The Ability of Bone Mineral Density and Microstructural Indices to Reflect Mechanical Properties of Trabecular Bone
The Ability of Bone Mineral Density and Microstructural Indices to Reflect Mechanical Properties of Trabecular Bone

by
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- ABSTRACT -

The Ability of Bone Mineral Density and Microstructural Indices to Reflect Mechanical Properties of Trabecular Bone

**Purpose:** The goals of this experimental study were to (1) apply high-resolution imaging techniques (micro-CT imaging) in combination with new computer modeling techniques (FEA) to quantify 3D microstructural and biomechanical properties of trabecular bone in the intertrochanteric region (2) investigate contribution of bone mineral density (BMD) and microstructure of trabecular bone to predicting its mechanical property, i.e., elastic modulus, and (3) determine if the prediction of bone elastic constant can be improved when BMD is combined with any one structural index, or the structural indices are associated each other as independent variable.

**Materials and Methods:** Total 15 trabecular bone core specimens were obtained from the proximal femurs with patients undergoing to total hip arthroplasty. BMD of all bone cores was measured using PIXIImus2 densitometer. A high-resolution micro-computed tomography (micro-CT) was used to scan each specimen to obtain histomorphology. Microstructural parameters such as bone volume fraction (BV/TV), trabecular number (Tb.Th), trabecular separation (Tb.Sp) were directly calculated from the 2-D and 3-D datasets, and then the hexahedron mesh models were created.
Micro-finite element analysis was performed to derive indices of mechanical properties of trabecular bone. The multiple relationships among BMD, structural parameters and mechanical indices were assessed using linear regression analyses. A p value < 0.05 was considered to be significant.

**Results:** Linear regression analysis showed that the BV/TV was the best predictor for Young’s modulus (R²=0.758, p<0.001), as well as BMD (R²=0.752, p<0.001). The structure model index (SMI), Tb.Sp and Tb.N could well explain the variance of Young’s modulus by 51%, 42% and 39%, respectively. If BMD is supplemented with any of the examined structural indices there is a clear improvement for predicting Young’s moduli. Likewise, the ability to explain variance of Young’s modulus is improved by combining the structural indices each other.

**Conclusion:** A combination of microstructural parameters each other or with bone mineral measurements could provide the best prediction of mechanical property of cancellous bone. Therefore, as regards detection of osteoporosis and evaluation of the efficacy of drug treatments for osteoporosis, BMD measurement should be supplemented with assessment of bone microarchitecture in vivo.

**Key Words:** Bone mineral density; Microstructure; Mechanical properties; Finite element analysis.
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ABBREVIATION

µCT: microcomputed tomography
FEA: finite element analysis
BMD: bone mineral density
Tb.Th: trabecular thickness
BV/TV: bone volume fraction
DOA: degree of anisotropy
SMI: structure model index
Tb.N: trabecular number
E: Young’s modulus (elastic modulus)
I. INTRODUCTION

Osteoporotic hip fracture is the worst complication in osteoporosis, resulting in significant morbidity and mortality (Riggs and Melton, 1995). Numerous studies have been performed to examine the potential causes and risk factors for fractures of the proximal femur. Despite significant associations between hip fracture and both low bone mass and falling, especially falls to the side (Cooper et al., 1987; Cummings, 1985; Lotz and Hayes, 1990), neither bone mass nor falling are sufficient to definitively categorize who will sustain a fracture. Previous work has shown that fracture patients as a whole may have lower bone mass than controls, but there is still substantial overlap in measurements between groups (Reckoff, 1993). Other studies demonstrated no differences in bone mineral content of the femoral neck (Bohr and Schaadt, 1983) or femoral head (Wicks et al., 1982) between patients with femoral neck fracture and healthy age-matched controls. In addition, it is estimated that 90% of hip fractures result from a fall, but only 5% of falls result in a hip fracture (Greenspan et al., 1994). Thus it seems evident that factors other than bone mass and falls are important to hip fracture risk. It has been shown that the trabecular microarchitecture is closely associated with biomechanically determined bone strength, which has a substantial effect on fracture risk (Chevalier et al., 1992; Cooper, 1993; Dempster et al., 1993; Vesterby et al., 1991). Therefore, the idea with respect to “microstructural deterioration” of trabecular bone was include into the
current definition of osteoporosis by the World Health Organization (WHO).

