Micro-Computed Tomography Assessment of Human Alveolar Bone: Bone Density and Three-Dimensional Micro-Architecture

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ABSTRACT

Background: Micro-computed tomography (micro-CT) is a valuable means to evaluate and secure information related to bone density and quality in human necropsy samples and small live animals.

Purpose: The aim of this study was to assess the bone density of the alveolar jaw bones in human cadaver, using micro-CT. The correlation between bone density and three-dimensional micro architecture of trabecular bone was evaluated.

Materials and Methods: Thirty-four human cadaver jaw bone specimens were harvested. Each specimen was scanned with micro-CT at resolution of 10.5 μm. The bone volume fraction (BV/TV) and the bone mineral density (BMD) value within a volume of interest were measured. The three-dimensional micro architecture of trabecular bone was assessed. All the parameters in the maxilla and the mandible were subject to comparison. The variables for the bone density and the three-dimensional micro architecture were analyzed for nonparametric correlation using Spearman's rho at the significance level of $p < .05$.

Results: A wide range of bone density was observed. There was a significant difference between the maxilla and mandible. All micro architecture parameters were consistently higher in the mandible, up to 3.3 times greater than those in the maxilla. The most linear correlation was observed between BV/TV and BMD, with Spearman's rho = 0.99 ($p = .01$). Both BV/TV and BMD were highly correlated with all micro architecture parameters with Spearman's rho above 0.74 ($p = .01$).

Conclusions: Two aspects of bone density using micro-CT, the BV/TV and BMD, are highly correlated with three-dimensional micro architecture parameters, which represent the quality of trabecular bone. This noninvasive method may adequately enhance evaluation of the alveolar bone.

KEY WORDS: alveolar bone, bone density, bone mineral density, bone volume fraction, micro architecture, micro-CT

INTRODUCTION

The success of a root-form dental implant is dependent on many factors. These include placement of the implant within encasing bone with correct position, no impingement of vital structures (i.e., nerves, adjacent tooth roots, etc.), and the density of the encasing bone.[1,2] Proper diagnosis and treatment planning are crucial for these determinations.

The various objective methods of bone density measurements in the literature include the bone volume fraction (BV/TV) using histomorphometry,[3] Hounsfield unit values using computed tomography,[4–7] and the bone mineral density (BMD), either with quantitative computed tomography[8–11] or dual energy X-ray absorptionmetry referred to as a DXA.[12,13] Currently, cone beam computed tomography (CBCT) is available. However, the reliability of the bone density measurement is not confirmed.[14–16]

The two existing "gold-standard-of-bone-density" measures are histological/histomorphometric analysis and micro-computed tomography (micro-CT).[17,18]

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Several studies have compared histometric results to computer imaging on undemineralized methylmethacrylate[19,20] and celloidin-paraffin[21] embedded sections. These studies reported a very high correlation of the BV/TV to various micro-CT scans ($r = 0.94–0.97$). Müller and colleagues[22] demonstrated a 6.8% lack of agreement measuring the BV/TV between sequential surface image analyses on sequentially cross-sectioned human radius biopsy blocks. Other investigators[23,24] have reported similarly high correlative values comparing the two methods; however, the micro-CT densities consistently exceeded the absolute histomorphometric numbers. Another study[25] using ground sectioning demonstrated higher histologic measurements when compared with their micro-CT counterparts. Further evidentiary support is provided by a study examining the micro-CT bone densities in rat tibias following sequential administration of parathyroid hormone doses.[26] From these studies, it appears that the micro-CT method is adequate to establish the necessary *gold-standard-of-bone-density* measure. Advantages to rely on micro-CT rather than histomorphometric analysis include less error of the method due to shrinkage, less time, and lower cost.[19]

The micro architecture of trabecular bone is considered an important aspect of bone quality.[27–30] The micro architecture assessment is based on either two-dimensional histomorphometry or three-dimensional evaluation using micro-CT.[31–35]

Micro-CT can provide various information such as bone density in the BV/TV, BMD with proper calibration, and three-dimensional micro architectural data. Although it presently has no clinical application, micro-CT is a valuable means to evaluate and compare the human necropsy samples and small live animals.[27,28,35] Recently in the literature, the micro-CT method has been utilized as a technique to evaluate ridge augmentation and degree of osseointegration both qualitatively and quantitatively.[21,36–40]

Other than a pilot report on a single human cadaver specimen,[41] there were no available data related to alveolar bone density assessment with micro-CT in the literature. Accordingly, this study was designed to assess bone density of alveolar jaw bone in human cadavers using micro-CT. The correlation between bone density and three-dimensional micro architecture of trabecular bone was also determined.

