Cone-Beam Computed Tomography as a Prediction Tool for Osteoporosis in Postmenopausal Women: A Systematic Literature Review

Abulfaz Isayev (✉ isayev@bu.edu)

Boston University

Svitlana Koval

Boston University

Nigiar Velieva

Russian Medical Academy of Postgraduate Education

Luljeta Isedisha

Boston University

Mamoona Javed

University of London

Kivanç Kamburoğlu

Ankara University

Research Article

Keywords: CBCT, DEXA, postmenopausal, bone mineral density, osteoporosis

Posted Date: February 18th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-199883/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Objective: To analyze the capability of cone-beam computed tomography (CBCT) to accurately identify low bone mass density in women.

Methods: A systematic search of Medline, Embase, Scopus, Google Scholar, Cochrane Library, and Science Direct was conducted to identify the relevant articles. A detailed inclusion and exclusion criterion was developed and implemented to screen the abstracts. Full texts of the selected studies were then evaluated to establish their inclusion or exclusion in our review. Cochrane risk of bias criterion was used to determine the methodological quality of the included studies. All relevant data were extracted, and the results were summarized narratively.

Results: Ten studies met out inclusion-exclusion criteria and were included in this systematic review. All of the included studies assessed primary research on the capacity of CBCT to accurately diagnose insufficient bone mineral density. The results indicated that CBCT has good sensitivity and specificity, and high accuracy in predicting osteoporosis. Four of the included studies measured qualitative values while others concentrated on quantitative values and found lower values in osteoporosis patients compared to osteopenic and healthy patients. All of these studies compared CBCT grayscale values with DEXA scores which strengthened our confidence in the accuracy of CBCT diagnostic capability.

Conclusion: Given the common use of CBCT in dental practices and the high prevalence of osteoporosis in postmenopausal women, the evidence on the capacity of CBCT to predict osteoporosis is somewhat finite. Although this systematic review provides good evidence regarding the ability of CBCT for predicting osteoporosis, further research is needed to confirm the evidence and enhance its generalisability.

1. Introduction

Osteoporosis, a silent skeletal disease, is characterised by the low bone mass and deterioration of the bone structure(1). It occurs as a result of the aging process of bone that increases from infancy to approximately 30 years of age. However, there is a gradual and progressive increase in bone loss, occurring at a higher rate specifically in post-menopausal women. Following this period, the rate of bone loss declines at a more gradual rate(2).

Osteoporosis, a generalized loss of bone mass, is a disease affecting mostly post-menopausal women population which compromises bone strength and increases the risk of bone fractures in any area of the skeleton excluding the face(3). Diagnosis of osteoporosis is made by the measurement of bone mineral density (BMD) which allows the delivery of preventive and therapeutic intervention if necessary. BMD is defined through the values of T and Z scores. Mean value of standard deviations (SD) in young healthy individuals is a reference for the T score while mean values of SD expected for healthy individuals within the same age and sex describes the Z score. T value of 2.5 SD or more below the young female adult mean is an indication of osteoporosis. T score between - 1 and - 2.5 SD defines the status of osteopenia(4). Although, Z-scores are not routinely used to diagnose osteoporosis, low Z-scores can be an indication of osteoporosis and should be evaluated for metabolic bone diseases or secondary causes of osteoporosis(5).

Osteoporosis exerts a significant social and economic impact on the global population due to high treatment costs and humanistic burden(6). According to international guidelines, all women over 65 years old should perform bone densitometry, as should younger postmenopausal women with associated risk factors(7) such as; amenorrhea, low estrogen level, hyperthyroidism, chronic rheumatoid arthritis and chronic hepatitis C(8).

The silent nature of this condition contributes to the difficulty of its detection and diagnosis. Hence, all medical professionals should partake in identifying osteoporotic patients and refer them to specialists for timely diagnosis and suitable treatment(1).

Early detection may be crucial in dentistry as it has the potential to prevent higher failure of dental implants. The dentists are commonly consulted by a majority of the population, and dental radiographs are widely used for diagnosing teeth and jaw

conditions in the adult population. These radiographs can be used as a screening tool in order to diagnose osteoporosis(3).

