Trabecular bone structure parameters from 3D image processing of clinical multi-slice and cone-beam computed tomography data

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--Manuscript Draft--

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Abstract:	<p>Objective. Bone strength depends on both mineral content and bone structure. The aim of this in vitro study was to develop a method for quantitative assessment of trabecular bone structure by applying three-dimensional image processing to data acquired with multi-slice and cone-beam computed tomography using micro-computed tomography as reference.</p> <p>Material and Methods. 15 bone samples from the radius were examined. After segmentation, quantitative measures of bone volume, trabecular thickness, trabecular separation, trabecular number, trabecular nodes and trabecular termini were obtained.</p> <p>Results. Both clinical machines overestimated bone volume and trabecular thickness and underestimated trabecular nodes and number but cone-beam CT to a lesser extent. Parameters obtained from cone beam CT were strongly correlated to μCT, with correlation coefficients between 0.93 and 0.98 for all parameters except trabecular termini.</p> <p>Conclusions. The high correlation between cone-beam CT and micro-CT suggest the possibility to quantify and monitor changes of trabecular bone microarchitecture in vivo using cone beam CT.</p>

Revision Note

This document gives a point-by-point response to the comments made by the Reviewers. Most of these comments have led to changes in the manuscript. In order to facilitate the task for the Editor and the Reviewers, the changes are marked with Reviewer 1 or Reviewer 2 with the following subtitles.

Comment:

Response:

Changes:

Proposed changes from the Reviewers in italics.

In this document we have noted Page XX and Line XX, were to find the changes in the manuscript.

Comment about weakness in the study:

Weaknesses: Small sample population may affect study power. Unfortunately no a priori power analysis has been performed; it may be worth to include it (post-hoc).

Response:

We agree that for planning the current study it might have been wise to perform power calculations. With the high correlation coefficients obtained for CBCT (0.73 and above), post-hoc power calculations yield power estimates of at least 95% for all studied parameters (exact distribution, one-tailed test, $\alpha=0.05$). However in this study, we think that the relevant research question is not whether there is a positive correlation, but how strong the (expected) correlation is. This is the main reason for including confidence intervals rather than p values in Table 3. In accordance with this, we find it less relevant to include power calculation post hoc.

Reviewer 1

Comment 1:

It may be worth to include "Cone Beam Computed Tomography" in the title. CBCT is presently a topic of interest and it may appeal to the readers, focusing their attention on this paper, especially due to the study conclusion

Response:

We agree with the reviewer and CBCT is now included in the title

Changes:

The new title is:

Trabecular bone structure parameters from 3D image processing of clinical multi-slice and cone-beam computed tomography data

Comment 2:

Introduction: Page 5 Line 16: Consider adding the following reference: Boutry N, Cortet B, Dubois P, Marchandise X, Cotten A. Trabecular bone structure of the calcaneus: preliminary in vivo MR imaging assessment in men with osteoporosis. Radiology. 2003 PubMed PMID:12676974.

Response:

We absolutely agree that MRI studies of trabecular bone structure is interesting to add to the article.

Changes:

The recommended article as well as text describing trabecular bone structure by MRI is now included in the Introduction. Page 1, line 17-20.

Comment 3:

Introduction: Page 5 Line 34: Consider adding the following reference: Phan CM, Macklin EA, Bredella MA, Dadrich M, Flechsig P, Yoo AJ, Hirsch JA, Gupta R. Trabecular structure analysis using C-arm CT: comparison with MDCT and flat-panel volume CT. Skeletal Radiol. 2011 PubMed PMID: 20658286.

Response:

The proposed article is interesting. However, we think that including it in this paper is not relevant since we are not describing any use of C-arm CT in the paper.

Comment 4:

M&M: Page 6 Line 22: Consider condensing Fig. 1 a to f, in a single mosaic-image, with a single explanatory legend describing each single image.

Response:

We agree that it could be easier to read if we make the legend more explanatory.

Changes:

We have now used a more descriptive legend for the images allowing them to be inserted as a single mosaic-image. See Legend to Fig. 1 a-f.

