HISTOMORPHOMETRIC AND BONE DENSITOMETRIC ANALYSIS OF DENTAL IMPLANT SITES.

by

RANIA LIVADA

MICHAEL S. REDDY, COMMITTEE CHAIR
NICOLAAS GEURS
MARIA L. GEISINGER
PHILIP J. VASSILOPOULOS.

A THESIS

Submitted to the graduate faculty of The University of Alabama at Birmingham, in partial fulfillment of the requirements for the degree of Master of Science

BIRMINGHAM, ALABAMA

2009
HISTOMORPHOMETRIC AND BONE DENSITOMETRIC ANALYSIS OF DENTAL IMPLANT SITES.

RANIA LIVADA

MASTERS IN CLINICAL DENTISTRY

ABSTRACT

Purpose: The purpose of this study was to assess bone density at implant sites by four types of means: a) clinical measurements b) radiographic measurements c) histological measurements d) measurements from micro-computed tomography scan of the bone biopsies obtained and find if there is a correlation between these measurements. Materials and Methods: 28 patients that underwent dental implant surgery were included in this study. Subjective bone density measurements based on the tactile sense of the surgeon were obtained during drilling of the implant bed and compared with radiographic measurements of bone density in Hounsfield Units obtained with a cone beam computed tomography (CT) scan analysis. During implant surgery a bone biopsy was obtained that was subsequently analyzed histologically and scanned with a micro-CT machine in order to determine bone density. These different measurements of bone density were subsequently analyzed statistically to determine the degree of correlation between them. Results: There was a significant association between the clinician’s pre-surgical assessment of bone density as that was recorded prior to implant surgery with the clinician’s clinical assessment of bone density as that was measured during drilling of the recipient bone (Table 1). Although repeated radiographic measurements of bone density were highly
correlated and reproducible (Table 2), no association was found between them and the other bone density measurements (Table 1). In conclusion, no association was found between clinical, radiographical, histological and micro – CT measurements of bone density. **Conclusions:** While the use of a classification scale is widely used in clinical practice today, these subjective assessments of bone density are of limited value, as according to these data, a surgeon cannot classify bone density accurately, based only on his tactile sense. Also the use of a CT scan in diagnosis and treatment planning is very accurate and valuable; however its use in measuring bone density is not accurate in reflecting the actual histomorphometric image of the bone.

Keywords: bone density, bone quality, Hounsfield units, dental implants.
DEDICATION

I dedicate this thesis to my loving parents Renos and Daphne Livada. Without your unconditional love, support and encouragement I would not be where I am today.

Also this thesis is dedicated to the memory of my beloved Grandmother, who is not here today to see me achieve my dreams; not a day goes by that I don’t love and miss her.
ACKNOWLEDGEMENTS

I would like to express my sincere appreciation and thanks to my mentor Dr. Michael Reddy for all of his help, guidance and valuable advice throughout this research study. I would also like to thank Drs. Maria Geisinger, Nicolaas Geurs and Philip Vassilopoulos who served as my committee members and provided me with valuable input, guidance and encouragement during the course of my thesis work.

I am also grateful for the help and support from Dr. Kevin Sims and Mrs. Sandre McNeal.

This work would not have been possible without the help of the Orthopedic Research Lab and Mrs. Patty Lott, Dr Wang and all of the other staff members. Special thanks also go to Dr. Johnson and Dr. Li from the UAB Small Animal Phenotypic Core as well as to Mr. Nate Powell and Mr. Ty Primm for their support with my research endeavor.

Finally I would like to recognize the faculty members of the Department of Periodontics, of the University of Alabama, School Of Dentistry for their mentorship over the course of my studies.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>iii</td>
</tr>
<tr>
<td>DEDICATION</td>
<td>v</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>vi</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>ix</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>x</td>
</tr>
<tr>
<td>LIST OF ABBREVIATIONS</td>
<td>xii</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>Importance of Bone Quality.</td>
<td>2</td>
</tr>
<tr>
<td>Etiology of Variable Bone Density</td>
<td>3</td>
</tr>
<tr>
<td>Classification of Bone Quality:</td>
<td>5</td>
</tr>
<tr>
<td>Evaluation of bone quality</td>
<td>8</td>
</tr>
<tr>
<td>DENTAL IMPLANT SITE IMAGING</td>
<td>8</td>
</tr>
<tr>
<td>Computed Tomography (CT)</td>
<td>9</td>
</tr>
<tr>
<td>Cone Beam Computed Tomography (CBCT)</td>
<td>10</td>
</tr>
<tr>
<td>Micro – computed tomography</td>
<td>14</td>
</tr>
<tr>
<td>HYPOTHESIS AND SPECIFIC AIMS OF RESEARCH STUDY:</td>
<td>16</td>
</tr>
<tr>
<td>MATERIALS AND METHODS:</td>
<td>17</td>
</tr>
<tr>
<td>Type of Data Obtained During Research Study</td>
<td>18</td>
</tr>
<tr>
<td>Statistical Analysis</td>
<td>38</td>
</tr>
<tr>
<td>RESULTS</td>
<td>38</td>
</tr>
<tr>
<td>DISCUSSION</td>
<td>41</td>
</tr>
</tbody>
</table>
## LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1 Results of statistical analysis examining the degree of association between the different parameters of bone density</td>
<td>39</td>
</tr>
<tr>
<td>Table 2 Results of statistical analysis examining the degree of association between repeated radiographic measurements of bone density</td>
<td>40</td>
</tr>
<tr>
<td>Figure</td>
<td>Page</td>
</tr>
<tr>
<td>----------</td>
<td>------</td>
</tr>
<tr>
<td>Figure 1 CT Scan image screen shot</td>
<td>18</td>
</tr>
<tr>
<td>Figure 2 Edentulous area #10</td>
<td>19</td>
</tr>
<tr>
<td>Figure 3 3-D image from CT software with virtual implant in edentulous area</td>
<td>19</td>
</tr>
<tr>
<td>Figure 4 Bone density measurements in HU from CT software</td>
<td>20</td>
</tr>
<tr>
<td>Figure 5 Pre-operative view of edentulous area #10</td>
<td>21</td>
</tr>
<tr>
<td>Figure 6 Intra-operative view of edentulous area #10</td>
<td>22</td>
</tr>
<tr>
<td>Figure 7 Bone biopsy harvested with trephine</td>
<td>22</td>
</tr>
<tr>
<td>Figure 8 3-D model matching position and angulation of trephine used</td>
<td>23</td>
</tr>
<tr>
<td>Figure 9 Surgical guide was used to verify position and angulation</td>
<td>24</td>
</tr>
<tr>
<td>Figure 10 Bone biopsy harvested with surgical trephine</td>
<td>24</td>
</tr>
<tr>
<td>Figure 11 Implant placed in area #10</td>
<td>25</td>
</tr>
<tr>
<td>Figure 12 Post-operative radiograph of implant in area #10</td>
<td>26</td>
</tr>
<tr>
<td>Figure 13 Bone biopsy within trephine immediately after harvesting</td>
<td>27</td>
</tr>
<tr>
<td>Figure 14 Bone biopsy placed in 10% neutral buffered formalin</td>
<td>27</td>
</tr>
<tr>
<td>Figure 15 Bone biopsy extracted from trephine</td>
<td>27</td>
</tr>
<tr>
<td>Figure 16 Plastic cassettes used to place bone biopsies during dehydration</td>
<td>28</td>
</tr>
<tr>
<td>Figure 17 Embedded bone biopsies on pre-polymerized bases</td>
<td>28</td>
</tr>
<tr>
<td>Figure 18 Embedded bone biopsies on pre-polymerized bases</td>
<td>29</td>
</tr>
<tr>
<td>Figure 19 Outline of the whole bone core with blue color (2x)</td>
<td>30</td>
</tr>
<tr>
<td>Figure 20 Outline of bone with yellow color (10x)</td>
<td>31</td>
</tr>
</tbody>
</table>
Figure 21 Outline of connective soft tissue with green color (10x) ........................................... 31

