THE JOURNAL OF THE ACOUSTICAL SOCIETY OF KOREA Vol.22, No.2E 2003. 6. pp. 69~77

Correlations Among Speed of Sound, Broadband Ultrasonic Attenuation, Broadband Ultrasonic Reflection, and Bone Density in Bovine Cancellous Bone

Kang Il Lee*, Bok Kyoung Choi**, Suk Wang Yoon*

*Acoustics Research Laboratory and BK21 Physics Research Division, Department of Physics, SungKyunKwan University

**Global Environment Research Laboratory, Korea Ocean Research and Development Institute

(Received March 14 2003; revised April 17 2003; accepted June 9 2003)

Abstract

Correlations between acoustic properties and bone density have been investigated in bovine cancellous bone. Speed of sound (SOS), broadband ultrasonic attenuation (BUA), and broadband ultrasonic reflection (BUR) were measured in 10 defatted bovine cancellous bone specimens *in vitro*. SOS showed a significant correlation with the apparent density of the bone. A comparable correlation was observed between BUA and the apparent density. BUR was rather highly correlated with the apparent density. It was shown that BUR had a weak correlation with BUA and a significant correlation with SOS. This indicates that the parameter BUR can provide important information that may not be contained in BUA and SOS and, therefore, can be useful as an alternative diagnostic parameter of osteoporosis. As expected, a linear combination of all three ultrasonic parameters in a multiple regression model resulted in a significant improvement in predicting the apparent bone density.

Keywords: *Osteoporosis, Cancellous bone, Apparent bone density, Speed of sound (SOS), Broadband ultrasonic attenuation (BUA), Broadband ultrasonic reflection (BUR), Multiple regression model*

I. Introduction

Quantitative ultrasound (QUS) technique is now widely used for non-invasive assessment of osteoporosis[1-5]. Bone mineral density (BMD) is regarded as one of the most important parameters for the assessment of osteoporotic fracture risk. BMD can be measured at specific fracture-related skeletal sites by dual energy X-ray absorptiometry (DEXA) and quantitative computed tomography (QCT). Ultrasound has been found to easily measure bone characteristics of calcaneus, tibia, and patella. This technique has some advantages over its X-ray counterparts: DEXA and QCT. It is less expensive, relatively simple, portable, and does not apply ionizing radiation. Moreover, ultrasonic parameters reflect bone structural characteristics as well as BMD.

Most commercial ultrasonic devices screening bone density utilize values for speed of sound (SOS), broadband ultrasonic attenuation (BUA), or their combination in the os calcis[3]. SOS is related in a predicted manner to elasticity and density of cancellous bone, whereas BUA is related to both density and structure. Calcaneal SOS and BUA have been shown to highly correlate with

Corresponding author: Suk Wang Yoon (swyoon@skku.ac.kr)
Department of Physics, SungKyunKwan University, 300 Chunchun-dong, Jangan-gu, Suwon, Kyunggi-do 440-746, Republic of Korea

calcaneal BMD[1,5], which is in turn a useful indicator of osteoporotic fracture risk in the hip[6]. Linear combination of SOS and BUA has been demonstrated to be predictive of hip and other fractures in women in prospective[7] and retrospective[8] studies.

Transmission measurements only partially exploit the information related to the interaction between elastic wave and bone. The assessment of bone strength demands increasing specific knowledge about microscopic bone quality and structure. Ultrasonic reflection or backscatter may be useful for the measurement of these specific material and structural properties. In addition, skeletal sites, which are difficult to reach by transmission, could be evaluated by such echoed ultrasounds.

Reflection or scattering from the bone has received less attention than speed of sound and attenuation. From theory and also from previous experience of backscatter measurements in soft tissue, it is known that the backscatter signal should be dependent on the scatter structure, in this case the bone microstructure. A few studies have shown *in vitro* and *in vivo* the feasibility of the backscatter approach at the calcaneus[9,10]. The frequency-averaged backscatter coefficient from 0.2 to 0.6 MHz has been termed broadband ultrasonic backscatter (BUB). The relationship between BUB and future fracture risk has been documented by Roux *et al*[11]. However, the study failed in demonstrating that a combination of the parameters measured in transmission (SOS or BUA) with BUB improves the prediction of the fracture risks. In addition to usual QUS parameters, the clinical utility of BUB at the heel or at different skeletal sites has yet to be proven.

