

Ultrasonic Assessment of Human and Bovine Trabecular Bone: A Comparison Study

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Abstract—A comparison study is reported on the ultrasonic assessment of human trabecular and bovine trabecular bone samples. Both ultrasonic velocity and ultrasonic attenuation were evaluated through a transmission insertion technique and correlated with bone mineral density as determined with single photon absorptiometry. For a 1-MHz ultrasonic transducer pair and the human cancellous bone samples the correlations were 0.91 and 0.89 between density and velocity and attenuation, respectively. For a 500-kHz ultrasonic transducer pair the correlations were 0.89 and 0.81 between density and velocity and attenuation, respectively. For the bovine bone samples, the correlations were 0.90 and -0.31 for the velocity and attenuation, respectively, for the 1 MHz transducer pair. For the 500-kHz transducers, the correlations were 0.85 and -0.17 for the velocity and attenuation, respectively. By combining both velocity and attenuation in a multivariate regression, an improvement was achieved in the estimation of bone density in the human samples for both the 500-kHz and 1-MHz transducer pairs. No significant improvement was achieved in the multivariate regressions for the bovine bone samples. In conclusion, the results indicate that ultrasonic measurements are in general highly correlated with bone mineral density in trabecular bone samples. This correlation is more consistent and strong in relatively low density human samples compared with the higher density bovine samples.

I. INTRODUCTION

ULTRASONIC assessment of bone for managing osteoporosis and other metabolic bone diseases has been proposed [1], [2] as an alternative to radiation-based bone densitometry technology, e.g., single photon absorptiometry or dual energy x-ray absorptiometry (DEXA). In contrast with the ionizing electromagnetic radiation of such clinical bone densitometric techniques, ultrasound is a mechanical wave and thus interacts with bone in a fundamentally distinct manner. Ultrasound is viewed as having great potential for assessing bone since its propagation is affected by the structure, composition, and mass of the bone tissue being interrogated [1]. Since

the risk of bone fracture is related to the combined interactions of these latter features [3], ultrasonic measurements may be able to provide important information on bone quality and more accurate estimates of the risk of bone fracture.

Numerous clinical [4]–[13] and *in-vitro* human [14]–[16] and animal [17]–[21] ultrasonic studies have been reported. For example, Evans and Tavakoli [20] measured the correlation between velocity of ultrasound and broadband ultrasound attenuation (BUA) with physical density in 44 samples of cancellous bovine femora. The results showed a correlation of $r = 0.85$ and $r = 0.33$, respectively. An *in vitro* study on the human *os calcis* by McKelvie *et al.* [15] compared bone density, as measured by quantitative computed tomography, to BUA and reported a correlation coefficient of $r = 0.92$, in the frequency range 200 kHz–600 kHz. In a clinical study, both ultrasonic velocity and BUA were measured in the *os calcis* in 64 subjects [8]. They found respective correlations of 0.66 ($P < 0.01$) and 0.74 ($P < 0.73$) with bone density at the same site using DEXA.

Most prior studies, for example those summarized above, have been carried out on bones for which the associated densities varied over relatively narrow ranges. Another aspect of these investigations was their respective use of univariate regression methods in establishing relationships between ultrasonic velocity and attenuation and bone density. This has produced less than optimal estimates of bone density since all the available data has not been used.

The objectives of this study were threefold. First, we wanted to explore in a comprehensive and consistent manner the interrelationships between ultrasonic velocity, ultrasonic attenuation, and bone density over a very broad range of density values. Both human and bovine cancellous bone samples were used in order to obtain a set of specimens with a wide range of bone densities. The second objective was to determine if the combined use of ultrasonic attenuation and velocity in multivariate regressions would lead to improved accuracy in the estimation of bone density, in comparison to using either ultrasonic attenuation or velocity alone. Finally, we wanted to see what effect different nominal ultrasonic transducer frequencies would have on the measured velocities and attenuations.

II. MATERIALS AND METHODS

A. Ultrasonic Setup and Analytic Framework

In the experimental setup, Fig. 1, two ultrasonic transducers are used, one acting as transmitter and the other as a

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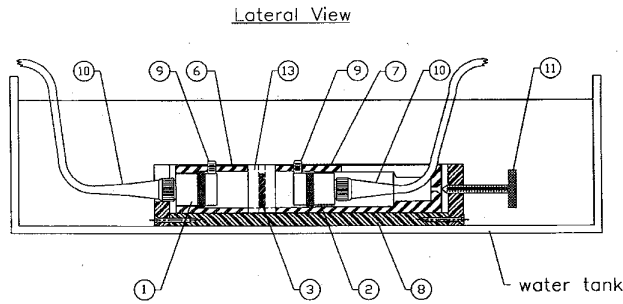


Fig. 1. The ultrasonic measurement apparatus: 1) receiver transducer, 2) transmitter transducer, 3) bone sample, 6) receiver transducer holder, 7) transmitter transducer holder, 8) plate, 9) set screw, 10) transducer cable, 11) compression screw, and 13) bone holder.

receiver of the ultrasound wave. In a typical experiment, a bone specimen of thickness d is placed between the two transducers. The transducers and bone are then submerged in water. In this configuration, there exist two water layers through which the ultrasonic wave propagates—one between the transmitter transducer and sample, the other between the receiver transducer and sample. The two transducers are coaxially positioned and separated by a fixed distance L . The transmitting transducer is excited by an input signal, $u(t)$, so that an ultrasound pulse is transmitted through the water, into and through the sample, and through the water to the receiving transducer. The output voltage of the receiving transducer is denoted either by $v_s(t)$ or $v_r(t)$, depending on whether the measurement is made with a bone sample present or absent. In the latter case, the signal is termed a reference signal and corresponds to a measurement made through the water bath only. In the former case, the signal, $v_s(t)$, corresponds to propagation through the water-sample-water path. The techniques for estimation of the ultrasonic attenuation and velocity are distinct and are carried out in the frequency and time domains, respectively. Each technique will be described in turn.