Figure 22 Outline of bone graft with red color (10x) ..................................................................... 32

Figure 23 Paragon stain 20x-depicting very clearly bone, bone graft and soft tissue. .......... 33

Figure 24 Von Kossa stain (2x) ........................................................................................................ 34

Figure 25 Bone under polarized light microscopy (4x). ................................................................. 36

Figure 26 3-D view of bone biopsy as produced with the Micro-CT scan............................... 37
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAT</td>
<td>Computerized Axial Transverse</td>
</tr>
<tr>
<td>CBCT</td>
<td>Cone Beam Computed Tomography</td>
</tr>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>IIT</td>
<td>Image Intensifier Tube</td>
</tr>
<tr>
<td>FPI</td>
<td>Flat Panel Imager</td>
</tr>
<tr>
<td>HU</td>
<td>Hounsfield Units</td>
</tr>
<tr>
<td>µ-CT</td>
<td>Micro – computed Tomography</td>
</tr>
<tr>
<td>FE</td>
<td>Finite Element</td>
</tr>
<tr>
<td>BV/TV</td>
<td>Bone Volume</td>
</tr>
<tr>
<td>Tb.Th</td>
<td>Trabecular Thickness</td>
</tr>
<tr>
<td>Tb.Sp</td>
<td>Trabecular Separation</td>
</tr>
</tbody>
</table>
INTRODUCTION

Dental implants have been a popular alternative in the oral rehabilitation after the introduction of osseointegration by Branemark in 1985. Osseointegration refers to the direct implant to bone contact at the light microscopic level.

Based on the healing response of bone leading to osseointegration, a desired type of anchorage of the endosseous part of dental implants can predictably be obtained. The nature of this bone – to- implant relationship is obviously capable of supporting the loads resulting from forces exerted onto the implant – borne suprastructures.

In addition, under standard clinical conditions a stable and competent soft tissue seal is established during the phase of tissue integration at the part of the implant penetrating the tissues and extending into the oral cavity. This soft tissue seal comprises an epithelial attachment and a connective tissue adaptation to the neck portion of the implant. A stable mechanical seal is thus provided by these tissues along with their capacity to mount a competent immunologic reaction to the microbial challenge occurring at the marginal area of the implant.

An understanding of the factors crucial for obtaining stable and lasting tissue integration of functional implants is important in order to obtain long term success. The successful outcome of any implant procedure depends on a variety of patient-related factors (general health, behavioral and environment influences such as oral hygiene habits, smoking habits) and procedure-dependent parameters, including the health of the implant
site, the implant system and type of implant chosen, biocompatibility of the implant material, the features of the implant surface, the surgical procedure and skills of the surgeon, the level of infection control during placement as well as the quality and quantity of the local bone at the recipient site.

During treatment planning, the clinician is faced with the challenge of making the right decisions for rendering implant success to an individual patient. In order to do so, the clinician has to be able to obtain all pertinent information regarding the patient and the recipient implant site (such as the amount and density of local bone). Unfortunately up to date there are not any scientifically proven diagnostic - non invasive tools or methods to determine bone density prior to implant surgery.

Importance of Bone Quality.

Multiple independent groups have reported higher failure rates in poor – quality bone compared with higher – quality bone:

1. Following a standard surgical and prosthetic protocol, Adell et al (1981) reported a nearly 10% greater success rate in the anterior mandible compared with the anterior maxilla.

2. Schnitman et al (1988) also noted lower success in the posterior mandible compared with the anterior mandible following the same protocol.

In general, the anterior mandible has greater bone density than the anterior maxilla. The posterior mandible has poorer bone density than the anterior mandible. The poorest bone quality in the oral cavity typically exists in the posterior maxilla and is associated with dramatic failure rates as the following studies showed:
1. Engquist et al (1988) reported a high percentage (78%) of all clinical failures were when implants were placed in soft bone types (type IV).

2. Jaffin and Berman (1991) reported a 44% failure when poor density was observed in the maxilla, with the majority of failures noted at second-stage surgery. Their study documented a 35% implant loss in any region of the mouth when bone density was poor.

3. Johns et al (1992) reported a 3% failure in type III bone but a 28% failure in type IV bone.

4. Friberg et al (1991) observed that 66% of their group’s implant failures occurred in the maxilla with soft bone. They reported that the reduced implant survival most often is related to bone density than location.

In general, clinical reports have indicated a higher survival rate for dental implants in the mandible as compared with the maxilla, particularly in the anterior region of the mandible, which has been related to better volume and density of the bone. Clinical studies have also indicated that the highest failure rate encountered in the posterior region of the maxilla is attributed to the fact that this region frequently lacks adequate volume and/or density of bone.

