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Bone Mineral Density through DEXA and CBCT: A Systematic Review with Meta-Analysis

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Featured Application: Opportunistic CBCT scans may be used to assess bone mineral density and fracture risk, improving the ability to track disease progression and helping clinicians to provide better care as osteoporosis can be detected early.

Abstract: Dual-energy X-ray absorptiometry is used to determine bone density in several pathologies, namely osteoporosis and fracture risk in post-menopausal women. The aim of this study was to identify, appraise and synthesize all available evidence about the correlation between Dual Energy X-ray Absorptiometry (DEXA) and Cone Beam Computed Tomography (CBCT) techniques through a systematic review. A systematic literature search was conducted in the following databases: PubMed via MEDLINE, Cochrane Library, EMBASE and Web of Science Core Collection, along with several sources of grey literature. The Cochrane Risk of Bias Tools were used to perform the qualitative assessment of the selected studies. A total of 913 articles were initially scrutinized and 11 were included for qualitative analysis, of which 3 were included in a meta-analysis. Most of the included studies revealed a low risk of bias (7 out of 11). A strong correlation (min r = 0.46 max r = 0.62) between DEXA and CBCT values were found. Thus, opportunistic CBCT scans may be used to assess the bone mineral density and fracture risk, improving the ability to track disease progression and providing better care.

Keywords: cone beam computed tomography; absorptiometry; Photon; bone density

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1. Introduction

Osteoporosis is the most common bone disorder worldwide affecting over 27 million people in Europe alone. This disease is associated with decreased bone density, structural bone changes and an increased fracture risk [1]. During the last 30 years, osteoporosis

prevalence has increased and with it, the capability of imaging technologies used for clinical assessment [2].

Dual-energy X-ray absorptiometry (DEXA or DXA) is used to determine bone density by combining two X-ray beans with different energy levels [3–6]. DEXA is used to monitor osteoporosis and assess fracture risk in mostly post-menopausal women [7]. From 1994 on, T-score (standard deviations compared with a young adult—reference population) has been used as a scale to classify bone mineral density (BMD) measurements in postmenopausal women. The T-scores evaluated were: (1) health: T-score value greater or equal to −1; (2) osteopenia: T-score value between −2.5 and −1; (3) osteoporosis: T-score value less or equal to −2.5. This classification was later adopted for all men, women and children by the International Society for Clinical Densitometry [7]. DEXA is regarded as the gold standard technique to assess BMD and despite being widely disseminated; it is scarcely used in Dentistry [7].

Computed Tomography (CT) has several uses in bone analysis and has been used in healthcare and diagnostic investigation, so it may be used to evaluate osteoporosis [1]. In dentistry, Cone Beam Computed Tomography (CBCT) scanners are increasingly used to evaluate morphologic information [8]. CBCT can additionally aid in bone density estimations through a linear correlation between CBCT voxels values (usually in Hounsfield units) and bone mineral content [8]. Knowing bone mineral density is crucial in some fields of dentistry such as Implantology [9]. To use CBCT for bone mineral density assessment, this exam must present with equal accuracy to the gold-standard technique (DEXA) [3].

If a strong correlation coefficient is established between DEXA and CBCT, this suggests that a CBCT can be used to evaluate patients with low BMD with the same level of assurance as DEXA. In dentistry the CBCT is commonly used to more accurately help plan future interventions, but it can be additionally used to detect low bone density without additional scans (e.g., DEXA), thus avoiding exposure to any additional radiation whilst reducing costs and saving time. The opportunity for osteoporosis diagnosis using CBCT has been reported in literature, albeit sparsely.

The aim of this systematic review is to identify, appraise and synthesize all available evidence regarding the correlation between Dual Energy X-ray Absorptiometry and Cone Beam Computed Tomography techniques in the evaluation of bone mineral density.

2. Materials and Methods

2.1. Protocol

The proposed systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The present systematic review aims to answer the following question according to the PICO model (P—population; I—intervention; C—Comparative Intervention; O—Outcome): "What is the correlation coefficient between DEXA and CBCT technologies in the determination of bone mineral density in osteoporosis patients?". The protocol for this systematic review was registered on PROSPERO with CRD42018100209 number.

2.2. Strategy and Study Selection

A systematic literature search was conducted on the following databases: MEDLINE via PubMed via MedLine, Cochrane Library, EMBASE and Web of Science Core Collection (All databases). The search for grey literature included ProQuest (Database, EBooks and Technology for Research), HSRProj and Onegrey. The search was performed until 6 March 2023, independently by two reviewers. The Search Strategies are detailed in Table S1. No restrictions on publication date were applied but language filters (English, Portuguese, and Spanish) were considered. A manual search of the reference list of the retrieved studies selected for critical appraisal was also conducted.

Results of all database searches were collated and uploaded to Mendeley v1.19.5 (Mendeley Ltd., Elsevier, Amsterdam, The Netherlands), and all duplicates were removed. Subsequently, the titles and abstracts were independently screened by two reviewers and

assessed according to the eligibility criteria. Any disagreements were resolved by a third review author. If the article did not have the information for the authors to make the decision, the article was collected for reading the full text.

The following inclusion criteria were used: (1) Participants: adults (aged 18 years and over), male or female, with or without a diagnosis of osteoporosis, and with or without bone fractures; (2) papers where a correlation coefficient was calculated to assess the relationship between BMD measured with CBCT and the lumbar spine or femoral neck BMD measured by DEXA; (3) Study design: randomized controlled trials (RCTs), controlled clinical trials (CCTs) and cohort studies that show the correlation coefficient between DEXA and CBCT; 4) studies in humans. The following exclusion criteria were considered: (1) Participants: children or animal studies; (2) papers where a correlation coefficient between DEXA and CBCT technologies was not calculated; (3) Study design: case reports, case series, editorials, conference abstracts, opinion letters, book chapters; (4) studies with missing data.

The full text of relevant papers was screened by two independent reviewers and whenever a consensus was not reached, a third researcher was consulted.