1) *Attenuation Estimation:* An expression for the Fourier transform magnitude, $|V_s(f)|$ associated with the bone sample signal, $v_s(t)$, is given by

$$|V_s(f)| = T_t(f)T_r(f)|H(f)||U(f)|. \quad (1)$$

In (1), $T_t(f)$ and $T_r(f)$ are the magnitude transfer functions of the transmitting and receiving transducers, respectively, $|U(f)|$ is the magnitude Fourier transform of the input excitation signal, $u(t)$, and $|H(f)|$ is the acoustic magnitude transfer function of the bone specimen.

The expression for the Fourier transform magnitude, $|V_r(f)|$, associated with the water-bath-only signal (i.e., without the bone sample present), $v_s(t)$, is given by

$$|V_r(f)| = T_t(f)T_r(f)|U(f)|. \quad (2)$$

An estimate of $|H(f)|$ may now be obtained by dividing (1) by (2). Thus we find that

$$|H(f)| = \left| \frac{V_s(f)}{V_r(f)} \right|. \quad (3)$$

The magnitude transfer function $|H(f)|$ can be written in terms of an attenuation function $\alpha(f)$ as follows:

$$|H(f)| = e^{-\alpha(f)}. \quad (4)$$

Note that in the above analysis, we have assumed that all reflection and transmission losses are included in the attenuation function $\alpha(f)$.

Alternatively, the specific attenuation function, $\mu(f) \equiv \alpha(f)/d$, may be used

$$|H(f)| = e^{-\mu(f)d}. \quad (5)$$

An estimate of $\mu(f)$ can then be obtained by taking the logarithm of $|H(f)|$ in (5) and using (3). Thus we find that

$$\mu(f) = \frac{[\ln |V_r(f)| - \ln |V_s(f)|]}{d}. \quad (6)$$

If $\mu(f)$ is modeled as an affine function, that is

$$\mu(f) = a + bf \quad (7)$$

then an estimate of the slope, b , of the specific attenuation can be obtained by a least squares regression curve fit of (7) to (6), over a specified frequency range. The frequency range is chosen according to the region where the specific attenuation function is approximately linear, as assessed by the mean squared error in the least squares curve fit and as shown in Section III. The constant, b , is known as the *differential specific attenuation* (DSA) and is expressed in units of $\text{dBcm}^{-1}\text{MHz}^{-1}$; in terms of the more commonly used BUA, it is given by $\text{DSA} = \text{BUA}/d$, where d is the thickness of the bone sample.

2) *Velocity Estimation:* The estimation of velocity is carried out in the time domain, according to the straightforward principle of time of arrival of signal energy. The estimation of velocity can also be achieved in the frequency domain, through the use of phase unwrapping and linear models, as described by Kaufman *et al.* [22]. However, since most prior studies have relied on the pulse transit time technique, we choose to use that method here as well.

The time of arrival of the reference and sample signal is defined to be the first time at which three consecutive absolute values of the signal remain above a prespecified amplitude level. In this study, this level is chosen to be three times (3σ) the standard deviation of the additive noise in the waveform from the portion of the acquired reference or sample data waveforms where no ultrasonic signal is present.

Using τ_s and τ_r to denote the time of arrival of the sample and reference signals, respectively, the ultrasonic velocity v , can be evaluated according to the following expression:

$$v = \frac{1}{\frac{1}{v_r} - \frac{(\tau_r - \tau_s)}{d}} \quad (8)$$

where v_r is the velocity of ultrasound in the reference medium, in this case water.

B. Bone Sample Preparation

1) *Human Bone Specimens*: Fresh lumbar vertebrae were acquired within three hours after extraction from human cadavers. In total, 27 vertebral bodies from 14 cadavers ranging in age from 35 to 93 years were employed in this study. A 2-cm diameter cylindrical core was cut from the central portion of each vertebral body using a drill with an attached drill corer. The cortical shell at both ends of the core was removed using a Buehler Isomet low-speed saw under constant irrigation, so that the samples consisted only of vertebral trabecular bone. The samples were then defatted using a warm water rinse, submerged in xylene for approximately 48 hours and then rinsed in water again. Bone samples were frozen at -20°C until ultrasonic and densitometric testing. Although xylene changes the properties of the bone matrix, the principal relationships between ultrasonic parameters and bone density are largely retained. This is due to the fact that these relationships arise primarily out of the interactions of the ultrasonic wave with the bone matrix-pore fluid structure and less from (changes in) the bone matrix material *per se*. This has been previously demonstrated in [23], which showed little effect on ultrasonic velocity and attenuation in fresh human trabecular bone treated with formalin fixation.

2) *Bovine Bone Samples*: Twelve fresh bovine femurs were used, and a 2.7-cm \times 0.8-cm thickness cylinder of trabecular bone were cut from each distal medial and lateral condyle (Fig. 2), respectively, using a drill with an attached drill corer and a two blade saw with constant irrigation. The marrow was removed by placing a solution of ethyl-methyl-isopropyl and acetone with a 3:1 proportion in an ultrasonic cleaner for approximately 100 hours with five changes of alcohol/acetone solution. The samples were kept in 0.9% saline solution at 4°C until ultrasonic and densitometric testing.