Etiology of Variable Bone Density

In bones there are two different types of bone tissue: The first type is cortical or compact bone, which is a low porosity solid material, mainly found in the shaft of long bones and it comprises the outer part of the maxilla and mandible. The second type is tra-
trabecular bone. It has a complex three-dimensional structure consisting of struts and plates and is mainly found near joint surfaces, at the end of long bones, within vertebrae and it comprises the inner part of the maxilla and the mandible. Cortical and trabecular bone throughout the body is modified constantly by modeling or remodeling. These phenomena have been associated with the alteration of the mechanical stress and strain environment within the host bone.

Already in 1892 Wolff found that the orientation of trabeculae coincides with the direction of the stress trajectories. He proposed that bone loading is somehow sensed and that the bone adapts its structure accordingly. This principle of functional adaptation is generally known as ‘Wolff’s Law’ (Wolff, 1892). It occurs in conditions of disuse, such as during immobility, space flight and long term bed rest, when bone is lost and in overloading which causes a gain in bone mass. It also occurs in growth, when the refined trabecular bone in childhood is changed to coarser trabecular morphology in maturity, after fracture healing and in relation with implant incorporation.

The ability of bone to adapt to mechanical loads is brought about by continuous bone resorption and bone formation. If these processes occur at different locations, the bone morphology is altered. Frost defined this as modeling (Frost, 1990a).

In a homeostatic equilibrium resorption and formation are balanced. In that case old bone is continuously replaced by new tissue. This ensures that the mechanical integrity of the bone is maintained but it causes no global changes in morphology. Frost defined this as remodeling (Frost, 1990b). The modeling and remodeling processes are conducted by specialized bone-resorbing and bone-forming cells, called osteoclasts and osteoblasts respectively.
A number of research studies over the years confirmed and expanded Wolff’s theories. Overall today it is believed that modeling and remodeling are controlled primarily, in part or whole, by the mechanical environment of microstrain and that bone density is a result of the bone’s response to microstrain. A series of clinical studies also confirm this:

1. MacMillan\textsuperscript{13} (1926) and Parfitt\textsuperscript{14} (1962) noted that the bone is most dense around the teeth (cribriform plate) and denser around the teeth at the crest compared with the regions around the apices.

2. Neufeld\textsuperscript{15} (1958) reported that generalized trabecular bone loss in the jaws occurs in regions around a tooth from a decrease in mechanical strain.

3. Similarly Orban\textsuperscript{16} (1953) demonstrated a decrease in the trabecular bone pattern around a maxillary molar with no opposing occlusion, compared with a tooth with occlusal contacts on the contralateral side.

Another fact supporting this is that bone density is usually decreased after tooth loss. The density decrease in the jaws is related to the length of the time the region has been edentulous and not loaded appropriately, the original density of the bone, muscle attachments, flexure and torsion in the mandible, parafunction before and after tooth loss, hormonal influences and systemic conditions.

Classification of Bone Quality:

\textbf{Bone quality} is a collective term referring to the mechanical properties, architecture, degree of mineralization of the bone matrix, and chemistry and structure of the bone mineral crystals as well as the remodeling properties of the bone.
The importance of bone density and its relation to dental implants was noted since the 1970s when Linkow and Chercheve classified bone density into 3 categories:

1. Class I bone structure: this ideal bone type consists of evenly spaced trabeculae with small cancellated spaces.

2. Class II bone structure: the bone has slightly larger cancellated spaces with less uniformity of the osseous pattern.

3. Class III bone structure; large marrow – filled spaces exist between bone trabeculae.

Linkow and Chercheve stated that Class III results in a loose – fitting implant, Class II bone was satisfactory for implants; and Class I bone was a very satisfactory foundation for implant prostheses.

However, the most popular conventional bone quality classification with four different types was proposed by Lekholm and Zarb (1985) which was based on the amount of cortical versus cancellous bone as this was observed on a pantograph film. According to them:

1. Type 1 bone: consists almost of homogenous compact bone;

2. Type 2 bone has a thick layer of compact bone which surrounds a core of dense trabecular bone;

3. Type 3 bone has a thin layer of cortical bone which surrounds a core of dense trabecular bone; and

4. Type 4 bone is characterized as a thin layer of cortical bone surrounding a core of low density trabecular bone of poor strength.
Another popular classification was proposed by Misch in 1988. He related bone density to the clinical hardness of the bone as subjectively perceived during drilling prior to implant placement. According to that:

1. D1 bone is primarily dense cortical bone.
2. D2 bone has dense-to-thick porous cortical bone on the crest and within coarse trabecular bone.
3. D3 has a thinner porous cortical crest and fine trabecular bone.
4. D4 bone has almost no crestal cortical bone. The fine trabecular bone composes almost all of the total volume of bone next to the implant.
5. D5 is very soft bone, with incomplete mineralization – immature bone.

Also in order to communicate more broadly to the dentists the tactile sense of the different bone densities, Misch compared the different bone densities with different materials. He stated that:

1. Drilling and placing implants into D1 bone is similar to drilling into oak or maple wood.
   - D2 bone is similar to the tactile sensation of drilling into white pine or spruce.
   - D3 bone is similar to drilling into balsa wood.
   - D4 is similar to drilling into Styrofoam.

However, this analogy to the different types of bone is not helpful in the clinical practice of dentistry.

In the clinical setting of dental implant placement, there is a quantitative and qualitative difference in bone density between patients and between different areas of the oral cavity in the same patient. This innate characteristic of our patients, has led clini-
cians over the years to the use of various modalities, in an attempt to classify and even predict the quality of bone of individual patients.

Evaluation of bone quality

The means currently available to the clinicians for evaluation of the patient’s bone density are:

1. Radiographs: Radiographic examination only allows clinicians to crudely evaluate the bone quality of the edentulous site. Computer tomography (CT) offers the best radiographic method for the morphological and qualitative analysis of the residual bone.

2. Tactile perception: Clinically, bone density is evaluated by tactile perception during the preparation of the implant site. However, this method is very subjective and cannot be standardized between different clinicians.

3. Histological analysis: It is considered the best biologic method for evaluating the density of a bone sample. However, this approach is not applicable to the clinical practice of implant dentistry as the histomorphometric analysis is tedious and time consuming.

