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Ultrasound Attenuation in the Assessment of Bone Mineral Density and Elastic Modulus of Human Trabecular Bone

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요 약 : 본 연구에서는 뼈의 특성을 파악하는 초음파감쇠 파라미터를 재평가하였다. 초음파 속도, 특정 주파수(0.5MHz)에서의 초음파감쇠 및 광역 밴드 초음파감쇠와 같은 초음파 파라미터들을 해면골 입방체 시편의 세 직교방향(전/후, 내/외, 상/하)에서 측정하였다. 그리고 컴퓨터 영상장치를 사용하여 골 밀도를 측정했으며, 골 시편의 무게와 부피를 이용하여 외형 밀도(apparent density)도 함께 얻었다. 이와같이 구해진 외형밀도와 초음파 속도로부터 초음파 탄성영률을 계산하였다. 주파수 0.5MHz에서의 초음파감쇠와 광역밴드감쇠는 골 밀도 및 세 직교방향의 초음파 영률과 서로 관련시켜 연관성을 조사하였다. 그 결과 특정 주파수 초음파감쇠가 골밀도 및 탄성영률을 평가하는 능력에 있어서 광역밴드 감쇠보다 우수함을 알 수 있었다. 따라서 광역밴드 초음파감쇠를 측정하여 골의 상태를 평가하는 현행 초음파 진단 기법이 재검토 되어야 하며 본 연구에서 증명된 특정주파수(0.5MHz) 초음파감쇠를 이용하여 골 다공증 진단 예측율을 향상시킬 수 있다.

Abstract : The objective of this study was to re-evaluate ultrasound attenuation as an indicator of bone properties. Ultrasound parameters, such as ultrasound velocity, ultrasound attenuation at a particular frequency (0.5 MHz), and broadband ultrasound attenuation (BUA), were measured in the three orthogonal directions of trabecular bone cubes. Measurements of bone mineral density (BMD) were made using quantitative computed tomography and apparent density by weighing bone specimens and measuring their volume. Ultrasonic modulus was calculated from the standard equation with apparent density and ultrasound velocity. Ultrasound attenuation at a frequency of 0.5 MHz and BUA were correlated with BMD and ultrasonic modulus in the anterior/posterior, medial/lateral, and superior/inferior directions. Analysis of correlations demonstrated that attenuation at 0.5 MHz was superior to BUA in describing both BMD and elastic modulus of trabecular bone. This result may be used to improve current ultrasound diagnostic techniques for assessing bone status.

Key words : Ultrasound attenuation, Ultrasound velocity, Broadband ultrasound attenuation, Bone mineral density, Trabecular bone, Elastic modulus

INTRODUCTION

Osteoporosis is defined as a marked and continual decrease in skeletal mass. It clinically presents itself as a large decrease in bone mass and symptomatically as bone fracture. In osteoporosis, a bone fractures either spontaneously (i.e., due to normal loads) or from minimal trauma such as a simple fall. Currently, diagnosing osteoporosis relies heavily on densitometers, which use ionizing radiation to obtain information about bone and soft tissue through the attenuation of high energy beams. Although bone strength is strongly correlated with bone mass (Turner and Eich 1991), as much as 30% of bone strength may be due to non-mass parameters such as bone microstructure and remodeling state (Kleerekoper *et al.* 1985, Turner *et al.* 1988). Bone density measurements using some form of ionizing radiation are unable to reflect the direct effect of these factors due to the inevitable limitation of radiation dosage. There is, therefore, a strong need of non-invasive assessment that determines how bone will respond to mechanical loads and is likely to fracture.

The application of ultrasound to the non-invasive assessment of bone properties has become increasingly popular over the past decade. Ultrasound is in the form of mechanical (i.e. acoustic) waves instead of electromagnetic radiation. Not only does ultrasound allow for inexpensive and radiation-free measurements, it may also provide information on bone structure and strength as well as the BMD due to the potential for sound to be modified by bone microstructure, composition, and mass. The application of ultrasound techniques in the medical field originally focused on BUA measurements (Langton *et al.* 1984, Baran *et al.* 1988).

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Langton *et al.* (1984) described a BUA technique for the diagnosis of osteoporosis, suggesting that BUA provides direct information on trabecular bone structure as well as mineral density. Many subsequent studies (McKelvie *et al.* 1989, McCloskey *et al.* 1990, Gluer *et al.* 1992, Lees *et al.* 1993, Kolthoff *et al.* 1995, Han *et al.* 1996, Han *et al.* 1997) have demonstrated a positive relationship between BUA and BMD acquired through traditional radiographic measurements.