Material and Methods page 2 line 20.

Comment 5 and 6:

M&M: Page 6 Line 40: As described the ARG algorithm has been performed, it may be worth to describe the hardware used to perform the analysis in order to allow method reproducibility.

M&M: Page 6 Line 49: Consider describing the specific hardware used to perform the MATLAB analysis, in order to allow method reproducibility.

Response:

We agree with both comments.

Changes:

The hardware and the software used are now described in Material and Methods as follows:

The MATLAB code used for segmenting the images was developed in house. The computer used was a standard PC with Intel Core i5, CPU at 2.60GHz, 4GB of RAM and 64-bit operating system.

Material and Method. Page 2 line 46-49.

Comment 7:

Discussion and Conclusion: Page 9 Line 30: "Our measurements describing Tb.N, Tb.Th as well as Tb.Sp are in good agreement with other studies indicating that the results are credible"...Please reference those studies.

Response:

We agree the need for references and the references below are included in the discussion.

Changes:

We have now included the following references in the discussion in the article:

The effect of voxel size on high-resolution peripheral computed tomography measurements of trabecular and cortical bone microstructure. Tjong W, Kazakia GJ, Burghardt AJ, Majumdar S. Med Variations in morphological and biomechanical indices at the distal radius in subjects with identical BMD. Kazakia GJ, Burghardt AJ, Link TM, Majumdar S. J Biomech. 2011 Jan 11;44(2):257-66.

Discussion. Page 5 line 31.

Comment 8:

Discussion and Conclusion: Page 9 Line 47: Consider including the following reference: Koskinen SK, Haapamäki VV, Salo J, Lindfors NC, Kortessniemi M, Seppälä L, Mattila KT. CT arthrography of the wrist using a novel, mobile, dedicated extremity cone-beam CT (CBCT). Skeletal Radiol. 2013 PubMed PMID: 22990597

Response:

We agree that the reference is important to include in the discussion.

Changes:

The reference is now included in the discussion as reference [30].
Discussion. Page 5 line 44.

Reviewer 2

Comment 1:

Abstract. "The clinical machines grossly overestimated bone volume and trabecular thickness. Trabecular nodes and number were underestimated. "This seems to tell only one side of the story, looking at figures 4 and 5 it is clear that the overestimation and underestimations happens also for the CBCT method. A less biased sentence would be something like: both machines overestimate bone volume and trabecular thickness and underestimate trabecular nodes and number, but CBCT to a lesser extent

Response:

We agree with the reviewer.

Changes:

We have changed the text in accordance with the comments from the reviewer.

New text: Both clinical machines overestimated bone volume and trabecular thickness and underestimated trabecular nodes and number, but cone-beam CT to a lesser extent.

Comment 2:

Introduction. Lines 16-23 the authors omit the current in vivo clinical use of high resolution MRI to quantify trabecular bone architecture, used for at least the past 15 years, and it has obvious advantages. Also HR-QPCT could be mentioned here, since this is already used in vivo with very good results. There is no need to omit these to elevate the potential and novelty of CBCT.

Response:

We agree that MRI is an important method for describing bone structure and have now added a discussion of the matter in the Discussion. In addition, both MRI and HR-pQCT are mentioned in the Introduction with appropriate references [8-12].

Changes:

In the Discussion: page 5 line 15-18, and in the Introduction: page 1 line 17-20.

Comment 3.:

Introduction. Line 25 " MSCT" I did not find an early definition, should be: multislice CT (MSCT)

Changes:

The change has been done.

Introduction: page 1 line 23

Comment 4:

Materials and methods. Image processing: lines 33-34, it is not clear how the voxels are averaged and why, it is perfectly possible and common to do reconstructions with non isometric voxels.

Response:

We agree with the reviewer that the article benefits from more explanation in this matter.

Changes:

We have made explanatory changes in Material and Methods on page 2 line 35-39.

