	**4**
nextEDSS>5	**2**

Table E.8: Results for the *One sample one patient* database using the AUC performance method.

Label	Score
msCourse	0
first2EDSS >3	0
first2EDSS >5	not performed
highestEDSS >3	0
highestEDSS >5	not performed
mediumEDSS>3	0
mediumEDSS>5	0

E.1.1.2 Clinical databases

Table E.9: Results for the *Static* database with the standard procedure using the AUC performance method.

Label	Score
msCourse	**26**
mediumEDSS >3	**20**
mediumEDSS >5	not performed
highestEDSS >3	**45**
highestEDSS >5	not performed
first2EDSS >3	4
first2EDSS >5	not performed

Table E.10: Results for the *Static* database with the investigation procedure using the AUC performance method.

Label	Score
msCourse	0
mediumEDSS >3	**5**
mediumEDSS >5	not performed
highestEDSS >3	**14**
highestEDSS >5	not performed
first2EDSS >3	**9**
first2EDSS >5	not performed

Table E.11: Results for the *Groundzero* database with the standard procedure using the AUC performance method.

Label	Score
msCourse	**6**
highestEDSS >3	**11**
highestEDSS >5	not performed
first2EDSS >3	6
first2EDSS >5	not performed
mediumEDSS >3	**20**
mediumEDSS >5	not performed

Table E.12: Results for the *Groundzero* database with the investigation procedure using the AUC performance method.

Label	Score
msCourse	0
highestEDSS >3	0
highestEDSS >5	not performed
first2EDSS >3	0
first2EDSS >5	not performed
mediumEDSS >3	0
mediumEDSS >5	not performed

Table E.13: Results for the *Momentaneous* database with the standard procedure using the AUC performance method.

Label	Score
msCourse	33
currentEDSS >3	65
currentEDSS >5	5
nextEDSS >3	**122**
nextEDSS >5	50
highestEDSS >3	**82**
highestEDSS >5	80
first2EDSS >3	76
first2EDSS >5	not performed
tendencyEDSS	0
mediumEDSS>3	**115**
mediumEDSS>5	not performed

Table E.14: Results for the *Momentaneous* database with the investigation procedure using the AUC performance method.

Label	Score
msCourse	not performed
currentEDSS >3	not performed
currentEDSS >5	not performed
nextEDSS >3	**94**
nextEDSS >5	6
highestEDSS >3	61
highestEDSS >5	63
first2EDSS >3	**64**
first2EDSS >5	not performed
tendencyEDSS	21
mediumEDSS>3	**83**
mediumEDSS>5	not performed

Table E.15: Results for the *Momentaneous with past* database with the standard procedure using the AUC performance method.

Label	Score
msCourse	53
currentEDSS >3	**110**
currentEDSS >5	26
nextEDSS >3	**123**
nextEDSS >5	59
highestEDSS >3	**124**
highestEDSS >5	92
first2EDSS >3	80
first2EDSS >5	not performed
tendencyEDSS	3
mediumEDSS>3	73
mediumEDSS>5	not performed

Table E.16: Results for the *Momentaneous with past* database with the investigation procedure using the AUC performance method.

Label	Score
msCourse	23
currentEDSS >3	74
currentEDSS >5	7
nextEDSS >3	**109**
nextEDSS >5	21
highestEDSS >3	**142**
highestEDSS >5	**90**
first2EDSS >3	50
first2EDSS >5	not performed
tendencyEDSS	0
mediumEDSS>3	62
mediumEDSS>5	not performed

E.1.2 Classification performances measure method

E.1.2.1 Image databases

Table E.17: Results for the *MRI Total Head* database using the stats performance method.

Label	Score
msCourse	0
currentEDSS >3	18
currentEDSS >5	6
nextEDSS >3	**42**
nextEDSS >5	6
highestEDSS >3	**131**
highestEDSS >5	0
first2EDSS >3	0
first2EDSS >5	0
tendency >EDSS	20
mediumEDSS_ >3	**48**
mediumEDSS_ >5	0

Table E.18: Results for the *One sample one lesion* database using the stats performance method.

Label	Score
msCourse	0
currentEDSS >3	0
currentEDSS >5	0
first2EDSS >3	0
first2EDSS >5	0
highestEDSS >3	0
highestEDSS >5	0
mediumEDSS>3	**6**
mediumEDSS>5	0
nextEDSS>3	0
nextEDSS>5	0

Table E.19: Results for the *One sample one lesion* database with lesion ensembling using the stats performance method.

