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7 **Treatment failure prediction for head-and-neck cancer patients treated with radiation therapy**  
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11 **Prédiction de l'échec du traitement pour les patients atteints du cancer de la tête et du cou, traités par**  
12 **radiothérapie**  
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53 Running title: RT treatment prediction for H&N cancer  
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## Abstract

**Purpose** Treatment outcome prediction is an important emerging topic in oncologic care. To support radiation oncologists on their decisions, with individualized, tailored treatment regimens increasingly becoming the standard of care, accurate tools to predict tumor response to treatment are needed. The goal of this work is to identify the most determinant factor(s) for treatment response aiming to develop prediction models that robustly estimate tumor response to radiation therapy (RT) in patients with head-and-neck cancer.

**Patients and methods** A population-based cohort study was performed on 92 head-and-neck cancer patients treated with RT from 2007 until 2014 at the Portuguese Institute of Oncology of Coimbra (IPOCFG). Correlation analysis and multivariate binary logistic regression analysis were conducted in order to explore the predictive power of the considered predictors. Performance of the models is expressed as the area under the curve (AUC) of the receiver operating characteristics (ROC) curve. A nomogram to predict treatment failure was developed.

**Results** Significant prognostic factors for treatment failure, after multivariate regression, were older age, non-concomitant RT and larger primary tumor volume. A regression model with these predictors revealed an AUC of .78 for an independent data set.

**Conclusion** For patients with head-and-neck cancer treated with definitive RT, we have developed a prediction nomogram based on models that presented good discriminative ability in making predictions of tumor response to treatment. The probability of treatment failure is higher for older patients with larger tumors treated with non-concomitant RT.

**Keywords** head-and-neck cancer; radiation therapy; primary tumor volume; prognosis

## Résumé

**Objectif de l'étude** La prévision des résultats du traitement est un sujet émergent et très important dans le domaine des soins oncologiques. Pour soutenir les radio-oncologues sur leurs décisions, les régimes de traitement sur mesure deviennent, de plus en plus, la norme des soins. En ce sens, des outils précis pour prédire la réponse tumorale au traitement s'avèrent nécessaires. Ce travail se propose, donc, d'identifier le(s) facteur(s) le(s) plus pertinent(s) pour déterminer la réponse au traitement, visant à développer des modèles de prédiction qui puissent estimer, le plus efficacement possible, une réponse tumorale à la radiothérapie (RT), chez les patients atteints du cancer de la tête et du cou.

**Patientes et méthodes** Une étude de cohorte basée sur la population a été réalisée sur 92 patients atteints d'un cancer de la tête et du cou, traités par RT à partir de 2007 jusqu'en 2014, à l'Institut portugais d'oncologie de Coimbra (IPOCFG). Une analyse de corrélation, ainsi qu'une analyse multivariée par régression logistique binaire ont été menées afin d'explorer le pouvoir prédictif des prédicteurs présentés. La performance des modèles est exprimée par la surface située sous la courbe (AUC) de la courbe des caractéristiques opérationnelles du récepteur (ROC). Il a été développé un nomogramme pour prédire l'échec du traitement.

**Résultats** Des facteurs pronostiques déterminants pour l'échec du traitement, après une régression multivariée – les patients étaient plus âgés, traités avec une RT non-concomitante et ils avaient un plus grand volume de tumeur primaire. Un modèle de régression avec ces prédicteurs a démontré une AUC de 0,78 pour un ensemble de données indépendantes.

**Conclusion** Pour les patients atteints du cancer de la tête et du cou, traités par RT définitive, nous avons développé un nomogramme de prédiction basé sur des modèles qui ont présenté une bonne capacité discriminative à faire des prédictions de la réponse tumorale au traitement. La probabilité d'échec du traitement est plus élevée pour les patients plus âgés, ayant de plus grandes tumeurs et étant traités avec des RT non-concomitantes.

**Mots clés** cancer de la tête et du cou; radiothérapie; volume de la tumeur primaire; pronostic

## 1 Introduction

2 Treatment outcomes prediction is an important emerging topic in oncologic care, with individualized  
3 tailored treatment regimens increasingly becoming the standard of care [1]. Outcomes in oncology  
4 treatments include the risks and benefits of cancer therapy in terms of side-effects, tumor response to  
5 treatment and follow-up outcomes such as local recurrences, evolution to metastatic disease, survival or  
6 a combination of these endpoints. Recently, online predicting tools have become available [2-4]. These  
7 aim to supplement clinical judgment by giving information to physicians and health professionals about  
8 possible outcomes. The involvement of the patients in the treatment decisions is becoming generalized  
9 and ultimately these tools will also be assessed by patients with all the associated pros and cons. These  
10 tools have been validated by peer review for a variety of tumor sites including lung [5], colorectal [6],  
11 head-and-neck [7,8], breast [9], ovarian [10], endometrial [11], gastric [12] or prostate [13]. Although the  
12 prediction models were validated by peer review, they require validation for different populations and  
13 treatments. Moreover, the factors found relevant during the model development stage concern a given  
14 population and different factors may prove to be important for different populations. For instance,  
15 different drugs or different RT treatment modalities may be used in different countries or even in  
16 different cancer institutes within the same country.