MATERIALS AND METHODS

Specimen Preparation

Human cadaver heads obtained from the Division of Anatomy, School of Medicine at Loma Linda University, fixed in formalin, were screened. A total of 34 edentulous bone block specimens from various regions of the jaw were selected, which consisted of 18 maxillary and 16 mandibular block specimens in 12 donors. Each bone block specimen was at least 5 mm wide buccolingually and 11 mm high occlusoapically. The alveolar bone quantity having no root tips was verified with periapical radiographs. A 2-mm twist drill was used to make a 5-mm deep osteotomy. Then a reference marker, 2 mm in diameter and 10 mm long, made with nonscattering radiopaque material (plastic catheter cannula), was inserted in each site. The reference marker was extended 5 mm coronal to the bone level to locate a region of interest (Figure 1).

Acquisition of Micro-CT Images

Micro-CT scans were performed with the Scanco Viva-CT40 scanner (Scanco Medical AG, Bassersdorf, Switzerland). The scanner was set at 55 kVP with 0.16 mAs in a resolution of 10.5 μm voxels. It was calibrated with a phantom using known density hydroxyapatite (HA) disks to calculate the mineral density of the bone provided by the manufacturer of the scanner.

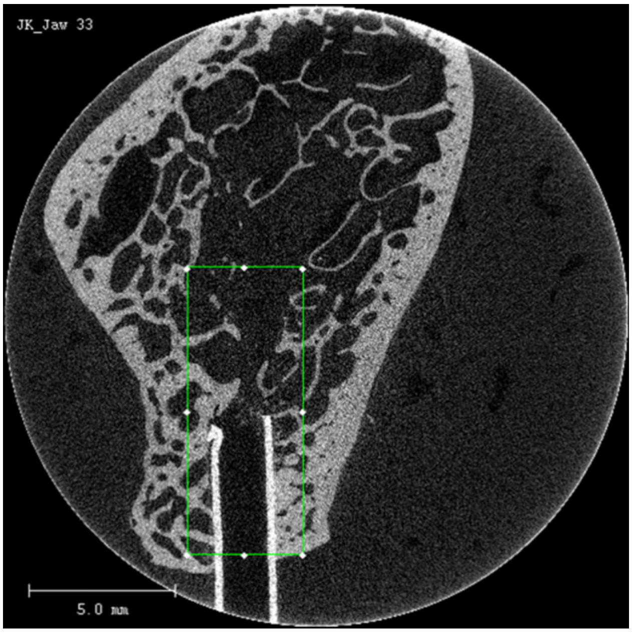

Figure 1 Center of the reference marker and region of interest. The reference marker was not included in the area of measurement.

Each specimen was scanned individually in a cylindrical container filled with distilled water. The container was positioned in a same manner each time for consistency.

Bone Density Measurement and Micro Architecture Assessment

Each scan was reviewed using the Scanco Viva-CT40 software program provided with the scanner (Scanco Medical AG) at the threshold of 420. The images were reviewed in a manner such that buccolingual slices were serially screened from the mesial to distal aspect of the reference marker. The center of the reference marker was located and the most distal part of the marker was identified. A template of the region of interest (4 mm × 10 mm, a rectangular box parallel to the marker) was created on the image with the center of the marker present (Figure 1).

The volume of interest (VOI), identified by consecutive images representing 1.5 mm thick immediately distal to the marker was selected for analysis; the marker itself was not included in the analysis. The total volume, bone volume, and BV/TV in % within VOI were all measured. BMD value within VOI was expressed in mg HA/cm^3.

The three-dimensional micro architecture of trabecular bone was assessed following the protocol of Parfitt and colleagues[3] and various parameters[42] were measured (Table 1).

TABLE 1 Parameters for the Micro Architecture Assessment

Bone Volume Fraction[3]: BV/TV	Proportion of Volume Occupied by Bone Volume (%)
Trabecular number[3]	Number of trabeculae per unit length (1/mm)
Trabecular thickness[3]	Average thickness of trabeculae (mm)
Trabecular separation[3]	Average thickness of nonbone (mm)
Connectivity density[42]	Three-dimensional connectivity index, normed by total volume (1/mm^3)
Structure model index[42]	Estimation of the plate-rod characteristic of the structure
Bone mineral density	Mean in units of hydroxyapatite density (mg HA/cm^3)

Statistical Analysis

Descriptive statistics were used to compare the maxillary bone versus the mandibular bone. The correlation between bone density, as measured in the BV/TV and BMD values, was analyzed using nonparametric correlation Spearman's rho at the significance level $p < .05$. The variables for bone density and the micro architecture were also assessed for the correlation using nonparametric correlation Spearman's rho at the significance level $p < .05$.

