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Method to measure bone mineral density through CT images – Meta-analysis

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Método para determinar densidade óssea a partir de imagens CT – Meta-análise

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Resumo

Introdução: Com a evolução das especialidades médicas e médico-dentárias, como a cirurgia maxilo-facial e a ortodontia, tem-se verificado a crescente necessidade do estudo da densidade óssea, cuja avaliação poderá condicionar e/ou melhorar planos de tratamento e técnicas cirúrgicas empregues em determinadas patologias. A técnica *gold standard* para medição da densidade óssea é o sistema DEXA (do inglês, *Dual energy x-ray absorptiometry*) que combina duas energias de raios X com diferentes picos de energia e que permite calcular a densidade mineral. Este sistema encontra-se amplamente disseminado, no entanto, é raramente utilizado em Medicina Dentária. A tomografia computorizada de feixe cónico (TCFC) é um exame frequentemente requisitado por médicos dentistas e usa uma fonte de raios X de largo espectro que permite estimar a densidade óssea. Contudo, o uso das imagens TCFC para determinação da densidade óssea parece estar pouco difundida.

Objetivos: O objetivo deste trabalho é explorar a possibilidade de estabelecer uma correlação entre os valores do DEXA e da tomografia computorizada através de uma meta-análise.

Materiais e Métodos: Inicialmente foi feita uma pesquisa bibliográfica nas bases de dados PubMed/Medline, LILACS e Cochrane com as palavras-chave: “Densitometry”, “Absorptiometry”, “DEXA” e “Computed Tomography” conjugadas pelos conectores booleanos "AND" e “OR”, de acordo com os critérios de inclusão e exclusão definidos previamente, a fim de responder à questão PICO. Para além deste estudo, foi construído um fantoma com o intuito de obter uma curva de calibração entre os valores de densidade e os valores de CT.

Resultados: A revisão sistemática com meta-analise mostrou que existe uma correlação forte entre os valores do DEXA e da tomografia computorizada (média do coeficiente de correlação é 0.77 IC95%[0.70; 0.84]).

Conclusões: Há uma forte correlação entre os valores do DEXA e do CT, pelo que a avaliação oportunista da densidade óssea nas imagens de tomografia computorizada é uma mais valia que pode permitir identificar doentes com elevado risco de fratura, diminuindo desta forma a morbilidade e mortalidade associadas à osteoporose.

Palavras-Chave: “Densitometria”, “Absorciometria”, “DEXA”; “Tomografia Computorizada”

Abstract

Introduction: With the evolution of medical and dental specialties, such as maxillofacial surgery and orthodontics, there has been a growing need to study bone density, which assessment may condition and/or improve treatment plans and surgical techniques employed in particular pathologies. Bone mineral density (BMD) knowledge is very important in several areas of Dentistry. The state-of-the-art technique for measuring BMD, *in vivo,* is the DEXA technique, which combines two X-ray beams with distinct peak energy making possible to compute the mineral density of bone. DEXA has become widely disseminated, however, it is rarely used in Dentistry. Cone-beam computed tomography (CBCT), on the other hand is vastly used as a diagnostic technique and it has the capacity estimate BMD. Nevertheless, CBCT images are not usually employed to assess BMD.

Objectives: The aim of work is to explore the possibility of establishing a correlation between DEXA and CT through a systematic review with a meta-analysis.

Materials and Methods: Firstly, a systematic literature search was conducted in the databases: Medline, Cochrane and LILACS. The following keywords: densitometry, absorptiometry, DEXA and computed tomography, combined with Boolean operators "AND" and “OR” were utilized accordingly to the inclusion and exclusion criteria that were defined along with the PICO question. Apart from this study, a phantom was constructed in order to obtain a calibration curve between density values and CT values.

Results: The systematic review with meta-analysis showed a strong correlation between DEXA and CT values (mean coefficient of correlation is 0.77 (CI95%[0.70; 0.84])).

Conclusions: There is a strong correlation between DEXA and CT values, so that opportunist osteoporosis screening with a CT routine scan is an excellent opportunity to identify individuals with a high risk of fracture, reducing morbidity and mortality associated with osteoporosis.

Keywords: “Densitometry”, “Absorptiometry”, “DEXA”, “Computed Tomography”

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1. Introduction

Dentistry is a field with high growth and rapid evolution that has been taking advantage of several other areas notably, bioengineering, biochemistry and informatics to name a few, that has helped promote new materials and new clinical procedures. X-ray technology is commonly used either in diagnosis or at the planning phase, yet, other possibilities given by X-rays are less common such as measuring bone density. On the other hand, dentistry is not isolated from other medical areas contributing to signalize patients to other specialties (e.g. Orthodontics maxillofacial surgery, oncology, hematology) or to work along with other doctors to provide better care to patients. Therefore, X-rays could be explored even further helping, for example, as a tool for screening tests, namely to detect augmented risk of fracture in some patients. This would be provided as long as bone density could be measured from X-rays techniques used in dentistry. Hence, in this work we analyzed the correlation between the values given by computed tomography images and DEXA images, which are the *gold-standard* for measuring bone density. And so, the main objective is to demonstrate a correlation between CT and DEXA images resorting to a systematic review with meta-analysis. In addition, a phantom for calibrating CBCT (cone beam CT) images was devised and constructed and the calibration curve was computed.