Dual Energy X-Ray Absorptiometry (DEXA) is recognised as the gold standard method for identifying those at risk for low bone mineral density (BMD). Primarily, the proximal femur and lumbar spine are measured by using DEXA to assess BMD. DEXA is an accurate and non-invasive method, however; high patient doses and costs make the application of this tool unfeasible for routine examination(9).

Cone-beam computed tomography (CBCT) has been used widely since the beginning of its introduction in dentistry in 1998(10). CBCT enables submillimetre accuracy assessment of bone quantity(11) and offers 2-dimensional (2D) and 3-dimensional (3D) images at lower radiation doses and lower costs than medical computed tomography, with improved image sharpness and minimal distortion(12). Previous studies have provided some evidence of CBCT capacity to detect low BMD and suggested the use of CBCT as an early screening tool. Moreover, a previous systematic review(12) compiled the evidence of capacity of CBCT to detect BMD, however, this systematic review included both male and female population. As low BMD is primarily a women health issue, this systematic review therefore focused to compile the evidence only on female population.

1.1. Objective

The objective of the present systematic review was to analyse the capacity of cone-beam computed tomography to accurately identify low bone mass density in women.

2. Methods

This systematic review was conducted in an attempt to identify evidence demonstrating the capacity of CBCT to diagnose low BMD. Protocol of this systematic review was registered at PROSPERO (the International Prospective Register of Systematic Reviews) under number CRD209839. We followed PRISMA reporting guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) for this systematic literature review(13). We applied a rigorous and transparent methodology in order to reduce bias in the selection of relevant studies.

1.1. Eligibility criteria

We included comparative diagnostic studies assessing the capacity of CBCT scan to identify low BMD in comparison to gold standard DEXA. Studies only conducted on adult female participants and published in the English language were included in this systematic review.

A detailed eligibility criterion is reported below in Table 1.

1.2. Data Sources and search strategy

Databases searched for this review included: Medline, Embase, Scopus, Google Scholar, Cochrane library and Science Direct.

The search strategy used for Embase and Medline is reported in the appendix, which was generated from search terms related to CBCT, DEXA and osteoporosis. Filters applied to limit the studies only to the English language, human and adults. The search was not limited by any geographical location. References of the compatible studies were also searched in order to identify other similar studies and included the study. Final data were downloaded and uploaded into the reference management software 'Zotero'(14).

1.3. Study selection

Abstracts were assessed against the eligibility criteria shown in Table 1. The studies were screened in abstract screening software 'Rayyan'(15) by two researchers by title and abstracts and discrepancies were resolved through discussion and consensus. The full texts were obtained for all citations that met the inclusion criteria after the title and abstract screening. Full texts were screened using the same inclusion criteria as abstract screening and concentration was given to identify methods used in the studies. Two researchers independently conducted full-text screening and resolved the disagreements through discussion.

Table 1: Inclusion &exclusion criteria

Category	Inclusion criteria	Exclusion criteria
Population	- Adult female patients - Studies assessing the capacity of dental CBCT scan in assessing low BMD in comparison to DEXA.	- Studies assessing other imaging technologies. - Mixed population studies - Non-comparative studies - Studies comparing diagnostic capacity of CBCT with technologies other than DEXA
Intervention	CBCT	Studies with imaging modalities other than CBCT
Comparator	DEXA	- Studies with comparator other than DEXA - Non-comparative studies i.e., studies without DEXA comparator
Outcomes	- Sensitivity - Specificity - Accuracy	
Study design	- Randomised controlled trials - Non-randomised studies - Cohort studies - Case-control studies - Cross-sectional studies - SLRs/NMAs^a	- Letters to the editor - Narrative reviews - Editorials - Expert opinions - Case studies - Book chapters
Language	English language	Non-English language

Filters applied: Human, adults

^a Citations of systematic literature reviews (SLRs) and network meta-analyses (NMAs) will be thoroughly reviewed to find and include any additional relevant studies.

1.4. Data Extraction

We extracted the relevant data into a pre-agreed Microsoft Excel template. Below mentioned data were extracted for each eligible study:

1. Study characteristics: Study name, authors, the title of the study, objectives of the study, study design, year of publication, study setting, country, patients' sampling design, and sample size.
2. Patients characteristics: Study population (diagnosis), age, co-morbidities, previous fracture, and patients' classification.
3. Intervention (CBCT) characteristics: Unit, version, the field of view, voxel size, and viewer software.
4. Comparator (DEXA) characteristics: Name, reference, characteristics.
5. Outcomes: Sensitivity, specificity, accuracy, CBCT grayscale values, DEXA T-score, and Z score.