In this study, the frequency-averaged reflection loss from 0.5 to 1 MHz, which is referred to as broadband ultrasonic reflection (BUR), is introduced for some advantages over backscatter measurements. Backscatter measurements must be compensated for several sources of error including the signal loss caused by the partial transmission at the bone-tissue interface, the frequency dependence of the volume insonified by the transducer, and the effect of the gating function. In addition, not accounting for the frequency-dependent attenuation in the bone leads to poor estimation of backscatter coefficients. The larger attenuation and longer time gate give the poorer estimates of backscatter coefficients without compensation. Although the attenuation is not negligible and has a frequency dependency, which is almost always the practical case for the bone, BUR is not needed to account for the frequency-dependent attenuation compensation.

In the present study, SOS, BUA, and BUR were measured in 10 defatted bovine cancellous bone specimens *in vitro*. One objective of the present study is to investigate relationships between BUR and more common ultrasonic parameters of SOS and BUA. Another objective is to investigate the degree of correlation by which BUR can be used to predict bone density. Toward these objectives, BUR was evaluated by itself as well as in combination with SOS and BUA with multiple regression models for prediction of bone density. A high predictive value would suggest that linear combinations of the ultrasonic parameters may be used as surrogates for bone density.

II. Materials and Methods

2.1. Bone Specimens

Ten cancellous bone specimens were obtained from the proximal ends of one fresh frozen bovine tibia. The specimens were cut by using a rotary electric saw to make parallel and smooth surfaces without any soft tissue. The surfaces of each specimen were finished with a fine silicon carbide abrasive paper. Care was taken to produce parallel surfaces. The resulting specimens had flat and parallel faces with thicknesses varying from 14 to 20 mm. The opposing planar surfaces were kept as parallel within $\pm 0.5°$ by caliper measurements of thickness throughout each specimen. The surface of the bone specimens was large enough to cover the receiving transducer face. The specimens were all oriented in the same direction in relation to the bone. Their orientations were chosen so that the ultrasound could pass through the specimens along the mediolateral (ML) direction of the tibia where the trabeculae are aligned in the perpendicular direction to propagation at normal incidence. They are the same orientations with those *in vivo* measurements commonly performed with commercial bone sonometers.

In order to decrease the risk of microorganism contamination of bone specimens, they were defatted by boiling for 1 hour in water. Defatting process was assumed not to significantly affect their acoustic properties because the acoustic properties of defatted trabecular bone have shown just slightly different from those of bone with marrow left intact[12]. Although boiling may change the bone matrix, correlations between ultrasonic parameters and bone density are largely retained. This is due to the fact that these relationships arise primarily from the interactions of the ultrasonic wave with the bone matrix-pore fluid structure and less from changes in the bone matrix material by itself. To remove air bubbles, the specimens were degassed under vacuum. After removing air bubbles, they were kept at room temperature prior to ultrasonic measurements.

Apparent density is defined as the ratio of defatted bone mass to bulk volume of the specimen. It was assessed from separate measurements of mass and volume. Mass was measured with a balance. Volume was determined by measuring the volume difference with and without the specimen using a mass cylinder.

2.2. Transmission Measurements

The schematic diagram of the experimental setup for ultrasonic measurements is shown in Figure 1. Ultrasonic measurements were performed in a water bath maintained at room temperature between 16℃ and 18℃. A 200 MHz computer controlled pulser/receiver (Panametrics 5900PR) was used. A pair of coaxially aligned transducers with the center frequency of 1 MHz (Panametrics V303, 0.5″ diameter) was vertically oriented to make it possible to place the specimen on the face of the receiving transducer. The faces of transducers were separated by 50 mm, a distance greater than the 26.5 mm near-field distance stated by the manufacturer. Received ultrasound signals were acquired using a 500 MHz digital storage oscilloscope (LeCroy LT322) and were stored on a computer for off-line analysis.

A through-transmission method was used to measure SOS and BUA. Using two opposing coaxially aligned transducers, transmitted signals were recorded both with and without the bone specimen in the acoustic path. SOS was estimated in the time domain with the straightforward principle of time of arrival of signal energy. SOS can be also estimated in the frequency domain using phase unwrapping and linear models. Since most commercial bone QUS devices have employed the pulse transit time method, we used that method here as well. To measure SOS, arrival times of received broadband pulses were measured with and without the specimen in the water path. SOS, c_s, can be estimated from

