Bone Mineral Density and Bone Histomorphometry are Statistically Related

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Purpose: *The aim of this study was to evaluate how closely analysis of bone quality performed using the bone mineral density (BMD) values obtained by quantitative computerized tomography (QCT) reflected the histologic bone density.* ***Materials and Methods:*** *Eighteen patients requiring implant therapy underwent CT scanning. Their data were processed using Image Master software, and the BMD was calculated by measuring the Hounsfield units and relating those values to a phantom (Calibration Phantom, Quantitative Technologies). Each patient wore a radiographic-surgical template in which titanium cylinders were placed as a drilling guide for preparation of the implant site. The mouth regions where the titanium guides were placed (on the CT images and in the patient's mouth) corresponded to the implant sites where the BMD was measured and where tissue specimens for histomorphometric analysis retrieved. Forty specimens measuring 6 mm in length and 2 mm in diameter were obtained. Histomorphometric analysis was performed by digitizing the images, which were subsequently analyzed using the image analysis software IAS 2000. The bone volume (BV) was calculated as a percentage by dividing the area occupied by the mineralized bone over the entire microscopic field.* ***Results:*** *The results of the statistical analysis showed a Pearson correlation coefficient of 0.691 between the BV and BMD values, with a* P *value < 0.01, which was considered significant.* ***Discussion and Conclusion:*** *The results of this study support the use of QCT to assess the bone quality before implant placement to improve the planning of implant treatment.* INT J ORAL MAXILLOFAC IMPLANTS 2005;20:898–904

Key words: *bone density, computerized tomography, histomorphometry*

Although bone classification has been described, at present there are no clear tools for obtaining an accurate analysis of bone density. Lekholm and Zarb[1] classified bone tissue based on the radiographic evaluation of the proportions of cortical and trabecular bone. They labeled bone that was thick and cortical with an almost total absence of spongy tissue type I bone; bone with a thick layer of cortical and high-density trabecular bone type II bone; bone with a thin layer of cortical bone and a well-represented layer of dense trabecular bone type III bone; and bone with a thin layer of cortical bone with very low-density trabecular bone and wide marrow spaces type IV bone.

The success rate of dental implant therapy is influenced by both the quality and quantity of bone, and clinical reports have indicated that implant prognosis is significantly affected by bone quality.[2–5] Therefore, the bone density of potential implant sites is a critical parameter when planning prosthetic and surgical implant treatment. Very dense cortical bone, less vascularized bone, and low-density trabecular bone do not offer optimal conditions from a prognostic point of view.

Misch[6] classified bone density according to the clinical hardness assessed during drilling the implant site. According to Misch, bone density may be grossly estimated by radiographic evaluation with tomograms. Conventional dental radiographs, including periapical, panoramic, or lateral cephalometric studies, are less useful for diagnostic purposes.

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Trisi and Rao[7] compared the histomorphometric evaluation of bone volume (BV) to the method of manual perception during drilling described by Misch.[6] They found good possibilities of recognizing D1 and D4 bone (according to Misch classification[6]), but less capability for distinguishing D2 and D3 bone.

Evaluating bone strength in patients is an important problem, not only in treatment of osteoporosis[1,2] but also in implant dentistry. Radiographic measurements of bone mineral density (BMD)[3,4] by dual-energy x-ray absorptiometry or quantitative computerized tomography (QCT)[5] are important indices of bone strength. With the QCT method it is possible to analyze BMD and provide quantitative data on trabecular and cortical bone.[8] Norton and Gamble[9] compared the bone density subjectively registered according to the Lekholm and Zarb classification to bone density in Hounsfield units (HU) in the various regions of the mouth and found an overall correlation.

HU was defined on the basis of the x-ray attenuation coefficient when various materials are crossed by x-rays. A range between –1000 (dry air value) and +3000 (the densest metal) has been created. Zero is the value produced by water. When the density of soft tissues is measured, values very close to 0 or negative values are obtained. For bone, the HU range is between 100 and 1,900 HU, and variations can be found between 100 and 350 HU for type IV bone, between 350 and 700 HU for type III bone, between 700 and 1,200 HU for type II bone, and usually between 1,200 and 1,900 HU for type I bone.[10]

Since small changes in the x-ray energy of the CT scan setting results in bone images with different HU values, bone density was related to BMD values that were independent from the machine settings because they were adjusted using standard phantoms.