1.5. Quality Appraisal

All included studies were assessed using a revised diagnostic accuracy quality assessment tool, Quality Assessment Tool for Diagnostic Accuracy Studies-2 (QUADAS-2)(16).

1.6. Synthesis of Findings

A narrative synthesis was performed to synthesize the findings of the included studies. A narrative synthesis constituted the best instrument to synthesise the findings of the studies as the studies were heterogeneous due to the variations in the index test devices, areas assessed and analytical approaches.

A preliminary synthesis was conducted in the form of a thematic analysis that involved study characteristics and results in tabular form. The results were then discussed again and structured into themes. Included studies were summarised narratively in each theme. The themes were based on the sampling design of each study and risk of bias criteria. Within each theme, the outcomes were summarised in groups as our outcome measures varied considerably among various studies. This framework comprised of the following factors: the study design (case-control, cohort), the accuracy measures (sensitivity, specificity).

3. Results

In the first phase of the selection 624 references identified, of which 315 were duplicates, leaving 309 unique references for screening phase (Table 4). Full texts of seventeen articles were retrieved being considered potentially to possess the inclusion criteria. However, after full text review, 7 of these articles were excluded for not meeting determined inclusion criteria. Remaining ten studies matching inclusion criteria included in this systematic review for final analysis (Figure 1).

3.1. Study characteristics

All ten studies included in this systematic review investigated the capacity of dental CBCT imaging to accurately diagnose osteoporosis. Studies included female participants only and used observational cross-sectional methodologies. Three studies were conducted in Syria(1,3,17), three in Brazil(6,9,18), one in Iran(19), one in Egypt(20), one in Korea(2) and one in the United States(21). All studies were published in English language.

All ten studies reporting on our outcomes of interest enrolled a total of 510 participants. Case-control was the most common method of sampling and was used in 6 of 10 studies(1–3,6,17,20) while cohort sampling was used in remaining four studies(9,18,19,21). Summary of included studies is reported in Table 2.

3.2. Participants' characteristics

All studies enrolled female participants only; 3 of 10 studies enrolled menopausal and post-menopausal women(1,3,17) while 7 of 10 studies enrolled post-menopausal women only(2,6,9,18–21). Participants' ages ranged from 46 to 83 years across the

studies.

3.3. Intervention (CBCT) characteristics

There was extensive variation among studies in the characteristics of CBCT devices used to assess low BMD. Three studies used WhiteFox® version 3(1,3,17), two used KODAK 9000 C 3-D system(9,18) while remaining five studies used different devices. Field of view (FOV), voxel size and viewer software varied across included studies. Characteristics of CBCT devices are reported in Table 2.

3.3. Quality Assessment

Quality assessment and applicability concerns for each of the included articles were outlined in Figure 2 and Figure 3 and represent review of authors' judgements regarding each section across studies included in this systematic review. Overall, there were large variations among studies in cases and controls classifications, CBCT devices and viewer software. Small sample sizes and insufficient data ruled out the meta-analysis. Only one study fulfilled all of the methodological quality criteria (9).

3.3.1. Patient Selection

Patient selection posed a high risk of bias (ROB) in six of ten because of case-control sampling. Two studies were placed into the low risk of bias category because of the use of cohort sampling technique and random sampling strategy. ROB was unclear for two of ten studies; Shokri et al. (2019)(19) and Tadinada et al. (2013)(21). Shokri et al. (2019)(19) avoided case-control design for patients' selection but did not report the sampling method, whereas Tadinada et al. (2013)(21) did not present sufficient information to assess selection bias. Patients and settings did coincide with the review question; hence applicability concern was low for all ten studies.

3.3.2. Index Test

ROB was unclear in 7 of 10 studies, primarily due to the lack of information about masking for conducting and interpreting the index test results. Moreover, the authors in these studies provided no information on the use and pre-specification of thresholds. However, the remaining three studies had a low risk of bias(6,9,19). Index test applicability concerns were low in all studies except one which had unclear applicability concern due to lack of information.