$$c_s = \frac{c_w}{1 - \frac{c_w \Delta t}{d}} \qquad (1)$$

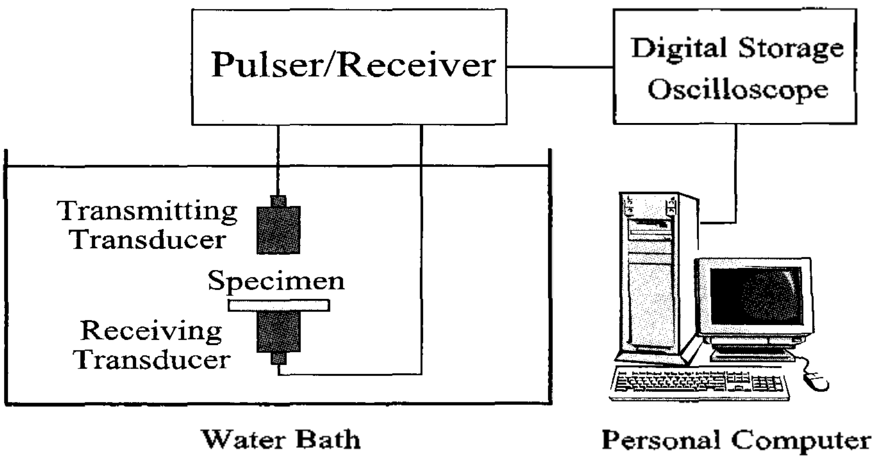

Figure 1. Schematic diagram of the experimental setup for ultrasonic measurements.

where d is the thickness of the specimen and Δt is the difference in arrival times. The temperature-dependent speed of sound in distilled water, c_w, is given by[13]

$$c_w = 1402.9 + 4.835 \times T - 0.047016 \times T^2 + 0.00012725 \times T^3 \quad (2)$$

where T is the temperature in ℃. Each arrival time was taken by the first zero crossing time. Five measurements were obtained at five different sites on a specimen. The measurements were repeated for the opposite direction in the same specimen. Total ten measurements of two directions in each specimen were averaged to obtain the mean value of SOS.

BUA was determined using the same signals acquired for the SOS measurements. A fast Fourier transform (FFT) was used to obtain the power spectra of the transmitted signals with and without the specimen in the water path. The signal loss as a function of the frequency was obtained by subtracting the power spectrum level of the signal transmitted through the specimen from that propagated through water taken as a non-attenuating reference medium.. A linear fit was performed over a bandwidth of interest, and the slope of the fitted line was divided by the thickness of the specimen to obtain a value of BUA in units of dB/cmMHz. This parameter is often referred to as "normalized broadband ultrasonic attenuation" (nBUA). Clinical systems do not generally normalize attenuation to calcaneal thickness. Due to the anatomical variations in the bone size of human subjects, it is reasonable to normalize for bone thickness.

Figure 2 shows a reference signal propagated through water only and a typical signal transmitted through a bone specimen. The typical bone signal exhibits an earlier arrival time due to the faster speed of sound in bone than that in water. Figure 3 shows the power spectra corresponding to the signals presented in Figure 2. It is apparent that the center frequency of the signal is shifted to a lower frequency, resulting from the increasing attenuation with frequency. The usable frequency bandwidth from 0.5 to 1 MHz was selected to reduce the effect of noise at low signal levels particularly at the high frequency region, in which there is a significant attenuation by the bone specimens. The measured spectral data within the bandwidth of 0.5-1 MHz were found to be reliable and not subject to the poor signal to noise ratio.

2.3. Reflection Measurements

Ultrasonic reflection was measured using a monostatic pulse-echo method. In this method, the transmitting transducer was also used as the receiving transducer. A

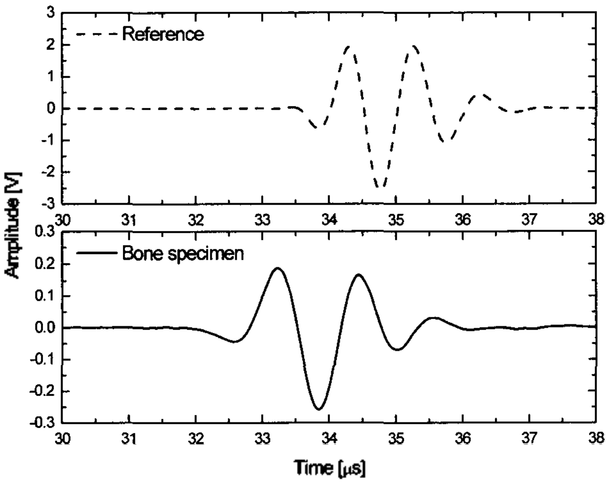

Figure 2. Reference signal propagated through water only and a typical signal transmitted through a bone specimen. The typical bone signal exhibits an earlier arrival time due to the faster speed of sound in bone than that in water.