The authors are not acquainted with reports that verify a correlation between objective data such as the HU, obtained from CT images, and the histomorphometric examination of the site analyzed in the jawbones. This was the aim of the present study.

MATERIALS AND METHODS

Twenty-three patients undergoing implant therapy for fixed prosthetic rehabilitation were included in this study. All the patients were in good health, with no systemic disorders. All were accurately informed about the procedures, and all signed an informed consent form. The study was approved by the Ethics Committee of the Lombardy Region (Milan, Italy).

The patients underwent CT scanning for implant treatment planning. The implant treatment was performed at the S. Anna Clinic (Brescia, Italy). The CT scan was carried out using a Toshiba x-press/GX scanner (Toshiba, Tokyo, Japan), set to produce 2-mm-thick slices with 120 kV voltage and a dose of 150.0 mA. The data were processed (reformatted CT) using Image Master (Image Master; CSI, Columbia, MD). The BMD calibration was performed by measuring HU values in the 3 compartments of the dental phantom (Calibration Phantom; Quantitative Technologies, San Francisco, CA) and relating these values to the known BMD phantom using a linear relation. Using the resulting calibration constant, the HU values were converted to BMD values.

Fig 1 Radiographic-surgical template that each patient wore. Titanium cylinders with a length of 8 mm and an internal diameter of 2.5 mm were inserted into the template and used as guides for drilling the bone during the preparation of the implant site.

Each patient wore a radiographic-surgical template. During surgery, titanium cylinders with a length of 8 mm and an internal diameter of 2.5 mm were placed in the template and used as a guide for drilling the bone during the preparation of the implant site (Fig 1).

The alveolar process below the titanium cylinder on the CT images and in the patient's mouth corresponded to the implant site where bone density was recorded in HU and from which the specimens for histomorphometric analysis were retrieved.

For HU analysis interactive software (SIM/Plant; CSI) was used that allowed mapping of the volume of bone tissue where implant placement was planned (Fig 2). The reference point was the titanium cylinder, and the interactive implant (6 mm in length, 2 mm in diameter) was placed below this, thus recording the HU of the bone in that particular region.

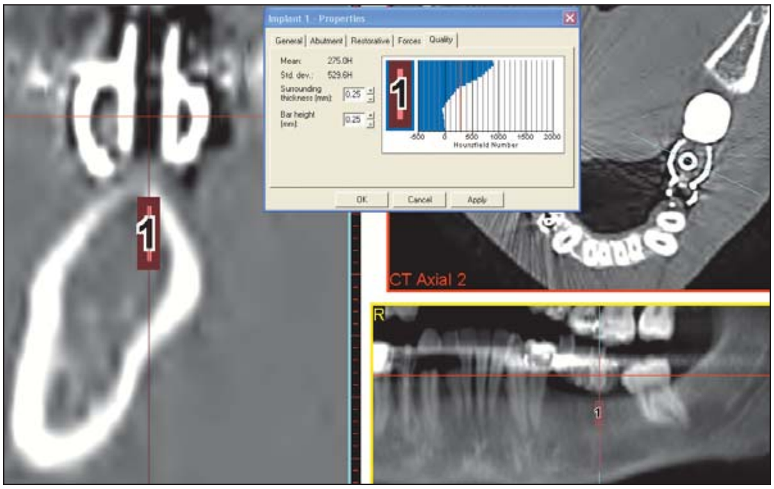

Fig 2 Digital image from the interactive SIM/Plant software, which allowed mapping of volume of bone tissue at potential sites for implant placement.

During surgery a trephine (6 mm in length, with an external diameter of 2.3 mm and an internal diameter of 2 mm) was passed through the titanium cylinder to retrieve the bone biopsy samples. After retrieval, the implant site was prepared, and the implant was placed in the conventional manner. Forty specimens measuring 6 mm in length and 2 mm in diameter were collected.