17 RT is one of the main treatment modalities for cancer, along with surgery and chemotherapy, being used  
18 for around 60% of all patients. RT is generally used as a locoregional treatment, irradiating tissues with  
19 proven or suspected disease with ionizing radiation. In many cases, RT alone, or combined with  
20 chemotherapy and/or surgery, is a successful treatment, curing patients or giving important symptom  
21 relief. However, even with state-of-the-art practice, the tumor is not eradicated in all patients treated  
22 with curative intent. Moreover, mild or severe complications may occur, having a large impact on  
23 patients' quality of life. In head-and-neck cancer cases, complex cases to treat with RT due to the large  
24 number of organs at risk, radiation induced side-effects with significant impact on health-related quality  
25 of life include xerostomia or swallowing dysfunction [8].

1 For head-and-neck cancer cases treated with RT, there are few prediction models available [7], the  
2 existing ones are focused on subpopulations (e.g. larynx cases [8]), and many of the outcomes of interest  
3 have no prediction model yet. Furthermore, in RT, the abundance of new treatment options and the  
4 numerous patient parameters that nowadays can be assessed accurately have created new challenges.  
5 There is thus a growing need for the development of prediction models testing the increasingly amount  
6 of information that is becoming easily assessed.

7 In this study, we aim to identify the most determinant factor(s) for the specific outcome of tumor  
8 response to RT. Then construct prediction models that robustly estimate tumor response to treatment in  
9 patients with head-and-neck cancer treated with RT, integrating all the relevant information in a  
10 quantitative manner. To implement personalized RT, clinical decisions based on validated and quantified  
11 factors (predictors) will be crucial. We aim to contribute to a long term objective that will consider the  
12 incorporation of the developed model in treatment planning systems for inverse treatment planning  
13 optimization.

## 15 **Patients and methods**

### 16 **Patients**

17 Population-based cohort included head-and-neck cancer patients treated with RT at IPOCFG.  
18 Demographic and clinical characteristics of consecutively treated patients with head-and-neck cancer  
19 were recorded from May 2007 to June 2014 in RESPONSE, the electronic health information system used  
20 at IPOCFG to store patient response to RT [14]. Exclusion criteria were palliative and re-irradiated  
21 patients, patients with distant metastasis at presentation and post-operative patients. Thus, a total of 92  
22 patients were included in our cohort study (Table 1). The demographic and clinical characteristics  
23 assessed for this investigation included age at diagnosis, gender, tumor location, T – classification and N  
24 – classification of tumor–node–metastasis (TNM) system of the American Joint Committee on Cancer  
25 (AJCC), anemia, RT concomitant or non-concomitant, primary tumor volume (the volume of the

1 macroscopic volume of the tumor), overall treatment time and mean doses delivered to the total  
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7 1 macroscopic volume of the tumor), overall treatment time and mean doses delivered to the total  
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9 2 planning target volume (PTV) and planning target volume of the primary tumor (PTV-T). Other dosimetric  
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11 3 features were initially considered but to simplify the analysis only these metrics were included in this  
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13 4 study.