In the past, several investigators have tried to relate the biomechanical properties of trabecular bone to mineral density and structural changes (Goulet et al, 1994; Turner, 1990). A few limitations in these studies should be noted. First, the BMD as measured by dual x-ray absorptiometry (DXA) in predisposed fracture sites is most common used method in clinical practice. However, because it provides only a 2-D image of apparent density, its ability to assess early fracture risk is limited. Moreover, DEXA cannot differentiate trabecular from cortical bone. This is unfortunate since the effects of bone loss are more prevalent in trabecular bone due to its much higher surface area, and because the greater amount of bone mineral content in cortical bone can conceal small changes in trabecular bone. Second, traditionally, trabecular structure has been assessed using two-dimensional (2D) analysis of histomorphometry sections obtained from iliac crest biopsies (Recker, 1993; Hordon and Peacock, 1990; Uitewaal et al., 1987). While measures of trabecular number and thickness can be quantified from histological sections, the anisotropy of trabecular orientation, the plate- or rod-like structure and connectivity of trabecular bone, which is a three-dimensional (3D) quantity, cannot be determined. These 3-D structures are likely to play an important role in determining bone strength. In addition, the ilium is commonly used in bone histomorphometry studies since this site lends itself most conveniently for biopsy and samples can therefore be obtained from a greater number of subjects. However, it has been suggested that a substantial heterogeneity of microstructural properties exists among various skeletal sites (Amling et al., 1996;
Hildebrand et al., 1999; Goldstein, 1987), and that this heterogeneity also applies to
different regions within the same bone (Issever et al., 2002; thomsen et al., 2002).
The use of an iliac model to study osteoporotic fracture has been questioned. To
determine if architecture has a role in osteoporotic fracture, systematic, regionally
specific three-dimensional architectural measurements made at the site of the high
fracture risk are needed. Third, the mechanical properties of excised bone cubes were
usually determined from compression test of mechanical experiment. This direct
assessment of the mechanical properties of cancellous bone from experiments is
subject to large errors and significant uncertainties, mostly due to the small samle
sizes and the relatively large length scales of the inhomogeneities. As a result,
mechanical load-frame measurements are very sensitive to the amount of friction
between the sample and the load platens and depend significantly on the size and
shape of the sample. A further complication is that mechanical tests are unable to
distinguish between variations in bone architecture and variations in tissue modulus.
Thereby, unexplained variation remained, and the relationships found between
different studies were not the same. The precise relationship between density,
structure, and mechanical properties is still under investigation.

Recently, high-resolution microcomputed tomography (µCT) reconstruction of
trabecular bone has been introduced that allow assessment of the bone
microarchitecture in three dimensions (Hildebrand et al., 1999; Muller et al., 1998).
With these techniques, the microstructure of the bone is reconstructed in a computer
by stacking the images in a 3D voxel grid. The 3D voxel grid can be used to assess
structural indices characterizing the 3D microarchitecture of cancellous bone. Furthermore, the voxel matrix can be used as input for microstructural finite element analysis (µFEA) models. These µFEA can be used to simulate real mechanical tests for eliminating experimental artifacts and to evaluate the elastic properties of trabecular bone specimens (van Rietbergen et al., 1995).

Thus, with reference to the discussion above, the goals of this experimental study therefore were to (1) apply high-resolution imaging techniques in combination with new computer modeling techniques to quantify 3D microstructural and biomechanical properties of trabecular bone in the intertrochanteric region (2) investigate contribution of bone mineral density and microstructure of trabecular bone to predicting its mechanical property, i.e., elastic modulus, and (3) determine if the prediction of bone elastic constant can be improved when BMD is combined with any one structural index, or the structural indices are associated each other as independent variable.
Ⅱ. MATERIALS AND METHODS

A. Materials:

Specimens Preparation

Trabecular bone core samples were obtained from 15 patients (6 male, 9 female) undergoing total hip arthroplasty. There were 6 male (55.3 ± 13.4 years) and 9 female (65.3 ± 16.7 years) with a mean age of 60.1 ± 15.5 years, in which indications for the surgery were 8 patients with femoral neck fracture, 7 patients with femoral head osteonecrosis.

The specimens were obtained according to the method described by Matthews et al. (Fazzalari et al., 1998; Matthews et al., 1992). A 10 mm internal diameter cylindrical saw was used to take the bone core biopsy of the intertrochanteric region of the femur. The cylindrical saw was directed down the shaft of the femur so that the biopsy was taken in line with the femoral medullary canal (Fig. 1). The removed specimen was wrapped in saline wet tape and put into tube plastic, the proximal site of bone cores marked by marking pen. All of specimens were stored in bone bank with -70°C.
Fig. 1. A 10 mm tube saw used to biopsy the intertrochanteric region of the proximal femur. A plain X-ray image of biopsy specimen is also shown.