Histologic and Histomorphometric Procedure

The retrieved biopsies were immediately rinsed in saline solution fixed in 10% neutral buffered formalin and processed to obtain thin ground sections. The specimens were dehydrated in an ascending series of alcohol rinses and then embedded in methacrylate resin. After polymerization, sections 200 to 250 µm wide were made using a Micromet high-speed rotating blade microtome (Remet, Bologna, Italy). The sections were then ground to about 40 to 50 µm wide using an LS2 (Remet) grinding machine. The histologic slides were routinely stained with toluidine blue and basic fuchsin staining solutions.

Histomorphometric analysis was performed by digitizing the images from the microscope via a JVC TK-C1380 color video camera (JVC Victor, Yokohama, Japan) and a frame grabber. The images were acquired with a 10× objective and included the entire biopsy sample. Subsequently the digitized images were analyzed by the image analysis software IAS 2000 (Delta Sistemi, Rome, Italy). For each specimen, the most central section was analyzed. The parameter calculated using the IAS 2000 software was the BV percentage, ie, the area of the microscopic field occupied by the mineralized bone matrix. This was measured by outlining the bone surface area to determine the surface area of bone in the microscopic field and expressed as a percentage of the total biopsy area.

Statistical Analysis

Because some biopsy samples were retrieved from the same subjects, the statistical independence was biased. Thus, a separate analysis was performed in which only 1 sample per patient was included. It was not possible to make an analysis of within-subject correlation because of the small number of cases in which more than 1 sample was retrieved from the same subject. Therefore, the correlation of the overall samples was calculated, but statistical significance was not measured.

One biopsy sample from each subject was randomly selected, and the correlation coefficient between the BMD and the BV was calculated. Since the values were skewed, a Spearman rank correlation test was calculated to evaluate the statistical significance of the correlation. Finally, r^2 was calculated and scatterplots were made to address the question of the clinical importance of the correlation. Three samples were not included in the analysis because of poor tissue preservation and difficult readings.

RESULTS

The Spearman correlation coefficient of all the biopsies was 0.706; $r^2 = 0.429$. The correlation coefficient among different subjects was calculated on 23 samples found to be 0.699 ($P = .01$). There was only a small difference between these 2 correlations, which suggests that the influence of intraindividual sampling was small.

Figure 3 shows the scatterplot of all the values; Fig 4 shows the scatterplot for the interindividual data. The results of the histomorphometric analysis and the BMD values are plotted in Fig 3 and summarized in Table 1.

Table 2 illustrates mean (SD) BMD and BV values in the different regions of the mouth. It shows that

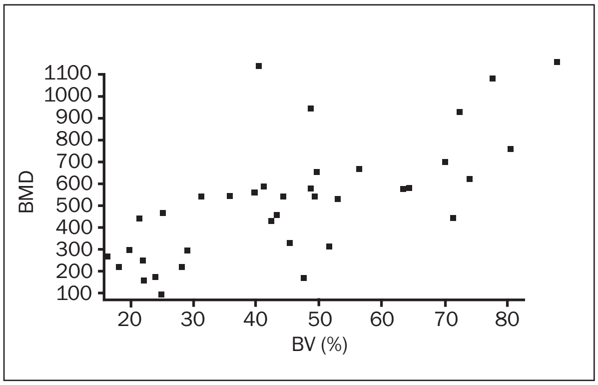

Fig 3 Scatterplot of the data points for all biopsy specimens.

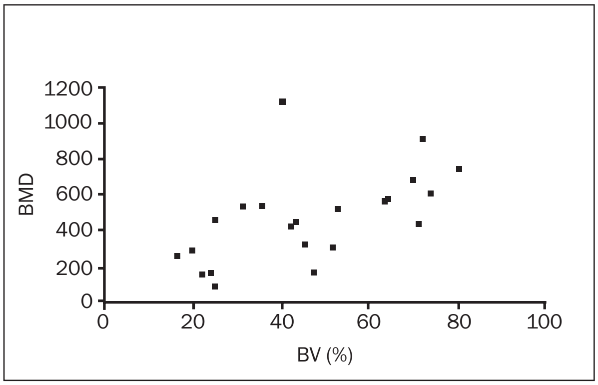

Fig 4 Scatterplot of the interindividual data points; 1 biopsy specimen per patient, selected at random, was used.