Ultrasound attenuation (dB/cm), in general, measures a decrease in signal amplitude of waves propagating through a medium at a particular frequency, while BUA (dB/MHz/cm) calculates the ratio of change of attenuation over a selected range of frequency. Although BUA was favorably introduced instead of attenuation, little is known in the literature concerning why BUA was originally preferred over attenuation. In fact, in an earlier study (Evans and Tavakoli 1990), it was reported that attenuation appeared to be better than BUA in correlation with bone density, however, this was not emphasized.

Ultrasound velocity has been successfully applied to determining the elastic property of cortical bone (Ashman *et al.* 1984). Efforts to extend wave theory of ultrasound to assessing the elastic modulus and strength of cancellous bone were also made in vitro (Ashman *et al.* 1987, Turner *et al.* 1991). Ashman *et al.* (1987) reported that Young's modulus obtained from mechanical testing was highly correlated with ultrasonic modulus calculated from ultrasound velocity and bone density.

This study was undertaken to compare ultrasound attenuation at a particular frequency (0.5 MHz) with BUA in assessing BMD and elastic modulus. This would determine whether this new attenuation parameter is superior to BUA in prediction of bone fracture.

MATERIALS AND METHODS

Seventy-one trabecular bone cubes (approximately 9.5 × 9.5 × 9.5 mm) were obtained from four human cadaveric tibiae. The cubic specimens were removed from underneath the proximal subchondral bone plate using a low-speed diamond saw (South Bay Technology Inc., San Clemente, CA). Three orthogonal axes of these specimens were aligned in the superior/inferior (SI), medial/lateral (ML), and anterior/posterior (AP) directions. Bone marrow was removed with a water jet (Water Pik, Teledyne Inc., Fort Collins, CO) to measure apparent density. Specimens were kept in moisture in 1:1 saline/ethanol solution between procedures.

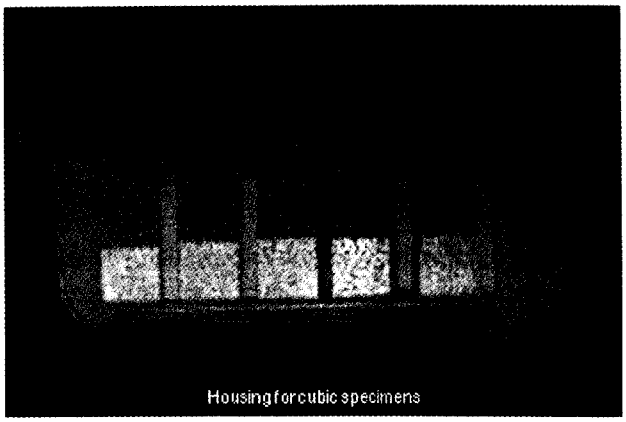

Fig. 1. Representative CT image for BMD measurement of cubic cancellous bone specimens in the water-filled Plexiglas® containers

Measurements of apparent density were accomplished by weighing the trabecular bone specimens and measuring their volume. The BMD of cubic specimens was measured by quantitative computed tomography (QCT). Prior to CT measurements, specimens were degassed under vacuum to remove air bubbles, and placed in water-filled Plexiglas® containers (Figure 1). The CT images were transferred to a computer (Sun Sparc Station 10) and analyzed using image analysis software (C-MED, Virtual Vision, Cupertino, CA). The average pixel intensity of at least three consecutive slices for each specimen was related to a BMD value (mg/cm^3).

The method used to measure the ultrasonic wave velocities in this experiment was a pulse transmission technique in the longitudinal mode of the wave with a pair of longitudinal contact transducers (Panametrics V101, Waltham, MA). This technique measures time delay of the propagation between the transmitted and received ultrasonic waves. The ultrasound velocities of all specimens were measured These transducers, a transmitter and a receiver, had a center frequency of 0.5 MHz and were fixed on a mount at the opposite ends of each specimen. The probes provided tight contact with the specimen by using a spring which pushed one of the transducers against the specimen (Figure 2). Once the specimen and probes were adjusted, water was sprayed at the interface between the transducers and specimen to complete the contact. The water was used as a coupling medium to prevent the wave scattering in the air at the interfaces. Ultrasonic waves were transmitted from one transducer to the other using a pulse generator