B. Methods:

1. Bone mineral density measurements

Specimens for BMD measurement were thawed at room temperature for 24 hours. Bone mineral density (BMD) of all 19 bone cores was measured using PIXImus2 densitometer (PIXImus™ Series; GE LUNAR, Madison, WI, USA) with 80/35 X-ray source, beam current 500µA, and scan resolution 0.18 × 0.18 mm, specifically designed for small animals. To ensure clinical integrity of the PIXImus, calibration of the instrument was conducted using a quality control phantom (BMD=0.669g/cm2 and %Fat=11.8%) provided by the manufacturer. The specimens were scanned in the core longitudinal axis matched with phantom body axis, where proximal site of bone
cores were corresponding with phantom head. The scanned image was analyzed with the PIXImus software provided by the manufacturer. A rectangular region of interest with 10mm length and 5mm width in each bone cores was manually defined at 4 mm level below the inner border of proximal cortical bone. The mean of the BMD value were calculated from three scans in same location. All measurements and analyses were performed by one investigator (Dr. Cui). The accuracy of BMD measurements by PIXImus was assessed from six trabecular bone cores with three times repositions. The intraoperator variability for the PIXImus facility used was less than 2%. The triplicate determinations of the six bone cores, with repositioning, showed a 0.0042 of standard deviation and CV of 4.2%.

2. Bone Micro-morphometry

All specimens were scanned with a high-resolution micro-computed tomography (µCT) system (Skyscan 1072, Belgium) at a spatial resolution of 21.31µm (Voxel dimension) (Ruegsegger et al., 1996). For each bone core, a total of 1024 consecutive microtomographic slices were acquired. From the resulting voxel data, a rectangular volume of interest with a resolution of 85 µm was selected at a side length of 5mm and height of 10mm, which was matched with the location and size of ROI as measured by BMD. To limit the computational requirements of the FE analyses, the µCT voxel data were resampled at an isotropic size of 85 µm prior to converting the three-dimensional bone volume directly into hexahedron-based FE meshes. Bone tissue was segmented from marrow using a global thresholding procedure. After
scanning, 2D image data was transferred to a workstation, and 3D reconstruction was made (Muller and Ruegsegger, 1997). With the µ-CT scanner’s built-in software, the following three-dimensional structural parameters were calculated, including relative bone volume (BV/TV), trabecular number (Tb.N), thickness (Tb.Th) and separation (Tb.Sp), structure model index (SMI), and degree of anisotropy. Structural indices were assessed from the 3D µCT images using direct structural analysis techniques. Tb.Th, Tb.Sp and Tb.N were assessed using the distance transformation method described by Hildebrand et al. (Hildebrand and Ruegsegger, 1997), i.e. Tb.Th was calculated as the mean diameter of spheres filling the trabecular structure, while similarly Tb.Sp was calculated as the mean diameter of spheres filling the marrow phase. Inversing the mean diameter of spheres filling the skeletonized structure resulted in the Tb.N. The Structure Model Index (SMI), a parameter describing the general shape of the structure, was calculated using the method described by Hildebrand and Ruegsegger (Hildebrand and Ruegsegger, 1997). BV (bone volume) is calculated from a surface generated by a triangle meshing technique based on the Marching Cubes method (Lorensen and Cline, 1987). Total tissue volume was the volume of the entire scanned sample. The normalized indices, trabecular bone volume fraction (BV/TV) were then calculated from these values. The degree of anisotropy (DA) was determined from the ratio between the maximal and minimal radii of the mean intercept length (MIL) ellipsoid (Harrigan and Mann, 1984).
3. Finite Element Analysis

The segmented reconstructions of the VOI were converted to μFE models by converting the voxels (size 85 × 85 × 85um) that represent bone tissue to equally shaped 8-node brick elements using (a mass-compensated) hexahedron meshing technique (Fig. 2) (Ulrich et al., 1998).

Fig. 2. 3D reconstruction image, imaged-based 3D mesh model and micro-FE image.