Table 1 Summary of Histomorphometric and Radiographic Data

	BV (%)	BMD
Mean	45.624	513.17
SD	19.728	271.76
SE	3.243	44.677
Minimum	16.510	89.570
Maximum	88.010	1148.3
Median	44.500	535.88

Data for 37 samples shown.

Table 2 Mean BMD and BV in Different Regions

	BMD (HU)		BV (%)	
Region	Mean	SD	Mean	SD
Maxilla				
Anterior	399	211	45.50	19.99
Premolar	433	114	33.83	10.92
Molar	246	128	30.62	14.08
Mandible				
Anterior	890	331	48.49	11.25
Premolar	709	232	58.05	12.79
Molar	571	234	56.75	21.27

the density values in the mandible were almost double those in the corresponding areas of the maxilla. Moreover, the highest values in the mouth were found in the anterior and premolar regions of the mandible; the lowest values were found in the molar region of the maxilla.

DISCUSSION

In implant therapy, bone density assessment has always been one of the most important parameters for predicting long-term success. Currently this topic is fundamental in the protocols for early and immediate loading. Bone density can influence implant surface and shape (eg, threads and anatomy) chosen and the length of the healing period.[6]

Bone quality classification according to Lekholm and Zarb[1] is not clinically estimable; however, Misch[6] has suggested evaluating bone quality using manual perception during implant site preparation.

Unfortunately, the subjective evaluation of bone density with any classification system is a limitation of any protocol, both in clinical studies and in routine clinical practice. Since there is interoperator variability in manual bone quality assessment during implant site preparation, bone density data assessed using this system will always be approximate. Trisi and Rao[7] demonstrated that D4 bone could be distinguished from all other types using manual perception, but the method failed to assess the intermediate levels of bone density. This means that a more objective and reliable method is needed for both routine clinical practice and clinical research studies.

QCT is able to measure true volumetric density 3-dimensionally. It has been mainly used to study the cancellous bone properties of the vertebral bone owing to its ability to distinguish between cortical and cancellous bone. QCT has proven to be more sensitive than dual-energy x-ray absorptiometry in discriminating between vertebral fracture and bone loss.[11,12] Even though it is a good tool for measurement of vertebral cancellous bone in cases of osteoporosis and fracture, its high cost and higher radiation dose may limit its use.

Although the use of QCT for the evaluation of bone quality in preoperative implant planning has been evaluated in several studies,[9,13,14] a correlation has never been made between QCT recordings and histomorphometric findings. In a study by Norton and Gamble,[9] the relationship between manual perception of bone quality and HU values, HU values (mean ±SD) of 951 ± 209, 706 ± 275, 657 ± 281, and 463 ± 290 were found for bone of types I, II, III, and IV, respectively.

In the present study, a comparison between bone density evaluated using QCT and the histologic structure of tissue removed from the implant sites was attempted. Since the results were obtained using a single brand of CT scanner (Toshiba) of the many commercially available, and since this scanner may have differed from other available tools, the BMD technique was used to transform the original values into the more universal BMD values using a phantom. The CT density measurements were compared to standard known x-ray values, which allowed standardization of the values of each single CT machine to compare the bone density values to each other objectively. The resulting data were defined as BMD values.

In the present study, multiple measurements were made within the same subject, which biased statistical independence. For this reason, it was possible that the correlation between the BMD and the BV within the same subject would be different than the correlation observed between different subjects. For this reason, an unbiased analysis of interindividual correlation was calculated by randomly selecting one sample from each subject. The difference between the unbiased interindividual correlation and the overall sample correlation was almost irrelevant (0.699 versus 0.706), which demonstrated that bias in the statistical independence caused by multiple measurements within the same subject was not a problem in this instance.