2.3. Data Extraction

The data gathered from the papers included in this review was the following: author and year of publication, size and type of samples analyzed (experimental/control group, sex, age, pathologies), description of DEXA and CBCT equipment, locations analyzed by DEXA and CBCT, software used to analyze CBCT images, field of view (FOV) and Voxel size used, the correlation coefficients between BMD values obtained with DEXA and CBCT, and the main conclusions of each study). Authors of papers were contacted to request missing or additional data when required. Any disagreements between the reviewers were solved by a third reviewer.

2.4. Risk of Bias

Selected papers were assessed by two independent reviewers for methodological quality. The Cochrane Risk of Bias Tools were used to perform the qualitative assessment of the selected studies. Depending on the type of study, the corresponding Cochrane Risk of Bias Tool was chosen, and the quality assessment was performed independently by two review authors. Any disagreements between the reviewers were solved by a third reviewer. The overall risk of individual bias studies was categorized into three categories: low- all domains evaluated with low risk of bias; moderate- low or moderate risk of bias for all domains; severe if at least one domain presents a severe risk assessment bias.

2.5. Statistical Analysis

Based on the coefficients of correlation between BMD values obtained with DEXA and CBCT extracted from the included papers, a meta-analysis was conducted to determine the strength of correlation between the two imaging techniques regarding their ability for measuring BMD. The summary measure adopted for the meta-analysis was the correlation coefficient between CBCT and DEXA values. As some of the studies acquired images in more than one location showing various correlation values, it was decided that two meta-analysis studies would be persormed: one with the minimum correlation value and one with the maximum value. A forest-plot was produced for each study. The summary measure was calculated using the random effects model, and heterogeneity was assessed using Cochran's Q test and the I^2 statistic. Meta-analysis was performed in R using the metafor package and a 5% significance level was adopted.

3. Results

In the first stage of this study, a total of 913 articles were identified from the electronic databases. A total of 11 papers met the eligibility criteria and were included in this Systematic Review. Figure 1 shows the flowchart that illustrates the references search and selection process.

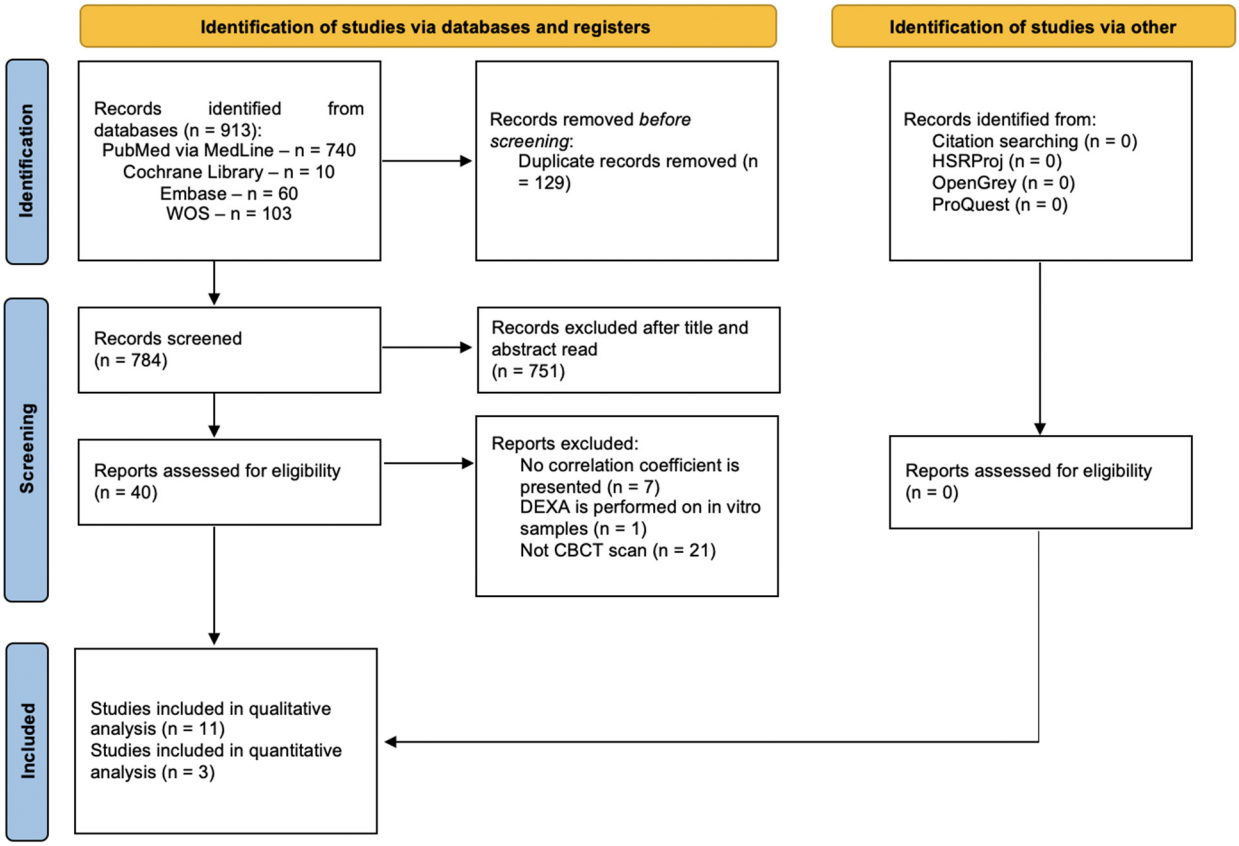

Figure 1. PRISMA flowchart diagram. This diagram represents all the information during the different phases, from identification, screenning and inclusion of studies.

3.1. Description of the Included Studies

Only one study mentions a random patient sample, and the sample group sizes varied from 23 to 81 individuals [10]. Out of the 11 studies that were assessed, five contained sample groups solely comprised of female individuals [10–15], another five studies analyzed samples with both male and female individuals [10,16–19], and only one study assessed an exclusively male group [20]. Four of the eleven studies specifically evaluated post-menopausal females [11,13–15], one study evaluated acromegaly patients [20] and one study evaluated diabetic patients [20].