The specified threshold level is chosen such that the best possible agreement between the BV/TV in the FE-model during conversion course. For the coarser FE-models, this thresholding procedure caused a loss of trabecular connections which resulted in unconnected bone parts which were removed because they do not contribute to stiffness. For all models, the element material properties were considered to be isotropic, linear elastic, and uniform with a tissue Young’s modulus of 10 Gpa and a tissue Poisson’s ratio of 0.3. Boundary conditions of the FE model
were applied to represent the situation in a compressive-test setup with 1%-strain level, in which at the bottom face the displacements in the z-direction were constrained, all other faces of the cube were unconstrained (Fig. 3). The FE-problems for the hexahedron models were solved with a special-purpose solver (van Rietbergen et al., 1995). Hence, the cube is in a state of uniaxial stress at the apparent level. The apparent Young’s modulus in the z-direction for the specimen as a whole was calculated from the formula \( E_z = \frac{\dot{\sigma}_z}{C_z} \), where \( \dot{\sigma}_z \) is the apparent stress and \( C_z \) the apparent strain in the z-direction. The apparent stress was calculated from \( \dot{\sigma}_z = F_r / (h_x h_y) \), where \( F_r \) is the total reaction force at the top face, \( h_x \) and \( h_y \) represent the external dimensions of the cube in the x-and y-direction, respectively (Fig. 3). The apparent Young’s modulus was calculated for the compressive-test model only.

**Fig. 3. The simulated compression-test model.** The 1% strain was applied at the top face while displacements were constrained at the bottom face, but only in the direction perpendicular to this face.
4. Statistical analysis

All statistical computations were processed with SPSS 8.0 software. Results were expressed as average ± SD. The distribution of each parameter value was examined. All values are shown as mean ± SD. Relationships between the biomechanical measure, and trabecular structure parameters, as well as BMD were assessed using linear regression and two-tailed t-tests of significance. Furthermore, a stepwise multiple-regression model was used to determine the combined effect of density and microstructural indices on predicting the biomechanical properties (elastic moduli.) of the specimens. The determination coefficients ($r^2$) were used to express the proportional variation due to linear or multiple regressions. A p value<0.05 was considered to be significant.
III. RESULTS

2D and 3D reconstruction images of samples with different age stages from μCT showed different microstructure patterns, as presented in Fig. 4 and Fig. 5. With aging, some trabeculae are lost, resulting in reduction of bone mass and structural changes, and plate-like trabeculae are perforated toward rod-like structure.

Fig. 4. 2D tomographic images extracted from consecutive microtomographic slices of micro-CT in the same location of samples.
Fig. 5. 3D micro-CT reconstruction images of four samples with aging from human cancellous bone of intertrochanteric area.

The descriptive statistics of BMD, 3D structural and mechanical parameters are presented in Table 1. The specimens included in this study ranged in BMD from 0.05 to 0.19 g/cm². The values of structural parameters ranged in bone volume fraction from 5.73 to 25.5%, degree of anisotropy from 0.10 to 0.37, structure model index from 1.03 to 2.1. The trabecular thickness varied from 0.10 to 0.20 mm and had a separation of 0.53-1.32 mm. Frequency distribution plots of the various BMD, structural and mechanical measures are not shown in Figure.
Table 1. Basic descriptive statistics of BMD, the structural and mechanical parameters of the data.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>n</th>
<th>Mean</th>
<th>S.D.</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>15</td>
<td>61.4</td>
<td>16.4</td>
<td>63</td>
<td>31–89</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>15</td>
<td>0.13</td>
<td>0.05</td>
<td>0.15</td>
<td>0.05–0.19</td>
</tr>
<tr>
<td>Tb.Th (mm)</td>
<td>15</td>
<td>0.15</td>
<td>0.03</td>
<td>0.15</td>
<td>0.10–0.20</td>
</tr>
<tr>
<td>Tb.Sp (mm)</td>
<td>15</td>
<td>0.72</td>
<td>0.22</td>
<td>0.69</td>
<td>0.41–1.32</td>
</tr>
<tr>
<td>BV/TV (%)</td>
<td>15</td>
<td>17.1</td>
<td>6.39</td>
<td>16.78</td>
<td>5.73–30.5</td>
</tr>
<tr>
<td>DOA</td>
<td>15</td>
<td>0.26</td>
<td>0.10</td>
<td>0.26</td>
<td>0.06–0.43</td>
</tr>
<tr>
<td>SMI</td>
<td>15</td>
<td>1.55</td>
<td>0.34</td>
<td>1.67</td>
<td>1.03–2.10</td>
</tr>
<tr>
<td>Tb.N (/mm)</td>
<td>15</td>
<td>1.21</td>
<td>0.27</td>
<td>1.23</td>
<td>0.69–1.77</td>
</tr>
<tr>
<td>E. (Gpa)</td>
<td>15</td>
<td>0.37</td>
<td>0.25</td>
<td>0.37</td>
<td>0.01–0.87</td>
</tr>
</tbody>
</table>

The determination coefficients from the linear analyses between Young’s modulus and BMD/microstructural parameters are summarized in Table 2, detailed in Fig.6. Linear regression analysis showed that the BMD and BV/TV were equally good as the best predictors for the Young’s modulus, both of which could strongly explain 75% and 76% of the variance of Young’s modulus, respectively ($r^2=0.75$, $r^2=0.76$, Table II, Fig. 6). Other structural parameters, Tb.Sp, SMI, and Tb.N could well also explain the variance of Young’s modulus by 42%, 51%, and 39%, respectively. No significant relationship was found between the Tb.Th or the DOA and the Young’s modulus, whereas Tb.Th or DOA added to BMD or combined with SMI and other structural indices could improve to explain for Young’s modulus clearly, reaching values of between 46% and 75%, as shown in Table 2.
Table 2. $R^2$ values of the linear regression analyses between BMD, the structural indices and the Young’s modulus.