The statistical correlation between BMD values and the histomorphometric evaluation of the BV was quite high. This implies that the CT measurement of the bone density is related to its histologic structure, defined by the percentage of mineralized bone per unit volume (BV). These results are in accordance with the data gathered from a similar previous study, which showed good correlation between the histometric bone parameters and the QCT values in different skeletal sites.[15]

However, the strength of the correlation found in the present study was not very high, since r^2 was 0.4286, which explains that only 42.86% of the variance in BMD was explained by the model. This means that not all the variance in the histologic BV was seen under the QCT examination, most likely because of the resolution limits of the CT scan, which cannot convey true trabecular bone thickness. Standard CT scanning has been suggested as a useful tool for measurement of the bone structure, but pixel size is a major limitation of this technique. At best, a pixel is 200 to 300 µm[16] wide, while the mean size of the trabeculae in cancellous bone is around 100 µm. Thus, CT is not able to detect fine bone structure correctly.[17] Another explanation could be related to the 2-dimensional nature of the histometric measurements, as compared to the 3-dimensional nature of the CT scan.

In a recent study[18] which compared the histometric bone structure measured by the 3-dimensional micro-CT to that measured by multi-slice spiral CT or single-slice CT a higher correlation (r^2 = 0.84) was also shown with the maximum compressive strength of the bone sample.

Bone volume has been related significantly to bone-implant contact (BIC), which has been shown to be related to the removal torque of the implant.[19] It may now be possible to predict, from the preoperative CT scan, not only the height and width of the bone, but also its quality, which has been shown to be a strong predictor of implant success and failure.[3] It appears possible to achieve higher values of BIC[20–24] and superior resistance to reverse torque removal[25–28] using an implant with a rough surface, such as a coated, abrasive blasted, acid-etched, blasted, or etched surface. It seems to be very important to define the bone density prior to placement for successful immediate loading, as primary stability and the control of micromovement appear to be crucial to the prediction of success in these procedures.

Esposito's literature review on implant failure[29] confirmed the general trend of maxilla to have almost 3 times more implant losses than the mandible for early and late failures. The maxilla tends to have insufficient bone volume; deficient bone quality and overload were the major determinants for the late failures. A higher failure rate was also reported in the posterior segments of both jaws, which has been explained by differences in the bone type and quality and the loading conditions in these locations.[30]

Precise knowledge of the bone structure for treatment planning could permit the definition of the bone density limit for an immediate loading protocol, once all other variables have been defined. Among these other variables, the height and width of the bone must be considered, since it has been shown that placing longer implants improves the success rate[31,32]; the number and position of the implants also appears to affect success.[29,30] The possibility of controlling the amount of load in the early loading period has been suggested to reduce the risks of failure in soft bone.[33]

Using this technique for the analysis of the bone quality, it may be possible to accurately describe bone quality limits for a reasonable prognosis in adopting the surgical and prosthetic protocols. This could reliably result in improved success in the more challenging situations of low bone density and reduce the healing time in the more predictable clinical cases of high bone density.

QCT is an established method for measurement of BMD and provides quantitative data regarding trabecular and cortical bone. Furthermore, in investigating an implant site, the oral surgeon requires information on BV, topography, and relation to important anatomic structures. However, adoption of these techniques into routine practice might lead to a significant increase in the radiation burden of the patient without a proper risk-benefit analysis. Clinicians should decide, on the basis of the clinical examination and treatment planning, whether QCT will be of benefit. Conventional tomography in such circumstances results in significantly lower radiation doses and may therefore be preferred.[34] A limited number of slices can be obtained with conventional tomography, while a scanning of a complete jaw has to be done with CT.

Considering the importance of bone density in some surgical and prosthetic implant protocols, there is a clear need for developing objective assessment techniques of this parameter. However, clinicians should have specific reasons in mind when they request QCT or any radiologic procedure, as it is important to choose a method that will minimize the amount of radiation exposure.

CONCLUSIONS

The present study showed a statistically significant correlation between histologically measured bone density and the radiographic bone density as measured by CT. CT scan evaluation of the bone density may be a good tool with which to evaluate bone density in the preoperative treatment planning of complex cases. Moreover, the quantitative approach of CT scan evaluation of bone quality may be extremely helpful in understanding the implications of bone quality in implant success and failure rates.

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