Comment 5:

Materials and methods. Lines 41-45 "The image processing is then repeated with a higher threshold and the procedure is iterated a segmentation, that was used to calculate the parameters, was defined as the iteration where the assessment function attained its minimum. "Should be : The image processing is then repeated with a higher threshold and the procedure is iterated. A segmentation, that was used to calculate the parameters, was defined as the iteration where the assessment function attained its minimum."

Changes:

We agree with the reviewer and the typo has been corrected.
Material and Methods page 2 line 41.

Comment 6:

Also it is not clear here if the segmentation was performed with a commercial package or with in house software (i.e. written in Matlab), please clarify.

Changes:

We have made changes in the text also in accordance with Reviewer 1 – Comment 5.
Material & Methods Page 2 line 46-49.

Comment 7:

Discussion. Again no mention of high-resolution MR imaging, diffusion MR imaging and in-vivo MR spectroscopy techniques.

Response:

We agree with the reviewer about the importance to include MRI in the article. In accordance with

Comment 2 from Reviewer 2 and also in accordance with Comment 2 from Reviewer 1 we have made changes.

Changes:

References [8-10] is included in the Introduction page 1 line 17-18. Reference [10] is discussed in the Discussion page 6 line 17.

Comment 8

Discussion. Since there was an effect based on the filter used (e.g. bone) and exhaustive analysis of these seems warranted for the clinical machines. And it should have been included for at least on sample in this study.

Response:

For the GE machine we have used two different filters: Bone and bone plus. The effect of the filters are analyzed and described in the text and in the tables. We have also added a comment on this paragraph in the Discussion.

Changes:

New text added in the Discussion page 5 line 7-11.

Comment 9:

Discussion. The time required for the scan combined with motion artifacts in vivo at micron level resolutions seem to be quite a big obstacle for the application of this method in vivo, also the extention to other parts of the body seems very difficult.

Response:

The issue of the acquisition time is certainly critical for in vivo studies and are discussed in the Discussion page 5 line 34-35.

Trabecular bone structure parameters from 3D image processing of clinical multi-slice and cone-beam computed tomography data

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Abstract

Objective. Bone strength depends on both mineral content and bone structure. The aim of this in vitro study was to develop a method for quantitative assessment of trabecular bone structure by applying three-dimensional image processing to data acquired with multi-slice and cone-beam computed tomography using micro-computed tomography as reference.

Material and Methods. 15 bone samples from the radius were examined. After segmentation, quantitative measures of bone volume, trabecular thickness, trabecular separation, trabecular number, trabecular nodes and trabecular termini were obtained.

Results. Both clinical machines overestimated bone volume and trabecular thickness and underestimated trabecular nodes and number but cone-beam CT to a lesser extent. Parameters obtained from cone beam CT were strongly correlated to μ CT, with correlation coefficients between 0.93 and 0.98 for all parameters except trabecular termini.

Conclusions. The high correlation between cone-beam CT and micro-CT suggest the possibility to quantify and monitor changes of trabecular bone microarchitecture in vivo using cone beam CT.

Keywords

trabecular bone structure; cone-beam computed tomography; micro computed tomography; multi-slice computed tomography; bone segmentation

Introduction

Bone strength, which is an important determinant of osteoporosis-related fractures, depends on the mineral content as well as the internal structure [1]. To assess the bone mineral content, the method most frequently used in clinical practice is measuring bone mineral density (BMD) with dual energy X-ray absorptiometry (DXA) [2]. This method estimates the mineral content per projected bone area (g/cm^2) from a two-dimensional image, but does not describe the trabecular bone structure. This limits its ability to fully predict the mechanical properties of the bone.

Several studies have shown that mainly the trabecular bone is affected in osteoporosis, and that the bone structure has great importance for the biomechanical competence [3]. Clinical studies show that the risk of vertebral fractures is higher with disconnections in the trabecular bone network [4, 5].