Radiomorphometric analysis were used to assess BMD from CBCT images in several of the included studies. One author was involved in 3 studies [13–15] using the same sample comprised of 38 post-menopausal female patients. Although it is the same sample, the analyzes performed are from different bone zones and therefore were included as independent studies. The main results of both studies concluded that CBCT-derived radiographic density (RD) measurements of the body and ramus of the mandible and cervical vertebrae could help predict osteoporosis with an accuracy of 75% for lumbar vertebrae (LV) and 78.4% for femoral neck(FN) [15], accuracy of 90.8% for LV and 86.4% [13]. A strong correlation with LV and FN in trabecular bone structure of jawbones and odontoid process comparision, thus the authors concluded the dens-derived measures can accurately predict osteoporosis [14].

The majority of the studies chose the lumbar spine as the preferred structure to assess BMD and to posteriorly compare the results to the CBCT of the mandibular cortical and cancellous bone. Four of the included studies compared the mandibular cortical bone with the lumbar spine DEXA obtaining an r value that fluctuated from 0.411 to 0.857 [12,16,17,19,20]. The highest correlation value that was observed among all the selected articles was of r = 0.924 and it was attained when comparing the cortical foramen and the femoral neck [17], in contrast, the lowest correlation value was observed between

the distal epiphysis border of the radius and the femoral neck with an r = 0.17 [19]. In general, it was concluded that BMD presents lower values in osteoporotic groups when compared to osteopenia and/or control groups.

Regarding the software used [16,17] of the eleven studies made no mention of the chosen software to analyze CBCT images. Three of the studies by the same author used the WhiteFox ® Imaging v.3 (Acteon Group Ltd., Milan, Italy) software [13–15]. The i-Cat vision (Imaging Sciences International Inc., Hatfield, PA, USA) software was only used in oneof the studies [10]. Two out of the 11 studies assessed used Planmeca Romexis (Helsinki, Finland), another two [11,18] used the OnDemand 3-D Dental Software (CyberMed, Seoul, Republic of Korea) and only one studyused the BoneJ 1.3.9 program, (U.S. National Institutes of Health, Bethesda, MD, USA) [19].

FOV and voxel size are also important factors to take into account and two studies [16,17] did not provide any information about these variables. Shokri et al. [11] provided information regarding the FOV: 13 × 14 cm and Sghaireen et al. [18] only provided information about the Voxel Size: 0.2 mm. Three studies [13–15] used values of FOV: 13 × 15 cm and Voxel size: 0.25 mm. All other studies used different FOV and voxel values with one of these using FOV: 13 × 15 cm and Voxel size: 0.25 mm [10], another using FOV: 8 × 8 cm and Voxel size: 0.2 mm [12]; an additional one using FOV: 8 × 8 cm and Voxel Size: 0.75 mm [19] and lastly, another one using FOV: 4 × 4 cm and Voxel size: 0.4 mm [20]. Table 1 summarize the characteristics of the articles included.

3.2. Quantitative Analysis

A meta-analysis was conducted to determine the strength of correlation between the two imaging techniques regarding their ability for measuring BMD. Of the included articles, three were chosen for the quantitative assessment of the results given that these are the ones that establish a correlation between the CBCT/CT and DEXA values and presented eligibility to compare the results. The remaining articles use measures that do not allow this comparison since they use t-scores to measure the relationships between cortical bone and trabecular bone.

The following forest-plots illustrate the results for the minimum values of correlation (Figure 2).

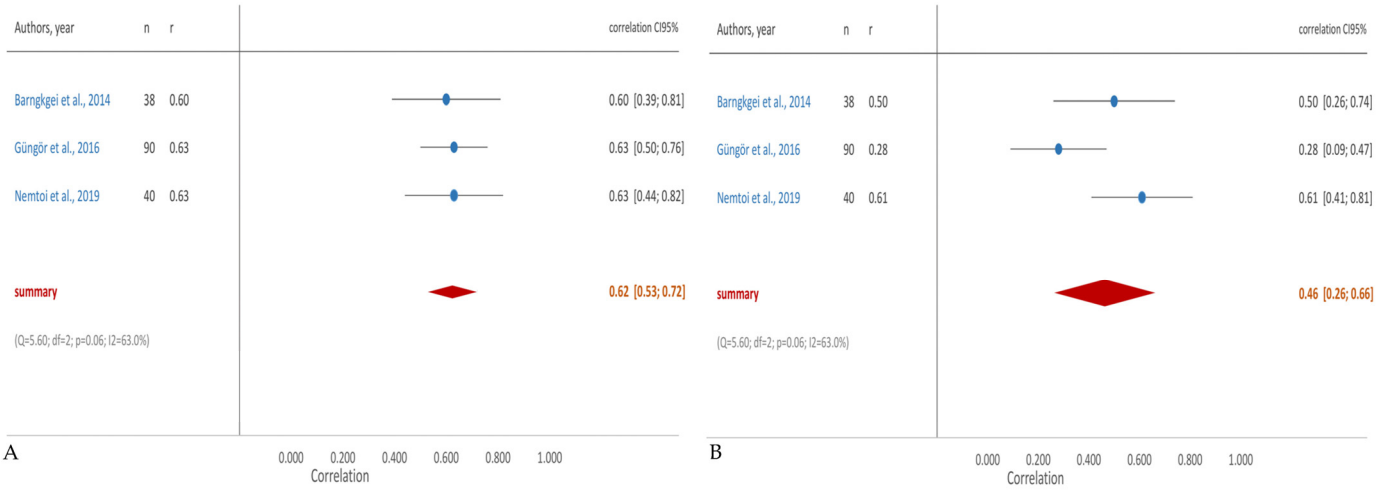

Figure 2. Forest plot of quantitative analysis between the CBCT/CT and DEXA: (**A**) minimum correlation value; (**B**) maximum correlation value [10,15,20].

Table 1. Characteristics of included studies in the qualitative analysis.