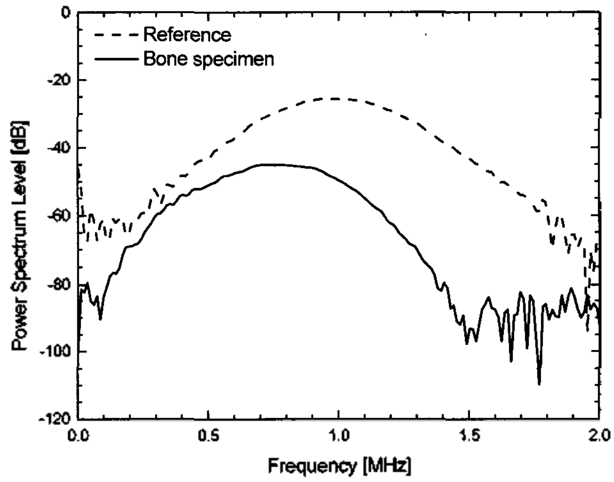

Figure 3. Power spectra corresponding to the signals presented in Figure 2. The usable frequency bandwidth from 0.5 to 1 MHz was selected to reduce the effect of noise at low signal levels particularly at the high frequency region, in which there is a significant attenuation by the bone specimens.

reference signal was acquired by reflecting an ultrasonic pulse from a standard reflector, 15.85 mm thick steel plate. The reflector was placed on the face of the receiving transducer that was disconnected for reflection measurements, and then was aligned by maximizing the amplitude of the reflected signal. Pulse-echo signals from the bone specimens were acquired by replacing the reflector with the specimen of interest.

A reference pulse-echo signal from the reflector and a typical pulse-echo signal from a bone specimen are shown in Figure 4. The gated region of the reflected signal from the bone specimen includes specular echoes produced at the water-specimen and specimen-water interfaces as well as the backscattered signals from the trabecular volume between the echoes. This gate location and duration are attributed to a total tissue volume of the specimen. Power spectra of the reference signal from the reflector and those of the reflected signals corresponding to the gated region were obtained using a FFT. Figure 5 shows the power spectra corresponding to the signals presented in Figure 4. The frequency bandwidth used for analysis was taken to be from 0.5 to 1 MHz, as was the same for attenuation. The reflection loss in dB, $RL(f)$, is obtained from

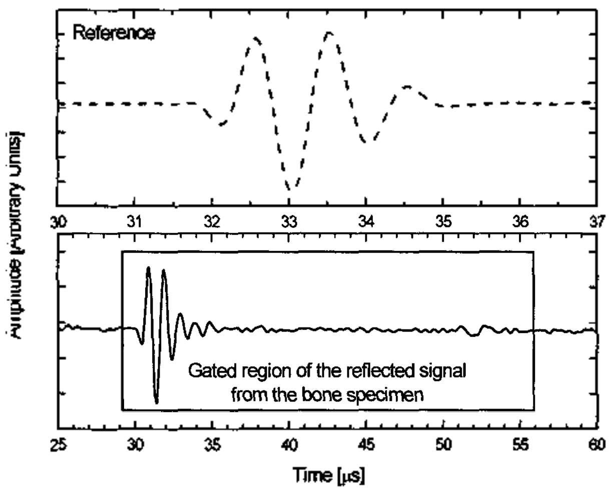

Figure 4. Reference pulse-echo signal from the reflector and a typical pulse-echo signal from a bone specimen. The gated region of the reflected signal from the bone specimen includes specular echoes produced at the water-specimen and specimen-water interfaces as well as the backscattered signals from the trabecular volume between the echoes.

$$RL(f) = 20\log\frac{R_0(f)}{R_B(f)} \tag{3}$$

where $R_0(f)$ is the amplitude power spectrum of the pulse-echo signal from the reflector and $R_B(f)$ is that from the bone specimen. Figure 6 shows the frequency-dependent reflection loss for a typical bone specimen. The $RL(f)$ was averaged (or integrated) over the frequency bandwidth of 0.5-1 MHz to obtain a representative value for reflection loss in dB, and was multiplied by 1 to be negative. This value is termed broadband ultrasonic reflection (BUR) hereafter. Five measurements were obtained at five different sites on the specimen. The measurements were