In the following document the results of the work are presented. Firstly, a brief introduction of the theme is made aiming at exploring the main issues of both DEXA and CT technologies. Secondly, the systematic revision is described as well as the construction of a phantom to calibrate the CT values to density. In the final parts of the work the results obtained are presented along with the limitations of the work, in the discussion chapter, and the concluding remarks.

1.1. Context

X-rays are particularly known for their application in imagiology, however there are other uses less familiar but not of lesser importance, such as the determination of bone mineral content or absorptiometry, which is fundamental in several areas of Medicine, including Dentistry.[1]

The evaluation of bone density can be performed either directly or indirectly. To measure it directly a biopsy is required, which makes this procedure quite rare because it is invasive and there are few laboratories able at processing the samples. The alternative is to measure bone density by indirect means.[2–5]

The most common indirect method to assess bone mass and density *in vivo*, involves the use of radiation, namely X-rays.[3,6] In this measuring technique, an X-ray beam passes through different tissues (e.g. bone, muscle or fat) and suffers attenuation, that depends both on the tissue physical characteristics and on the energy of the X-ray photons.[3,6] The detected X-rays intensity is then compared to the incidence intensity obtaining indirect information about the density of the irradiated tissue.[6] Resorting to image processing techniques, a grey scale is created from the attenuation values, mapping the bone density in order to produce an image. Finally, technical features (bone area, bone size or cortical width) can be calculated by several algorithms.[3,5]

The usual technique for determining bone density is dual-energy X-ray absorptiometry, known as DEXA (or DXA), which combines two X-ray beams with distinct peak kilovoltage in the same measurement, allowing the assessment of mineral density.[3,4,7–11] Despite DXA is the gold standard technique to assess bone density, *in vivo*, it is not widely spread in dentistry mainly due of its impractical use in the clinical set. [2,4,12–16]

Another technique that can also be used to evaluate bone density is computed tomography (CT), which has had a great impact in both health care and diagnostic investigation, namely in Orthodontics and Implantology.[1,6,13,17–19] Cone beam computed tomography (a variation of CT that uses a large spectral X-ray source) is frequently asked by dentists who are mainly interested in structural information but could also benefit from the knowledge of bone density.[12,13] For example, it is known that bone density is highly probable to change during orthodontic treatment, as dental movement is accompanied by bone deposition and resorption, and therefore alterations in bone mineral content (BMC) may occur.[12,13] These changes are often radiographically identifiable, as variations of radiopacity tend to occur around teeth in orthodontic movement.[12,13,20] During this movement, there is a profound bone remodeling (turnover of previously existing bone), causing detectable decreases of mineral density, which is translated into changes in cortical bone radiolucency. [13,20]

Knowledge of bone density is equally important in planning the anchoring strategy for orthodontic treatment.[12,21–23] Frequently, orthodontists resort to temporary anchorage devices to optimize the clinical procedure and obtain better results.[21–25] As so, it is advisable that during the planning step, careful evaluation should be considered in order to establish the most favorable locations for microscrews. The placement of these microscrews could dictate the overall success of the procedure as anchorage stability is highly dependent both on bone quality and density. [12,21–25] Panoramic and periapical radiographs are commonly used, however, they give little information about trabecular bone density or even the thickness of the cortical bone. [23,24]

Besides morphologic information, CT images can estimate bone density through a linear correlation between CT voxels values (generally in Hounsfield units) and bone mineral content.[1,6,12,13,18,19,21,24,26] Since bone density is related to the risk of failure of dental anchorage, it is desirable that CTs can predict it with the same accuracy as the gold-standard test (DXA). [1,6,12]

Recently, there has been an upraise in publications exploiting the possibility of CT opportunistic screening to detect low BMD that would then be used to prevent osteoporosis. [2,15,27,28] Thus, whenever a CT scan is performed for some indication, the images can be used to point out patients with osteoporosis or at higher risk of fracture, without additional scans (e.g. DXA) avoiding extra radiation exposure and reducing costs and time. [2,14,15,27] The same could happen with CBCT scans, that can be used not only to help dentists planning their interventions more accurately regarding the positioning of temporary devices but may also be exploited to determine bone density, thus having a reliable estimation of the risk of failure. Moreover, the implementation of a simple method effective at estimating bone density from CT images, would allow to detect osteoporosis in the population that goes under CBCT scans. This opportunistic screening would allow early detection of osteoporosis increasing the treatment success while reducing the radiation exposition and cost.[2,14,15,27,29]

1.2. Dual-energy X-ray absorptiometry

Dual-energy X-ray absorptiometry (DEXA) was introduced in the late 1980s in clinical routine to monitor osteoporosis and to assess fracture risk mostly in post-menopausal women. [30] Since 1994, T score (standard deviations compared with a young adult reference population) has been used as a scale to classify BMD measurements and to help diagnose osteoporosis in postmenopausal women considering as:

- normal: T score value greater or equal to -1;
- osteopenia: T score value between -2.5 and -1;
- osteoporosis: T score value less or equal to -2.5

Later, the International Society for Clinical Densitometry adapted this definition to all women (both pre and postmenopausal), men and children. [15,30] Currently, DEXA is consider the gold standard technique to assess bone mineral density (BMD) in general population. [3,8,30–33]

DEXA uses an X-ray source that produces radiation with two energies (differing peak kilovoltage, 30 to 50 keV and greater than 70 keV). X-rays pass through soft and hard tissue, suffering attenuation but emerging with less intensity that is finally detected and measured. The combination of these two X-ray energies allows to subtract the soft tissue component and compute the bone mineral density, namely areal bone mineral density (grams per square centimeter) that results from the projection of a 3D object onto a 2D image. [3,31] Usually, DXA is used to measure the BMD in the proximal femur (intertrochanteric and trochanteric regions and femoral neck), lumbar spine (L1-4 vertebral bodies) and distal radius, generally through an automatic segmentation, that can be corrected by the operator. [30] Besides BMD and T scores, DEXA can also give Z scores, which represent the number of standard deviations of the BMD of a patient compared to an age-matched reference population. This type of measuring is quite useful to detect deviation within an age group, for example Z score < -2 is considered to be meaningfully bellow the expected range for that age. [3,30]

DEXA is a low-cost, minimally invasive, widely accessible and low radiation dose technique. [3,30,34] However, DEXA has some disadvantages, notably it is a two dimensional projection of a 3D object, and therefore only capable of measuring density per area and not density per volume (volumetric density). Besides, it is not capable of differentiating cortical from trabecular bone which values are added to get the areal bone mineral density (aBMD) and these bone compartments become indistinguishable. In addition, DEXA is sensitive to bone size and, for that reason, BMD measurements tend to be lower in children or patients with small body frame when compared to normal-sized individuals. Moreover, DEXA is unable to evaluate bone microstructure and bone geometry and finally, hip and spine DEXA measurements are sensitive to degenerative diseases that may lead to areal BMD augmentation. Other known factors affecting aBMD are structures overlying the spine, anatomic abnormalities, aortic calcification and artifacts in the images obtained. [30,31]

1.3. Computed tomography

The word tomography derives from the greek words "tomos" (τομοσ), which means "slice", and graphos (γραφοσ) which means "to write", thus tomography stands for depicted images by slices. Tomographic images are obtained in different imaging modalities, such us PET (Positron Emission Tomography), OCT (Optical Coherence Tomography) and CT (Computed Tomography). In the latter, the tomographic images, also known as slices, are obtained by reconstruction of X-ray projections. These projections are produced by an X-ray generator that rotates around the patient at great velocity. The X-rays passing through the patient's body suffer attenuation and reach the radiation detectors at the opposite side of the X-ray emitter. The information acquired by the detectors, in a complete turn of 360º, is then used to feed a mathematical algorithm that constructs one cross-sectional image – this process is commonly labeled by reconstruction step. For a long time, for each turn of the X-ray generator a slice was produced, but modern CTs incorporate wider detectors that allow to obtain more than one slice; these scanners are known as multi detector CT (MDCT). A different kind of scanners, are the cone beam CT that have an X-ray generator emitting a diverging beam to form a cone that is detected by a large square detector. These type of CT scanners have been used with great success in different dentistry applications.[6]

Computed tomography, particularly, cone beam computed tomography allows a detailed 3D evaluation of head structures, assisting to accurately analyze anatomical details that generally escape to other exams, such as panoramic radiographs and periapical radiographs.[1,17,21,24]

A simple way to use CT scans for measuring BMD is to use a calibration phantom with different concentrations of a hydroxyapatite equivalent material, which can be scanned at the same time and in the same patient's field. As X-ray attenuation is measured in Hounsfield units, it can then be converted into milligrams of hydroxyapatite per cubic centimeter through the standardized phantom. [3,11,16,30,31,34] Images produced by CT scanners that undergo this calibration process are best known as Quantitative Computed Tomography (QCT). This principle can be applied to set volumetric bone mineral density or bone volume in cortical, trabecular or integral (even periosteal surface) bone. [34]

Computed tomography is highly repeatable in several body sites and able to detect structural changes that DEXA is not, namely the integrity of bone tissue. [34,35] Due to a three dimensional projection technique, it is capable of discriminating trabecular and cortical bone and to measure true volumetric bone density (mg/cm3), which is independent of bone size, enhancing fracture prediction (comparatively to DEXA). [3,9,32,35,36] However, CT has its own limitations, notably the high radiation dose and cost. [30,34,37]

2. Methods

In this chapter the procedure employed to perform the systematic review is described as well as how the phantom for calibrating the CBCT values was developed.