Trabecular bone microarchitecture can be described using different parameters [6]. *In vitro*, bone structure can be described and measured by destructive histomorphometry and by micro-computed tomography (μCT). Good agreement between μCT and destructive histomorphometry has been demonstrated [7]. *In vivo* imaging of the trabecular bone is feasible by using magnetic resonance imaging (MRI) [8-10]. High-resolution peripheral CT (HR-pQCT) is used for visualization of trabecular bone structures in the peripheral skeleton e.g. calcaneus and wrist [11, 12]. It would be attractive to be able to use also other clinical available CT scanners for osteoporotic research of more central parts of the body.

A pilot study using images acquired through multi-slice CT (MSCT) and the ARG-algorithm to describe skeletal microstructure evaluated, with promising outcome, the results using μCT as reference [13].

A relatively recently developed acquisition technique, cone-beam computed tomography (CBCT), is used in diagnosing dental, maxillofacial and temporal bone structures [14]. CBCT provides images with isotropic voxels in the range of 80-400 μm . A few articles are published in the field of describing bone microstructure on images acquired by CBCT [15, 16]. Several studies describe the microstructure of bone imaged by μCT [17-19]. There are also articles analyzing trabecular bone with MSCT, comparing it with μCT [20-22]. It would therefore be interesting to compare measures describing the bone microstructure obtained from MSCT and CBCT with such from μCT in order to quantitatively describe trabecular bone structure with a technique potentially applicable *in vivo*.

The aim of this work was to develop a method for quantitative assessment of trabecular bone structure by applying three-dimensional (3D) image processing methods to data acquired with MSCT and CBCT *in vitro* and to correlate it to the reference method μCT .

Material and methods

Material

The samples in this study consisted of 15 bone biopsies from the radius, the forearm, of human cadavers donated for medical research. The research was in accordance to the ethical guidelines regulating such donations. The biopsies were approximately cubic with a side of 10 mm. Each cube included a portion of cortical bone on one side to facilitate orientation. The bone samples were placed in a test tube filled with water and the tubes were placed in the center of a paraffin cylinder, with a diameter of approximately 10 cm, representing soft tissue to simulate measurements in vivo. After imaging, a cube, approximately 8 mm in side, with only trabecular bone was digitally extracted from each dataset for analysis.

Image acquisition and reconstruction

The specimens were examined in two different 64-slice MSCT machines, one Siemens Definition (Siemens AG, Erlangen, Germany) and one Light Speed VCT (GE Medical Systems, Milwaukee, WI, USA). On the Siemens MSCT, two levels of the slice thickness and of the mAs setting were used. The images from GE MSCT were reconstructed with two different reconstruction filters, “bone” and “bone plus”. The CBCT machine used was 3D Accuitomo FPD 80 (J. Morita Mfg. Corp., Kyoto, Japan). Acquisition parameters are found in **Table 1** and sample images in **fig 1 a-f**.

The μ CT data were acquired with a small desktop CT used for analyzing biopsies and other specimens (μ CT 40; SCANCO Medical AG, Bassersdorf, Switzerland). The tube voltage was set to 70 kVp and the voxels had an isotropic resolution of 0.02 mm.

Image processing

CBCT and μ CT voxels were isotropic. The CBCT had voxel sizes of 0.125 mm and 0.08 mm and the μ CT had a voxel size of 0.02 mm. To obtain almost isotropic voxels from the MSCT, the sections were averaged to voxel size 0.188x0.188x0.200 mm for the GE MSCT and to 0.098x0.098x0.098 mm for the Siemens MSCT datasets.

Segmentation, an important part of the 3D image processing in this study, aims at delineating bone from other tissues. Voxels representing bone are then assigned the value one and the remaining voxels the value zero, resulting in a binary image. We have used the automated 3D region growing algorithm based on an assessment function (ARG) [23]. Similarly to many other mathematical morphology-based techniques, ARG has been devised for images with isometric voxels. Thus it is necessary to perform an interpolation before ARG is applied, in case the images have non-isometric voxels. In our case such an interpolation was necessary for the MSCT images. The ARG method starts with a very limited homogeneity threshold which results in an under-segmented region. The image processing is then repeated with a higher threshold and the procedure is iterated. A segmentation, that was used to calculate the parameters, was defined as the iteration where the assessment function attained its minimum. Representative images demonstrating raw image, segmented image and 3D image from μ CT data are shown in (**Fig 1c** and **Fig 2a-b**).