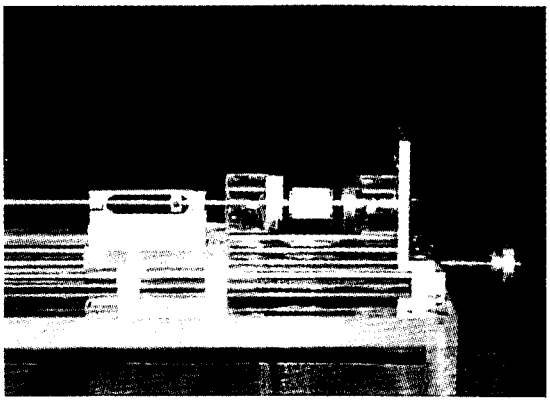

Fig. 2. Photograph of the special mount for the ultrasonic contact transmission technique. Tight contact was achieved by the spring pushing one of transducers against the specimen

(Panametrics 5055). The pulses were recorded with a digital storage oscilloscope (Tektronix 2232, Beaverton, OR), which can display and measure the time delay between the transmitted and received waves. Separate channels were used to display the transmitting and receiving signals simultaneously on the oscilloscope. The time delay associated with the propagation of the wave through the specimen was the interval from the start of the transmitted wave to the start of the received wave on the oscilloscope. The sonic velocities (UV = d / t) were calculated from the thickness (d) of the specimen measured using a digital caliper and the time delay (t) measured from the oscilloscope.

A pulse transmission technique was used with a pair of broadband ultrasound immersion transducers (0.5 MHz, Panametrics V301) to measure BUA and ultrasound attenuation at a frequency of 0.5 MHz. These transducers were mounted coaxially on opposite sides of a water-filled Plexiglas® tank and connected to an analyzer (Panametrics 5055). The analyzer contained transmitting, receiving and "stepless" gate sections. The transmitting section was operated in through-transmission mode. This section has two outputs, one that supplies voltage to the transmitting transducer, and one that allows visualization of the pulse on an oscilloscope. Controls on the analyzer allowed for the setting of the transmission signal pulse rate, energy and damping. Damping and energy affect the signal shape and amplitude. These controls were kept constant during all phases of testing. The receiving section of the ultrasound analyzer contained one input for the receiving transducer, and amplified the signal via adjustable gain (40 or 60 dB) and receiver attenuation controls (0 to 60 dB, in steps of 2 dB). Thus, a signal with both a gain and an attenuation of 40 dB is unamplified. These settings were appropriate for the "water only" signal. For transmission through bone, gains of up to 20 dB were often applied to provide appropriate resolution. Adjustment of signal gain should not affect attenuation slope. The last section of the ultrasound analyzer (the stepless gate) allows for the selection of any desired portion of the received signal by moving a window to the desired location. The window is viewed as a 40 mV pedestal on the received signal and can be adjusted in both start time and width. In addition, the stepless gate section has two outputs. The "marked RF" output allows for viewing of the entire received signal with the gate pedestal superimposed. The "gated RF" output shows only the portion of the signal within the gated window. The gated window was chosen so that the entire received pulse was analyzed (usually two or three peaks). After the "main-bang", a distinct leveling of the signal was observed and this marked the end of the gate window. Two outputs from the stepless gate section were connected to each channel of the digital storage oscilloscope. A serial board (RS-232C) was installed into the oscilloscope to allow for interfacing with a microcomputer (Macintosh Iici), which allowed for acquisition of both moving and stored signals from the oscilloscope. Signal acquisition, plotting, and analysis were performed using a custom program written in LabVIEW (National Instruments, Austin, TX). In this program, time domain signals captured by the storage oscilloscope were converted to the frequency domain using fast Fourier transformations (FFT). A spectrum obtained with a specimen in place was subtracted from a spectrum obtained with water only. The difference was plotted over the entire frequency range. The slope from the best linear fit between 0.3 and 0.7 MHz was normalized using the specimen's thickness. This value was expressed in units of dB/MHz/cm and is referred to as BUA. Ultrasound attenuation of each specimen was measured at the center frequency of the transducers (0.5 MHz) and normalized using the specimen's thickness. Ultrasound attenuation measurements for each specimen were made in the three orthogonal directions. In order to make all the ultrasound propagation pass through, a wave-blocking holder with holes slightly smaller than the specimen was used.