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15 5 Patient and clinical characteristics are shown in Table 1 for the entire study cohort and for two groups  
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17 6 corresponding to patients with different tumor response to the initial treatment protocol. All patients  
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19 7 were subjected to a standardized follow-up program prior to, during and at regular intervals after  
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21 8 curative RT that prospectively registered tumor response to the initial protocol and toxicity. Tumor  
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23 9 response to treatment is evaluated six to eight weeks after the end of the RT treatment and is assessed  
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25 10 using clinical and imaging (CT and MRI) evaluations complemented with a functional study (PET-CT)  
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27 11 and/or other complementary exams if required. The tumor response to treatment is stated complete if  
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29 12 all signs of disease disappear or stated partial/progression if signs of disease still exist and are  
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31 13 reduced/augmented compared to the beginning of the treatment. For the entire study cohort, mean age  
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33 14 at diagnosis was 53.0 (SD = 12.0) and the majority of the patients were male, 73 (79.3%). Of the 92  
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35 15 patients included in our cohort study, 38 (41.3%) of these patients had a T4 tumor while 54 (58.7%) had  
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37 16 lower T-classification. Most of the patients, 70 (76.1%), had N2 status while 22 (23.9%) had a N0 or N1  
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39 17 status. Concerning the tumor site, the majority (54 patients, 58.7%) was located at Oropharynx or  
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41 18 Nasopharynx and the other locations included Larynx, Pharyngeal – Laryngeal, Oral Cavity and  
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43 19 Hypopharynx (38 patients, 41.3%). The mean volume of the primary tumor was 42.0 cm<sup>3</sup> (SD = 38.2)  
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45 20 ranging from 1.8 to 161.7 cm<sup>3</sup>.

#### 21 **RT Treatment**

22 All target volumes and organs at risk were delineated by a radiation oncologist on the axial CT images in  
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24 the software Velocity AI® (version 2.8.1). This software was also used to construct 3-dimensional (3D)  
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25 Primary tumors were treated with prescribed doses ranging from 66.0 to 70.2 Gy in five fractions per

1 week of 1.8 – 2.12 Gy with an overall treatment time varying accordingly. Due to treatment toxicity, and other factors, the overall treatment time may have some variations. The overall treatment time is recorded in days and embeds useful information regarding possible treatment interruptions. To correct for differences in the fractionation scheme, all dose distributions were converted to a fractionation of 2 Gy [15]. Dosimetric predictors were assessed using the dose distributions generated by the ONCENTRA® treatment planning system.

Radiation was delivered with a Siemens ONCOR Avant-Garde® linear accelerator. Depending on the difficulty of the tumor case, two different radiation techniques were used: 3D Conformal RT (3D-CRT) or Intensity-Modulated RT (IMRT). All patients were treated with curative RT either alone or in combination with concomitant chemotherapy (cisplatin) or cetuximab [16].

### Statistical Analysis

All patient data used in this study was withdrawn from RESPONSE [14]. Anonymity and confidentiality of the study participants was granted by assigning a code for each participant assuring no nominal identification of the participants. Data were analyzed with software SPSS® (*Statistical Package for the Social Sciences*) version 21.

The development of models to predict response to treatment followed the several stages of model development. Predictors were selected not only according to the literature but after a review of potential features conducted by an expert panel. The use of clinical knowledge in feature selection cannot only improve the predictive performance of the model, but can also increase its clinical credibility since the medical team finds a model including well-known predictors more trustful than one model constructed in the basis of variable screening techniques [17]. Thus, the features considered were age at diagnosis, gender, tumor location, T – and N – classification, anemia, type of RT, primary tumor volume, overall treatment time and mean dose delivered to the PTV and the PTV-T. Age, primary tumor volume and dosimetric measures (mean dose delivered to the PTV and the PTV-T) were considered as continuous variables and their distribution treated as normal since a non-significant Kolmogorov-

1 Smirnov test was found for all the continuous variables. A correlation matrix was computed to check for  
2 high correlations between potential prognostic features and to rank the predictors on their strength of  
3 correlation with the outcome.

4 A multivariate binary logistic regression analysis was conducted in order to explore the predictive power  
5 of the univariate significant factors. The outcome of the study assumed the value 1 if we have a  
6 treatment failure, i.e. a partial response or progression and 0 if we have a complete tumor response to  
7 treatment. For model performance we calculated the measure of model fit (Nagelkerke pseudo- $R^2$ ) and  
8 measures of classification (hit rate, improvement over chance index, specificity and sensibility).

### 9 **Model Validation**

10 In order to validate the predictive model we used a 10-fold cross-validation procedure. This process  
11 consisted in the partitioning of the original dataset, into 10 complementary subsets, each with 9 patients  
12 (except the 10<sup>th</sup> with 11). Each subset is used once as testing set, whereas the remaining patients are all  
13 used to train the model. This process is applied 10 times such that each complementary subset is used  
14 once as testing set while the 9 separated elements are then used to validate the model. The  
15 performance of the model was then assessed by calculating the area under the curve (AUC) of the  
16 receiver operating characteristics (ROC) curves to measure the discriminative ability of the model in  
17 making predictions of tumor response to treatment.