2.1. Systematic review and meta-analysis

In order to answer the question "What is the correlation between aBMD of DEXA and CT values in adults?" a systematic review was organized according to the following PICO[1] model:

P: Adults

I: Scans from both DEXA and CT

C: aBMD values from the hip, femoral or lumbar spine

O: Correlation coefficient between DEXA and CT values

A systematic literature search was conducted in the following databases: Medline, Cochrane and LILACS. The keywords used in the search were: densitometry, absorptiometry, DEXA and computed tomography. These keywords were combined using Boolean operators (Table I) to identify relevant publications addressing the PICO question. Besides the articles directly found in the automatic search we have also manually included other articles that were found by cross search.

In the first stage of the systematic review, all the article titles were analyzed and screened for eligibility. Those that met the eligibility criteria, moved on to the second stage where the abstracts of the publications were independently review by 2 researchers, who decided whether or not the articles should be included, according exclusion criteria. Whenever consensus was not reached a third researcher was asked to decide in favour or against the inclusion.

[1] The letters stand for P- population; I- intervention, C- comparison and O – outcome

Table I – Search terms used in each database according to the syntax of each one.

Databases	Search Items
MedLine	"DEXA [All Fields] AND (CT[All Fields]) AND (Cone beam[All Fields] Or "Cone Beam"[MeSH Terms]) AND (computed tomography) OR computed tomography[MeSH Terms]) AND Absorptiometry[All Fields] AND (Densitometry[All Fields])"
Cochrane	"(Densitometry OR Absorptiometry) AND DEXA AND Computed Tomography"
LILACS	"(tw:(DEXA)) AND (tw:(Computed Tomography)) AND (tw:(densitometry)) AND (tw:(absorptiometry))"

The articles were selected according to the following inclusion criteria: published between 2001 e 2017 with available abstract, human studies and *in vitro* or *in vivo* studies. Studies in phantoms, in cadavers or in soft tissue were excluded as well as computer simulations. The search was limited to Portuguese and English written papers. In the second stage of the systematic review all the studies in paediatric populations were excluded as well as those presenting only T-scores for DEXA values and studies that did not mention the coefficient of correlation (r).

The coefficients of correlation between BMD values obtained with DEXA and CT were collected from the selected articles. Besides the coefficient correlations, the size of the samples was also gathered. Based on these values a meta-analysis was conducted to determine the strength of the correlation between the two imaging techniques regarding their ability for measuring BMD.

The analysis was carried out resorting to the R statistical platform, in particular to the "metafor" package.[38]

2.2. Calibration phantom

With the purpose of evaluating the correlation between DEXA and CT values, a phantom of several materials was developed. Five different materials were included in the phantom each one with distinct density, which was determined experimentally. The materials were:

1. Dental plaster (ISO- type III - Hydrock/Rapid Stone, Kerr ®)
2. Polyvinyl siloxane Impression Material (Aquasil Ultra LV Wash Material, DENSPLY Caulk®),
3. Impression Compound Color Red (Kerr®)
4. Join Wax (Cera REUS®)
5. Acrylic (Orthocryl EQ, DENTAURUM GmbH & Co. KG®).

The composition of the materials, according to manufacturers, is shown in Table II.

Each of one of the above described materials was transformed into a block (± 4 x 1 x 1 cm^3). A mold made from Polyvinyl siloxane Impression Material (Aquasil Ultra Soft Putty / Regular Set, DENSPLY Caulk®) was used to cast the materials. Later, this mold served as support of the described blocks. (see Fig. 1)

Fig. 1. Phantom materials on the mold made from Polyvinyl siloxane Impression Material (From right to left: Acrylic, Plaster ISO-type III, Join Wax, Impression Compound Color Red and Polyvinyl siloxane Impression Material)

Table II – Composition of the phantom's components, according to manufacturers

Materials	Composition
Plaster ISO-Type III	Calcium sulphate (60-100%) Plaster of Paris (30-60%) Crystalline silica respirable (0.1-1%)
Polyvinyl siloxane Impression Material (ISSO 4823 Type 3)	Polydimethylsiloxane polymer Polymethylhydrogen Siloxane Silicon Dioxide Sodium Aluminosilicate Organic Platinum Complex Surfactant Titanium Dioxide Metallic Oxide Pigments Peppermint Oil
Impression Compound Color Red	Rosin (5-10%) Oleic acid (1-5%) Titanium dioxide Chromium (III) oxide (1-5%) Naphthalene
Join Wax	Wax Paraffin
Acrylic	Polymethyl methacrylat Methyl methacrylat

The calibration curve between the real density of the blocks and the CT values, in Hounsfield units, was obtained by determining the density of the blocks and scanning them in a CBCT scanner. To achieve the density of the bocks the mass and the volume were experimentally measured resorting to a graduated micro beaker and a precision weighing-machine.

The scan of the phantom was performed with CBCT scanner (ICAT - Gendex KaVo Dental Group®) at 5 mA and voltage of 120 kV. The images were saved in DICOM format and analyzed with Matlab v2016 (Mathworks©). A single ROI (region of interest) was selected in each block in a central coronal slice of the CBCT scan to calculate HU value of CT attenuation. This results were combined with the density values of each block.