Ultrasonic elastic modulus of each specimen was calculated from the standard equation ($E = \rho v^2$) with ultrasound velocity and apparent density in the three orthogonal direc-

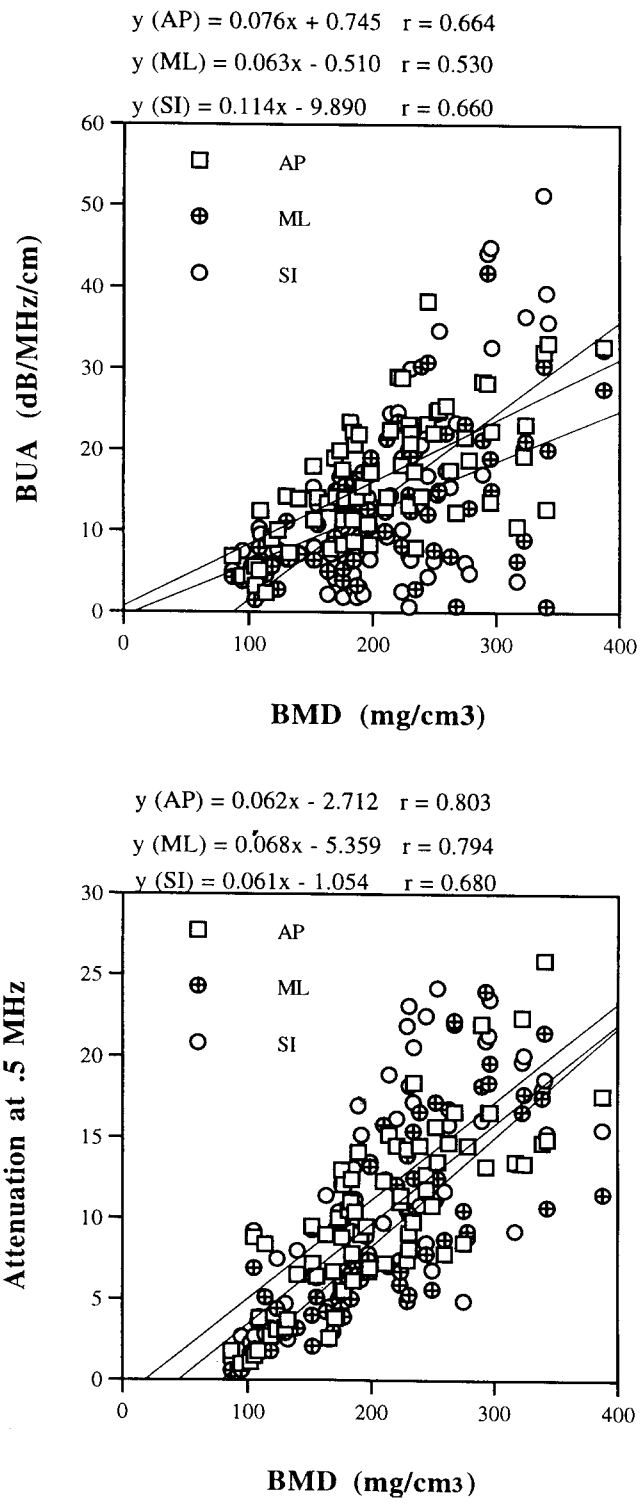

Fig. 3. (a) and (b). Relationships of BMD with BUA (a) and ultrasound attenuation at 0.5 MHz (UA) (b) in the AP, ML, and SI directions. UA was better correlated with BMD