C. Bone Densitometry

The samples' bone mineral densities were measured by single photon absorptiometry (Model 2780, Norland Corp, Fort Atkinson, WI, USA). The scanner was calibrated using the manufacturer's bone standard on a weekly basis. The bone sample's circular surface was divided into eight regions and rectilinear scans, with the sample submerged in water, were taken encompassing the entire sample. The area of each region was used to calculate the bone mineral density area weighted mean in g/cm^2 , which was divided by the sample thickness d to get a value of bone density (BD) in units of g/cm^3 . This BD, is closely related to that which would be obtained through direct physical weighing of the (dried) bone samples and dividing the weight by the associated sample volume [24].

D. Ultrasonic Measurements

Each trabecular sample was ultrasonically tested by an insertion technique as outlined earlier to obtain its associated velocity and attenuation values. The sample was placed in a water bath between two unfocussed ultrasound transducers of 1.9-cm diameter—each having a 0.5-MHz nominal center frequency and near-to-far field transition point of 3.0 cm (Model #V318-SU, Panametrics Inc., Waltham, MA, USA),

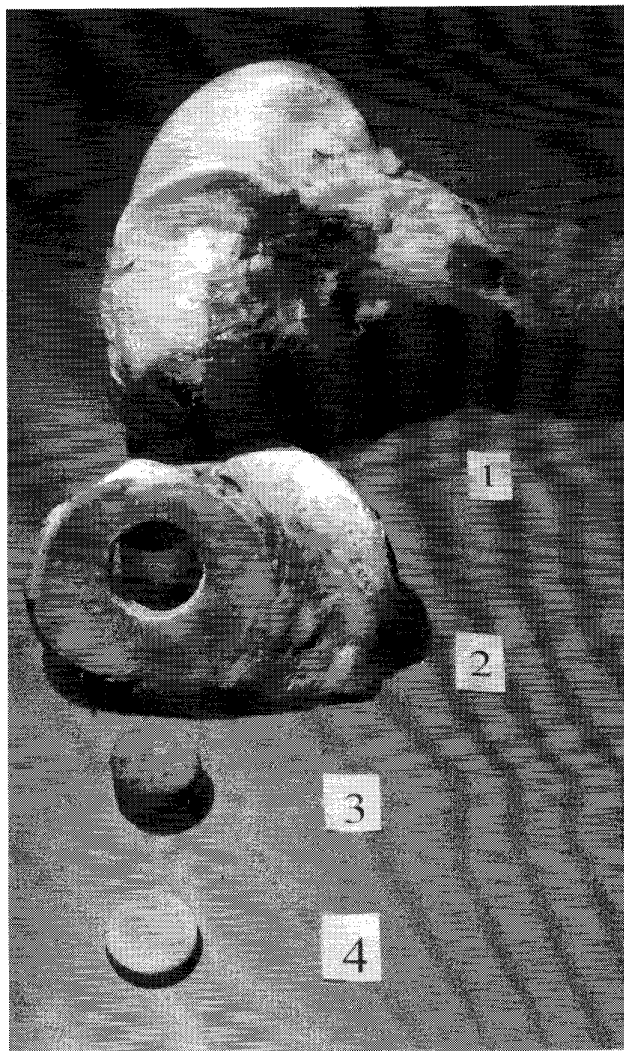


Fig. 2. Drilling and slicing of the trabecular bovine bone core. (1) Distal femur, (2) condyle slice, (3) raw core, and (4) final core.

coaxially located on either side of the core and 6.9 cm apart (Fig. 1). One transducer served to transmit an acoustic pulse driven by a pulser receiver card (Model SR-9000, Matec Inc., Hopkinton, MA, USA) directly into one surface of the sample and out the opposite side, where the signal was detected by the other transducer acting as receiver. The received ultrasound waveform was collected on a digital oscilloscope card (Model Compuscope 220, Gage Applied Science Inc., Montreal, Quebec, Canada) at a 40-MHz sampling rate and uploaded to a microcomputer for storage and subsequent off-line analysis. A waveform that propagated through the water only was also collected and served as a reference in the signal analysis.

The waveforms were processed using the discrete Fourier transform, and estimates of the sample's DSA were obtained using a least-squares straight line fit over the frequency range 300 kHz–700 kHz (Matlab 4.0, The MathWorks Inc., Natick, MA, USA). The ultrasonic velocity, v , was evaluated using a pulse transit time approach (8), in which the earliest arrival