3. Results

3.1. Systematic Review and meta-analysis

On the first stage of this study, a total of 2480 articles were identified from the bibliographic databases Medline (1907), Cochrane (465) and LILACS (108) and screened for eligibility, of which 92 were selected to second stage of the systematic review (Medline: 63, Cochrane: 11, LILACS: 18), but 59 were excluded because they did not address the PICO question. Seven (7) articles were added at this stage, making a total of 40 articles designated for review eligibility. The remaining articles (Medline: 13, Cochrane: 1, LILACS: 0, Cross added: 3) were review thoroughly resulting in 17 articles that were utilized in the meta-analysis (see Fig. 2). Description of included studies is in Table 2.

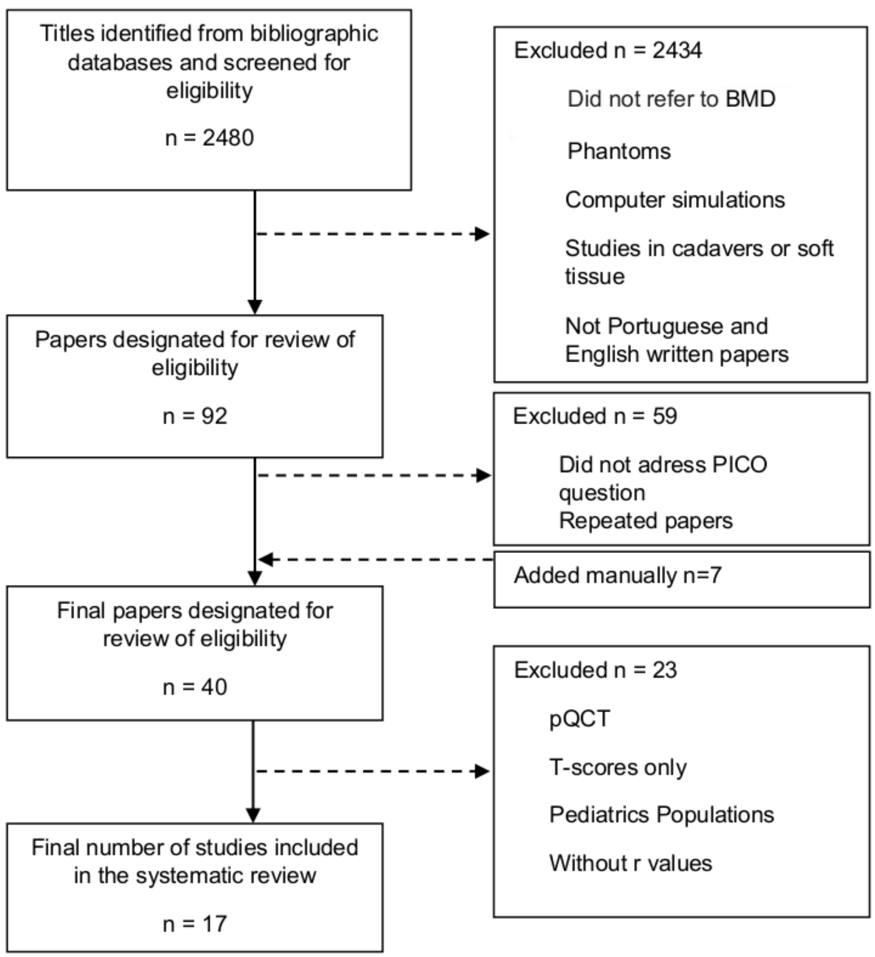

Fig. 2 Flow Chart of the search performed

Autor, year	Techniques	Regions analyze with DXA	Regions analyze with CT	Sample	Correlation Coefficient	
Blomquist, 2016[4]	DXA/QCT	Hip, femoral neck, spine	Iliac crest bone	46	r=0.97, r=0.97, r=0.65	Chronic kidney disease patients. 24/22 F/M, 51 years
Johnson, 2016[39]	DXA/CT	Hip, femoral neck, spine	Capitate	45	r=0.64, r=0.69, r=0.47	Female with distal radius fractures. 66.9 years
Islamian, 2016[40]	DXA/MDCT	L1 lumbar vertebra	L1 to L4	61	r=0.766	Patients suffering from weak damaged trauma on lumbar spine and suspect from osteoporosis. 38/23 F/M. 60.2 years
Amstrup, 2015[35]	DXA/QCT	Hip	Hip	98	r=0.74	Postmenopausal women. 63 years
Sapthagirivasan, 2015[41]	DXA/CT	Femoral neck	Femoral neck	50	r=0.551	Healthy women. 49 years

Table III – Description of the included studies in the systematic review and meta-analysis