The quantitative parameters of bone structure were calculated using MATLAB. The MATLAB code used for segmenting the images was developed in house. The computer used was a standard PC with Intel Core i5, CPU at 2.60GHz, 4GB of RAM and 64-bit operating system. Six different parameters were measured and are listed below:

Bone volume over total volume (BV/TV) is measured by dividing the number of voxels classified as bone trabecula by the total number of voxels in the bone sample. (**Fig 3a**)

Trabecular thickness (Tb.Th) is measured in mm, the mean trabecular bone diameter (**Fig 3b**)

Trabecular separation (Tb.Sp), also measured in mm, the mean distance between the boundaries of the segmented trabeculae. (**Fig 3c**)

Trabecular number (Tb.N) is the number of the trabeculae, measured as the inverse of the mean spacing between the midlines of the trabeculae. (**Fig 3c**)

Trabecular nodes (Tb.Nd) is the number of trabecular intersections per volume. (**Fig 3b**)

Trabecular termini (Tb.Tm) is the number of free ends of trabeculae per volume. (**Fig 3b**)

Statistical methods

Results are presented as mean values with standard deviations. Parameters are related to each other using Pearson correlation with 95% confidence intervals.

Results

With all clinical machines, BV/TV and Tb.Th were consistently overestimated relative to μ CT. The CBCT machine overestimated Tb.Th three times or more and the GE MSCT overestimated Tb.Th almost five times. (**Fig 4 and 6; Table 2**).

Both MSCT machines overestimated BV/TV more than four times and the CBCT machine more than three times. Tb.Nd was highly underestimated by all the clinical machines relative to μ CT. (**Fig 5 and 7; Table 2**).

The GE MSCT machines underestimated Tb.Nd more than 10 times and showed very small variations in this parameter between the bone samples.

All clinical CT machines showed strong correlation with μ CT regarding BV/TV ($r>0.86$) (**Table 3**). For the Tb.Th, both the CBCT and the Siemens MSCT showed strong correlation ($r>0.86$).

When images reconstructed with the two different reconstruction filters from the GE MSCT (“bone” and “bone plus”) were compared, the “bone plus” filter had slightly stronger correlations to the μ CT measurements for all parameters than those of the “bone” filter (**Table 3**). The differences between the mean values obtained with the two filters were small (**Table 2**).

Regarding the Siemens MSCT, the obtained Tb.Sp, Tb.N and Tb.Nd had weak correlations with those of μ CT when using 0.6 mm slice thickness ($r=0.12$, 0.15 and 0.02 respectively), but was much stronger when using 0.4 mm slice thickness ($r=0.52$, 0.66 and 0.70 respectively). Tb.Th and BV/TV had almost the same correlation to those of μ CT regardless of the slice thickness ($r = 0.88$ - 0.92) (**Table 3**).

The bone samples were imaged by CBCT with two different isotropic voxel sizes, $80\ \mu\text{m}$ and $125\ \mu\text{m}$. For both voxel sizes the observed correlations to μ CT were above 0.80 for all parameters except for Tb.Tm where the correlation was 0.73 . When using a voxel size of $80\ \mu\text{m}$ the correlation coefficients ranged from 0.93 to 0.97 for BV/TV, Tb.Th, Tb.N and Tb.Nd (**Table 3**).