## 19 **Results**

### 20 **Correlation Analysis**

21 Significant and positive correlations were found between treatment failure and age at diagnosis, T –  
22 classification, type of RT (concomitant vs non-concomitant) and primary tumor volume. The primary  
23 tumor volume presented the strongest correlation between predictors and outcome ( $r = .385$ ,  $p < .01$ ).  
24 The correlation between the dosimetric factors ( $r = .863$ ,  $p < .01$ ) is the highest significant correlation  
25 between predictors. This strong correlation occurred between most of the dosimetric factors tested. The



1 primary tumor volume and the T-classification ( $r = .472$ ,  $p < .01$ ) is the second highest significant  
2 correlation between predictors. The magnitudes of correlations between other predictors were low  
3 (Table 2).

#### 4 **Binary Logistic Regression**

5 A multivariate binary logistic regression was carried out for the significant predictors and the results are  
6 presented in Table 3 that displays the significance level (p-value), the odds ratio (OR) and the 95%  
7 confidence intervals (95% CI) for each predictor. The significant predictors for treatment failure were  
8 older age (OR = 1.07,  $p = .011$ ), non-concomitant RT (OR = 4.60,  $p = .047$ ) and larger primary tumor  
9 volume (OR = 1.02,  $p = .008$ ), after controlling the remaining variables. These results are in accordance to  
10 the univariate (correlation) analysis except for T – classification that was dominated by the primary  
11 tumor volume. While the results of the binary variable (type of RT) present a large odds ratio, results of  
12 the continuous variables are not so straightforward to read. For each decade increase in the patient's  
13 age, there was a 1.97 times greater chance of treatment failure and for each 10 cm<sup>3</sup> increase on the  
14 primary tumor volume, there was a 1.22 times greater chance of treatment failure when the remaining  
15 predictors were controlled. The predictive power given by a Nagelkerke pseudo R<sup>2</sup> of .452 indicated a  
16 model that accounted for 45.2% of the total variance which suggests that the set of predictors  
17 discriminated well between patients with complete tumor response to treatment and treatment failure.  
18 This logistic regression model classification power presented an overall hit rate of 81.5%, leading to a  
19 23.9% increase compared to the proportional percentage of correct classification by chance:  
20  $[(64/92)^2 + (28/92)^2] * 100 = 57.6\%$ , corresponding to an improvement over chance index of 40.3%  
21  $([(83.7\% - 57.6\%) / (1 - 57.6\%)] * 100)$ , which means 56.4% less classification errors than those made if  
22 classification was done by chance. This model presented correct prediction rates of 66% for patients with  
23 treatment failure (sensitivity) and 94% for patients with complete tumor response to treatment  
24 (specificity).

25 Since the T – classification was not significant in the multivariate analysis, being dominated by the

1 primary tumor volume, a multivariate binary logistic regression considering the remaining three  
2 significant variables was carried out. The interest of this new regression model is to perceive how much  
3 of the outcome is explained by the T-classification that is not explained by the primary tumor volume  
4 and most importantly if removing the T-classification from the regression model has a strong impact on  
5 the model's prediction ability. The model without the T-classification presented similar hit rates (80.3%),  
6 sensitivity (64%) and specificity (91%) compared to the model with the T-classification. It is worth to  
7 highlight that a 3-variable predictive model obtained by removing the primary tumor volume instead of  
8 removing the T-classification will clearly lead to worst results: overall hit rate of 77.2%, sensitivity of 46%  
9 and specificity of 90%.

#### 10 **Model Validation**

11 We validated the predictive models using a 10-fold cross-validation procedure. The logit regression  
12 model with all 4 predictors (model with T-classification) revealed an AUC of .79 (95% CI .69 - .89) while  
13 the model obtained by removing the T-classification revealed similar performance with an AUC of .78  
14 (95% CI .67 - .88) (Figure 1). These results confirm that the 3 predictors' model (age, type of RT and  
15 primary tumor volume) have good discriminative ability in making the predictions of tumor response to  
16 treatment for new head-and-neck cancer patients.

#### 17 **Nomogram**

18 The logistic regression model with age, type of RT and PTV-T volume as predictors, can be easily  
19 incorporated in treatment planning systems by using its regression coefficients to compute the  
20 probability of treatment failure:

$$21 \text{ Prob. of Treatment Failure} = \frac{1}{1 + e^{-(-6.223 + .072 * \text{Age} + .89 * \text{TypeRT} + .026 * \text{PTVTvolume})}} \cdot$$

22 This logistic model was used also to develop a visual, ready to use nomogram for prediction of treatment  
23 failure in head-and-neck cancer patients treated with RT (Figure 2).