Author, Year of Publication	Location Analyze with CBCT	Location Analyze with DXA	Software Used to Analyze CBCT Scans	Information about FOV and Voxel Size	Information about CBCT Equipment	Information about DXA Equipment	Methods	Control Group Analyzed	Case Group Analyzed	Main Results
Barngkgei et al., 2016 [13]	Dens and first and second vertebrae	Femoral neck and lumbar vertebrae	White Fox Imaging ® Version 3 (Acteon Group Ltd., Milan, Italy)	FOV: 13 × 15 cm Voxel size: 0.25 mm	WhiteFox ® Imaging v.3 (Acteon Group Ltd., Milan, Italy)	Hologic Discovery QDR ® (Hologic Inc., Bedford, MA, USA)	3 groups for FN and LV were assessed Radiographic density values were assessed from the dens and first and second vertebrae	Post-menopausal normal BMD females plus osteopenic females regarding LV T-score (n = 25) and FN T-score (n = 28) and normal BMD females concerning LV T-score (n = 10) and FN T-score (n = 17)	Post-menopausal osteoporotic females concerning LV T-score (n = 13) and FN T-score (n = 10) and osteoporotic plus osteopenic females concerning LV T-score (n = 28) and FN T-score (n = 21)	Radiographic density derived from CBCT analysis of the first and second vertebrae show high accuracy (90.8% for LV and 86.4% from FN) in predicting osteoporosis
Barngkgei et al., 2014 [15]	Body and ramus of the mandible	Lumbar vertebrae (L1–L4) e Femoral Neck	WhiteFox ® Imaging v.3 (Acteon Group Ltd., Milan, Italy)	FOV: 13 × 15 cm; Voxel size: 0.25 mm	WhiteFox ® Imaging v.3 (Acteon Group Ltd., Milan, Italy)	Hologic Discovery QDR ® (Hologic Inc., Bedford, MA, USA)	3 Groups for FN and LV were assessed Radiographic Density values of body and ramus of the mandible was evaluated	Post-menopausal normal BMD females and osteopenic females concerning to LV T-score (n = 25) and FN T-score (n = 28)	Post-menopausal osteoporotic females concerning LV T-score (n = 13) and FN T-score (n = 10)	Osteoporosis can be predicted with accuracy (75% for LV and 78.4% for FN) from radiographic density using CBCT
Barngkgei et al., 2015 [14]	Jawbones and odontoid process	Lumbar Spine (L1–L4) and Femoral Neck	WhiteFox ® Imaging v.3 (Acteon Group Ltd., Milan, Italy)	FOV: 13 ×15 cm; Voxel size: 0.25 mm	WhiteFox ® Imaging v.3 (Acteon Group Ltd., Milan, Italy)	Hologic Discovery QDR ® (Hologic Inc., Bedford, MA, USA)	3 groups for FN and LV were assessed Histomorphometric analysis was extracted from ImageJ (Tb.Th, Tb.Ts, BV/TV, BV/TV); Cuboids from jawbones extracted from CBCT scans and connectivity density were calculated by BoneJ	Post-menopausal normal BMD females and osteopenic females concerning to LV T-score (n = 25) and FN T-score (n = 28)	Post-menopausal osteoporotic females concerning LV T-score (n = 13) and FN T-score (n = 10)	Measures extracted from dens showed high accuracy of osteoporosis prediction (78.9% for LV and 84.2% for FN)

Table 1. *Cont.*

Author, Year of Publication	Location Analyze with CBCT	Location Analyze with DXA	Software Used to Analyze CBCT Scans	Information about FOV and Voxel Size	Information about CBCT Equipment	Information about DXA Equipment	Methods	Control Group Analyzed	Case Group Analyzed	Main Results
Güngör et al., 2016 [10]	Jawbones	Lumbar vertebra (L1–L3) or hip	i-Cat Vision (Imaging Sciences International Inc.) software, using 0.21 mm slices	FOV: 13 × 10 cm Voxel size: 0.3 mm	i-CAT vision (Imaging Sciences International Inc., Hatfield, PA, USA)	Hologic Discovery QDR; Hologic Inc., Belford, MA	3 groups were assessed Histomorphometric analysis and Fractal dimension analysis were taken using ImageJ. CT values and radiomorphometric index measurements (CTMI, CTI(S), CTI(I) were assessed	Normal BMD patients (n = 31)	Osteoporotic patients (n = 26) and Osteopenic patients (n = 33)	Histomorphometric analysis and Fractal dimension analysis, CT values and radiomorphometric index measurements can evaluated changes in the jawbones associated to osteoporosis
Jeong et al., 2016 [16]	Forearm (carpal bone to the elbow)	Femoral neck	-	-	Peripheral CBCT (Phion, Nano Forcus Ray, Jeonju, Republic of Korea)	Discovery-W scanner, Hologic Inc., Bedford, MA, USA	2 groups were assessed Ratio between Bone Volume/Trabecular volume, mean trabecular thickness, mean trabecular separation, cortical thickness and cortical porosity were calculated from High-Resolution CBCT	Healthy Volunteers (n = 21; 10 females and 11 males)	Acromegaly patients (n = 40; 24 females and 16 males)	High- Resolution CBCT may be a useful tool to measure the deleterious effects on trabecular and cortical bone microarchitecture of acromegaly patients
Ko et al., 2017 [17]	Forearm (carpal bone to the elbow; with included forearm mid-shaft)	Total femur, femoral neck, femoral trochanter, femoral inter-trochanter and femoral ward's triangle	-	-	Peripheral CBCT (PHION, Nano Focus Ray, Jeonju, Republic of Korea)	Discovery-W scanner, Hologic Inc., Bedford, MA	2 groups were assessed Bone Mineral density values of forearm were estimated though the ratio of the forearm cortical bone to the cross-sectional area measured by CBCT	Non-osteoporosis patients (n = 14; 7 male and 7 females)	Osteoporosis Patients (n = 14; 1 male and 13 females)	Forearm CBCT images can be used to estimate hip bone mineral density and be a useful tool for screening osteoporosis