DENTAL IMPLANT SITE IMAGING

In 1972 Godfrey Hounsfield presented a novel imaging technique referred to as computerized axial transverse (CAT) scanning. Since then, there has been a rapid evo-
olution in radiology imaging types and techniques – especially the ones used for medical
and most recently for oral and maxillofacial purposes.

Oral implant imaging can involve 3 distinct imaging modalities: conventional
spiral tomography, spiral multislice Computed Tomography, and Cone Beam Computed
Tomography (CBCT). Their superiority in implant imaging over plain radiographs is at-
tributable to their ability to produce cross-sectional images along the arches. These im-
ages provide details of bone morphology and bone dimensions, as well as the locations
of vital structures \(^{21,22}\) – all of which are critical for implant planning. Although CT scans
have been available for medical use since 1973, it was not until 1987 that this innovative
technology became available for dental application.

In 1987, Schwarz \(^{23}\) introduced the concept of using computerized tomography
(CT) scans for pre-operative quantitative assessment of patients requiring dental implant
treatment and since then, the use of CT in the patients requiring implant therapy has con-
tinued to grow.

**Computed Tomography (CT)**

In CT implant imaging, multiple thin axial slices are obtained through the jaws,
and then the data are reformatted with special software packages to produce cross-
sectional and panoramic views. Computer software is also available to analyze the CT
scans and to help in planning implant placement with electronically simulated fixtures.

The advantages of CT-based systems are (1) uniform magnification; (2) a high-
contrast image with a well defined image layer free of blurring; (3) easier identification
of bone grafts or hydroxyapatite materials used to augment maxillary bone in the sinus
region than with conventional tomography; (4) multiplanar views; (5) 3-dimensional reconstruction; (6) simultaneous study of multiple implant sites; and (7) the availability of software for image analysis.

The disadvantages of CT include (1) limited availability of reconstructive software; (2) expense; (3) higher doses of radiation compared with conventional tomography; (4) lack of understanding of the dentist’s imaging needs by the radiologic technologists and medical radiologists who acquire and interpret the CT images; and (5) lack of usefulness for implant-interface follow-up because of metallic streak artifacts.

Computed tomography can be divided into 2 categories based on acquisition x-ray beam geometry; namely: fan beam and cone beam tomography.

**Cone Beam Computed Tomography (CBCT)**

In this research study all of the Computed Tomography scans were taken with an i-CAT™ Cone Beam CT Scan machine. (Imaging Sciences International).

The cone-beam technique involves a single 360° scan in which the x-ray source and a reciprocating area detector synchronously move around the patient’s head, which is stabilized with a head holder. At certain degree intervals, single projection images, known as “basis” images, are acquired. Software programs incorporating sophisticated algorithms including back-filtered projection are applied to these image data to generate a 3D volumetric data set, which can be used to provide primary reconstruction images in 3 orthogonal planes (axial, sagittal, and coronal).

Most CBCT units for maxillofacial applications use an image intensifier tube (IIT)–charge-coupled device. Recently a system employing a flat panel imager (FPI) was
released (i-CAT™). The FPI consists of a cesium iodide scintillator applied to a thin film transistor made of amorphous silicon. Images produced with an IIT generally result in more noise than images from an FPI and also need to be preprocessed to reduce geometric distortions inherent in the detector configuration.24

The use of CBCT technology in clinical practice provides a number of potential advantages for maxillofacial imaging compared with conventional CT:

1. X-ray beam limitation: Reducing the size of the irradiated area by collimation of the primary x-ray beam to the area of interest minimizes the radiation dose. Most CBCT units can be adjusted to scan small regions for specific diagnostic tasks. Others are capable of scanning the entire craniofacial complex when necessary.

2. Rapid scan time: Because CBCT acquires all basis images in a single rotation, scan time is rapid (10–70 seconds) and comparable with that of medical spiral CT systems.

3. Dose reduction: Published reports indicate that the effective dose of radiation (average range 36.9–50.3 [µSv])25 is significantly reduced by up to 98% compared with “conventional” fan-beam CT systems (average range for mandible 1,320–3,324 µSv; average range for maxilla 1,031–1,420 µSv).26 This reduces the effective patient dose to approximately that of a film-based periapical survey of the dentition (13–100 µSv)27 or 4–15 times that of a single panoramic radiograph (2.9–11 µSv).28 Some machines—for example, Classic i-CAT—make use of pulsating x-ray emission, which further reduces the radiation dose.29 In this mode, x-ray emission is paused when the detector transfers signals to the computer.
4. Image accuracy: The volumetric data set comprises a 3D block of smaller cuboid structures, known as voxels, each representing a specific degree of x-ray absorption. The size of these voxels determines the resolution of the image. In conventional CT, the voxels are anisotropic — rectangular cubes where the longest dimension of the voxel is the axial slice thickness and is determined by slice pitch, a function of gantry motion. Although CT voxel surfaces can be as small as 0.625 mm square, their depth is usually in the order of 1–2 mm. All CBCT units provide voxel resolutions that are isotropic — equal in all 3 dimensions. This produces submillimeter resolution (often exceeding the highest grade multi-slice CT) ranging from 0.4 mm to as low as 0.125 mm.

5. Reduced image artifact: With manufacturers’ artifact suppression algorithms and increasing number of projections, our clinical experience has shown that CBCT images can result in a low level of metal artifact, particularly in secondary reconstructions designed for viewing the teeth and jaws.

6. Display modes unique to maxillofacial imaging: Access and interaction with medical CT data are not possible as workstations are required. Although such data can be “converted” and imported into proprietary programs for use on personal computers, this process is expensive and requires an intermediary stage that can extend the diagnostic phase. Reconstruction of CBCT data is performed natively by a personal computer. In addition, software can be made available to the user, not just the radiologist, from various vendors. This provides the clinician with the opportunity to use chair-side image display, real-time analysis of the patient’s scan.
Currently computed tomography (CT) is the only readily clinically available imaging technique that allows at least rough conclusions about the structure and density of the jawbones. It is an excellent tool for assessing the quantity of available bone in areas of the oral cavity.

In addition, bone density can be estimated using Hounsfield Units with the help of CT software programs. This method has been used since the late 1990s in an effort to facilitate the classification of bone density. Lacan and Terman\textsuperscript{30} in 1999 reported a new classification as that was determined by Hounsfield Units (HU): very dense cortical bone (>600 HU); dense cortical-spongy bone (between 400 and 600 HU), cortical-spongy bone of low density (<200 HU).