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## 1 Discussion

2 Personalized and accurate prediction of different type of outcomes in oncology would most certainly  
3 improve therapeutic and care strategies, minimizing risks of under-treatment or over-treatment. For  
4 head-and-neck cancer patients treated with RT, there are many outcomes of interest well studied in the  
5 literature including survival, disease-free survival, local and locoregional control, recurrence or distant  
6 metastases [5-13]. However, most of the previous studies concern a specific tumor location. In 2001, a  
7 survival prediction model based on 1662 head-and-neck cancer patients was published using age,  
8 gender, TNM classification, tumor location and history of tumor as predictors for survival [18]. However,  
9 conclusions are difficult to compare since the outcome studied is different. As far as we know, there are  
10 no studies of prediction factors or models for treatment failure in patients with head-and-neck cancer  
11 treated with RT. Moreover, in most of the previous works, these patients are excluded from the studies.  
12 Despite the fact that treatment failure is not a desirable outcome, it is a non-ignorable clinical reality of  
13 the utmost importance to study. Another distinctive aspect of this study is the fact that patients were  
14 treated with definitive RT and the prescribed (and delivered) doses lay in a narrow interval with most of  
15 the primary tumors treated with 70.2 Gy. In clinical practice, following increasingly stricter treatment  
16 protocols, many patients will be treated with very similar plans in terms of dosimetric features.  
17 Therefore, it is of the utmost interest to develop prediction models based on predictors other than  
18 dosimetric ones.  
19 Many potential predictors for different outcomes are presented in numerous studies in the literature [1].  
20 With the availability of 3D tools, the primary tumor volume can be easily quantified. Thus, this measure  
21 has recently shown prognostic significance for different cancer locations [5]. Opposite results were  
22 reported in a small group of head-and-neck cancer patients where the primary tumor volume had no  
23 prognostic significance [19]. In the present study we showed that for head-and-neck cancer patients the  
24 primary tumor volume was a significant predictor of tumor response to treatment in both univariate and  
25 multivariate analysis. Moreover, it presented the strongest correlation with treatment failure compared

1 to the remaining predictors.

2 Typically, prognostic decisions are mainly guided by the TNM classification which might be limited as  
3 described by Byron J Bailey, Chairman of the Committee to study the TNM classification of the Laryngeal  
4 Cancer Association [20]: “Physicians are focused on optimal treatment while patients are interested in  
5 their prognosis, and the TNM is not designed to provide answers to either sets of questions.” Moreover,  
6 the clustering of various subsets of TNM classification into four stages for prognostic decisions might  
7 result in a greater loss of accuracy. Stage IV of AJCC staging system includes patients with a T4N0M0  
8 carcinoma and patients with a T1N2M0 carcinoma which may biologically be very different. In this study,  
9 as expected, a significant and positive correlation was found between the primary tumor volume and T –  
10 classification. However, 20.7% of the patients with primary tumor volume under the mean (42.0 cm<sup>3</sup>)  
11 had a T4 status and two of the ten largest primary tumor volumes ( > 100 cm<sup>3</sup>) had other status than T4  
12 (one patient with T2 status and other patient with T3 status). This result suggests that the current TNM  
13 classification system has still some limitations in separating larger tumors from smaller tumors.  
14 Moreover, in our study, in a multivariate analysis, the T – classification lost its univariate significance,  
15 being dominated by the variable that is strongly correlated, the primary tumor volume.

## 16 17 **Conclusion**

18 For patients with head-and-neck cancer treated with definitive RT, we have developed a 3-predictor  
19 model that presented a good discriminative ability in making the predictions of tumor response to  
20 treatment. To the best of our knowledge this study is pioneering in predicting treatment failure of head-  
21 and-neck cancer patients treated with RT. The results obtained suggest that the primary tumor volume is  
22 a highly significant predictor of tumor response to treatment and it should be added as a quantitative  
23 measure for evaluating tumor response to treatment prognosis in addition to age and type of RT. The  
24 prediction nomogram developed aims to assist doctors on the decision-making process for newly  
25 diagnosed head-and neck patients incorporating in a quantitative manner all relevant information

1 available for the population at hand. The results of the regression models may be used in clinical decision  
2 making and quality maintenance after external validation.

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#### 6 7 **Disclosure of interest**

8 The authors declare that they have no potential conflict of interest relevant to this article.

9  
10 Fig. 1. ROC curve of the predictive logit models for tumor response to treatment.