RESULTS

A wide range of bone densities was observed. The BV/TV ranged from 2.4% to 48.2%, and BMD using micro-CT ranged from 47.9 mg HA/cm^3 to 619 mg HA/cm^3.

The result of three-dimensional micro architecture evaluation showed a huge variation similar to the bone density variables. The variation of trabecular thickness was the smallest items studied among the parameters. The average of trabecular thickness of all the specimens was 0.09 mm (SD 0.02).

There was a clear difference between the maxilla and mandible (Table 2). Compared with the maxilla, the mandible presented nearly two times greater in BV/TV, trabecular number, and BMD. The connectivity density

TABLE 2 Comparison between the Maxilla and Mandible

	BV/TV	Tb N	Tb Th	Tb Sp	Conn D	SMI	BMD
Maxilla	14.59 ± 7.68	2.07 ± 0.80	0.10 ± 0.02	0.63 ± 0.18	95.63 ± 100.83	0.98 ± 1.87	214.15 ± 95.04
Mandible	27.28 ± 10.19	3.76 ± 1.99	0.09 ± 0.02	0.42 ± 0.18	242.59 ± 145.01	−3.23 ± 5.09	382.41 ± 118.46
Ratio	1.9	1.8	0.9	0.7	2.5	3.3	1.8

BMD, bone mineral density; BV/TV, bone volume fraction; Conn D, connectivity density; SMI, structure model index; Tb N, trabecular number; Tb Th, trabecular thickness; Tb Sp, trabecular separation.

TABLE 3 Correlation between Parameters

	BV/TV	Tb N	Tb Th	Tb Sp	Conn D	SMI	BMD
BV/TV	1*	0.91	0.18	−0.87	0.76	0.74	0.99
Tb N		1	0.41	−0.99	0.86	0.69	0.93
Tb Th			1	0.41	0.59	0.23	−0.21
Tb Sp				1	−0.85	−0.66	−0.89
Conn D					1	0.65	0.78
SMI						1	0.75
BMD							1

*Spearman's rho. $p < .01$.
BMD, bone mineral density; BV/TV, bone volume fraction; Conn D, connectivity density; SMI, structure model index; Tb N, trabecular number; Tb Th, trabecular thickness; Tb Sp, trabecular separation.

and structure model index (SMI) were 2.5 times and 3.3 times higher, respectively, in the mandible than the maxilla. In contrast, the trabecular separation was more in the maxilla than in the mandible by the nature of this measurement. It was found that the average trabecular thickness was very similar between the maxilla and the mandible, with average thickness 0.10 mm and 0.09 mm, respectively (Table 2).

The correlation between the different parameters is presented in Table 3. As the trabecular thickness was consistent, it demonstrated low to modest correlation with other parameters. The most linear correlation was observed between the BV/TV and BMD, with Spearman's rho = 0.99 ($p = .01$). Both the BV/TV and BMD were highly correlated with all micro architecture parameters, with Spearman's rho being above 0.74 and inversely correlated with the trabecular separation (Table 3).

DISCUSSION

As a "gold standard of bone density," micro-CT provides various information such as bone density in the BV/TV, BMD with proper calibration, and three-dimensional micro architectural data. It is a valuable tool for small live animals, and human biopsy and necropsy samples.[27,28,35] Recently in the literature, micro-CT analyses have been utilized, not only qualitatively but also quantitatively for different clinical situations.[21,36–41] However, there has not been any study available regarding bone density measurement in the BV/TV and BMD using micro-CT in alveolar bone. The results of this study present the density and the micro architecture of alveolar bone.

In the current study, it was noted that there was a huge variation in bone density, as the BV/TV ranged from 2.4% to 48.2%. The bone block specimens were collected from various regions of the maxilla and mandible from 12 different donors. Due to the lack of information of the donors' age, gender, and health history, it was impossible to make any clinically relevant application from this result. There was an obvious difference found between the maxilla and mandible. All the parameters for the bone quality assessment were consistently higher in the mandible than those of the maxilla. The most distinctive parameter was SMI with a ratio of 3.3 of maxilla to mandible, which means that the mandible presents more plate-like architecture than the maxilla. Understanding the quantitative difference in bone density and the comparative micro architecture between the maxilla and mandible may enable clinicians to provide and prepare optimal dental treatment options for patients.