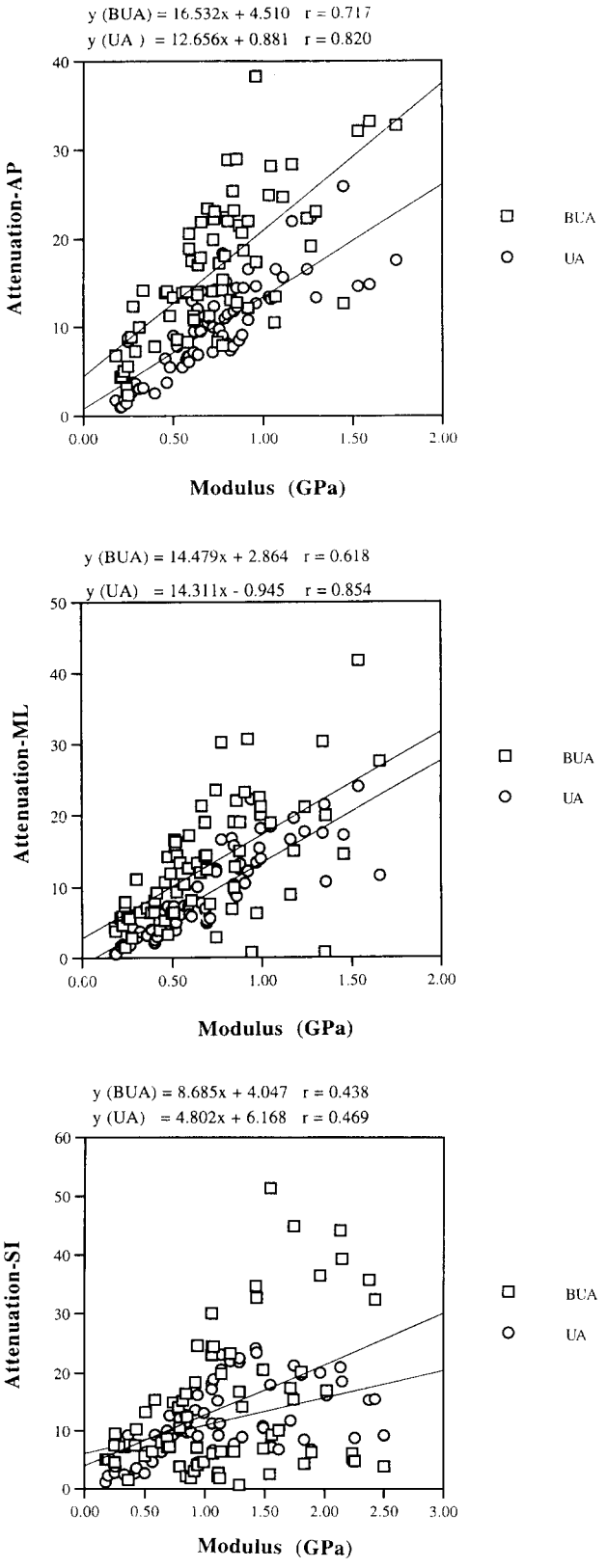

Fig. 4. (a), (b), and (c). Regressions of ultrasonic modulus with BUA and ultrasound attenuation at 0.5 MHz (UA) in the AP (a), ML (b), and SI (c) directions

tions.

Linear regression analysis was performed to determine

the correlation coefficient (r) among variables, and the differences in means were considered statistically significant for p-values less than 0.05.

RESULTS

The experimental data for apparent density, BMD, attenuation at 0.5 MHz, BUA, UV, and ultrasonic modulus are summarized in Table 1. The correlations between the variables were highly significant in all cases ($p<0.0001$) (Table 2). Attenuation at 0.5 MHz was better associated with both BMD and ultrasonic modulus in all three directions than was BUA. Its enhanced correlation was pronounced in the AP and ML directions. Figures 3 (a) and (b) describe the general trend of the relationship between BMD and attenuation parameters. Ultrasound attenuation tended to linearly increase with increasing BMD. The ultrasonic elastic modulus correlated well with attenuation at 0.5 MHz, in the AP and ML directions [Figures 4 (a), (b), and (c)].

DISCUSSION

The results demonstrated that ultrasound attenuation at a frequency of 0.5 MHz was superior to BUA in the prediction of BMD and elastic modulus. Most published reports on the clinical assessment of bone using ultrasound showed a wide range of coefficients of determination ($0.29<r<0.92$) for correlations between BMD and BUA (McKelvie *et al.* 1989, McCloskey *et al.* 1990, Gluer *et al.* 1992, Lees *et al.* 1993, Kolthoff *et al.* 1995, Han *et al.* 1996, Han *et al.* 1997). This questioned the reliability of ultrasound to predict BMD.

Until recently, there has been little discussion on preference of BUA over attenuation. With the results obtained from this investigation, current methodology of ultrasound measurements may be altered for more accurate ultrasound assessment of bone property. Since the correlations of BUA and attenuation with modulus were significantly better than those of BMD in the AP and ML directions, these attenuation parameters might reflect trabecular architectural properties, which is independent of BMD but contribute to elastic modulus. It was shown in the previous study (Gluer *et al.* 1994) that the mean attenuation across the selected frequency reflects trabecular separation, while BUA reflects a combination of trabecular separation and connectivity. Although BUA and attenuation might be influenced by different aspects of trabecular architecture, ultrasound attenuation surpassed BUA in the predictability of BMD and elastic modulus.

Consequently, the results in the present study suggest that current ultrasound diagnostic techniques for assessing bone status may be replaced with new ultrasound attenuation measurement using a particular frequency of 0.5 MHz. However, the results in this study might not provide sufficient evidence concerning better prediction of fracture risk with attenuation since both BMD and modulus do not completely represent bone quality and fracture risk. Future studies need to apply these findings to in vivo bone fracture.

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