<table>
<thead>
<tr>
<th></th>
<th>BMD</th>
<th>Tb.Th</th>
<th>Tb.Sp</th>
<th>BV/TV</th>
<th>DOA</th>
<th>SMI</th>
<th>Tb.N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young’s</td>
<td>0.75</td>
<td>0.16</td>
<td>-0.42</td>
<td>0.76</td>
<td>0.20</td>
<td>0.51</td>
<td>0.39</td>
</tr>
<tr>
<td>P value</td>
<td>0.0002</td>
<td>0.135</td>
<td>0.009</td>
<td>0.0002</td>
<td>0.096</td>
<td>0.003</td>
<td>0.012</td>
</tr>
</tbody>
</table>

P value < 0.05 is considered to be significant.
Fig. 6. Regression coefficients between BMD/structural indices and Young's modulus.
Likewise, if BMD is supplemented with any of the examined structural indices there is a clear increase in the $r^2$ values for the Young’s moduli of the samples, reaching values of between 75% and 79%, as shown in Table 3. The ability to explain variance of Young’s modulus is improved by combining the structural indices each other (Table 4). The best prediction of Young modulus is found in combination of SMI, Tb.N and Tb.Th ($r^2=0.80$), as shown in (Table 5).

Table 3. The determination coefficients $R^2$ of stepwise multiple-regression analyses between BMD combined with any of structural indices and Young’s modulus.

<table>
<thead>
<tr>
<th></th>
<th>BMD Tb.Th</th>
<th>BMD Tb.Sp</th>
<th>BMD BV/TV</th>
<th>BMD DOA</th>
<th>BMD SMI</th>
<th>BMD Tb.N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young’s</td>
<td>75.2%</td>
<td>75.4%</td>
<td>79%</td>
<td>75.3%</td>
<td>77.9%</td>
<td>76%</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.005</td>
<td>&lt;0.005</td>
<td>0.0001</td>
<td>0.0002</td>
<td>0.0001</td>
<td>0.005</td>
</tr>
</tbody>
</table>

P value <0.05 is considered to be significant.

Table 4. Regression coefficients between two structural indices together and Young’s modulus.

<table>
<thead>
<tr>
<th></th>
<th>Tb.Th</th>
<th>Tb.Sp</th>
<th>DOA</th>
<th>SMI</th>
<th>Tb.N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tb.Th</td>
<td>/</td>
<td>0.56 *</td>
<td>0.26</td>
<td>0.65 **</td>
<td>0.66 **</td>
</tr>
<tr>
<td>Tb.Sp</td>
<td>0.56 *</td>
<td>/</td>
<td>0.46 *</td>
<td>0.60 **</td>
<td>0.42 *</td>
</tr>
<tr>
<td>DOA</td>
<td>0.26</td>
<td>0.46 *</td>
<td>/</td>
<td>0.51 *</td>
<td>0.50 *</td>
</tr>
<tr>
<td>SMI</td>
<td>0.65 **</td>
<td>0.60 **</td>
<td>0.51 *</td>
<td>/</td>
<td>0.60 **</td>
</tr>
<tr>
<td>Tb.N</td>
<td>0.66 **</td>
<td>0.42 *</td>
<td>0.50 *</td>
<td>0.60 **</td>
<td>/</td>
</tr>
</tbody>
</table>
Table 5. Regression coefficients between combination of three structural indices and Young’s modulus.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DOA</td>
<td>Tb.Th</td>
<td>Tb.N</td>
<td>DOA</td>
<td>Tb.Th</td>
</tr>
<tr>
<td>Y’s modulus</td>
<td>0.60</td>
<td>0.74</td>
<td>0.60</td>
<td>0.61</td>
<td>0.80</td>
</tr>
<tr>
<td>P value</td>
<td>0.015</td>
<td>0.0015</td>
<td>0.014</td>
<td>0.013</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