Hounsfield Units are directly related to tissue attenuation coefficients. Each individual element of the CT image is called a voxel and has a value, expressed in Hounsfield units, that describes the density of the CT image at that point. In general, the higher the CT number, the denser the tissue is.

\textit{Hounsfield Units.}\textsuperscript{31} The Hounsfield scale is based on density values for air, water and dense bone, which are assigned arbitrarily values of -1000, 0, and +1000 respectively. The images, which are reconstructed by the algorithm of the CT scanner, are not given by the attenuation coefficients for each point in the volume but by the CT number which is expressed in Hounsfield Units (HU). The HU of a material A are calculated with this formula:\textsuperscript{32}

\[
HU_A = \frac{\mu_A - \mu_{H_2O}}{\mu_{H_2O}} \cdot 1000
\]
Where $\mu_A$ represents the linear attenuation coefficient of material A and $\mu_{\text{H}_2\text{O}}$ represents the linear attenuation coefficient of water. With this definition, the HU of air and water are respectively -1000 and 0.

**Micro-computed tomography**

Until recently, readily available CT equipment was not useful during laboratory investigations of small samples, mainly because of limitations in spatial resolution. Recent technical advances such as the Micro-Computed Tomography (\(\mu\)CT) have made it practical to obtain such high-resolution CT images of small-specimens and animals during research investigations.

Micro-computed tomography uses analysis of x-rays to create cross-sections of a 3-D object that later can be used to recreate 3-D models without destroying the original sample. The term *micro* is used to indicate that the pixel sizes of the cross sections are in the micrometer range.

Since its introduction by Feldkamp\(^3\)\(^3\) (1989) \(\mu\)CT has become an important tool to quantify the morphometry of the trabecular structure of bone biopsy specimens of humans and of whole bones of small animals like rats or mice. It has become a technique that replaces or augments histological analysis, with a major advantage being that it does not interfere with any additional anatomical or mechanical study on fresh or fixed tissue. Other advantages of \(\mu\)CT except from being a non-destructive method of analyzing and quantifying bone volume are: that is a fast and easy to perform procedure; the areas of interest can be isolated and imaged independently and it can also provide 3 dimensional
images of the scanned tissue. In addition, μCT provides the possibility to set up finite element (FE) models to determine the strength and stiffness of the bone sample based solely on the trabecular architecture.\textsuperscript{34}

Some of the disadvantages of the μCT are: a) the large amount of electronic data that needs to be stored b) difficulty with living tissue as there may be possible damage to DNA with the x-ray doses required for the scanning and c) the information given by scanning is at the supracellular level and it cannot be used to obtain information about the cellular bone-healing response.

A number of studies have validated the accuracy of μCT. Comparison with histology showed relative small to rather high deviations in 2D morphometric parameters depending on scan resolution and especially on which segmentation method was used.\textsuperscript{35} In another study Chappard\textsuperscript{36} et al (2005) comparing bone measurements with histomorphometry and μCT, noted that correlations between all parameters \{(Bone volume (BV/TV), Trabecular thickness (Tb.Th), and trabecular separation (Tb.Sp))\} were highly significant, but μCT overestimated bone volume. They suggested that overestimation may have been caused by a double threshold used in micro-CT, giving trabecular boundaries less well defined than on histological sections.

In a similar study design Thomsen\textsuperscript{37} (2005) compared bone structural measurements obtained from 3D micro-CT data sets with those obtained by histological sections using human tibial bone biopsies. Their study revealed high correlations between measures of bone structure obtained from conventional 2D sections and 3D micro-CT data. They concluded that 3D micro-CT data sets can be used as a substitute for conventional histological sections for bone structural evaluations.
HYPOTHESIS AND SPECIFIC AIMS OF RESEARCH STUDY:

The purpose of this study is to assess bone density at the implant sites by four types of means: a) clinical measurements b) radiographic measurements with the help of a cone beam computed tomography (CT) scan c) histological measurements from histomorphometric analysis of the bone biopsies d) measurements from micro – computed tomography (micro – CT) scan of the bone biopsies obtained and find if there is a correlation between these measurements.

The hypothesis was that:

- There is a significant correlation between clinical, radiographic, histological and micro – computed tomography data of bone density.

The aims of the study were to help answer specific questions such as:

1. Does the pre-surgical assessment of the clinicians correlate with their clinical assessment of bone density during surgery?
2. Does the clinical assessment of bone density correlate with the histological and the micro-CT analysis of the bone biopsy taken during surgery?
3. Does the clinical assessment of bone density correlate with the radiographic measurements obtained by the patient’s CT scan analysis?
4. Does the radiographic measurement of bone density correlate with the histological and micro – CT analysis of the bone biopsy taken during surgery?
MATERIALS AND METHODS:

This study was approved by the Institutional Review Board of the University of Birmingham in Alabama (UAB) (protocol number X081007004.)

A total of 28 patients that fulfilled the inclusion criteria were selected and included in the research study.

The inclusion criteria were:

1. Patients at least 19 years of age that are able to read and understand written English without the aid of ad hoc interpretation and they are able to consent for their own inclusion in the study.

2. Patients of any race or ethnicity.

3. Patients that have existing treatment plans for implant therapy (could be either partially or completely edentulous)

4. Patients with an existing Cone Beam CT scan (performed as part of their pre-surgical work-up).

5. Patients may have bone grafting procedures of any type prior to implant placement and at least 12 weeks must have elapsed since bone grafting surgery.

The exclusion criteria were:

1. Women who self-reported pregnancy.
Type of Data Obtained During Research Study

A. Radiographic Data:

All patients received an initial CT scan at the treatment planning appointment with an i-CAT™ Cone Beam CT Scan machine. (Imaging Sciences International). The scanning conditions (tube voltage 120 kVp, tube current: 3-8 mA (pulse mode), focal spot: 0.5 mm, voxel size: 0.4 mm (typical), image acquisition: single 360 degree rotation, scan time: 20 seconds.)

In case that a patient had a bone grafting procedure prior to implant placement, then a second CT scan was taken within the last month prior to the implant surgery. Axial, cross-sectional and coronal images for both the maxilla and the mandible were obtained for every patient.