3.3.3. Reference Test

ROB was low in 6 of 10 studies. However, the remaining four studies had unclear ROB due to lack of blinding information, and it was not clear whether or not findings were evaluated without knowing the results of the study. Reference test applicability concerns were low in all studies except one which had unclear applicability concern due to lack of information.

3.3.4. Flow and timing

ROB was high in the study conducted by De Castro et al. (2020)(6). Although the time interval between index test and reference test was not a matter of concern, the authors excluded osteopenia patients, which raised the concern of false increase in sensitivity; hence we assessed it high ROB. ROB was unclear in Koh and Kim (2011)(2) study as the authors did not report timing between two tests. All other included studies had low flow and timing ROB.

3.5. Outcomes

Reporting of outcome variables varied across included studies. Six of ten studies reported sensitivity and specificity(1,3,6,9,17,19) while accuracy was reported in half of the included studies [1], [3], [5], [7], [15]. Four of the included studies, measured qualitative radio-morphometric indices and linear measurements on the CBCT scans(2,9,18,20).

Brasileiro et al. (2017) performed measurements on CBCT derived cross-sectional images to determine mean values of computed tomography mandibular index, computed tomography index (inferior) and computed tomography index (superior). The authors concluded that the mean values of all indices were significantly lower in osteoporosis group compared to osteopenic and healthy patients ($p < 0.02$)(18).

Mostafa et al. (2016) conducted a study to assess the capability of using box-counting fractal dimension (FD) and mandibular CBCT radio-morphometric indices to detect osteoporosis in 25 postmenopausal women in comparison to 25 healthy females in control group. The authors found significant differences for the CT mental index, CT cortical index scores, and CT mandibular index between the cases and control. The osteoporotic group showed lower mean values compared to the healthy group. However, FD values of control group were not found to be significantly higher in comparison to osteoporotic group. Authors suggested that CBCT is a useful secondary diagnostic tool to implement in patients at risk of insufficient bone density for further diagnostic assessment.(20)

Koh and Kim (2011) studied the possible use of the radio-morphometric indices derived from CBCT images for diagnosis of osteoporosis in the sample of 21 postmenopausal osteoporotic women and 21 postmenopausal healthy women. The authors found that there were statistically meaningful differences between two groups in the values of CTI(S), CTI(I), and CTCl while no statistically significant difference was observed in the values of computed tomography mental index (CTMI)(2).

Barra et al. (2020) conducted the study to evaluate four new radio-morphometric indices: symphysis (S), anterior (A), molar (M) and posterior (P). The authors found that there was no statistically significant difference in mean values of the S index and A index between normal, osteopenia and osteoporosis groups. However, mean M index showed noticeable lower values in osteopenia ($p < 0.001$) and osteoporosis ($p = 0.001$) compared to healthy individuals. Mean P index was markedly lower in osteoporosis than in healthy patients ($P = 0.008$) while showing no significant difference between osteopenia and healthy group ($p=0.031$). These findings demonstrate that M and P indices may become useful tools in dental CBCT images of the mandible for the evaluation of bone density and diagnosis of osteoporosis in postmenopausal women(9).

Barngkgei et al. (2014, 2015) studied lumbar spine and femoral neck T score and its correlation with radiographic density (RD) derived from dental CBCT for evaluation of osteoporosis in postmenopausal females (1,3). Authors demonstrated that RD values derived from the CBCT of the mandibular slice that passes through the lower borders of the mental foramina shows high accuracy in predicting osteoporosis and correlation with femoral neck and lumbar T-scores.

Barngkgei et al. (2015) also assessed RD from the cervical vertebrae. RD values derived from CBCT of

the left part of the atlas (C1) and the dens (odontoid process of the second cervical vertebra) showed the strongest correlation coefficients ($r = 0.6, 0.7$; $P < .001$) and the highest sensitivity (70%, 76.9%), specificity (92.9%, 92%), and accuracy (86.4%, 90.8%) in predicting osteoporosis in the femoral neck and the lumbar vertebrae, respectively(3). The dens and the trabecular bone structure of jawbones in osteoporotic and non-osteoporotic women was assessed by using CBCT in a separate study. Barngkgei et al. (2016) found that Jawbone-derived measures showed minor differences between osteoporotic and non-osteoporotic groups. Correlation of Jawbone-derived measures with femoral neck and lumbar vertebrae T scores (between osteoporotic and non-osteoporotic groups) was ≤ 0.4 ($P > 0.05$). However, the correlation between Dens-derived measures and femoral neck and lumbar neck was 0.34 to 0.38 ($p = 0.02-0.036$) and 0.48 to 0.61 ($p \leq 0.003$), respectively(17).