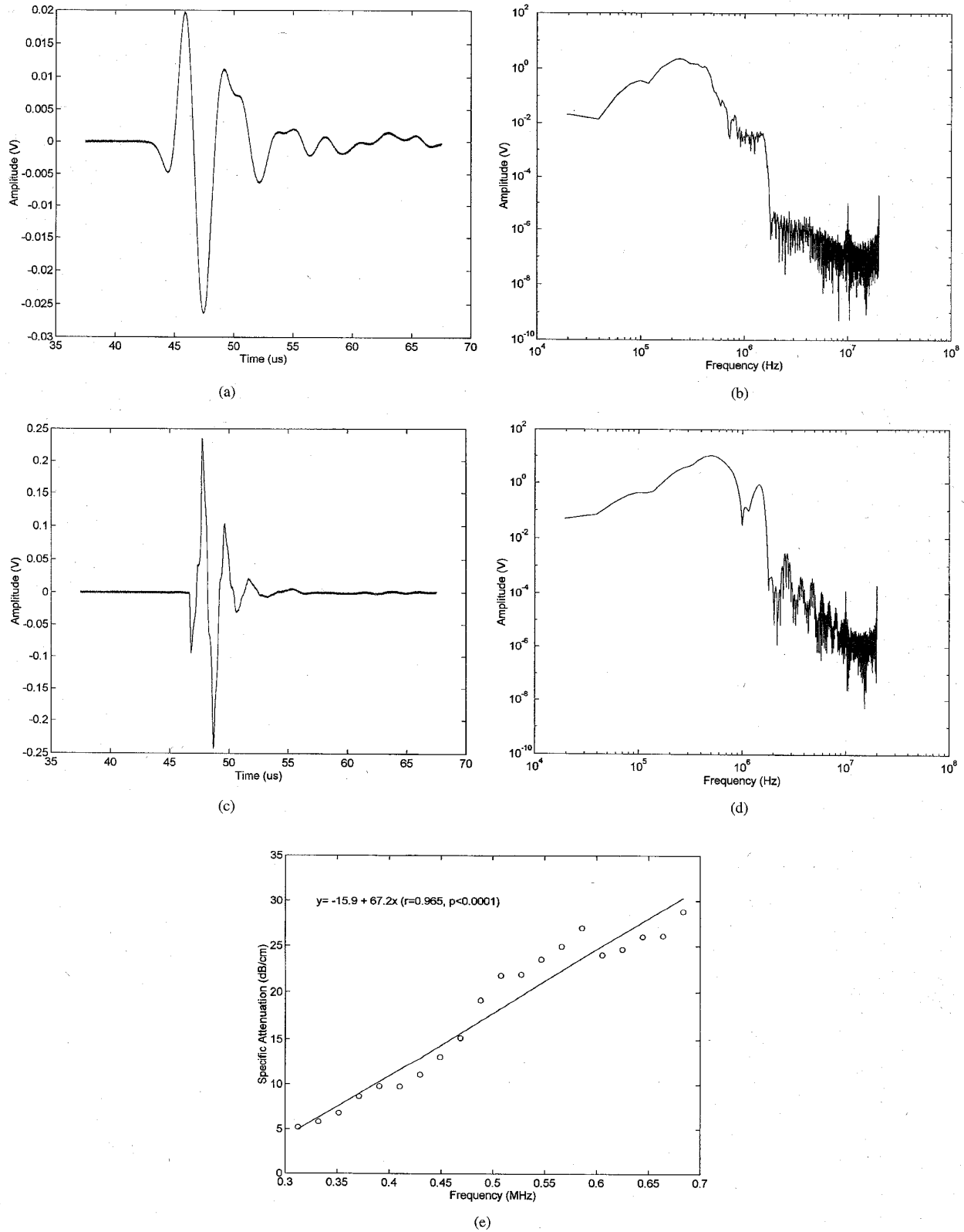


Fig. 3. (a) Time domain signal for a typical human vertebral trabecular sample (Transducers: 500 kHz/0.75"). (b) Frequency domain spectrum for the signal in (a). (c) Time domain signal for a typical reference medium measurement (Transducers: 500 kHz/0.75"). (d) Frequency domain spectrum for the reference signal in (c). (e) Attenuation data points and least squares curve fit for the sample and reference signals in (a) and (c).