P value<0.05 is considered to be significant.
IV. DISCUSSION

It is generally accepted that the mechanical strength of trabecular bone depends on both bone mass and bone quality. Several aspects of bone quality, which range from the macroscopic to the microscopic, should be considered. Macroscopically, bone geometry, the hip axis length, bone size and the ratio of cortical and trabecular bone volume are considered to be some of the crucial factors for the proximal femoral and vertebral bone strength (Faulkner et al., 1993; Reckoff et al., 1969). Microscopically, tissue properties, such as microdamage and the degree of mineralization, are also important measures of bone quality. The contribution of all the afore-mentioned factors of bone quality to the mechanical properties of trabecular bone should be evaluated separately. As for trabecular bone, its microstructure should be considered in determining bone quality. Therefore, this study focused attentions on the contribution of bone mass and its microstructure to the local mechanical properties of trabecular bone of the intertrochanteric region. An attempt to determine the contribution of pure architectural properties of trabecular bone to the mechanical properties without confusing the effects of other factors, 3D trabecular microstructural analysis using micro-CT and a micro-image based biomechanical technique (3D micro-FEA) were applied to calculate the elastic constant of trabecular bone. The data showed that BMD and apparent BV/TV as two parameters reflecting
amount of bone mass can explain 75% of the variance of Young’s modulus. In accordance to our results, significant correlations between BMD measured by DXA or pQCT and biomechanical parameters of trabecular bone calculated by experiment test from the intertrochanteric region (Cody et al., 1996; Lotz et al., 1990; Muller et al., 1998), tibia (Hodgkinson and Currey, 1993; Turner et al., 1990), and radius (Louis et al., 1995) have been reported. Nikolaus and Lotz et al. (Lotz and Hayes, 1990) as well as Lang et al. (Lang et al., 1997) showed, that intertrochanteric trabecular BMD measured by quantitative computed tomography explained about 73% of the variability of Young’s modulus and 80% of the variance of strength of the proximal femur. In the proximal human tibia, structural density (apparent density) and fabric explain 72%-94% of the variance in the modulus of cancellous bone.

Likewise, the results from the present study showed that structure parameters determined in high resolution micro-CT images of bone cores correlate significantly with Young’s modulus calculated by mico-FEA. The structure model index was the best predictor for Young’s modulus ($r^2=0.51$), followed by Tb.Sp and Tb.N ($r^2=0.42$ and $r^2=0.39$). SMI represents the ratio of plate- and rod-like structures. In a three-dimensional image, we can clearly observe changes from the plate-like structure of trabecular bone to the rod-like structure with aging that we cannot see in a two-dimensional image. A plate-like structure reflects high mechanical stress, whereas a rod-like structure indicates low mechanical stress for normal cancellous bone. The pathogenesis of bone is not completely understood. With aging and osteoporosis, a process of progressive reduced bone formation rather than increased bone resorption
occurs. Moreover, Plate-like trabeculae are perforated toward rod-like structure and some trabeculae are lost, resulting in reduction of bone mass and structural changes. These changes may cause loss in mechanical strength. Some investigations show that significant changes occur in microstructure of OP patients compared with normal control, despite only a slight reduction in bone volume fraction occurs. These structural changes might be a consequence of trabecular plate perforations. Our findings are consistent with previously published studies, as imaged by histomorphometry and micro-CT from the human femoral neck, vertebrae (Hildebrand et al., 1999) and tibia (Ding et al., 2002). Hildebrand et al. (Hildebrand, 1999) have found quantitatively that trabecular bone from the human vertebra and femoral neck and head represent two architectural extremes, the former having a “rod-like structure”, and the latter a “plate-like” structure. A micro-CT study in the tibia by Ming D. et al. (Ding et al., 2002) have shown that the structure model index was the best predictor for Young’s modulus (R²=0.45). Additionally, Cellular solid theory predicts different dominant deformation and failure mechanisms for different architectures (Gibson and Ashby, 1997). For instances, rod-like structures are more susceptible to large deformations such as bending and rotation of trabeculae than are plate-like structures. This theory is supported by the experimental data of Muller et al., who observed large deformations of trabeculae during compression tests in rod-like trabecular specimens but not plate-like specimens (Muller et al., 1998). Most clearly, it suggests that the type of structure played an important role in determining the mechanical properties of cancellous bone. Interestingly, in this study, Tb.Th alone
account for only a relatively small amount of the variation of Young’s modulus by only 16%. It is intriguing to speculate that, when bone structure deteriorates later in life caused by the loss of bone mass, compensatory mechanisms try to maintain bone strength by increasing trabecular thickness. This is an important function for bone adaptation to mechanical loading. Similar demonstrations have been shown in several animal studies and human vertebral studies (McNamara et al., 2004; Moselilide, 1998; Waarsing et al., 2004). Investigations have also shown a significant age-related decrease in the thickness of horizontal trabeculae, but not in the thickness of vertical trabeculae (Moselilide, 1998). The ovariectomized animal models have shown that single trabecular thickness and yield strength in ovariectomized group were greater than those of sham group. It has been demonstrated that the increase in the yield strength from ovariectomy is due to some mechanism whereby bone attempts to compensate for the decrease in bone mass by altering the mechanical properties of the tissue, perhaps through increasing the degree of mineralization of the tissue. DOA is an index reflecting the orientation of trabecular bone, isotropy or anisotropy. Thus DOA also reflects trabecular adaptation function for mechanical environment. The results of this study showed that DOA alone accounts for a relatively small amount of the variation of Young’s modulus by only 20% in local intertrochanteric region. There are some divergences with other studies for the femoral head and tibia. Recently, ciarelli et al. (Ciarelli et al., 2000) examined cancellous bone from age-matched woman with and without femoral neck fractures. Architectural parameters such as trabecular number, connectivity, and thickness were
not significantly different between the groups. The maximal elastic modulus and ultimate stress in the inferosuperior direction were also the same. The only difference found was a significantly greater architectural anisotropy in the fracture group. It has demonstrated that degree of anisotropy is important for prediction of the fracture risk. Ming D. et al. have believed that DOA is predominant factor in determining the mechanical properties of cancellous bone of tibia (Ding et al., 2002). We consider that these divergences are due to the interchanteric area undergoes different loads than the femoral head and tibia. Following aging and progression of bone loss, the remodeling occurred in the principal trabecular system of femoral head and subchondral bone of tibia are mainly adapted to compressive mechanical stress. Thus, trabecular orientation becomes more anisotropic. Whereas, the interchanteric area are undergone multiple and composite mechanical stress, such as tension stress, shear and torsion force, leading to more isotropy in trabecular orientation for adapting to mechanical loading from multiple direction. Although, the ability of DOA and Tb.Th to explain variance of Young’s modulus is poorly, once they are supplemented with BMD or are combined with other structural indices, their abilities of explanation for Young’s modulus are improved clearly. Our finding that a combination of microstructural parameter with bone mineral measurements provides the best prediction of bone elastic constant is in agreement with some of previous studies reported for bone samples from the proximal femur (Link et al., 2003; Ulrich et al., 1999) and tibia (Ding et al., 2002).