Discussion

When describing the micro architecture of the trabecular bone the image resolution turned out to be of great importance. When describing parameters sensitive to differences in the trabecular network such as Tb.Nd and Tb.N, CBCT showed much higher correlations with μ CT than MSCT did. The correlations of CBCT were as high as 0.93 and 0.95 respectively for the 80 μ m isotropic voxels, while the relatively low resolution of MSCT with >400 μ m isotropic voxels resulted in much lower correlations (Table 3). It should be noted that for MSCT, the choice of reconstruction filter ("bone" vs. "bone-plus" on the GE machine) did have an effect on the results. It cannot be excluded that even better results might be attained with a different filter, but with the hardware and software available, these were the filters that were expected to give the best results. On the other hand, when describing parameters less sensitive to image resolution, such as BV/TV all studied machines showed strong correlations to those of μ CT ($r>0.87$), regardless of resolution or filter. There was also a strong correlation for Tb.Th when using MSCT from Siemens, as well as when using the CBCT machine. However, both BV/TV and Tb.Th describe the mineral content, just like DXA, but fail to describe the complexity of the microarchitecture.

A recent article describing trabecular bone microarchitecture in the maxilla found positive correlations between μ CT and CBCT (with resolution 400 μ m) regarding BV/TV ($r = 0.77$), Tb.N ($r = 0.52$) and Tb.Th ($r = 0.49$) [24]. In our study, using CBCT with higher resolution (80 μ m), the correlations for the same parameters were considerably higher: BV/TV $r = 0.97$, Tb.N $r = 0.95$ and Tb.Th $r = 0.96$. CBCT either overestimated or underestimated the bone structure parameters compared to μ CT. Such systematic errors can be tolerated if the purpose is to make intra-individual comparisons over time to, e.g. evaluate medical treatment. High correlations with the gold standard can also make it possible to estimate the bone structure in individuals with measurements at only one occasion if one takes into account the known relationship between the measurements from different machines. Our study was an in vitro study and the bone specimens were defatted and surrounded by water. This may affect the results compared to studies on viable bone. Our measurements, imaged by μ CT, describing Tb.N, Tb.Th as well as Tb.Sp are in good agreement with other studies indicating that the results are credible [25, 26].

When imaging facial structures, CBCT machines are usually used with the patient in either sitting or standing position. The long acquisition time, between 10 and 35 seconds, increases the risk for motion artifacts, especially when the patient is standing. There are CBCT devices for patients lying down, but those are less widely used. Currently available CBCT equipment does not permit examination of the torso. The prospect of applying CBCT to e.g. vertebral examinations does therefore not seem realistic. Examination of cervical vertebrae is feasible [27], but the radiation dose to the thyroid would probably be an issue if one were to screen for osteoporosis. In order to decrease radiation dose to the thyroid imaging of the wrist could be an appealing alternative. Such a study, in a CBCT device permitting patients to lie down, has recently been published [28]. There are also studies describing finger fractures using CBCT devices, with high correlation with those of MSCT [29] and articles where the wrist is imaged by arthrography and CBCT [30]. If the wrist is going to be imaged in our CBCT machine, some kind of fixation device for the wrist needs to be developed in order to minimize the risk for motion artifacts and to ensure high reproducibility.

It has previously been shown that there is a correlation between the width of the mandible cortex and BMD of the lumbar spine [31]. By analyzing changes in mandible bone structures from panoramic dental radiographs it has been possible to identify 40-69 % of women at risk

for future fractures by observing sparse mandibular trabeculation [32]. This indicates that it might be possible to identify persons at risk for osteoporosis by also investigating the 3D trabecular network of the mandible when performing dental examinations by CBCT.

An already existing method for studying the trabecular bone structure at a resolution equivalent to CBCT is HR-pQCT [11]. In a study by Sode et al [33], HR-pQCT data sets of different voxel sizes were correlated to μ CT, also of different voxel sizes. The correlation for the structure parameters increased when the voxel size for HR-pQCT was close to the voxel size for the μ CT. This strengthens the conclusion that resolution plays an important role for the ability of the CBCT to describe trabecular bone structures. A disadvantage of HR-pQCT is that it is less wide-spread than CBCT and that it is only used for peripheral body parts. MSCT, on the other hand, is available in most general hospitals. The radiation dose is, however, considerably higher compared to CBCT [34]. Another drawback of MSCT is its lower resolution which, as shown by our present study, results in much lower correlations with μ CT for several of the bone structure parameters. MRI is appealing as it does not use any radiation, but susceptibility artifacts cause magnetic field dependent overestimation of the trabeculae [10] and also the cost per examination is rather high compared to many other imaging methods. In addition, the acquisition time is considerably longer than for CBCT.