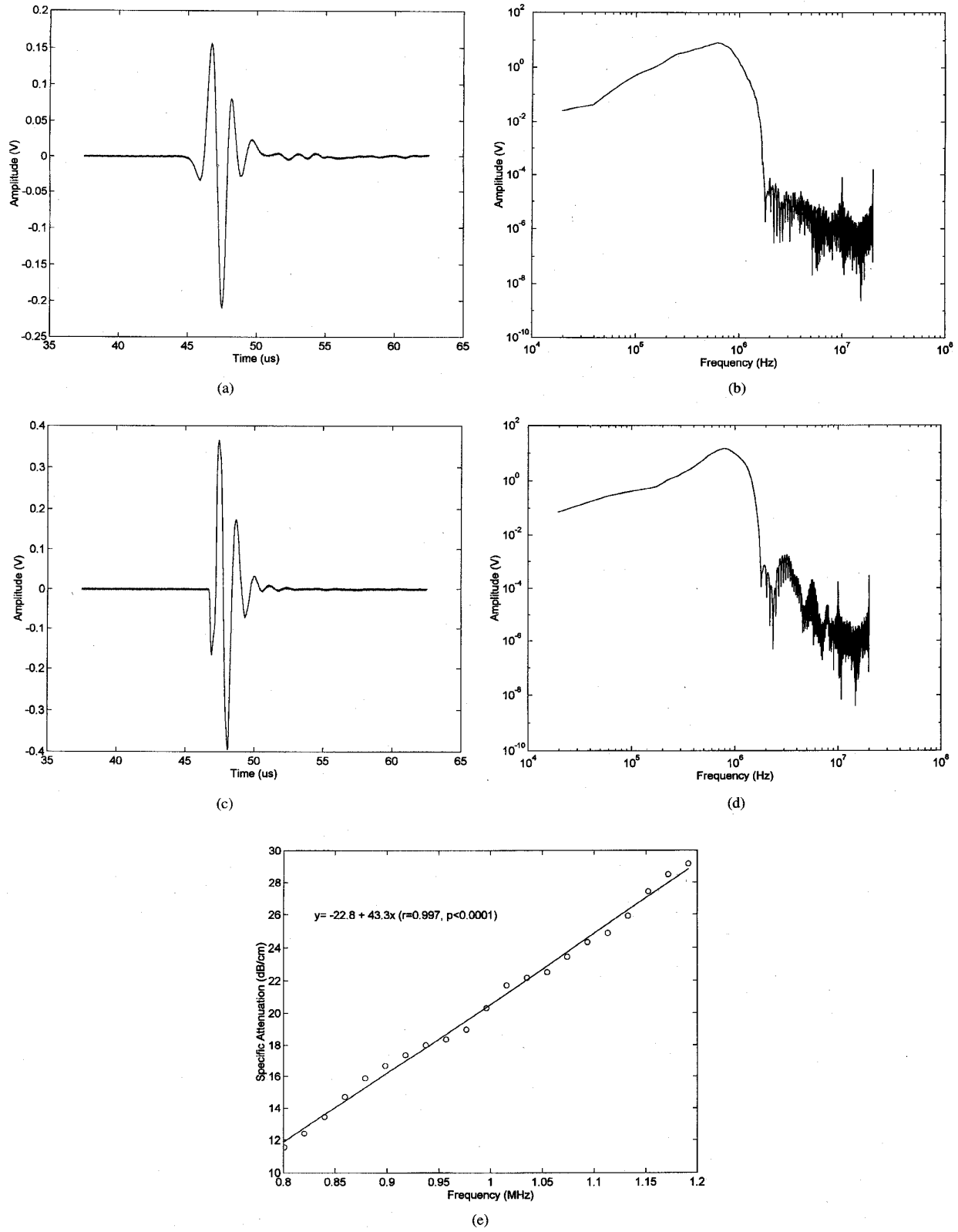


Fig. 4. (a) Time domain signal for a typical bovine femoral trabecular sample (Transducers: 1 MHz/0.75"). (b) Frequency domain spectrum associated with the signal in (a). (c) Time domain signal for a typical reference medium measurement (Transducers: 1 MHz/0.75"). (d) Frequency domain spectrum associated with the reference signal in (c). (e) Attenuation data points and least squares curve fit for the sample and reference signals in (a) and (c).

time of signal energy was recorded. Three independent sets of velocity and attenuation data from each sample were recorded and averaged to obtain the mean velocity and DSA for each sample. The ultrasonic measurements were repeated for all bone samples using another 1.9-cm diameter transducer pair, but with a 1-MHz nominal center frequency and a near-to-far field transition point of 6.0 cm (Model #V314-SU, Panametrics). In this case, the DSA was evaluated over the frequency range 0.8 MHz–1.2 MHz. The effect of the walls of the apparatus on the propagating acoustic pulse was determined to be negligible by comparing the reference waveforms to those obtained in absence of the apparatus (i.e., transducers only in water). No detectable difference in waveforms was observed.

Fig. 3(a)–(e) shows, for the 500-kHz transducer pair, respectively, an ultrasonic signal received after propagating through a human vertebral trabecular sample, the magnitude spectrum of the sample signal, a reference signal which propagated through water only, the magnitude spectrum of the reference signal, and the specific attenuation curve, $\mu(f)$. Similarly, Fig. 4(a)–(e) shows, for the 1-MHz transducer pair, respectively, an ultrasonic signal received after propagating through a bovine femoral condyle trabecular sample, the magnitude spectrum of the sample signal, a reference signal which propagated through water only, the magnitude spectrum of the reference signal, and the associated specific attenuation curve, $\mu(f)$.

E. Statistical and Correlation Analysis

Standard regression techniques were used to determine the correlation coefficients and statistical significance of the associated regressions [SigmaPlot, Jandel Scientific Software, San Rafael, CA]. The univariate and multivariate models for predicting bone density from the ultrasonic velocity and attenuation were evaluated using standard linear regression techniques. For example, the multivariate prediction of BD is based on the following regression equation:

$$BD = A + Bv + C \text{ DSA} \quad (9)$$

where A , B , and C are regression coefficients to be chosen according to the principle of least squares. The quality of the regression was assessed using the average absolute percent error (AAPE) between the actual and estimated bone density values (MATLAB, The MathWorks, Inc., South Natick, MA).

III. RESULTS

A. Human Bone Data

The BD of the human vertebral samples ranged from 0.057 to 0.142 g/cm^3 . For the 500-kHz transducers the ultrasonic velocity ranged from 1447 to 2019 m/s (Fig. 5) and the differential specific attenuation from 8.5 to 47 $\text{dBcm}^{-1}\text{MHz}^{-1}$ (Fig. 6). The correlation coefficients were $r = 0.91$ ($P < 0.0001$) and $r = 0.89$ ($P < 0.0001$) for the velocity and attenuation, respectively. For the 1-MHz transducers the bone velocity ranged from 1469 to 2343 m/s (Fig. 7) and DSA from 2.6 to 22 $\text{dBcm}^{-1}\text{MHz}^{-1}$ (Fig. 8). The correlation coefficients

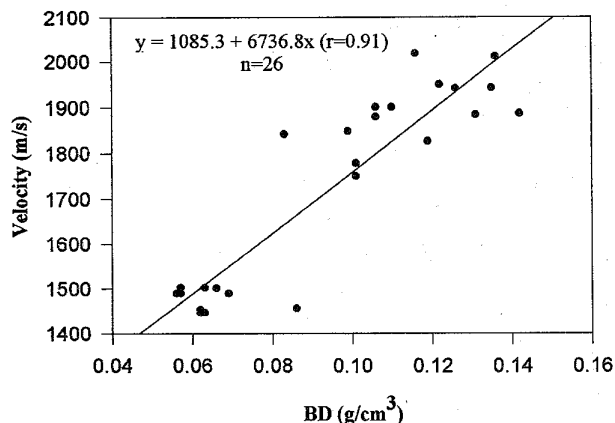


Fig. 5. Correlation between ultrasonic velocity and BD for the human vertebral trabecular samples. Transducer: 500 kHz/0.75". Frequency range: 300 kHz–700 kHz.