The interrelationship of trabecular mechanical and microstructural properties
allows better understanding consequences of trabecular remodeling, and for the potential improvement diagnostic measures for bone loss. The results of this study are able to shed some lights on both of these issues. However, some points of the present study must be noted. First, for the present study, using micro-FEA to calculate elastic constant rather than compression test was essential. The elastic constants calculated from the uFE analyses reflect the mechanical properties of the bone that are due purely to its architecture, while elastic constants determined form conventional compression tests are determined by the bone tissue properties and by experimental artifacts (Keaveny et al., 1997). High-resolution finite element modeling provides the ability to control tissue properties, thereby isolating the effect of architecture. This technique could be applied to explore contributions of architecture to apparent elastic behavior without confusing the results with other factors (Kabel et al., 1999). Additionally, a comparative study has been demonstrated that the results of compression tests and those of the uFE analyses show good agreement ($r^2=92\%$) (Kabel et al., 1999), indicating that the FE approach can provide information similar to mechanical tests. However, in a number of studies, inaccuracies in compression test experiment and their possible consequences for the apparent mechanical properties measured have been reported (Keaveny et al., 1993; Linde and Hvid, 1989; Odgaard and Linde, 1991; Zhu et al., 1994). It must be considered that the Young’s modulus can be underestimated by 20%-45% (Keaveny et al., 1993; Odgaard and Linde, 1991). The application of uFEA models to simulate compression tests can be used to reduce these errors (van Rietbergen et al., 1998).
Second, Bone strength is a central predictor of fracture risk. Although this study determined the elastic constant of bone by FEA rather than bone strength, bone strength can be estimated through the assessment of its elastic properties, which are highly correlated to strength ($R^2 \geq 0.95$) (Goulet et al., 1994; Hodgskinson and Currey, 1993; Hou et al., 1998). The strength is most commonly expressed in terms of yield or ultimate stress. Brown and Ferguson found a strong linear correlation between yield stress and modulus for specimens taken from different regions of the proximal femur (Brown and Ferguson, 1980). Hence, much research is devoted to estimating the stiffness properties of trabecular bone structures, which are easier to determine than strength. Third, we assumed the tissue modulus to be isotropic and homogeneous, while in reality it is neither. Kabel et al. have, however, demonstrated that the apparent elastic properties can be estimated using an isotropic and homogeneous tissue modulus (Kabel et al., 1999). Moreover, we used equal tissue moduli for all sample. Thus, we focused only on the contribution of volume fraction and cancellous bone architecture to apparent properties, ignoring the influence of the tissue mechanical properties. Fourth, a possible limitation of this study was the influence of thresholding the 3D µCT data to obtain a binary representation of mineralized trabecular bone. This could influence estimation of morphological parameters (Uchiyama et al., 1997). However, a consistently applied threshold ensures reliable comparison between specimens, although the absolute value of these measures may include a small amount of error. Despite these limitations, our study, along with previous other reports, support the concept that
structural analysis provides an additional tool to analyze bone quality of trabecular bone.