Future clinical studies are needed to evaluate effects of patient movement as well as other factors that may complicate in vivo acquisition. It would also be interesting to compare CBCT with HR-pQCT with μ CT as the reference. As most CBCT scanners are used for dental examinations, there may be free capacity during out-of-office hours, which potentially can be used for research studies and clinical trials.

In conclusion, the very high correlation between CBCT and μ CT, for several bone structure parameters, in particular Tb.Nd and Tb.N, suggest that it might be feasible to use CBCT for monitoring changes in the microarchitecture of trabecular bone *in vivo*.

Conflict of interest

No conflict of interest

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Figure 1 Mosaic
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(a)

(b)

(c)

(d)

(e)

(f)

Figure 1a

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Table 1. Imaging parameters

	MSCT GE Light speed	MSCT GE Light speed	MSCT Siemens Definition	MSCT Siemens Definition	CBCT Accuitomo FPD 80	CBCT Accuitomo FPD 80
Imaging voxel size [μm]	188 x 188 x 625	188 x 188 x 625	98 x 98 x 600	98 x 98 x 400	125 x 125 x 125	80 x 80 x 80
Reconstruction voxel size [μm]	188 x 188 x 200	188 x 188 x 200	98 x 98 x 98	98 x 98 x 98	125 x 125 x 125	80 x 80 x 80
Tube voltage [kV]	120	120	120	120	85	85
Effective [mAs]	130	130	130	400	-	-
[mA]	-	-	-	-	8	8
Field of view [mm]	96	96	50	50	60	40
Matrix	512 x 512	512 x 512	512 x 512	512 x 512	480 x 480	500 x 500
Reconstruction filter	Bone	Bone plus	U70u sharp	U70u sharp	G001 (dental)	G001 (dental)

MSCT = Multi Slice Computed Tomography; CBCT = Cone Beam Computed Tomography

Table 2. Measurements of trabecular bone structure parameters. Mean values and standard deviations

	MSCT GE Light speed 625 μm bone	MSCT GE Light speed 625 μm boneplus	MSCT Siemens Definition 600 μm	MSCT Siemens Definition 400 μm	CBCT Accuitomo FPD 125 μm	CBCT Accuitomo FPD 80 μm	μCT SCANCO 20 μm
Tb.Sp [mm]	0.80 $\pm$ 0.07	0.80 $\pm$ 0.05	0.55 $\pm$ 0.03	0.60 $\pm$ 0.04	0.67$\pm$0.09	0.57 $\pm$ 0.07	0.65 $\pm$ 0.12
Tb.Th [mm]	0.65 $\pm$ 0.03	0.63 $\pm$ 0.02	0.47 $\pm$ 0.04	0.50 $\pm$ 0.04	0.43 $\pm$ 0.02	0.39$\pm$0.03	0.13 $\pm$ 0.02
Tb.N [mm^{-3}]	0.64 $\pm$ 0.05	0.68 $\pm$ 0.04	0.95 $\pm$ 0.05	0.88 $\pm$ 0.05	0.85 $\pm$ 0.09	0.95$\pm$0.11	1.17 $\pm$ 0.16
BV/TV	0.40 $\pm$ 0.07	0.42 $\pm$ 0.06	0.46 $\pm$ 0.04	0.44 $\pm$ 0.67	0.30$\pm$0.08	0.31 $\pm$ 0.08	0.10 $\pm$ 0.03
Tb.Nd [mm^{-3}]	0.26 $\pm$ 0.05	0.30 $\pm$ 0.05	0.46 $\pm$ 0.04	1.1 $\pm$ 0.14	0.74 $\pm$ 0.2	1.53$\pm$0.43	5.11 $\pm$ 1.67
Tb.Tm [mm^{-3}]	0.14 $\pm$ 0.02	0.15 $\pm$ 0.03	0.88$\pm$0.08	0.79 $\pm$ 0.1	0.31 $\pm$ 0.07	1.01 $\pm$ 0.27	0.84 $\pm$ 0.08

MSCT = Multi Slice Computed Tomography; CBCT = Cone Beam Computed Tomography; μCT = micro Computed Tomography

Bold figures denote values closest to the reference method (μCT)

Table 3. Correlations with μ CT. Pearson correlation coefficients (r) with 95% confidence limits.