Shokri et al. (2019) assessed the correlation between BMD determined by CBCT gray values and BMD determined by DEXA. The authors found that 61 asymptomatic patients (47.5%) had abnormal BMD based on the T-scores of the femoral neck

while 55.7% of the patients had abnormal BMD based on the T-scores of lumbar spine. The correlations between the T-scores and the gray values of the maxillary incisor and tuberosity areas were significant(19).

De Castro et al. (2020) used cross-sectional and panoramic reconstructed images to evaluate mandibular cortical width (MCW) and cortical quality. The authors found significantly lower MCW values in osteoporotic women compared to women with normal BMD according to DEXA at all three bone sites; lumbar spine, femoral neck and total hip(6). New three-dimensional morphometric index on panoramic reconstructed images derived from CBCT has been found to be helpful to assess the osteoporosis status in postmenopausal women.

Tadinada et al. (2013) investigated the accuracy of pixel intensity values and width of the mandibular inferior cortical border measured on images derived from a CBCT in comparison to T scores on 32 postmenopausal women. The authors found a strong correlation between the right and left mental indices while no statistically significant correlation found between the T scores of hip, lumbar vertebra, and mental index values on the right or left sides. A Strong correlation was found between thickness of the mandibular cortical border, pixel intensity values, and age. There was no correlation between pixel intensity values and T-scores.

4. Discussion

This systematic review evaluated the available literature and compiled the evidence regarding the capacity of CBCT scan to detect low BMD accurately. All ten studies included in this systematic review provided evidence on CBCT's capability to accurately diagnose bone density and quality. All of these studies compared CBCT grayscale values with DEXA scores which strengthened our confidence on the accuracy of CBCT diagnostic capacity. Six of ten studies reported sensitivity and specificity. Four studies used radio-morphometric indices to successfully differentiate osteoporotic and non-osteoporotic individuals(2,9,18,20).

Density of bone is the main factor influencing bone strength. Therefore, osteoporosis related traumatic fractures occur in patients with compromised bone strength where bone microstructure changes and density of bone reduces. (20). Although osteoporotic fractures affect any area of the skeleton except the face, mortality and morbidity of the hip fractures are the worst and may cause 10–20% deaths within the first year. The survivors mostly suffer from disability that significantly affects the quality of their lives(1).

Findings of this systematic review are in line with previous review findings(12). Gungor et al. (2016) (22) also studied radio-morphometric indices by using CBCT images and concluded that osteoporotic changes could be accurately assessed through CBCT scans, however; we did not include this study in our systematic review as the authors did not report participants' gender. Similar results were also found in a mixed population study that was conducted in Saudi Arabia(23). T scores and GS values were obtained from all 81 participants. The authors concluded that the CBCT GS values of BMD at different jawbone regions significantly correlated with the DEXA T values in osteoporotic patients.

The methodological quality of all included studies was considered carefully in order to mitigate potential bias, however; many of the included studies failed to pay due diligence to patients sampling and selection. Moreover, small sample size, convenience sampling and case-control study designs played a major role in introducing a bias in many of the included studies. Although case-control studies are less expensive and easy to perform, they may lead to increase diagnostic accuracy to 2- or 3-fold in comparison to prospective cohort studies(24).

Ideally, index test should be performed before the gold standard test. However, in most of the included studies, DEXA was performed before CBCT. In fact, participants were selected based on the DEXA results. Many of the included studies failed to report tests interpretation blinding which might have induced bias in reporting. Likewise, some of the included studies excluded the patients with osteopenia, that could falsely increase sensitivity of the test.

Newer high-quality studies with standardised CBCT devices and viewer software are required to ensure accuracy and reproducibility.

5. Conclusions

This systematic review provided a cumulative evidence from the available literature suggesting that CBCT was capable of accurately detecting low BMD. Extending the use of CBCT in dental practices to detect osteoporosis may help to identify high risk patients and in turn reduce social and economic burden.