11 Fig. 2. Courbe ROC des modèles logistiques prédictifs pour la réponse tumorale au traitement.

12 Fig. 2. Nomogram for the prediction of failure to treatment.

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Table 1. Demographic and clinical information. Tableau 1. Données démographiques et cliniques.

| <b>Demographic and clinical features</b> | <b>Total<br/>(N=92)<br/>Frequency (%)</b> | <b>Complete<br/>response<br/>(N=64)<br/>Frequency (%)</b> | <b>Partial response<br/>/progression<br/>(N=28)<br/>Frequency (%)</b> |
|--|---|---|---|
| <b>Age at diagnosis</b>                  |   |   |   |
| Mean (SD)                                | 53.0 (12.0)                               | 50.6 (11.6)   | 58.6 (11.0)   |
| <b>Gender</b>                            |   |   |   |
| Female                                   | 19 (20.7)                                 | 16 (25.0)   | 3 (10.7)  |
| Male                                     | 73 (79.3)                                 | 48 (75.0)   | 25 (89.3)   |
| <b>Tumor location</b>                    |   |   |   |
| Oro/Nasopharynx                          | 52 (56.5)                                 | 38 (59.4)   | 14 (50.0)   |
| Other                                    | 40 (43.5)                                 | 26 (40.6)   | 14 (50.0)   |
| <b>T – classification</b>                |   |   |   |
| T1-3                                     | 54 (58.7)                                 | 43 (67.2)   | 11 (39.3)   |
| T4                                       | 38 (41.3)                                 | 21 (32.8)   | 17 (60.7)   |
| <b>N – classification</b>                |   |   |   |
| N0-1                                     | 22 (23.9)                                 | 18 (28.1)   | 4 (14.3)  |
| N2 <sup>+</sup>                          | 70 (76.1)                                 | 46 (71.9)   | 24 (85.7)   |
| <b>Anemia</b>                            |   |   |   |
| No                                       | 69 (75.0)                                 | 51 (79.7)   | 18 (64.3)   |
| Yes                                      | 23 (25.0)                                 | 13 (20.3)   | 10 (35.7)   |
| <b>Type RT</b>                           |   |   |   |
| Concomitant                              | 72 (78.3)                                 | 54 (84.4)   | 18 (64.3)   |
| Non – Concomitant                        | 20 (21.7)                                 | 10 (15.6)   | 10 (35.7)   |
| <b>Primary tumor volume</b>              |   |   |   |
| Mean (SD)                                | 42.0 (38.2)                               | 32.3 (29.2)   | 64.1 (47.0)   |
| <b>Overall treatment time</b>            |   |   |   |
| 39 – 45 days                             | 46 (50.0)                                 | 29 (45.3)   | 17 (60.7)   |
| >45 days                                 | 46 (50.0)                                 | 35 (54.7)   | 11 (39.3)   |
| <b>PTV mean dose</b>                     |   |   |   |
| Mean (SD)                                | 61.3 (3.1)                                | 60.9 (3.2)  | 62.1 (2.5)  |
| <b>PTV-T mean dose</b>                   |   |   |   |
| Mean (SD)                                | 70.4 (4.9)                                | 70.3 (5.4)  | 70.6 (3.5)  |



Table 1. Correlation analysis. Tableau 2. L'analyse de corrélation.

|                        | Treatment failure | Age    | Gender | Tumor location | T - classification | N - classification | Anemia | Type RT | Primary tumor volume | Overall treat. time | PTV mean dose | PTV-T mean dose |
|------------------------|-------------------|--------|--------|----------------|--------------------|--------------------|--------|---------|----------------------|---------------------|---------------|-----------------|
| Treatment failure      | 1                 | .313** | .162   | .087           | .261*              | .164               | .164   | .224*   | .385**               | -.142               | .251          | .228            |
| Age                    |                   | 1      | .118   | .100           | .074               | -.202              | .252*  | .333**  | -.043                | .013                | -.094         | -.094           |
| Gender                 |                   |        | 1      | .339**         | .046               | -.047              | .109   | .074    | .064                 | .027                | -.012         | .003            |
| Tumor location         |                   |        |        | 1              | .066               | -.080              | .203   | -.037   | .099                 | .088                | .106          | .154            |
| T - classification     |                   |        |        |                | 1                  | .127               | .178   | -.067   | .472**               | .044                | .306**        | .142            |
| N - classification     |                   |        |        |                |                    | 1                  | .101   | -.122   | .272**               | -.417*              | .364**        | .297**          |
| Anemia                 |                   |        |        |                |                    |                    | 1      | .061    | .012                 | .025                | .093          | .074            |
| Type RT                |                   |        |        |                |                    |                    |        | 1       | -.056                | -.211*              | -.205*        | -.151           |
| Primary tumor volume   |                   |        |        |                |                    |                    |        |         | 1                    | .025                | .360**        | .179            |
| Overall treatment time |                   |        |        |                |                    |                    |        |         |                      | 1                   | -.229*        | -.146           |
| PTV mean dose          |                   |        |        |                |                    |                    |        |         |                      |                     | 1             | .863**          |
| PTV-T mean dose        |                   |        |        |                |                    |                    |        |         |                      |                     |               | 1               |

Note: \*\* p &lt; .01; \*p &lt; .05.