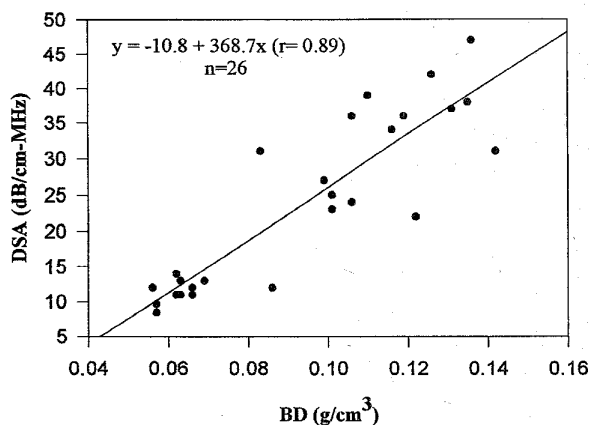


Fig. 6. Correlation between DSA and BD for the human vertebral trabecular samples. Transducer: 500 kHz/0.75". Frequency range: 300 kHz–700 kHz.

were $r = 0.89$ ($P < 0.0001$) and $r = 0.81$ ($P < 0.001$) for the velocity and DSA, respectively. For the 500-kHz transducer, the AAPE were 9.4% and 10.5% for the univariate velocity and attenuation estimates, respectively. Using both velocity and attenuation, the multivariate AAPE reduced to 8.4%, or about 11% lower than the smaller univariate error. For the 1-MHz transducer pair, the univariate AAPE were 9.5% and 16.1% for the velocity and attenuation based estimates, respectively. Using both attenuation and velocity, the multivariate AAPE reduced to 7.7%, or about 19% lower than the smaller univariate error. Table I displays the AAPE for both transducer pairs and for the univariate and multivariate regression estimates.

B. Bovine Bone Data

The BD of the femoral condyle samples ranged from 0.19 to 0.45 g/cm^3 . For the 500-kHz transducers the bone velocity ranged from 1510 to 1867 m/s (Fig. 9) and the DSA from 12 to 35 $\text{dBcm}^{-1}\text{MHz}^{-1}$ (Fig. 10). The correlation coefficients for the 500-kHz transducers for the univariate regressions were $r = 0.85$ ($P < 0.0001$) and $r = -0.17$ ($P < 0.44$)

TABLE I
AVERAGE ABSOLUTE PERCENT ERROR FOR UNIVARIATE AND MULTIVARIATE ANALYSIS (HUMAN VERTEBRAL TRABECULAR BONE)

Transducer (Frequency Range)	Univariate Analysis (Velocity versus BM)	Univariate Analysis (Attenuation versus BM)	Multivariate Analysis (Velocity and Attenuation versus BM)
500 kHz/0.75"			
300 kHz-700 kHz	9.4	10.5	8.4
1 MHz/0.75"	9.5	16.1	7.7
(0.8 MHz-1.2 MHz)			

TABLE II
AVERAGE ABSOLUTE PERCENT ERROR FOR UNIVARIATE AND MULTIVARIATE ANALYSIS (BOVINE FEMORAL TRABECULAR BONE)

Transducer (Frequency Range)	Univariate Analysis (Velocity versus BM)	Univariate Analysis (Attenuation versus BM)	Multivariate Analysis (Velocity and Attenuation versus BM)
500 kHz/0.75"			
300 kHz-700 kHz	9.4	18.7	9.1
1 MHz/0.75"	7.9	18.2	8.0
(0.8 MHz-1.2 MHz)			

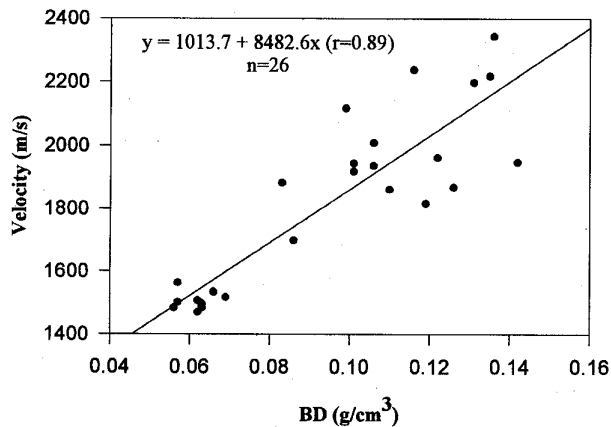


Fig. 7. Correlation between ultrasonic velocity and BD for the human vertebral trabecular samples. Transducer: 1 MHz/0.75". Frequency range: 0.8 MHz-1.2 MHz.