Although the micro-CT used in this study can only provide some important information about microstructure properties of trabecular bone with high resolution in vitro, recently developed magnetic resonance (MR) and peripheral quantitated computed tomography (pQCT) high-resolution imaging techniques can provide images of cancellous bone structure with a resolution that is good enough to resolve its trabecular architecture (150-500 µm) in vivo (Laib et al., 1997; Majumdar et al., 1997). Based on a resolution study, Muller et al. (Muller et al., 1996) concluded that, although structural indices show a strong resolution dependency, their values can be determined from 3D reconstructions with a resolution of about 175 µm when using calibration procedures. In a similar study, Kothari et al. (Kothari et al., 1998) showed that the determination of Tb.Sp and Tb.N, but not Tb.Th, is rather independent of the image resolution and can yield meaningful results when measured from MR images. Laib and Ruegsegger have recently calibrated an in vivo, three-dimensional, peripheral, quantitative computed tomography (3D pQCT) scanner with “gold-standard” µCT measurements on the same bones samples (Laib and Ruegsegger, 1999). Structural variables such as trabecular number and mean trabecular thickness and separation, obtained with the 3D pQCT scanner, correlated with the µCT data, with $r^2$ values in the range of 0.81-0.96. The pQCT scanner used in the study is a relatively small and low-dose device that can be used for routine patient examination. Application of the calibration equations obtained should lead to improvements in the
in vivo assessment of trabecular microarchitecture. These results thus indicate that
the determination of structural indices in vivo is feasible.
V. CONCLUSION

In conclusion, first, high-resolution imaging techniques in combination with new computer modeling techniques based on the finite-element method is a useful tool to provide insight into the structure-function relationship for trabecular bone. Second, it was demonstrated that, not only could BMD, but also purely microstructural indices quantified by µCT imaging could well predict the mechanical property of trabecular bone calculated by FEA. Third, a combination of microstructural parameters each other or with bone mineral measurements could provide the best prediction of mechanical property of cancellous bone. Therefore, as regards detection of osteoporosis and evaluation of the efficacy of drug treatments for osteoporosis, BMD measurement should be supplemented with assessment of bone microarchitecture in vivo.
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전자부 골소주의 골밀도와 미세구조 특성이 골소주의 기계적 성질에 미치는 영향

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목적: 본 연구의 목적은 골밀도와 미세 골구조의 성질이 전자부 골소주의 기계적 특성(예, 탄성계수)에 미치는 영향을 연구하는 것이다.

대상 및 방법: 인공관절 전치환술을 시행 받은 15명의 환자로부터 대퇴골 전자부에서 총 15개의 고관절 골소주 시편을 채취하여, 이들을 대상으로 PIXImus2 골밀도 측정기, 고해상도 미세 컴퓨터 단층촬영기, 유한요소법을 이용하여 골밀도와 2차 및 3차원 미세구조 지수, 그리고 기계적 특성을 분석하였다. 골밀도, 구조 지수, 탄성계수 간의 상관관계를 선형회귀분석을 이용하여 통계처리 하였다.

결과: 본 연구에서 골밀도 및 골 체적비는 기계적 특성을 예측하는데 가장 중요한 인자였으며, 3 차원 미세구조지수(예를 들어 구조 모델 지수) 또한 51%정도 통계적으로 의미 있게 기계적 특성을 예측하였다. 골밀도와 미세구조지수를 조합한 경우에 탄성계수의 변화량을 예측하는데 잘 반영하였다.
결론: 골밀도와 미세구조지수를 이용한 분석은 전자부에서 탄성계수를 예측하는데 가장 좋은 방법이다.

핵심어: 골밀도, 미세구조, 기계적 성질, 유한요소분석