Table 1. *Cont.*

Author, Year of Publication	Location Analyze with CBCT	Location Analyze with DXA	Software Used to Analyze CBCT Scans	Information about FOV and Voxel Size	Information about CBCT Equipment	Information about DXA Equipment	Methods	Control Group Analyzed	Case Group Analyzed	Main Results
Maffezzoni et al., 2016 [19]	Distal epiphysis border of radius	Lumbar spine, total hip, femoral neck and distal radius	BoneJ 1.3.9 program, (U.S. National Institutes of Health, Bethesda, MD, USA)	FOV: 8 × 8 cm^2 Voxel size: 0.75 mm	High-resolution CBCT system (Newtom 5 G; QR, Verona, Italy)	Explorer Hologic Inc., Waltham, MA	2 groups were assessed / Ratio between Bone Volume/Trabecular volume, mean trabecular thickness, mean trabecular separation, cortical thickness and cortical porosity were calculated from High-Resolution CBCT	Healthy Volunteers (n = 21; 10 females and 11 males)	Acromegaly patients (n = 40; 24 females and 16 males)	High- Resolution CBCT may be a useful tool to measure the deleterious effects on trabecular and cortical bone microarchitecture of acromegaly patients
Mostafa et al., 2016 [12]	Mandible	Lumbar spine	Planmeca Romexis ® (Helsinki, Finland)	FOV: 8 × 8 cm Voxel size: 0.2 mm	Planmeca ProMax ® 3D Classic, Helsinki, Finland.	-	2 groups were assessed / Fractal Dimension analysis were assessed using ImageJ; Radiomorphometric index measurements (CTMI, CTCI, CTI) were assessed	Normal BMD females (n = 25)	Osteoporotic females (n = 25)	Radiomorphometric index measurements obtain though CBCT can help refer patients at risk of osteoporosis
Nemtoi et al., 2019 [20]	Cortical and cancellous bone of the mandible	Lumbar spine (L1–L4) and Left femur	Romexis 3.0.1 (Helsink, Finland)	FOV: 4 × 4 cm Voxel size: 0.4 mm	Planmeca Promax 3D mid CBCT (Helsinki, Finland)	Hologic Delphi W densitometer DEXA scan	3 groups were assessed / Radiomorphometric indices and mandibular bone density were obtained in CBCT images.	20 osteoporotic male patients)	40 diabetic male patients (16-type I DM; 24 type II DM	CBCT examination offer sufficient radiographic information detect patients with mandibular osteoporosis.
Sghaireen et al., 2020 [18]	Jaws bones (anterior and posterior maxilla and anterior and posterior mandible)	Lumbar Spine (L1–L4)	OnDemand 3D (Yuseong-gu, Daejeon, Republic of Korea)	FOV: Medium Voxel size: 0.2 mm	SORDEX, Nahkelantie 160 Tuusula, Filand	-	2 groups were assessed / CBCT grayscale values of BMD jaws bones were measure in CBCT radiographs and compared to the results of DXA examinations	Non-osteoporosis patients (n = 39; 16 males and 23 females)	Osteoporosis Patients (n = 42; 6 males and 36 females)	CBCT grayscale values of BMD can be used to predict DXA T-score values

Table 1. *Cont.*

Author, Year of Publication	Location Analyze with CBCT	Location Analyze with DXA	Software Used to Analyze CBCT Scans	Information about FOV and Voxel Size	Information about CBCT Equipment	Information about DXA Equipment	Methods	Control Group Analyzed	Case Group Analyzed	Main Results
Shokri et al., 2019 [11]	Anterior, premolar, retromolar and tuberosity areas of mandible and maxilla	Femoral Neck and Lumbar spine	OnDemand 3-D Dental Software (CyberMed, Seoul, Republic of Korea)	FOV: 13 × 14 cm	Scanora 3-D CBCT system (Soredex, Tuusula, Finland)	Osteocore Bone Densitometer (Medilink, Paris, France)	3 groups were assessed Mean gray value of CBCT Cross-sectional images of anterior, premolar, retromolar and tuberosity areas of mandible and maxilla were used to calculated Bone mineral density	Post-menopausal non-osteoporosis females according to FN T-score (n = 32) and LV T-score (n = 27)	Post-menopausal osteoporotic and osteopenia females concerning LV T-score (n = 34; 24 with osteopenia and 10 with osteoporosis) and FN T-score (n = 29; 28 with osteopenia and 1 with osteoporosis)	A strong correlation was found between CBCT gray values of different parts of the maxilla and BMD values determinated by DXA.

BMD—bone mineral density; BV/TV—bone volume/trabecular volume ratio; CBCT—Cone Beam Computed Tomography; CT—computed tomography; CTMI—computer tomography mental index; CTI(S)—CT index (superior); CTI(I)—CT index (inferior); CTCI—computed tomography cortical index; CTI—Computer tomography mandibular index; DXA—dual-energy X-ray absorptiometry; DM—diabetes mellitus; FOV—field of vie; FN—Femoral Neck; LV—Lumbar Vertebra; Tb.Th, trabecular thickness.

The coefficients values found within the studies are described in Table 2. The highest value was r = 0.924 [17] and the lower value was r = 0.08 [19], with a discrepancy of 0.8 values between the higher and the lower values.

Table 2. Coefficients of correlation between BMD values obtained with DEXA and CBCT technologies.

Author, Year of Publication	Coefficients of Correlation
Barngkgei et al., 2016 [13]	Pearson correlation between Dens CBCT derived values and DEXA values: in osteoporotic group: r = 0.34–0.38 [p value = 0.02–0.036]; Non-osteoporotic group: r = 0.48–0.61 [p value $\leq$ 0.003]
Barngkgei et al., 2014 [15]	Pearson's correlation coefficients were 0.5 and 0.6 (p value = 0.037 and 0.009) between RD of bone area of the mandible and T-scores obtained from FN and LV, respectively
Barngkgei et al., 2015 [14]	Correlation Coefficients between CBCT-derived RD values of the left part of first cervical vertebra and the dens: r = 0.7, 0.6; $p < 0.001$
Güngör et al., 2016 [10]	Lumbar vertebrae DXA-derived measures and CTMI (r = 0.48, $p \leq 0.01$), CTI(I) (r = 0.40, $p \leq 0.01$), and CTI(S) (r = 0.32, $p \leq 0.01$) Femoral head DXA-derived measures and CTMI (r = 0.32, $p \leq 0.01$)
Jeong et al., 2016 [16]	Correlation factor of r = 0.857 between femoral neck BMD and the ratio of the cortical and total bone areas
Ko et al., 2017 [17]	RAFC and total femur (r = 0.889), RAFC and femoral neck (r = 0.924), RAFC and femoral trochanter (r = 0.821), RAFC and femoral inter-trochanter (r = 0.867), RAFC and femoral ward's triangle (r = 0.895)
Maffezzoni et al.,2016 [19]	Spearman correlation factor between BV/TV and lumbar spine, total hip, femoral neck and distal radius, respectively: 0.08, 0.26, 0.17 and 0.32.
Mostafa et al., 2016 [12]	Correlation found between CTI and CTMI with lumber spine BMD: $p < 0.05$, r = 0.340 and $p < 0.001$, r = 0.463, respectively
Nemtoi et al., 2019 [20]	Pearson correlation between lumbar spine BMD and cortical mandibular bone density and cancellous bone density in case group (diabetic male patients) was r = 0.63, $p < 0.01$ and r = 0.607, $p < 0.01$, respectively.
Sghaireen et al., 2020 [18]	Pearson's correlation between the T-scores of lumbar spine and the CBCT GS values at posterior maxilla: $r^2 = 0.849$
Shokri et al., 2019 [11]	Pearson's correlation between the T-scores of femoral neck and the gray values of cancellous and cortical bone at the site of maxillary tuberosity areas: r = 0.411, $p < 0.001$