The CT scans were analyzed with Facilitate™ Pro software (Astra Tech Dental) prior to the implant surgeries as shown in Figure 1.

![Figure 1 CT Scan image screen shot](image-url)
With the help of the software, a virtual implant was placed in the edentulous area at the desired position and angulation as the actual implant. (Figure 2 and 3)

![Figure 2 Edentulous area #10](image1)

![Figure 3 3-D image from CT software with virtual implant in edentulous area.](image2)
The virtual implant’s dimensions were 2 mm (width) and 6 mm (length) in order to match and replicate the dimensions of the trephine used and the bone biopsy obtained during implant surgery. The software was then asked to calculate the density of the bone within each virtual implant and the measurements given were expressed in Hounsfield Units (Figure 4). In order to verify the accuracy of results, repeated measurements were taken.

Figure 4 Bone density measurements in HU from CT software
In addition, by random coin toss the virtual implant was moved (from the ideal position) 1mm either to the mesial or distal, or buccal – lingual and a separate bone density measurement was taken for that patient. Later these “modified” measurements were compared with the “ideal” ones for accuracy and association.

B. Clinical Data:

All the implant surgeries were performed at the Periodontal Clinic at UAB and at the private office of a part – time faculty (limited to periodontics and implants) by experienced surgeons (experience ranged from 8-20 years). All surgeons were Board Certified periodontists. The oral examination, treatment planning, surgical procedures and post – operative follow up were performed by the treating surgeon on the same patient. Implant surgeries were performed according to standard surgical procedure and the implant manufacturer’s protocol (Figure 5 and 6).
Instead of using the standard 2 mm twist drill for the initial osteotomy, the surgeon used a 2mm diameter trephine bur (ACE Surgical Supply, Inc.) with external irrigation to harvest the bone biopsy from the future implant site (Figure 7 and 8).
The diameter of the trephine of the bur was always smaller than the diameter of the final drill used in the surgical protocol. In this way, it was possible to place the implants with primary stability. A study by Klinge et al. (1995) showed that implant preparation by trephine burs is a safe method of preparing the implant bed and that this type of surgical procedure does not affect the short term implant survival rate.

A surgical guide was used to verify the correct position and angulation of the implant in order to replicate the position and angulation of the virtual implant placed with the help of the CT software. (Figure 9)
Figure 9 Surgical guide was used to verify position and angulation.

Bone biopsy was harvested (Figure 10) from one only site from each patient (regardless of the number of implants the patient got). In case of multiple potential sites on one patient, the surgeon selected from where the bone biopsy would be obtained; based on the preoperative assessment of the patient’s CT scan as well as his clinical assessment for the most ”convenient site”. During surgery, clinical photos and radiographs were taken.

Figure 10 Bone biopsy harvested with surgical trephine
Prior and during implant surgery specific measurements were taken by the operating surgeon:

1. Pre-surgical assessment of bone density was recorded prior to implant surgery and was based on the Lekholm and Zarb classification.

2. Clinical assessment of bone density was recorded during bone drilling and was based on the Misch classification. (A modified Misch classification was used that included categories D1 –D4).

In addition, several other data were recorded for each patient such as: age, gender, race, smoking status, implant site number, bone grafting history (date, type and quantity of bone graft used), length and width of implant placed.

In order to decrease the variability in the data, only one type of dental implants was used in the study – Nobel Active™ (Nobel Biocare USA).(Figure 11 and 12)

Figure 11 Implant placed in area #10.
Figure 12 Post-operative radiograph of implant in area #10

C. Histological Data:

The retrieved bone biopsies along with the trephines were immediately placed in 10% neutral buffered formalin solution for fixation where they remained for at least 48 hours for fixation (Figure 13 and 14). A buffered solution is preferred as it prevents acidity, which would promote autolysis, causing precipitation of formol-heme pigment in the tissues.
Figure 13 Bone biopsy within trephine immediately after harvesting

Figure 14 Bone biopsy placed in 10% neutral buffered formalin

After fixation, the bone samples were carefully extracted from the trephines (Figure 15) placed in plastic tissue cassettes and processed for dehydration (Figure 16).

Figure 15 Bone biopsy extracted from trephine.
Dehydration follows fixation, and its goal is to remove all the water contained within the specimen to allow uniform penetration of the acrylic resin. It was achieved by processing the samples through alcohol solution of increasing concentration. Then the samples were transferred into Methylmethacrylate (MMA), (Fisher Scientific). Infiltrating solution was 95:5, MMA vs. n-Butyl Phthalate (Fisher Scientific) under vacuum, and finally, embedded in MMA embedding solution (95:5, MMA vs. n-Butyl Phthalate and 0.25% Perkadox) at room temperature. The blocks were allowed to polymerize, then trimmed and placed on pre-polymerized bases (Figure 17-18).
Embedding in plastic provides many advantages in hard-tissue histology. Using a sliding or heavy-duty rotary microtome, thin sections (several microns in thickness) can be made because of the better support given by the media to cellular components. When choosing a plastic-embedding medium, the goal is to match the hardness of the embedding medium to the hardness of the bone or cartilage in order to produce successful sections.

Eight-micron longitudinal thin sections were cut at the mid-line of the block, using a Leica 2265 microtome. Serial sections were chosen for Paragon staining and for Von Kossa staining for histomorphometric analysis under brightfield and polarized light microscopy.

**Histomorphometric analysis.** Histomorphometric analysis of bone biopsies provides quantitative information about bone volume, density and architecture. The histologic analysis was considered the “gold standard” for measuring bone density in this study. All the samples were analyzed to evaluate:

a) bone volume (measured as % of bone/total area)

b) volume of any remaining graft particles and

c) volume of connective soft tissue.
The histomorphometry was performed using the Bioquant ® Image Analysis Software. (Bioquant R & M Diagnostics, Nashville, TN). Sections with Paragon and von Kossa stains were both viewed by one observer.

The template involved outlining of the entire tissue section stained with Paragon stain at low magnification (2x) as shown in Figure 19 and then filling in the outline of the various tissue types with different colors at a higher magnification (10x)(Figures 19-22).

![Figure 19 Outline of the whole bone core with blue color (2x)](image-url)
Figure 20 Outline of bone with yellow color (10x)

Figure 21 Outline of connective soft tissue with green color (10x)
The computer then analyzed for area of each tissue type, and quantified the bone volume per total volume (BV/TV), as well as the percentage of bone, bone graft and fibrous connective tissue per total tissue area. The sum of the percentage of bone and bone graft was considered the percentage of mineralized tissue of the sample and was recorded as the histologic bone density of the sample.