	MSCT GE Light speed Bone	MSCT GE Light speed Bone plus	MSCT Siemens Definition 600 μ m	MSCT Siemens Definition 400 μ m	CBCT Accuitomo FPD 80 125 μ m	CBCT Accuitomo FPD 80 80 μ m
Tb.Sp	0.80 (0.49; 0.93)	0.91 (0.73; 0.97)	<i>0.12</i> (-0.42;0.60)	0.52 (0.01;0.81)	0.82 (0.52;0.94)	0.85 (0.59;0.95)
Tb.Th	<i>0.47</i> (-0.06;0.79)	0.58 (0.10;0.84)	0.89 (0.70;0.96)	0.88 (0.66;0.96)	0.87 (0.64;0.96)	0.96 (0.88;0.99)
Tb.N	0.76 (0.41;0.92)	0.79 (0.47;0.93)	<i>0.15</i> (-0.39;0.62)	0.66 (0.22;0.87)	0.90 (0.71;0.97)	0.95 (0.86;0.98)
BV/TV	0.89 (0.71;0.96)	0.94 (0.81;0.98)	0.92 (0.76;0.97)	0.87 (0.65;0.96)	0.96 (0.88;0.99)	0.97 (0.92;0.99)
Tb.Nd	0.74 (0.36;0.91)	0.78 (0.44;0.92)	<i>0.02</i> (-0.53;0.50)	0.70 (0.29;0.89)	0.86 (0.62;0.95)	0.93 (0.80;0.98)
Tb.Tm	<i>0.06</i> (-0.47;0.55)	<i>0.06</i> (-0.46;0.55)	0.63 (0.18;0.86)	0.53 (0.03;0.82)	0.73 (0.34;0.90)	0.73 (0.34;0.90)

MSCT = Multi Slice Computed Tomography; CBCT = Cone Beam Computed Tomography

Tb.Sp = Trabecular separation; Tb.Th = Trabecular thickness; Tb.N = Trabecular number; BV/TV = Bone volume; Tb.Nd = Trabecular number; Tb.Tm = Trabecular termini

Bold figures denote correlations above 0.90.*Italic* figures denote correlations not significantly different from 0.

Figure_2a
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BV/TV

TV

BV

Figure_4

Figure_5

Figure_6

Figure_7

Fig. 1 Slices (**a, b, c**) and volume renderings (**d, e, f**) of acquired images from multi-slice CT (**a, d**), cone-beam CT (**b, e**) and micro-CT (**c, f**)

Fig. 2 Segmentation result from micro-CT data, slice (**a**) and volume rendering (**b**)

Fig. 3 Description of trabecular bone structure parameters: volume fraction (BV/TV) (**a**); trabecular thickness (Tb.Th) and trabecular nodes (Tb-Nd) (**b**); trabecular spacing (Tb.Sp) and trabecular number (Tb.N) (**c**)

Fig. 4 Trabecular thickness of the 15 different bone samples measured from the different CT machines using the ARG segmentation algorithm

Fig. 5 Trabecular nodes of the 15 different bone samples measured from the different CT machines using the ARG segmentation algorithm

Fig. 6 Linear regression analysis of trabecular thickness [mm] measured from cone-beam CT (80 μm) and micro-CT (20 μm)

Fig. 7 Linear regression analysis of trabecular nodes [mm^{-3}] measured from cone-beam CT (80 μm) and micro-CT (20 μm)