RD—Radiographic density; FN—Femoral Neck; LV—Lumbar Vertebrae; CTMI—computer tomography mandibular index; CTI(S)—CT index (superior); CTI(I)—CT index (inferior); CTI—Computer tomography mandibular index; CTMI—computer tomography mental index; BV/TV—bone volume/trabecular volume ratio; RAFC—relative cross-sectional area of forearm cortical; CBCTI(S)—CBCT mandibular index (superior); CBCTI(I) mandibular index (inferior); CBCTMI: CBCT mental index; CBCTCMI: CBCT mandibular cortical index; GS—Grayscale values.

3.3. Risk of Bias

The risk of bias in randomized and non-randomized studies is summarized in Tables 3 and 4, respectively. The only randomized trial included had a low risk of bias [11]. Regarding non-randomized studies, most of the included studies revealed a low risk of bias (6 out of 10). The remaining four have methodological flaws, 2 of them in the domain of bias due to confounding [20,21], 1 in deviations from intended interventions domain [16], and 1 with a methodologic flaw in the missing data domain [12].

Table 3. Risk of bias in randomized trials with the analysis of the parameters: randomization process, deviations from the intended, missing outcome data, measurement of outcome, selection of the reported result and overall bias (Y green—Yes).

	Randomization Process	Deviations from the Intended	Missing Outcome Data	Measurement of Outcome	Selection of the Reported Result	Overall Bias
Güngör et al., 2016 [10]	Y	Y	Y	Y	Y	Y

Table 4. Risk of bias in non-randomized trials with the analysis of the parameters: randomization process, deviations from the intended, missing outcome data, measurement of outcome, selection of the reported result and overall bias. (Y green—Yes; N red—No).

	Bias Due to Confounding	Selection of Participants	Classification of Interventions	Deviations from Intended Interventions	Missing Data	Measurement of Outcomes	Selection of the Reported Result	Overall Bias
Barngkgei et al., 2014 [15]	Y	Y	Y	N	Y	Y	Y	Y
Barngkgei et al., 2016 [13]	Y	Y	Y	Y	Y	Y	Y	Y
Barngkgei et al., 2015 [14]	Y	Y	Y	Y	Y	Y	Y	Y
Jeong et al., 2016 [16]	Y	Y	Y	Y	Y	Y	Y	Y
Ko et al., 2017 [17]	Y	Y	Y	Y	Y	Y	Y	Y
Maffezzoni et al., 2016 [19]	N	Y	Y	Y	Y	Y	Y	Y
Mostafa et al., 2016 [12]	Y	Y	Y	Y	Y	Y	Y	Y
Nemtoi et al., 2019 [20]	N	Y	Y	Y	Y	Y	Y	Y
Sghaireen et al., 2020 [18]	Y	Y	Y	Y	Y	Y	Y	Y
Shokri et al., 2019 [11]	Y	Y	Y	Y	N	Y	Y	Y

4. Discussion

The use of CBCT scans daily in dentistry practices has increased in recent years. Dental CBCT have lower radiologic dosages relative to traditional CT scans and comparable precision CBCT scans could be used to detect patients with low BMD without additional scans (e.g., DEXA) and help refer those patients to further follow-up. The studies in this Systematic Review intended to study the possibility of using CBCT images to identify and differentiate patients with low BMD, patients with risk of developing osteoporosis and patients who had already recovered from this illness, from healthy individuals.

In this study, we intended to determinate the correlation coefficient between DEXA and CBCT derived values. In 2017 a systematic review was published, investigating the opportunist capability of CBCT to identify patients with low BMD [21]. This systematic review did not identify the correlation coefficient between DEXA and CBCT, and, consequently, did not had quantitative analysis of their results. The authors concluded that the evidence was restricted to endorse the use of CBCT derived images as a mean to diagnostic low BMD [21]. Meanwhile, new publications in recent years justify the elaboration of a new Systematic Review, particularly, with a quantitative analysis that allows the extraction of a correlation coefficient.

All included articles in this Systematic Review concluded that CBCT derived images can be used to estimate BMD and refer patients at risk of osteoporosis. However, the methodology of the included papers was different, different indices (qualitative and linear) were used in the included studies as an opportunist diagnostic tools for low BMD. Furthermore, seven of the included papers in this review, resorted to those indices to differentiate patients with low BMD from patients with normal BMD, according to DEXA results [10–12,16–19]. Relatively to the studies who performed their analysis in the jaw bones: Güngör et al. [10] study, assessed CT values and radio morphometric index measurements, and concluded that those values can evaluated the changes associated to osteoporosis and referred those patients for further treatment. Shokri et al. [11]. study calculated mean gray values of CBCT cross-sectional images and concluded that those where lower in post-menopausal osteoporotic and osteopenic females, than in postmenopausal normal BMD females. Furthermore, Mostafa et al. [12] analyzed the mandible CBCT derived images of normal BMD and osteoporotic females and calculated radio morphometric index measurements, concluding those were lower in osteoporotic patients, and so, could be used to refer patients in risk of osteoporosis. Sghaireen et al. [18] used CBCT-derived grayscale values (GS) from jawbones to discriminate normal BMD patients and osteoporotic BMD patients and concluded that CBCT GS values are able to predict the presence of osteoporosis and DXA T-score values. Therefore, based in the results of the aforementioned studies, we can conclude that radio morphometric measurements are a capable tool for the identification of low BMD patients.