The histomorphometric analysis requires the correct identification of the various tissue types prior to the outlining and analyzing of the included area. To verify the accuracy of the results, the sections were stained with two different types of stains and both were analyzed under brightfield microscopy and with circular polarized light microscopy.

- **Paragon stain.** Consists of toluidine blue, basic fuchsin and ethyl alcohol. It stained the different tissue types different shades of pink and purple. With in-
creased magnification (up to 20x) the characteristics of every tissue type were clearly seen and identified correctly (Figure 23).

**Figure 23 Paragon stain 20x-depicting very clearly bone, bone graft and soft tissue.**

- **Von Kossa stain.** The von Kossa stain works by substituting a silver ion for calcium in the tissue section, which appears dark black with brightfield illumination, after reduction with a strong light. It stains calcium phosphate and calcium carbonate- found in mineralized tissue- by binding the silver ion with the negative
phosphate or carbonate portion. This makes a new silver salt that we see as black thus creating an excellent contrast to the remaining –non mineralized tissue that stains brown to light yellow (as in the case of connective tissue and demineralized bone graft material). (Figure 24).

Figure 24 Von Kossa stain (2x)

- **Polarized light microscopy.** At the microscopic level, bone can be divided into two distinct types: woven and lamellar bone. In woven or immature bone, the collagen fibers are arranged randomly in a meshwork pattern. In lamellar bone, the collagen fibers are arranged in parallel sheets and bundles, and the orientation of collagen fibers alternates between successive lamellae. Orientation of collagen fi-
bers is typically evaluated based on the birefringence of bone under polarized light. Under polarized light, osteons with longitudinally oriented collagen fibers appear dark, whereas those with transversely oriented fibers appear bright.

In a linear polarizing light microscope, normal light is first passed through a polarizing filter and then through the microscope stage onto a similar filter. This filter is called an analyzer and has a transmission axis that rotates to form a 90° angle with the polarizer. If no specimen is present between the polarizer and the analyzer, no light can pass though the cross-polars to the eye piece. This point is called the angle of extinction. However, if a birefringence material is placed between the cross-polars, the light interacts with the molecular organization of the material. The light undergoes a phase shift or causes a rotation of the electromagnetic vector, which vibrates in a plane different from its original polarization. The material then becomes visible at the eyepiece.

In this research study circularly polarized light microscopy was used; its difference is that it does not produce the characteristic extinction angle points but, instead, illuminates all of the fibers nearly equally, regardless of their orientation. With the help of the polarized light, clear identification of the illuminate bone was achieved versus the remaining tissue types (soft tissue, bone graft) that appeared dark under the microscope. (Figure 25)
Prior to histomorphometric analysis, the embedded in MMA bone cores were sent to the “UAB Small Animal Phenotyping Core” where they were scanned using a “Scanco µCT 40” machine at an 8 µm resolution. Samples were marked to maintain orientation and were scanned longitudinally.

Scanning of the bone biopsies measured bone density expressed in mg HA/ mm³. Also it produced 3- dimensional (3-D) images of the bone biopsies architecture (Figure 26).

D. Micro – computed tomography data:
Micro-computed tomography (µCT) uses analysis of x-rays to create cross-sections of a 3-D object that later can be used to recreate 3-D models without destroying the original sample. The term *micro* is used to indicate that the pixel sizes of the cross sections are in the micrometer range.

For micro tomography, x-ray scanners typically use 2 methods for scanning; Fan beam reconstruction or Cone beam reconstruction.

The machine used in the present study was a Desktop Cone-Beam Micro-CT Scanner (This means the system is based on a 2-dimensional x-ray detector (camera) and an electronic x-ray source, creating projection images that subsequently were being used to reconstruct the image cross-sections).\textsuperscript{40} The “Scanco µCT 40” achieves the highest resolution.
Statistical Analysis.

Analyses of variance (ANOVAs) were used as well as Chi-squares. In the end, multiple regression analyses were used to adjust for potential confounders such as age, race, gender and smoking status. All statistical analysis was performed using SAS v9.2 (Cary, NC).

The statistical analysis of results helped answer the specific questions we posed in the beginning of the research study.

RESULTS:

The total sample consisted of 28 patients (13 males and 15 females) with an age of range of 19 -82 years at the time of implant placement. Out of 28 patients, 23 were Caucasians, 4 were African American and 1 was Hispanic.

The sample also included 20 non-smoker patients, 5 currently smoking and 3 former smokers (they had recently quitted). Out of the total of 28 implant sites included in the study, 12 were in the maxilla and 16 were found in the mandible.

The radiographical, clinical, histological and micro – computed tomography data were recorded and analyzed statistically as shown below: (Table 1 and 2).
**Table 1** Results of statistical analysis examining the degree of association between the different parameters of bone density

<table>
<thead>
<tr>
<th>Data type 1</th>
<th>Data type 2</th>
<th>P – value</th>
<th>r-value</th>
<th>Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preclinical assessment of bone density</td>
<td>Clinical assessment of bone density</td>
<td>0.0027</td>
<td></td>
<td>Highly correlated.</td>
</tr>
<tr>
<td>Clinical assessment of bone density</td>
<td>Histological assessment of bone density</td>
<td>0.5414</td>
<td></td>
<td>No association found</td>
</tr>
<tr>
<td>Clinical assessment of bone density</td>
<td>Micro – CT assessment of bone density</td>
<td>0.9920</td>
<td></td>
<td>No association found</td>
</tr>
<tr>
<td>Clinical assessment of bone density</td>
<td>Radiographical Assessment of bone density</td>
<td>0.9034</td>
<td></td>
<td>No association found</td>
</tr>
<tr>
<td>Radiographical Assessment of bone density</td>
<td>Histological assessment of bone density</td>
<td>0.6405</td>
<td>0.09</td>
<td>No association found</td>
</tr>
<tr>
<td>Radiographical Assessment of bone density</td>
<td>Micro – CT assessment of bone density</td>
<td>0.7816</td>
<td>-0.02</td>
<td>No association found</td>
</tr>
</tbody>
</table>
The aforementioned results remained the same, even after adjusting for possible confounders such as age, gender, race and smoking status.