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Competing interests: The authors declare that they have no competing interests.

Funding: Not applicable.

Authors' contributions: A.I. and N.V. executed the search strategy. A.I. and S.K. independently read and assessed the abstracts and selected the articles using the full text for this systematic review. AI and M.J. prepared the manuscript. N.V., L.I., and K.K. reviewed the manuscript. All authors have read and approved the final manuscript.

Acknowledgements: Not applicable.

Availability of data and materials: All data generated or analysed during this study are included in this published article.

References

1. Barnkgkei I, Al Haffar I, Khattab R. Osteoporosis prediction from the mandible using cone-beam computed tomography. *Imaging science in dentistry*. 2014;44(4):263–71.
2. Koh K-J, Kim K-A. Utility of the computed tomography indices on cone beam computed tomography images in the diagnosis of osteoporosis in women. *Imaging science in dentistry*. 2011;41(3):101–6.
3. Barnkgkei 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 surgery, oral medicine, oral pathology and oral radiology*. 2015;120(5):651–9.
4. Calciolari E, Donos N, Park JC, Petrie A, Mardas N. Panoramic measures for oral bone mass in detecting osteoporosis: a systematic review and meta-analysis. *J Dent Res*. 2015 Mar;94(3 Suppl):17S-27S.
5. WebMD. Bone Scans and Bone Health Screenings. In [cited 2021 Jan 7]. Available from: <https://www.webmd.com/osteoporosis/features/tests#3>
6. de Castro JGK, Carvalho BF, de Melo NS, de Souza Figueiredo PT, Moreira-Mesquita CR, de Faria Vasconcelos K, et al. A new cone-beam computed tomography-driven index for osteoporosis prediction. *Clinical oral investigations* [Internet]. 2020; Available from: <https://rsm.idm.oclc.org/login?url=https://www.rsm.ac.uk?url=https://dialog.proquest.com/professional/docview/2337557491?accountid=138535>
7. Baccaro LF, Conde DM, Costa-Paiva L, Pinto-Neto AM. The epidemiology and management of postmenopausal osteoporosis: a viewpoint from Brazil. *Clinical interventions in aging*. 2015 Mar 20;10:583–91.
8. MedicineNet. Osteoporosis risk factors. In [cited 2021 Jan 7]. Available from: <https://www.medicinenet.com/script/main/art.asp?articlekey=20363>

9. Barra SG, Gomes IP, Amaral TMP, Brasileiro CB, Abreu LG, Mesquita RA. New mandibular indices in cone beam computed tomography to identify low bone mineral density in postmenopausal women. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology* [Internet]. 2020; Available from: <http://www.sciencedirect.com/science/article/pii/S2212440320311214>
10. White SC, Pharoah MJ. The evolution and application of dental maxillofacial imaging modalities. *Dent Clin North Am*. 2008 Oct;52(4):689–705, v.
11. Bornstein MM, Scarfe WC, Vaughn VM, Jacobs R. Cone beam computed tomography in implant dentistry: a systematic review focusing on guidelines, indications, and radiation dose risks. *Int J Oral Maxillofac Implants*. 2014;29 Suppl:55–77.
12. Guerra EN, Almeida FT, Bezerra FV, Figueiredo PT, Silva MA, De Luca Canto G, et al. Capability of CBCT to identify patients with low bone mineral density: a systematic review. *Dentomaxillofacial Radiology*. 2017;46(8):20160475.
13. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *J Clin Epidemiol* 2009; doi:10.1016/j.jclinepi.2009.06.005. *Journal of Clinical Epidemiology*.
14. Zotero.org [Internet]. Available from: <https://www.zotero.org/>
15. Mourad Ouzzani, Hossam Hammady, Zbys Fedorowicz, and Ahmed Elmagarmid. Rayyan – a web and mobile app for systematic reviews. *Systematic Reviews* (2016) 5:210.
16. Whiting PF, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med*. 2011 Oct 18;155(8):529–36.
17. Barnkgkei 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. *Journal of investigative and clinical dentistry*. 2016;7(4):332–40.
18. Brasileiro CB, Chalub LFFH, Abreu MHNG, Barreiros ID, Amaral TMP, Kakehasi AM, et al. Use of cone beam computed tomography in identifying postmenopausal women with osteoporosis. *Archives of Osteoporosis* [Internet]. 2017;12(1). Available from: <https://rsm.idm.oclc.org/login?url=https://www.rsm.ac.uk?url=https://dialog.proquest.com/professional/docview/1877371652?accountid=138535>
19. Shokri A, Ghanbari M, Maleki FH, 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 Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. 2019;128(3):319–31.
20. Mostafa RA, Arnout EA, Abo El-Fotouh MM. Feasibility of cone beam computed tomography radiomorphometric analysis and fractal dimension in assessment of postmenopausal osteoporosis in correlation with dual X-ray absorptiometry. *Dento maxillo facial radiology*. 2016;45(7):20160212.
21. Tadinada A, Raisz L, Lurie A. Reliability of pixel intensity values derived from cone beam CT for early detection of osteoporosis. *Osteoporosis International*. 2013 Apr;24(1):S367–8.
22. Güngör E, Yildirim D, Çevik R. Evaluation of osteoporosis in jaw bones using cone beam CT and dual-energy X-ray absorptiometry. *Journal of oral science*. 2016;58(2):185–94.
23. Sghaireen MG, Ganji KK, Alam MK, Srivastava KC, Shrivastava D, Ab Rahman S, et al. Comparing the Diagnostic Accuracy of CBCT Grayscale Values with DXA Values for the Detection of Osteoporosis. *Applied Sciences*. 2020;10(13):4584.
24. Rutjes AWS, Reitsma JB, Vandenbroucke JP, Glas AS, Bossuyt PMM. Case-control and two-gate designs in diagnostic accuracy studies. *Clinical chemistry*. 2005 Aug;51(8):1335–41.

