NON-INVASIVE ASSESSMENT OF BONE STRENGTH AND DENSITY USING SCANNING ULTRASOUND

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INTRODUCTION

Musculoskeletal complications induced by age-related diseases like osteoporosis, and in long-term disuse osteopenia such as a lack of microgravity during extended space missions and long-term bed rest, represent a key health problem. Such a skeletal disorder changes both the structural and strength properties of bone, and the latter plays a critic role in ultimately leading to fracture [1]. Early diagnosis of progressive bone loss or poor bone quality would allow prompt treatment and thus would dramatically reduce the risk of bone fracture. Most osteoporotic fractures occur in cancellous bone. Hence, non-invasive assessment of trabecular strength and stiffness is extremely important in evaluating bone quality. The principal diagnostic method for osteoporosis is currently dual-energy X-ray absorptiometry (DEXA), which provides an index of bone mineral density and/or content, but not the bone's physical properties. Recently, advancements in ultrasonic techniques provide a method for characterizing the material properties of bone in a manner which is non-invasive, non-destructive, repeatable, safe and relatively accurate. Limitations with this approach, however, include the tissue boundary interaction, influence of soft tissue and cortical shell, and accuracy. These leave quantitative ultrasound (QUS) - in its current configuration - as a first order screening tool, rather than a highly accurate diagnostic for true fracture risk [2]. To overcome these hurdles and improve the specificity of non-invasive ultrasonic assessment, we have initiated a new modality of QUS by developing a scanning confocal acoustic diagnostic (SCAD) technology particularly for identifying the strength of trabecular bone [3]. The ultrasound resolution and sensitivity can be significantly improved by its configuration. The correlations using μCT determined bone architecture and mechanical testing parameters are used for verifying this SCAD in assessing bone quality.

METHODS

A total of 63 sheep trabecular bone cubes (1 x 1 x 1 cm), were harvested from the distal femoral condyle. Prior to cutting, the femoral shaft was placed at a 45° angle to the blade such that the axes of the resultant samples corresponded to the physiologic and anatomic directions, i.e., longitudinal (LG) (animal's weight-bearing direction), anteroposterior (AP), and mediolateral (ML). These bones were stored in equal amounts of 70% ethanol, and normal saline at 4°C, and tested using ultrasound, μCT and contact mechanical testing.

SCAD measurement: Using a newly developed SCAD technology, the bone cubes were measured in three orthogonal directions. The measurement procedure consisted of confocal scanning of ultrasonic beam through the central region (2-D plane) of the sample with a resolution of 0.5 mm pixel size. A recording ultrasound wave was made over a 24×24 array (12×12 mm field of view). These waveforms were processed to calculate the ATT (dB), the log-ratio of the energy of reference wave to testing wave, the broadband ultrasound attenuation (BUA) (dB/MHz), the slope of the frequency-dependent attenuation at bandwidth 300-800 kHz, and the ultrasound velocity (UV) (m/s). These signals were further processed to generate ATT, BUA and UV images. A 14×14 grid (0.5 mm pixel size, 7×7 mm field of view) region of interest (ROI) was then determined from each ATT, BUA and UV images to derive ultrasound parameters.

μCT determining microarchitecture and density of bone: Through a μCT 3-D reconstruction with a 20 μm resolution (μCT -20, Scanco Corp., USA), a number of parameters, such as the total volume (TV), bone volume (BV), bone mineral density (BMD), trabecular width (TbTh) and space, connectivity, and structural model index (SMI) were determined.

Tissue mechanical modulus: Contact force-displacement testing was used to determine the elastic modulus of trabecular bones. Using a mechanical testing machine (MTS Systems Corp., USA), the cubes were uniaxially loaded in compression using displacement control. To overcome slight deviations from surface parallelism, a smoothly curved nail head was placed above the bone cube such that the force would be distributed evenly to the bone in the loading direction. An upper limit of 300 N – determined by prior loading of non-experimental but otherwise identical bone cubes – was established to prevent the plastic yielding of any specimens while the loading was achieved in bone's elastic region. The loading rate was approximately 1000 με/s for the samples. Both displacement and force were digitized analyzed using MTS BasicTestware software.