According to the statistical analysis, there was a significant association between the clinician’s pre-surgical assessment of bone density as that was recorded prior to implant surgery with the clinician’s clinical assessment of bone density as that was measured during drilling of the recipient bone (Table 1). However, no significant association was found between clinical, radiographical, histological and micro–CT measurements of bone density (Table 1).

Repeated radiographic measurements of bone density were performed during the CT scan analysis. In addition by random coin toss the virtual implant was moved (from the ideal position) 1mm either to the mesial or distal, or buccal – lingual and a separate bone density measurement was taken for that patient. The comparison and association of these “modified” measurements with the “ideal” ones are shown in table 2 below:

Table 2 Results of statistical analysis examining the degree of association between repeated radiographic measurements of bone density

<table>
<thead>
<tr>
<th>“Ideal” measurements of bone density. (mean)</th>
<th>“Modified” measurement of bone density. (mean)</th>
<th>P-value</th>
<th>R-value</th>
<th>Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>552.62 HU</td>
<td>563.10 HU</td>
<td>&lt;0.0001</td>
<td>0.98</td>
<td>Highly correlated.</td>
</tr>
</tbody>
</table>
According to the statistical analysis, repeated radiographic measurements of bone density on the patient’s CT scans were highly correlated and reproducible. However, no association was found between them and the other bone density measurements as shown in Table 1.

DISCUSSION

According to the data, the hypothesis posed in the beginning of the research study that “there is a significant correlation between clinical, radiographic, histological and micro – computed tomography data of bone density” is rejected. The null hypothesis that “there is not any significant correlation between clinical, radiographic, histological and micro - CT data of bone density” is accepted.

In this study no significant association was found between the clinician’s tactile sense of bone density with the histological analysis of the bone biopsies taken. According to our data, in the clinical practice of dentistry a surgeon cannot classify bone density accurately, based only on his tactile sense.

In the literature one other study evaluated the correlation of the hand clinical assessment of the bone quality to the histologic structure as it was quantified by histomorphometric evaluation of the bone biopsy. Trisi & Rao in 1999 harvested small bone biopsies from 56 patients during dental implant surgery, and utilized them for histomorphometric evaluation. The bone quality was recorded during drilling of the implant bed, based on the hand-felt perception of the drilling resistance and scored based on the Misch
classification. It was found that the D1 and D4 classes had the highest and lowest histomorphometric density, respectively, while D2 and D3 presented similar densities. Also this study demonstrated that hand feeling allows distinguishing, with statistically significant confidence of D1 and D4 bone, but failed to distinguish between the intermediate classes of bone quality.

According to them a clinician could differentiate between the highest and lowest density (D1 vs. D4) but could not differentiate between the other classes. (D1 vs. D2 / D2 vs. D3 etc) Therefore, in clinical practice, tactile perception allows us to classify the bone quality into three categories: soft, normal and dense bone.

Based on the findings of the previous study and this study we can conclude that:

- The clinical assessments of bone density are of limited value.

Previous studies showed that in general, the anterior mandible has greater bone density than the anterior maxilla. The posterior mandible has poorer bone density than the anterior mandible. The poorest bone quality in the oral cavity typically exists in the posterior maxilla. However, this may vary in the individual patients. For example, in this study, the highest bone density was measured in the anterior maxilla, leading to the assumption that the generalizations about the distributions of bone density may not always be accurate. It would be great if we could repeatedly and accurately predict the patient’s bone density so we can treatment plan accordingly using reliable, objective methods. Especially now, with the advent of CT technology and the associate software, clinicians may have a tool in their hands to assess bone quality at the implant sites. However, ac-
cording to this study, while the bone density measurements on the patient’s CT scans are highly repeatable and reproducible, they are not accurate in reflecting the actual histomorphometric image of the bone.

In the literature there is one other study evaluating the association between the bone density measurements obtained with the CT scan and the ones obtained by histological analysis of the bone biopsies. Todisco and Trisi in 2005 used 18 patients undergoing implant placement. The results of their study showed that there was a statistically significant relationship between the bone volume (calculated from the histomorphometric analysis) and the bone density values (obtained by measuring the Hounsfield units from the CT) and they supported the use of computer tomography to assess the bone quality before implant placement to improve the planning of implant treatment.

In contrast to their study, in this study no significant correlation between the radiographic bone densities with the histological analysis of the bone biopsies was found.

**Conclusion:**

According to our data there is not a significant association between clinical, radiographical, histological and micro – CT data of bone density.

A great limitation of this study was the small sample of patients (28) that were included. Further studies should be done with a much greater sample of patients in order to exclude with certainty any association between the aforementioned parameters.
CLINICAL APPLICATIONS OF RESULTS:

Within the limits of this study we can suggest that:

- The classification of bone density has been used widely in clinical practice and in research. However, these subjective assessments of bone density are of limited value, as according to these data, a surgeon cannot classify bone density accurately, based only on his tactile sense. While, this classification may be important in assessment of individual patients, its use in research data and as modifying factor in treatment plans and patient care may not be accurate.

- The use of CT scan in diagnosis and treatment planning is valuable and very accurate. While the bone density measurements on the patient’s CT scans are highly repeatable and reproducible, they are not accurate in reflecting the actual histomorphometric image of the bone.
REFERENCES


APPENDIX A

IRB APPROVAL FORM
UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office for Human Research Protections (OHRP). The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56 and ICH GCP Guidelines. The Assurance became effective on November 24, 2003 and expires on October 26, 2010. The Assurance number is FWA00005960.

Principal Investigator: LIVADA, RANIA
Co-Investigator(s): GEISINGER, MARIA
REDDY, MICHAEL S
VASSILOPOULOS, PHILIP J
GEURS, NICOLAAS
SIMS, KEVIN M

Protocol Number: X081007004
Protocol Title: Correlation of Subjective Bone Density Observations with Radiographic and Histological Data

The IRB reviewed and approved the above named project on 10/4/08. The review was conducted in accordance with UAB’s Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

This project received EXPEDITED review.
IRB Approval Date: 10-4-08
Date IRB Approval Issued: 10/4/08

Marilyn Doss, M.A.
Vice Chair of the Institutional Review Board for Human Use (IRB)

Investigators please note:

The IRB approved consent form used in the study must contain the IRB approval date and expiration date.

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.