Label	Score
msCourse	0
currentEDSS >3	0
currentEDSS >5	0
first2EDSS >3	0
first2EDSS >5	0
highestEDSS >3	0
highestEDSS >5	0
mediumEDSS>3	0
mediumEDSS>5	0
nextEDSS>3	**1**
nextEDSS>5	0

Table E.20: Results for the *One sample one study* database using the stats performance method.

Label	Score
msCourse	0
currentEDSS >3	0
currentEDSS >5	0
first2EDSS >3	**12**
first2EDSS >5	not performed
highestEDSS >3	**61**
highestEDSS >5	0
mediumEDSS>3	10
mediumEDSS>5	not performed
nextEDSS>3	10
nextEDSS>5	**19**

Table E.21: Results for the *One sample one patient* database using the stats performance method.

Label	Score
msCourse	**54**
first2EDSS >3	40
first2EDSS >5	not performed
highestEDSS >3	**109**
highestEDSS >5	not performed
mediumEDSS>3	**76**
mediumEDSS>5	10

E.1.2.2 Clinical databases

Table E.22: Results for the *Static* database with the standard procedure using the stats performance method.

Label	Score
msCourse	**139**
mediumEDSS >3	**100**
mediumEDSS >5	not performed
highestEDSS >3	**231**
highestEDSS >5	not performed
first2EDSS >3	72
first2EDSS >5	not performed

Table E.23: Results for the *Static* database with the investigation procedure using the stats performance method.

Label	Score
msCourse	**7**
mediumEDSS >3	**66**
mediumEDSS >5	not performed
highestEDSS >3	**110**
highestEDSS >5	not performed
first2EDSS >3	4
first2EDSS >5	not performed

Table E.24: Results for the *Groundzero* database with the standard procedure using the stats performance method.

Label	Score
msCourse	26
highestEDSS >3	**145**
highestEDSS >5	not performed
first2EDSS >3	**124**
first2EDSS >5	not performed
mediumEDSS >3	**38**
mediumEDSS >5	not performed

Table E.25: Results for the *Groundzero* database with the investigation procedure using the stats performance method.

Label	Score
msCourse	**10**
highestEDSS >3	**71**
highestEDSS >5	not performed
first2EDSS >3	8
first2EDSS >5	not performed
mediumEDSS >3	**18**
mediumEDSS >5	not performed

Table E.26: Results for the *Momentaneous* database with the standard procedure using the stats performance method.

Label	Score
msCourse	62
currentEDSS >3	109
currentEDSS >5	4
nextEDSS >3	**146**
nextEDSS >5	92
highestEDSS >3	**176**
highestEDSS >5	136
first2EDSS >3	106
first2EDSS >5	not performed
tendencyEDSS	0
mediumEDSS>3	**189**
mediumEDSS>5	not performed

Table E.27: Results for the *Momentaneous* database with the investigation procedure using the stats performance method.

Label	Score
msCourse	not performed
currentEDSS >3	not performed
currentEDSS >5	not performed
nextEDSS >3	**136**
nextEDSS >5	6
highestEDSS >3	**146**
highestEDSS >5	110
first2EDSS >3	92
first2EDSS >5	not performed
tendencyEDSS	0
mediumEDSS>3	**132**
mediumEDSS>5	not performed

Table E.28: Results for the *Momentaneous with past* database with the standard procedure using the stats performance method.

Label	Score
msCourse	86
currentEDSS >3	104
currentEDSS >5	60
nextEDSS >3	**179**
nextEDSS >5	98
highestEDSS >3	**233**
highestEDSS >5	118
first2EDSS >3	**140**
first2EDSS >5	not performed
tendencyEDSS	0
mediumEDSS>3	104
mediumEDSS>5	not performed

Table E.29: Results for the *Momentaneous with past* database with the investigation procedure using the stats performance method.

Label	Score
msCourse	48
currentEDSS >3	97
currentEDSS >5	18
nextEDSS >3	**148**
nextEDSS >5	32
highestEDSS >3	**283**
highestEDSS >5	**126**
first2EDSS >3	80
first2EDSS >5	not performed
tendencyEDSS	0
mediumEDSS>3	104
mediumEDSS>5	not performed