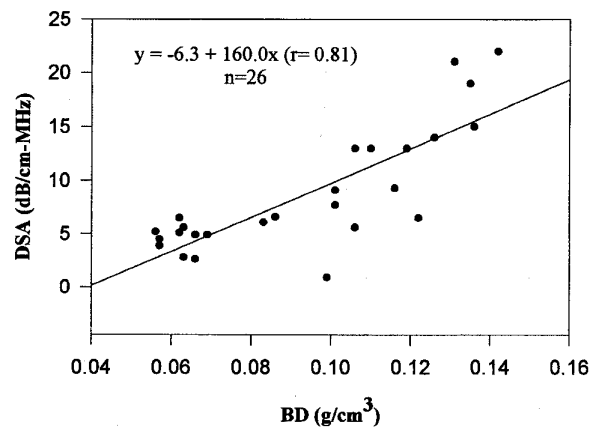


Fig. 8. Correlation between DSA and BD for the human vertebral trabecular samples. Transducer: 1 MHz/0.75". Frequency range: 0.8 MHz-1.2 MHz.

for the velocity and attenuation, respectively. For the 1-MHz transducers the bone velocity ranged from 1521 to 1914 ms^{-1} (Fig. 11) and DSA from 42 to 76 $\text{dBcm}^{-1}\text{MHz}^{-1}$ (Fig. 12). The correlation coefficients were $r = 0.90$ ($P < 0.0001$) and $r = 0.31$ ($P = 0.15$) for the velocity and attenuation, respectively. For the 500-kHz transducer, the univariate AAPE were 9.4% and 18.7% for the velocity and attenuation based estimates, respectively. Using both velocity and attenuation, the multivariate AAPE reduced to 9.1%, or about 3% lower than the smaller of the univariate errors. For the 1-MHz transducer pair, the univariate AAPE were 7.9% and 18.2% for the velocity and attenuation based estimates, respectively. Using both attenuation and velocity, the multivariate AAPE reduced to 8.0%, or about 1% higher than the lower univariate error. Table II displays the AAPE for both transducer pairs and for the univariate and multivariate regression estimates.

IV. DISCUSSION AND CONCLUSION

The results presented display the relationship between ultrasonic velocity and attenuation and bone mineral density

of cancellous bone. Both bovine and human bone samples were used in order to investigate the relationship over a relatively broad range of densities. The results demonstrate several facts. It is clear that for the range of bone densities studied, velocity was a more consistent and accurate estimator of bone density. For both the bovine and human data, the ultrasonic velocity was highly correlated with density, having correlation coefficients in the range of 0.9. This was true for both the lower frequency range (500-kHz transducer pair) and for the higher frequency range (1-MHz transducer pair). The same cannot be stated about attenuation. Although attenuation was highly correlated with density for the human bone samples, with correlations greater than 0.8, the relationship for the higher density bovine samples was much less strong. For the low and high frequency ranges the correlation was small and also negative. Thus while attenuation is strongly correlated with density for samples of relatively low density, the correlation is significantly weakened in the case of higher densities. This indicates that a nonlinear relationship exists between the attenuation and bone density, at least when taking into account both the human and bovine sample data. This finding is consistent with the recent results of Serpe and

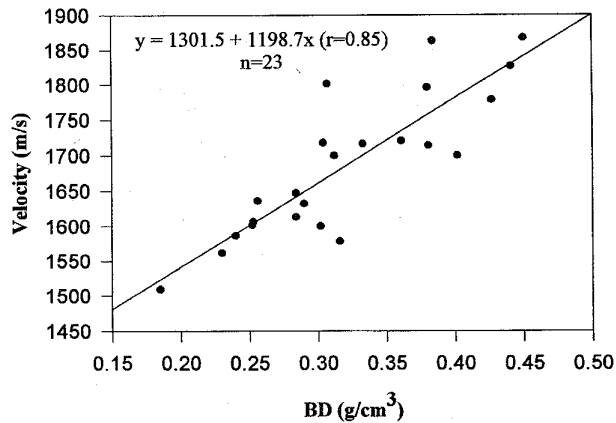


Fig. 9. Correlation between ultrasonic velocity and BD for the bovine femoral trabecular samples. Transducer: 500 kHz/0.75". Frequency range: 300 kHz–700 kHz.

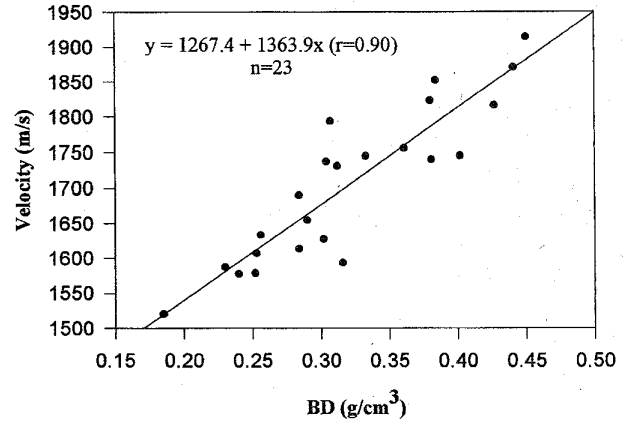


Fig. 11. Correlation between ultrasonic velocity and BD for the bovine femoral trabecular samples. Transducer: 1 MHz/0.75". Frequency range: 0.8 MHz–1.2 MHz.