Table 1. Logit regression results for predicting treatment failure. Tableau 3. Les résultats de la régression logistique pour prédire l'échec du traitement.

| <b>Logit Regression</b>                  | <b>p-value</b> | <b>OR</b> | <b>95% CI</b> |
|--|----------------|-----------|---------------|
| <b>Age at diagnosis</b>                  | .011           |           |               |
| Mean (SD)                                |                | 1.07      | 1.02-1.15     |
| <b>T – classification</b>                | .198           |           |               |
| T1-3                                     |                | 1.0       |               |
| T4                                       |                | 1.48      | 0.81-2.69     |
| <b>Type RT</b>                           | .047           |           |               |
| Concomitant                              |                | 1.0       |               |
| Non – Concomitant                        |                | 4.60      | 1.02-20.81    |
| <b>Primary tumor volume</b>              | .008           |           |               |
| Mean (SD)                                |                | 1.02      | 1.01-1.04     |
| <b>Pseudo-R<sup>2</sup></b> (Nagelkerke) | .452           |           |               |

# ROC Curve

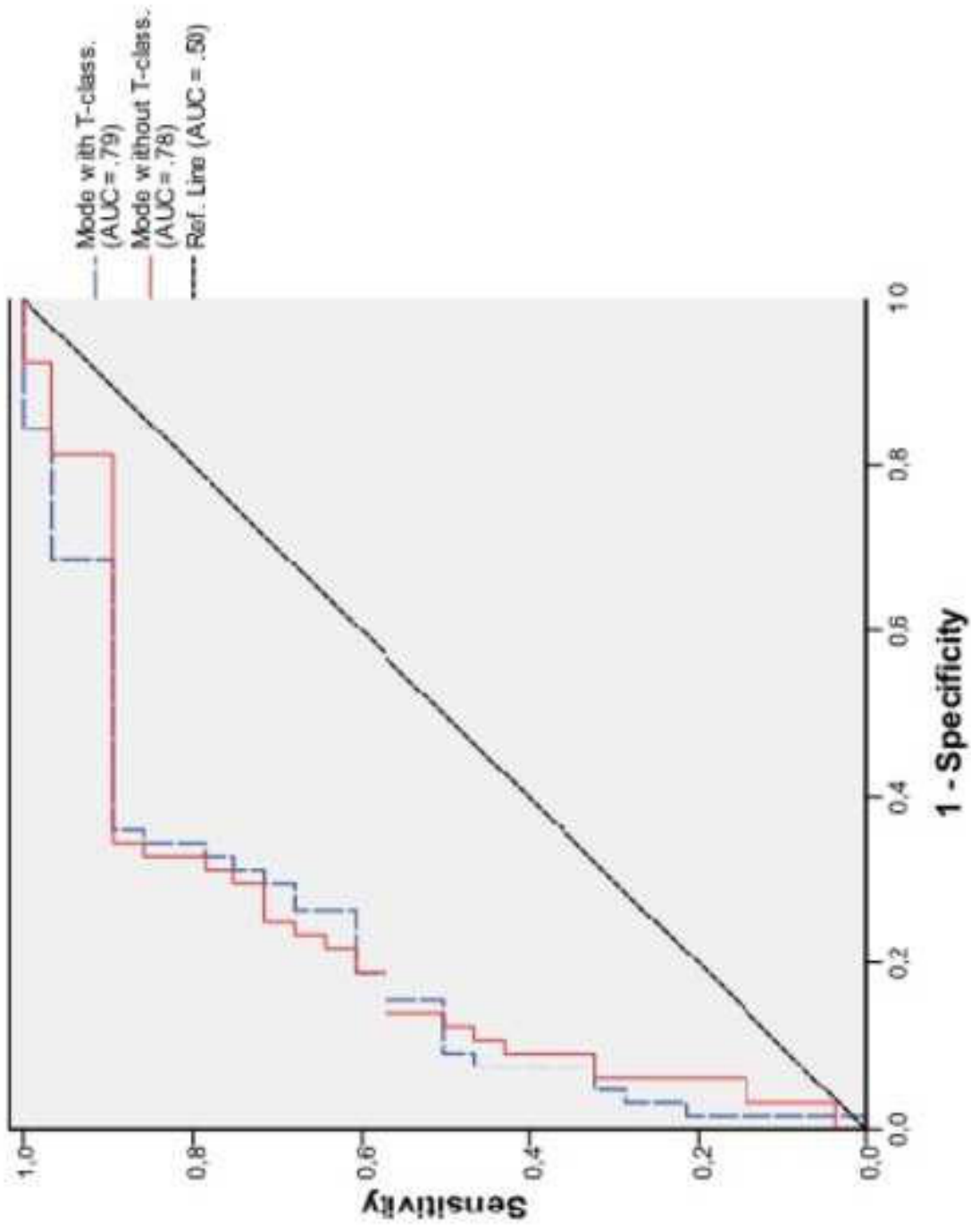


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Figure

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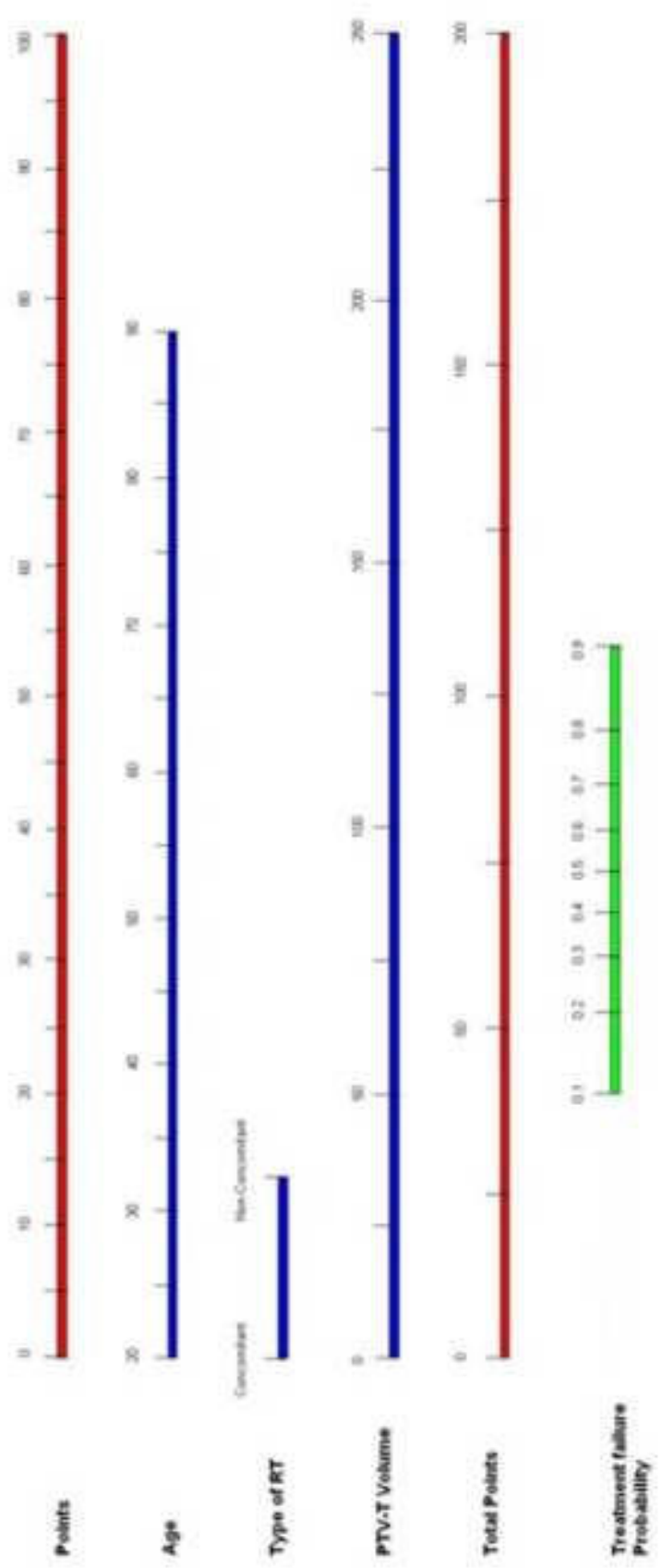


Fig. 1. ROC curve of the predictive logit models for tumor response to treatment.

Fig. 2. Courbe ROC des modèles logistiques prédictifs pour la réponse tumorale au traitement.

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