Autor, year	Techniques	Regions analyze with DXA	Regions analyze with CT	Sample	Correlation Coefficient	
Kim, 2015[42]	DXA/LDCT	Spine	T4, T7, T10 and L1	232	r=0.726	Retrospective study that collect exams from patients over 50 years. 154/78 F/M
Lee, 2015[2]	DXA/CT	Spine	Femoral Neck	292	r=0.514	Retrospective study. 212/80 F/M
Xiaoguang, 2014[33]	DXA/QCT	Spine	Hip, femoral neck	152	r=0.90, r=0.937	Chinese population F/M 103/49
Lee, 2013[43]	DXA/CT	Spine	L1 to L4	70	R=0.81	Female that underwent CT for back pain. 71.2 years
Gruber, 2012[28]	DXA/MDCT	Spine	femoral head and neck	41	r=0.864, r=0.841	Retrospective study. F/M 33/8. 63 years

Table III – Description of the included studies in the systematic review and meta-analysis

Autor, year	Techniques	Regions analyze with DXA	Regions analyze with CT	Sample	Correlation Coefficient	
Romme, 2012[16]	DXA/CT	Spine	T4, T7, T10	58	r=0.827	Patients with CPOD
Miyabara, 2012[44]	DXA/CT	Spine	T8	111	R=0.63	Women enrolled in the Kronos Early Estrogen Prevention Study
Ahmad, 2010[37]	DXA/QCT	Spine	Femoral neck	48	r=0.87	Women CAIFOS Age Related Extension.82.8 years
Engelke. 2008[5]	DXA/QCT	Spine	Distal Radius	141	r=0.658	Postmenopausal women. 58.8 years
Khoo, 2008[10]	DXA/QCT	Spine	Femoral neck	91	r=0.94	Women. 82.8 years

Table III – Description of the included studies in the systematic review and meta-analysis

Autor	Techniques	Regions analyze with DXA	Regions analyze with CT	Sample	Correlation Coefficient	
Prevrhal, 2007[11]	DXA/QCT	Spine	Hip	121	r= 0.90	Women. 58 years
Kaste, 2006[36]	DXA/QCT	Spine	Lumbar Spine	320	r=0.522	Retrospective study under survivors of childhood cancer

Table III – Description of the included studies in the systematic review and meta-analysis

The 17 selected articles represent 1977 subjects that underwent DEXA and CT scans enabling to compute the bone density from both techniques. In all studies the correlation coefficient between the BMD values was determined. Yet, not all studies addressed the same part of the body to perform the DEXA or the CT scan. Regarding DEXA it is well established which parts of the body should be scanned therefore the articles refer the hip, the femoral neck and the lumbar spine as the parts scanned. Two of them (Blomquist, 2016; Johnson, 2016) indicate more than one place analyzed. Only one paper mentioned a different place (Engelke, 2008), the distal radius, which was chosen to be in accordance to CT images that were acquired from the same part. Regarding CT scans, the variety of parts of the body are much higher, which is mainly due to the nature of most of the studies being retrospective and using samples of convenience. Studies reporting different scanned parts also report several coefficients of correlation and in these cases the femoral neck was selected whenever possible. Most of the samples comprised women (> 50 years old) which is expectable since osteoporosis is the main concern in the studies and the prevalence is greater in postmenopausal women. Nonetheless, samples other than postmenopausal women were analyzed because osteoporosis tend to be related with other diseases, such as chronic kidney disease (Blomquist, 2016), chronic obstructive pulmonary disease (Romme, 2012) and survivors of childhood cancer (Kaste, 2006). Hence, due to all these different approaches there is a high degree of heterogeneity across studies ($I^2 = 97.49\%$; $Q(17) = 376.45$; $p < 0.0001$).

Figure 3 shows the forest plot of the coefficients of correlation for the 17 studies and the global result obtained from a random effects model (restricted maximum-likelihood estimator - RMEL). There is significant correlation coefficient between DEXA and CT values where the mean coefficient of correlation is 0.77 (CI95%[0.70; 0.84]).