Table 2

Table 2: Summary of included studies

Study name	Country	Sample characteristics		Index test (CBCT) characteristics	Reference (DEXA) standards	Methodology	Conclusions
		Sample size (n)	Age (mean $\pm$ SD) years				
Almgkgei al. 14(1)	Syria	38 menopausal and post-menopausal women	57.9 $\pm$ 7.2	WhiteFox® version 3 Viewer software: WhiteFox Imaging® Version 3	DEXA Hologic Discovery QDR®	The lumbar spine and femoral neck were analysed. T-scores were calculated based on DEXA manufacturer's guidelines. Radiographic density (RD) derived from CBCT images of mandible and ramus were used to calculate gray values.	RD values of the body of the mandible on CBCT viewer program can be used to diagnose lumbar vertebrae and femoral neck osteoporosis.
Almgkgei al. 15(3)	Syria	38 menopausal and post-menopausal women	57.9 $\pm$ 7.2	WhiteFox® version 3 Viewer software: WhiteFox Imaging® Version 3	DEXA Hologic Discovery QDR®	The lumbar spine (L1-L4) and the femoral neck were analysed. T-scores were calculated based on DEXA manufacturer's guidelines. A coronal slice of the cervical vertebrae, was selected and the RD for the first and second vertebrae, and the dens was calculated by using CBCT-viewer software (WhiteFox imaging).	CBCT derived RD of cervical vertebrae can predict osteoporosis status using a CBCT-viewer program.
Almgkgei al. 16(17)	Syria	38 menopausal And postmenopausal women	57.9 $\pm$ 7.2	WhiteFox® version 3 Viewer software: WhiteFox Imaging® Version 3	DEXA Hologic Discovery QDR®	The lumbar spine (L1-L4) and the femoral neck were analysed. T-scores were calculated based on DEXA manufacturer's guidelines. Cuboids from various areas of the dens and jawbone were selected from each scan. Trabecular separation, Trabecular thickness, bone volume fraction, connectivity	Dens trabecular bone affected in osteoporosis as assessed by CBCT analysis.