The samples of the included studies were very distinct. Considering sex and health status, seven studies compared osteoporotic men and women, with healthy men and women with normal BMD, according to DEXA results [10–12,16–19]. Pathophysiology, aged-bone loss in women is related with a combination of a negative remodeling balance and an increase of bone remodeling (both in cortical and cancellous bone), and in men, the aged-related bone loss is mostly related with reduction of bone formation, and reduction of bone turnover, however, the World Health Organization and the International Society for Clinical Densitometry stated, recently, that risk of fracture in men and females occurs proximally at the same BMD [22]. Still on the issue of samples of the included studies, one study [20] performed their analysis in a group of diabetic patients (type I and II patients were analyzed). The neuropathy of diabetes mellitus (DM) amplified severally the possibility of developing osteoporosis, and consequently, the likelihood of disease-related fractures, morbidity, and mortality [23]. However, the risk of osteoporosis and the values of BMD in DM patients are not well described, and although most papers stated a lower BMD in DM type I patients, other studies claimed that BMD may be greater, similar or lower in DM type II patients [20]. Another study performed their analysis in acromegaly patients [19], and according to recent data, although BMD in acromegaly patients may be higher, similar or lower and there is no agreement of BMD and the appearance of fractures, a lower hip BMD founded in acromegaly patients has been related to the presence vertebral fractures in those patients [24].

Regarding to the coefficient values, we can state that Ko et al. [17] obtained the highest coefficient values, ($r = 0.924$). However, this study had a small sample of people included with 14 on the case group and 14 in the control group [17].

The present study has some limitations namely the discrepancy in anatomical structures chosen to perform the DEXA which can introduce a bias due to possible variations in DEXA values in different structures [25]. Also, several studies obtained radiographic density though grey values derived from CBCT images, and those values change with FOV and Voxel size [26]. In addition, BMD in some mandibular areas can be affected by local conditions, which must be taken into account.

Other limitations can be scrutinized such as the CBCT equipment used to evaluate BMD which was not the same for all studies and when technical parameters change (like FOV and voxel size), the quality of the image also changes, especially spatial resolution [27]. Five studies [10,11,13–15] used the similar FOV and voxel size, however 3 studies had different FOV and voxel sizes, and two studies [16,17] did not have any information about FOV and voxel size. In this study local factors such as occlusal forces and masseter muscle tensions were not considered despite their possible influence on the mandibular bony areas, constituting an additional limitation. Further investigation is mandatory to understand if these different technical parameters may change aforementioned results. Also, all included studies had a small and heterogenic sample of individuals analyzed. Control groups were quite diverse and some disagreement: some studies included only healthy normal BMD patients, but others included osteoporotic patients, and some studies included normal BMD and osteopenic patients in the control group.

Future studies should be performed in order to obtain further evidence, with standardized protocols taking into account the chosen structures for analysis, a more robust sample group and more homogenous in terms of heal status, sex, age and health characteristics.

5. Conclusions

A strong correlation (min r = 0.46 max r = 0.62) between DEXA and CBCT values were found. Thus, opportunistic CBCT scans may be used to assess the bone mineral density and fracture risk, improving the ability to track disease progression and providing better care.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/app13105962/s1, Table S1: Search Strategies.

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References

1. Grüneboom, A.; Kling, L.; Christiansen, S.; Mill, L.; Maier, A.; Engelke, K.; Quick, H.H.; Schett, G.; Gunzer, M. Next-Generation Imaging of the Skeletal System and Its Blood Supply. *Nat. Rev. Rheumatol.* **2019**, *15*, 533–549. [CrossRef] [PubMed]
2. Griffith, J.F.; Genant, H.K. New Advances in Imaging Osteoporosis and Its Complications. *Endocrine* **2012**, *42*, 39–51. [CrossRef] [PubMed]
3. Hsu, J.-T.; Chen, Y.-J.; Tsai, M.-T.; Lan, H.H.-C.; Cheng, F.-C.; Chen, M.Y.C.; Wang, S.-P. Predicting Cortical Bone Strength from DXA and Dental Cone-Beam CT. *PLoS ONE* **2012**, *7*, e50008. [CrossRef] [PubMed]
4. Khoo, B.C.C.; Brown, K.; Cann, C.; Zhu, K.; Henzell, S.; Low, V.; Gustafsson, S.; Price, R.I.; Prince, R.L. Comparison of QCT-Derived and DXA-Derived Areal Bone Mineral Density and T Scores. *Osteoporos. Int.* **2009**, *20*, 1539–1545. [CrossRef] [PubMed]
5. Bachrach, L.K.; Gordon, C.M.; Sills, I.N.; Lynch, J.L.; Casella, S.J.; DiMeglio, L.A.; Gonzalez, J.L.; Wintergerst, K.; Kaplowitz, P.B. Bone Densitometry in Children and Adolescents. *Pediatrics* **2016**, *138*, e20162398. [CrossRef] [PubMed]