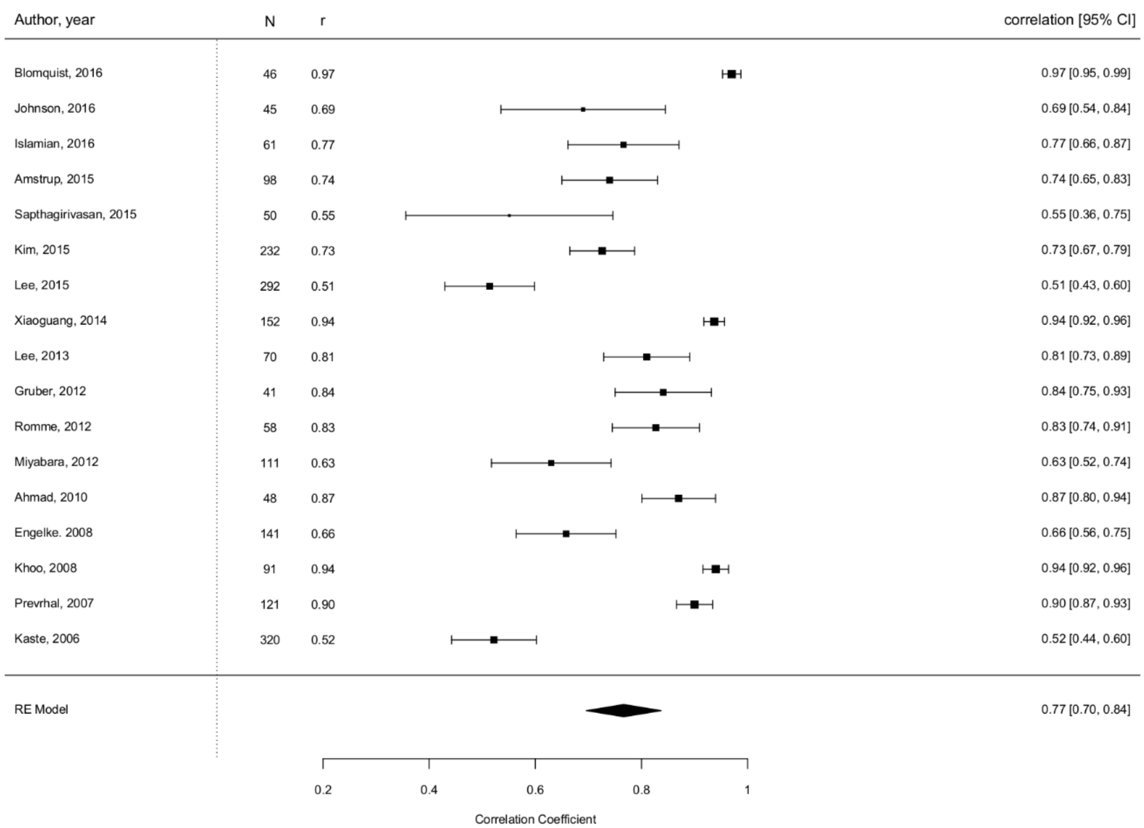

Fig. 3 – Forest plot depicting the coefficients of correlation of each study and the summary statistics.

3.2. Calibration phantom

The calibration phantom comprehends 5 blocks of different materials which densities were determined by measuring their mass and volume. The volume was measured using the displaced water volume in a beaker. Results are presented in the following table IV.

Table IV – Results of the determination of the density of the phantom blocks

Materials	Mass (g)	Initial Volume (ml)	Final Volume (ml)	Volume of each block (ml)	Density (g/ml)
Plaster ISO-Type III	4.30	15	18.0	3	1.43
Polyvinyl siloxane Impression Material (ISO 4823 Type 3)	4.04	15	18.0	3	1.35
Impression Compound Color Red	6.10	15	19.2	4.2	1.45
Join Wax	3.04	15	18.1	3.1	0.98
Acrylic	3.96	15	18.0	3	1.32

The corresponding values in Hounsfield units were obtained by drawing a small ROI in each block and computing the average value (Fig 4).

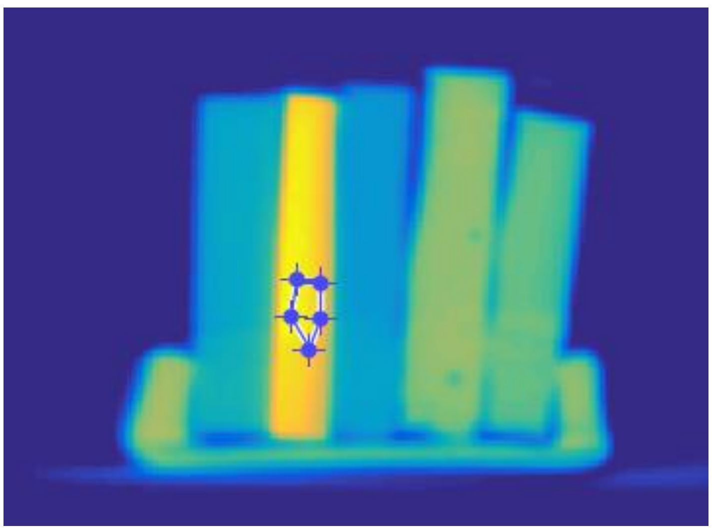

Fig. 4 – Coronal slice of the phantom CBCD showing a small ROI in the second block.

The process of drawing the ROI and computing the average value was repeated in three distinct slices for each block. The following chart (Fig. 5) shows the relationship between the density of the blocks and the Hounsfield units.