						density and specific bone surface were measured.	
rra et al. 20(9)	Brazil	48 post-menopausal women	61.4 ± 8.2	KODAK 9000 C 3-D Viewer software: Implant Viewer program version 3.5	Hologic Discovery DXA System	Mandibular inferior cortical bone thickness was evaluated. Cross-sectional images at four sites were assessed and divided into osteoporosis, osteopenia, and normal groups. The lumbar spine (L1-L4) and proximal femur (neck and total) regions were examined.	M and P indices in CBCT can identify low BMD in postmenopausal women.
asileiro et al. 17(18)	Brazil	60 postmenopausal women	Normal: 55.60 Osteopenia: 55.20 Osteoporosis: 58.66	KODAK 9000C 3D® Viewer software: Implant Viewer software®	Hologic Discovery DEXA System®	Cross-sectional images generated to measure the CTMI, CTI (S) and CTI (I)	Quantitative CBCT indices may help dentists to screen for women with low spinal and femoral BMD so that they can refer postmenopausal women for bone densitometry.
Castro et al. 20(6)	Brazil	103 post-menopausal women; 52 normal 51 osteoporotic	Normal: 64.8 ± 9.8 Osteoporosis: 63.9 ± 9.9	I-CAT Classic device. Viewer software: CBCT manufacturer software (Xoran 3.1.62).	DEXA	Mandibular cortical width and cortical quality were evaluated on cross-sectional and panoramic reconstructed images. The selected lumbar spine (L1-L4) and hip DXA scans were performed.	The newly developed 3D MOI enables distinguishing women with osteoporosis from those with normal BMD with good sensitivity and specificity.
h and n 11(2)	Korea	42 post-menopausal women; 21 osteoporotic & 21 healthy	Healthy: 60 ± 5.7 Osteoporotic: 66 ± 6.4	PSR-9000NTM Dental Viewer software: OnDemend3DTM	DEXA scanner, Hologic Discovery QDR®, Hologic Inc,	Density of the femur and lumbar vertebrae by DXA. The axial, coronal and sagittal samples were generated from the block images using OnDemend3DTM.	CTI(S), CTI(I), and CTI on the CBCT images can be used effectively in diagnosis of osteoporotic women.
stafa et al. 16(20)	Egypt	50 post-menopausal females	Normal: 60.1 ± 3.7 Osteoporotic: 61.1 ± 4.9	Planmeca ProMax® 3D	DEXA	Mandibular CBCT radio-morphometric indices and FD	CBCT radio-morphometric indices can be used as a

				Viewer software: Planmeca Romexis®		analysis were measured	secondary tool to assess population at risk for osteoporosis
okri et al. 2019(19)	Iran	61 postmenopausal women	64	Scanora 3-D CBCT Viewer software: OnDemand 3-D Dental software	DEXA	Six regions in the jaws were chosen for assessment of BMD to identify the region of the jaw that had the highest correlation with the results of DEXA. Locations included: Between the mandibular incisor roots, the maxillary incisor roots, the left maxillary premolar roots and the left mandibular premolar roots, in the retromolar area of the left mandible and in the left maxillary tuberosity. DEXA: bone densitometry of the femoral neck and lumbar spine	The correlation between the CBCT gray values at different sites in the maxilla and DEXA scores is strong. A gray value of less than 298 at the maxillary tuberosity can help identify patients with osteoporosis, with 66% to 67% accuracy and suggests the need for DEXA analysis.
Linada et al. 2013(21)	United States	32 postmenopausal women	NR	6- inch FOV CBCT exam of the facial skeleton	DEXA	Inferior cortical border thickness and PIV over a one mm2 area, at a standardised region inferior to the mental foramen measured on cross-sectional images from CBCT volumes was obtained	The study did not show a correlation between the inferior alveolar cortex thickness, density and DXA in this limited data set of patients.

Figures

Figure 1

PRISMA flow diagram

Figure 2

Risk of bias and applicability concerns graph

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Barnkgkei 2014	High	Unclear	Low	Low	Low	Low	Low
Barnkgkei 2015	High	Unclear	Low	Low	Low	Low	Low
Barnkgkei 2016	High	Unclear	Low	Low	Low	Low	Low
Barra 2020	Low	Low	Low	Low	Low	Low	Low
Brasileiro 2017	Low	Unclear	Unclear	Low	Low	Low	Low
De Castro 2020	High	Low	Low	High	Low	Low	Low
Koh 2011	High	Unclear	Unclear	Unclear	Low	Low	Low
Mostafa 2016	High	Unclear	Low	Low	Low	Low	Low
Shokri 2019	Unclear	Low	Unclear	Low	Low	Low	Low
Tadinada 2013	Unclear	Unclear	Unclear	Low	Low	Unclear	Low

High
 Unclear
 Low

Figure 3

Risk of bias and applicability concerns summary