There are various objective methods of bone density measurement and the correlation between them is of interest. Lindh and colleagues[10] reported that Pearson coefficient r ranged from 0.66 to 0.86 between BMD using quantitative computed tomography and the BV/TV using the contact radiography in human mandibles. Using a rat femur model, Keenan and colleagues, reported that BMD obtained using DXA showed a significantly high correlation with Archimedes density.[13] In contrast, results of a study by Rico and colleagues[43] presented low correlation between BMD obtained using DXA with the histomorphometric BV/TV (correlation $r = 0.35$). This study showed the most linear correlation between the BV/TV and BMD with Pearson's correlation coefficient $r = 0.99$. The two density parameters, the BV/TV and BMD, were retrieved from same micro-CT scan data in the current study. The micro-CT scanner was calibrated with an HA phantom so the machine is set for bone analysis. This explains the significantly high linear correlation between the variables.

It was reported that the bone density partially reflects the bone quality and the micro architecture of trabecular bone is one of the essential properties of bone quality.[29,34] Traditionally the micro architecture has been evaluated with histomorphometry.[3] However, histomorphometry is a two-dimensional assessment; it is unfortunately limited due to the destructive nature of the methodology. With the advent of micro-CT, three-dimensional micro architectural data are now available for greater analysis.

Different micro-CT parameters, such as trabecular number, trabecular thickness, trabecular separation, connectivity density, and SMI, have been considered to represent quality of bone. The *trabecular number* quantifies how many trabeculae exist in a given distance. The *trabecular thickness* measures the thickness of trabecular structures, which is related to bone formation. The *trabecular separation* measures spaces between non-bone structures.[3,42] The *connectivity density* is a three-dimensional connectivity index; it is the degree to which a structure is multiple-connected.[44] SMI is an indicator of plate-like versus rod-like trabecular architecture. The lower the ratio, the more rod-like the architecture, which translates to more bone resorption.[45,46]

From this study on human alveolar bone, the micro-CT parameters of bone quality related to the BV/TV and BMD. The linear correlation coefficient Spearman's rho of trabecular number, connectivity density, trabecular separation, and SMI were all above 0.74, which explains the significantly high correlation with bone density parameters. Teo and colleagues[47] also reported a strong correlation between the BV/TV and other parameters in porcine vertebrae. They also tested the mechanical property of trabecular bone and also found a good correlation with micro architecture parameters. In a rat model, compressive strength of bone was reported as 71–78% with the BV/TV and BMD.[48] However, among osteoporotic patients, a study by Burghardt and colleagues[34] suggested that both the bone density in BMD and the micro architecture parameters should be considered together to increase the predictive value of the risk of bone fracture.

The similar trabecular thickness in this study is an interesting finding, even though all other parameters presented a huge difference between the groups. In the current study, the trabecular thickness ranged from 0.07 mm to 0.12 mm. Other studies have reported similar results. In the work by Fanuscu and Chang,[41] trabecular thickness ranged from 0.09 mm to 0.13 mm using a three-dimensional analysis of a maxilla and a mandible from one human cadaver. Two-dimensional analysis of trabecular thickness of human maxillary alveolar bone was from 0.095 mm to 0.138 mm.[31] Still another animal study reported that the trabecular thickness decreased due to bone loss and increased after treatment in experimental osteoporosis.[33] In the study by Ding and Hvid,[49] these authors reported a variation in trabecular thickness among different age groups, which was statistically significant only after age 70. In this study, the bone specimens were harvested from various cadavers, but unfortunately, information of systemic health and the age of bone donors were not available for further evaluation.

The goal for three-dimensional imaging is to gather as much information as possible to make a proper diagnosis and formulate a treatment plan according to patients' needs. Although micro-CT has as yet no clinical application, the currently available clinical imaging methods, such as conventional computed tomography and CBCT, have shown a close correlation with micro-CT. The bone density measurement using CT and CBCT should be evaluated with micro-CT to verify their reliability, which will enhance the clinical assessment of the alveolar bone. This noninvasive method will enable clinicians to evaluate the alveolar bone adequately (i.e., preimplant sites when treatment planning) as there is significant variation in the jaw bone density as demonstrated in this study.

In conclusion, the present study showed a significant variation in bone density of human alveolar bone. Results have been presented that there is a *measurable quantitative difference* in the bone density between the maxilla and the mandible. This study investigated two aspects of bone density using micro-CT, BV/TV, and BMD. Both density values are highly correlated with three-dimensional micro architecture parameters which represent the quality of the trabecular bone.

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