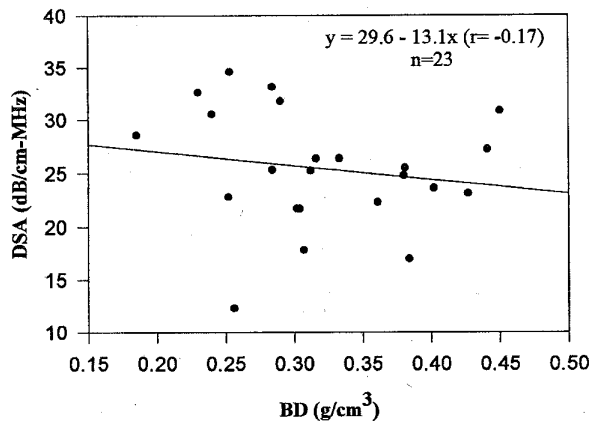


Fig. 10. Correlation between DSA and BD for the bovine femoral trabecular samples. Transducer: 500 kHz/0.75". Frequency range: 300 kHz–700 kHz.

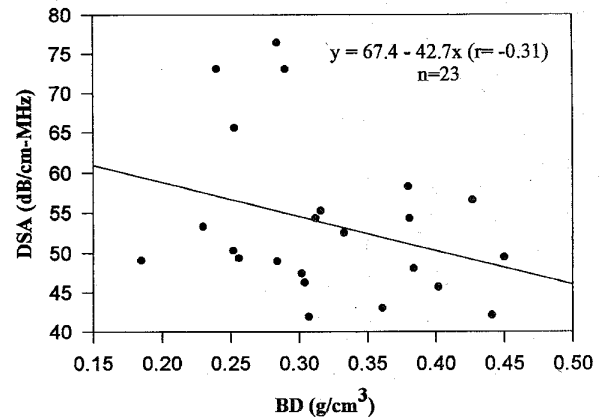


Fig. 12. Correlation between DSA and BD for the bovine femoral trabecular samples. Transducer: 1 MHz/0.75". Frequency range: 0.8 MHz–1.2 MHz.

Rho [25]. An interesting and possibly related observation arises from the nonlinear relationship between bone specific surface and porosity, as reported by Martin [26]. If attenuation can be assumed to arise from the scattering of the ultrasonic wave in the bone structure, and if this scattering can be assumed to be proportional to the relative amount of specific surface area present, then a nonlinear dependence of attenuation on bone density is consistent with the above observations and assumptions. Future investigations can be directed toward investigating this phenomenon and the related frequency dependence of the differential specific attenuation. In particular, it may be possible to identify a transition frequency, that is a frequency at which the dependence of DSA on density changes from a positive to a negative slope, and this could be useful for characterizing the mean pore size.

The range of ultrasonic velocity and attenuation values overlap for the human and bovine bone data. Thus it was not possible to analyze the human and bovine data together. The reasons for this may be related to two basic factors. First, the inherent assumed differences in trabecular architecture could

lead to different absolute values in the acoustic parameters. Second, the experiments on the groups of samples were not carried out at the same time and therefore may be susceptible to some uncontrolled factors in the procedure. Although each set of data, i.e., human or bovine, was acquired rapidly (within one week), there was a significant time interval between the experiments on the two data sets. Thus it was possible that a factor related to a change in the measurement conditions could have occurred.

A natural question to ask is whether or not the combination of ultrasonic attenuation and velocity may be able to better estimate bone mineral density together than with either feature alone. As may be expected, since the correlations of attenuation with bone density were so weak in the bovine data case, combining it with velocity did not lead to any significant improvement in the ability to estimate bone density. In contrast, however, for the human bone data the combination of both attenuation and velocity did produce improvements, providing about an 11% improvement for the 500-kHz transducer pair data and about a 19% improvement for the 1-MHz transducer pair data. This improvement was assessed by the AAPE, which

provides a measure of the relative errors one might expect in using ultrasonic measurements to estimate bone density. This best average error was obtained for the 1-MHz data, producing an AAPE of 7.7%.

This study did not consider the relationship of trabecular architecture to the ultrasonic measurements. This is an important aspect of the interaction of ultrasonic waves with trabecular bone, particularly with respect to the human bone samples [1]. Additional studies should be carried out in order to elucidate the effects of age, architecture, and bone quality on ultrasonic attenuation and velocity. In this regard, several recent reports have related ultrasonic measurements to osteoporotic fractures [29], which suggest that ultrasound may be useful for characterization and prediction of fracture risk as well.

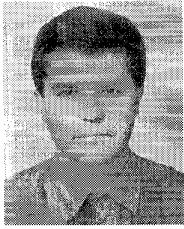
Our results indicate that ultrasonic measurements are, in general, highly correlated with bone density in trabecular bone samples. This correlation is more consistent and strong in relatively low density human samples compared with higher density bovine samples. Whether this is related to the density value alone, or a combination of the density with differences in microstructure (architecture) remains to be determined through further studies. Additionally, the combination of both ultrasonic velocity and attenuation as measured in human cancellous bone appears to offer a significant improvement in the accuracy of the bone density estimate. Studies are ongoing to investigate if the application of more complex multivariate estimation techniques, for example nonlinear neural network based methods, can further enhance the accuracy of bone density estimates [21]. Finally, the neural network approach is also being investigated to determine the ability of ultrasonic measurements to estimate bone architecture, strength, and clinical bone fracture risk.

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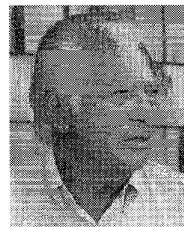
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