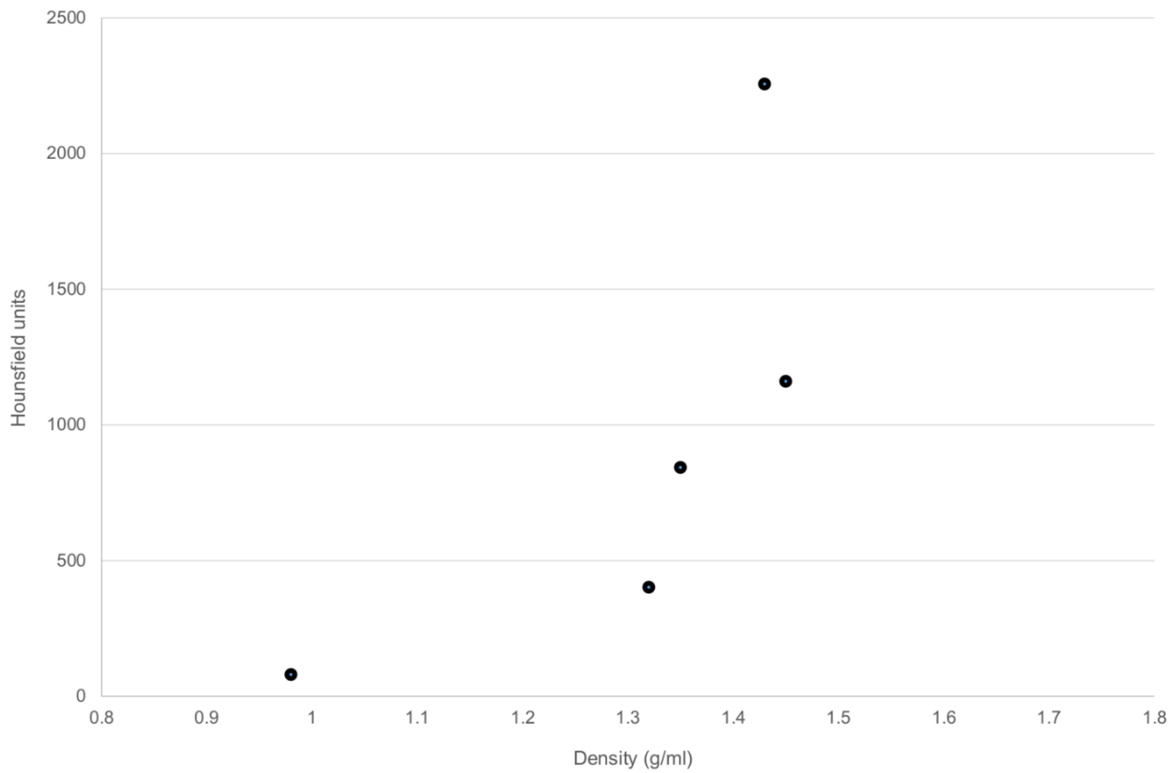

Fig. 5 – Scatter plot - relationship between the density of each block and the corresponding Hounsfield units in the CBCT image.

4. Discussion

In this study, we intended to estimate the correlation between DEXA and CT values. As many studies had already addressed this issue and, as far as we know, there are no systematic reviews or meta-analysis in literature dealing with this matter, we carried out a systematic review with meta-analysis to answer the question. Our data shows a strong correlation (r = 0.77, CI95%[0.70, 0.84]) between DEXA and CT values, therefore CT images may allow the identification of osteopenic and osteoporotic patients who present high risk of bone fracture, which may be the cause of premature death. Hence, opportunistic CT scans, which are performed by any other cause, may be used to assess bone mineral density and fracture risk, improving the ability to track disease progression and providing better care as osteoporosis may be detected early. Coefficient values of the selected studies range from 0.51 (Lee, 2015) to 0.97 (Blomquist, 2016), while sample sizes range from 41(Gruber, 2012) to 320 (Kaste, 2006).

The present study has some limitations worth of being mentioned. Although BMD has been determined in all studies, DEXA and CT equipments used to evaluate bone mineral density were not exactly the same in all studies. Another weakness of this study, is that regions analyzed by DEXA and CT varied from study to study. In most of them, DEXA evaluation was performed in the spine, but also the hip and femoral neck were assessed. In CT scans, the diversity of analyzed body parts were even higher. CT scans were performed on the hip, femoral neck, spine (either lumbar or thoracic spine), distal radius and even, capitate bone. Although the number of patients was high (1977 subjects undergone DEXA and CT scans), studies presented heterogeneous samples, creating a high degree of heterogeneity across studies ($I^2 = 97.49\%$; $Q(17) = 376.45$; $p < 0.0001$). Another source of heterogeneity is the population under study: nine studies were about women (> 50 years old) where osteoporosis is most common and the remaining have both men and women. In addition, subjects in the samples are different regarding their health status. Only one study (Sapthagirivasan, 2015) addressed a healthy population, while all others refer subjects suffering from different conditions, for example: CPOD (Romme, 2012), chronic kidney disease (Blomquist, 2016) and survivors from childhood cancer (Kaste, 2006).

Regarding the phantom, results show that although there is a positive correlation between the Hounsfield units and the density of the blocks, it is not linear, as can be observed in Fig.5. In fact, attenuation in CT is directly related to the electronic density which varies with the atomic number and the density of the material. The scatter plot (Fig. 5) suggests a nonlinear relation which might be related to the fact that the blocks are made of different materials.

5. Conclusion

Positive correlation between bone attenuation on CT and BMD in DEXA was described by many studies. However, as far as we know, there are no systematic reviews or meta-analysis in literature dealing with this matter. To answer this question, we developed this study, which shows there is a strong correlation between DEXA and CT values, proving that opportunist osteoporosis screening with a CT routine scan is an excellent form to identify and refer individuals with a high risk of fracture to other specialties, reducing morbidity and mortality associated with osteoporosis, but also the health costs associated to this disease.

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