6. Crabtree, N.; Ward, K. Bone Densitometry: Current Status and Future Perspective. In *Calcium and Bone Disorders in Children and Adolescents*; Karger Publishers: Berlin, Germany, 2015; pp. 72–83.
7. Link, T.M. Osteoporosis Imaging: State of the Art and Advanced Imaging. *Radiology* **2012**, *263*, 3–17. [CrossRef]
8. Yepes, J.F.; Al-Sabbagh, M. Use of Cone-Beam Computed Tomography in Early Detection of Implant Failure. *Dent. Clin. N. Am.* **2015**, *59*, 41–56. [CrossRef]
9. Jeong, K.-I.; Kim, S.-G.; Oh, J.-S.; Jeong, M.-A. Consideration of Various Bone Quality Evaluation Methods. *Implant. Dent.* **2013**, *22*, 55–59. [CrossRef]
10. Güngör, E.; Yildirim, D.; Çevik, R. Evaluation of Osteoporosis in Jaw Bones Using Cone Beam CT and Dual-Energy X-ray Absorptiometry. *J. Oral Sci.* **2016**, *58*, 185–194. [CrossRef]
11. Shokri, A.; Ghanbari, M.; Maleki, F.H.; Ramezani, L.; Amini, P.; Tapak, L. Relationship of Gray Values in Cone Beam Computed Tomography and Bone Mineral Density Obtained by Dual Energy X-ray Absorptiometry. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.* **2019**, *128*, 319–331. [CrossRef]
12. Mostafa, R.A.; Arnout, E.A.; Abo el-Fotouh, M.M. Feasibility of Cone Beam Computed Tomography Radiomorphometric Analysis and Fractal Dimension in Assessment of Postmenopausal Osteoporosis in Correlation with Dual X-ray Absorptiometry. *Dentomaxillofac. Radiol.* **2016**, *45*, 20160212. [CrossRef] [PubMed]
13. Barngkgei, I.; Al Haffar, I.; Shaarani, E.; Khattab, R.; Mashlah, A. Assessment of Jawbone Trabecular Bone Structure amongst Osteoporotic Women by Cone-Beam Computed Tomography: The OSTEOSYR Project. *J. Investig. Clin. Dent.* **2016**, *7*, 332–340. [CrossRef]
14. Barngkgei, I.; Joury, E.; Jawad, A. An Innovative Approach in Osteoporosis Opportunistic Screening by the Dental Practitioner: The Use of Cervical Vertebrae and Cone Beam Computed Tomography with Its Viewer Program. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.* **2015**, *120*, 651–659. [CrossRef]
15. Barngkgei, I.; Al Haffar, I.; Khattab, R. Osteoporosis Prediction from the Mandible Using Cone-Beam Computed Tomography. *Imaging Sci. Dent.* **2014**, *44*, 263. [CrossRef] [PubMed]
16. Jeong, K.; Ko, H.; Lee, C.-H.; Lee, M.; Yoon, K.-H.; Lee, J. A Novel Method for Estimation of Femoral Neck Bone Mineral Density Using Forearm Images from Peripheral Cone Beam Computed Tomography. *Appl. Sci.* **2016**, *6*, 113. [CrossRef]
17. Ko, H.; Lee, C.H.; Jeong, K.; Lee, M.S.; Nam, Y.; Yoon, K.H.; Lee, J. A Pilot Study on Hip Bone Mineral Densities Estimation from Forearm CBCT Images. *KSII Trans. Internet Inf. Syst.* **2017**, *11*, 6054–6068. [CrossRef]
18. Sghaireen, M.G.; Ganji, K.K.; Alam, M.K.; Srivastava, K.C.; Shrivastava, D.; Ab Rahman, S.; Patil, S.R.; Al Habib, S. Comparing the Diagnostic Accuracy of CBCT Grayscale Values with DXA Values for the Detection of Osteoporosis. *Appl. Sci.* **2020**, *10*, 4584. [CrossRef]
19. Maffezzoni, F.; Maddalo, M.; Frara, S.; Mezzone, M.; Zorza, I.; Baruffaldi, F.; Doglietto, F.; Mazziotti, G.; Maroldi, R.; Giustina, A. High-Resolution-Cone Beam Tomography Analysis of Bone Microarchitecture in Patients with Acromegaly and Radiological Vertebral Fractures. *Endocrine* **2016**, *54*, 532–542. [CrossRef]
20. Nemtoi, A.; Nemtoi, A.; Fochi, A.; Sirghe, A.E.; Preda, C.; Earar, K.; Beznea, A.; Onisor, C.; Iorgulescu, G.; Haba, D. CBCT Evaluation of the Mandibular Bone Quality in Relation to Skeletal Status after Treatment with Strontium Renelate in Diabetic Patients. *Rev. Chim.* **2019**, *70*, 4113–4118. [CrossRef]
21. Guerra, E.N.S.; Almeida, F.T.; Bezerra, F.V.; Figueiredo, P.T.D.S.; Silva, M.A.G.; De Luca Canto, G.; Pachêco-Pereira, C.; Leite, A.F. Capability of CBCT to Identify Patients with Low Bone Mineral Density: A Systematic Review. *Dentomaxillofac. Radiol.* **2017**, *46*, 20160475. [CrossRef]
22. Adler, R.A. Update on Osteoporosis in Men. *Best Pract. Res. Clin. Endocrinol. Metab.* **2018**, *32*, 759–772. [CrossRef] [PubMed]
23. Liu, C.; Lv, H.; Niu, P.; Tan, J.; Ma, Y. Association between Diabetic Neuropathy and Osteoporosis in Patients: A Systematic Review and Meta-Analysis. *Arch. Osteoporos.* **2020**, *15*, 125. [CrossRef] [PubMed]
24. Anthony, J.R.; Ioachimescu, A.G. Acromegaly and Bone Disease. *Curr. Opin. Endocrinol. Diabetes Obes.* **2014**, *21*, 476–482. [CrossRef]
25. Eckstein, F.; Lochmüller, E.-M.; Lill, C.A.; Kuhn, V.; Schneider, E.; Delling, G.; Müller, R. Bone Strength at Clinically Relevant Sites Displays Substantial Heterogeneity and Is Best Predicted from Site-Specific Bone Densitometry. *J. Bone Min. Res.* **2002**, *17*, 162–171. [CrossRef] [PubMed]
26. Ibrahim, N.; Parsa, A.; Hassan, B.; van der Stelt, P.; Aartman, I.H.A.; Wismeijer, D. The Effect of Scan Parameters on Cone Beam CT Trabecular Bone Microstructural Measurements of the Human Mandible. *Dentomaxillofac. Radiol.* **2013**, *42*, 20130206. [CrossRef]
27. Ibrahim, N.; Parsa, A.; Hassan, B.; van der Stelt, P.; Aartman, I.H.A.; Nambiar, P. Influence of Object Location in Different FOVs on Trabecular Bone Microstructure Measurements of Human Mandible: A Cone Beam CT Study. *Dentomaxillofac. Radiol.* **2014**, *43*, 20130329. [CrossRef]