The material properties studied include elastic moduli in 3 orthogonal directions, and bulk modulus. Finally, the samples were compressively loaded up to their failure in the longitudinal direction and the yield strength and the ultimate strength were recorded.

Interrelationships between QUS parameters and μCT determined structural values, and between QUS parameters and mechanical properties were evaluated through multiple correlations. Finally, while considering the complex structure of trabecular bone and its interactive influence on derived ultrasound signals, a new parameter that combined BUA and UV was determined by linear regression correlation between ultrasonic parameters and both μCT and mechanical properties. The data was analyzed using Pearson product moment correlation coefficients and the significance level was set at $p < 0.05$.

RESULTS

Among the quantity and quality parameters, these trabecular bone samples showed a variety of values of density and stiffness. The value of BV/TV averaged 49±7% (mean±s.d.), while the mechanical strength averaged 415±100 MPa for bulk modulus, 16.5±6.7 MPa for yield strength and 18.6±6.9 MPa for ultimate stress. Ultrasound scanning was capable of predicting the bone's quality parameters via multiple correlations.

Table 1 shows the overall correlation coefficients. While there are weak correlations between BUA and μCT determined structural parameters such as bone volume fraction (BV/TV) (R=-0.68), trabecular width (TbTh) (R=-0.34) and connectivity (R=0.07), as well as tissue bulk modulus (R=-0.31), it demonstrated strong correlations between UV and bone strength and structural parameters such as bulk modulus (R=0.82), BV/TV (R=0.93), and TbTh (R=0.69). The correlations were significantly improved by using a new parameter that combined BUA and UV in a linear regression analysis, yielding values of R=0.96 (BV/TV), R=0.67 (TbTh), and R=0.84 (bulk modulus). It can be seen that UV provides the best correlations with the strength of bone in that R value is consistently above .75 with regard to the elastic modulus, bulk modulus, yield or ultimate strength. All r values above 0.3 are significant.

TABLE 1. Relative correlation coefficients (r values) for QUS, μCT and mechanical testing

	ATT	UV	BUA	Combo BUA & UV
AP Modulus	-0.71	0.79	-0.66	-
LG Modulus	-0.75	0.79	-0.70	-
ML Modulus	-0.36	0.89	-0.34	-
Bulk Modulus	-0.75	0.82	-0.31	0.84
Yield Strength	-0.72	0.90	-0.85	0.93
Ultimate Strength	-0.75	0.90	-0.85	0.94
BV/TV	-0.37	0.93	-0.68	0.96
BMD	0.74	0.85	0.75	0.87
SMI	0.3	0.9	0.66	0.93
Connectivity	-0.12	-0.33	0.07	0.28
Trab.Thickness	-0.17	0.69	-0.34	0.67

These results have demonstrated the ability to pick up spatial differences among the samples, which is difficult to do by plane wave and non-scanning ultrasound methods.

DISCUSSION

Ultrasound holds promise as an efficient and non-invasiveness assessment tool for bone status. These results suggest that SCAD can provide detailed information for the prediction of bone mass and strength. Considering the complex architecture of trabecular bone, combining BUA and UV can provide a better prediction of bone's quality for determining osteogenic conditions. As such, various ultrasound methods are available to optimize the correlations with the true mechanical properties of bone and ultimately fracture risk. Thus, a well-established database using this newly developed system may provide an insight into non-invasive diagnosis of osteoporosis and bone quality using ultrasound.

More generally, it is both interesting and promising that when looking at either mechanical properties or μCT parameters, it is the more global and clinically relevant properties that are best described by ultrasound. That is, yield and ultimate strength (the best indicators of true fracture risk) are better correlated than elastic modulus (simply a measure of stiffness). Also, with respect to μCT, the ultrasound values are best correlated with overall parameters such as bone volume fraction and structural model index (which are again the best indicators of global quality of the bone), rather than specific parameters such as connectivity density and trabecular thickness. Acoustic mapping provides a true image for the region of interest, in which combining acoustic BUA and UV can provide better prediction of bone's quality in determining osteogenic conditions.

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