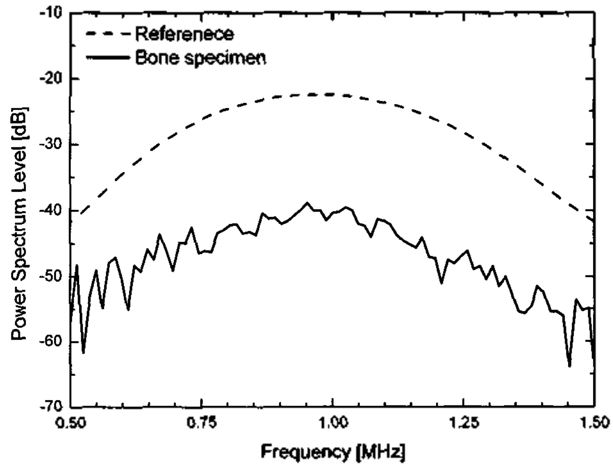

Figure 5. Power spectra corresponding to the signals presented in Figure 4. The frequency bandwidth used for analysis was taken to be from 0.5 to 1 MHz, as was the same for attenuation.

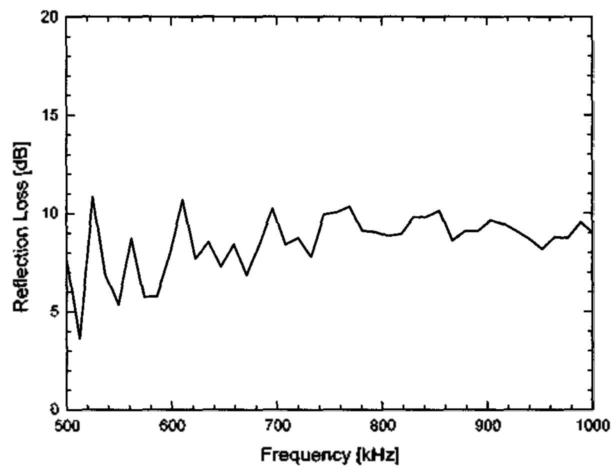

Figure 6. Frequency-dependent reflection loss for a typical bone specimen.

repeated for the opposite direction in the same specimen. Total ten measurements of two directions in each specimen were averaged to obtain the mean value of BUR.

III. Results

The mean value and standard deviation (SD) of the apparent density, SOS, BUA, and BUR for the 10 defatted bovine cancellous bone specimens are shown in Table 1. The correlation of each ultrasonic parameter with the apparent density is shown in Table 2. Figures 7 to 9 illustrate the results of SOS, BUA, BUR as functions of the apparent density. A linear fit was performed for each ultrasonic parameter to obtain the correlation coefficients. SOS showed a significant correlation with the apparent density (r = 0.64, $p < 0.04$). A comparable correlation was observed between BUA and the apparent density (r = 0.53, $p < 0.11$). These correlations are similar to those in high density bovine cancellous bone reported by others[14-16]. It was found that BUR was rather highly correlated with the apparent density (r = 0.73, $p < 0.01$). The p value is the probability that the correlation coefficient r is zero.

Table 2 also shows the correlation coefficients among SOS, BUA, and BUR. SOS and BUA were moderately correlated with each other (r = 0.44, $p < 0.20$). BUR showed a significant correlation with SOS (r = 0.62, $p < 0.05$), but a weak correlation with BUA (r = 0.23, $p < 0.51$). These suggest that BUR can provide important diagnostic information that may not be contained in SOS and BUA.

Table 1. Mean value and standard deviation (SD) of the apparent density, SOS, BUA, and BUR for the 10 defatted bovine cancellous bone specimens.

Apparent density [g/cm³]	0.735 ± 0.096	0.577 ~ 0.894
SOS [m/s]	1694 ± 48	1637 ~ 1785
BUA [dB/cmMHz]	26.1 ± 3.1	22.8 ~ 32.7
BUR [dB]	-9.3 ± 1.3	-12.3 ~ -7.9

Table 2. Correlation matrix for the apparent density, SOS, BUA, and BUR.

Parameter	Apparent density	SOS	BUA	BUR
Apparent density	1	0.64	0.53	0.73
SOS		1	0.44	0.62
BUA			1	0.23
BUR				1

Table 3. Correlation coefficient and root-mean-square error (RMSE) of the linear combinations of the parameters of SOS, BUA, and BUR with the apparent density of the bone.

Parameter	Correlation coefficient	RMSE
SOS	0.64	38.75
BUA	0.53	2.83
BUR	0.73	0.91
SOS + BUA	0.7	0.07
SOS + BUR	0.77	0.07
BUA + BUR	0.82	0.06
SOS + BUA + BUR	0.82	0.06

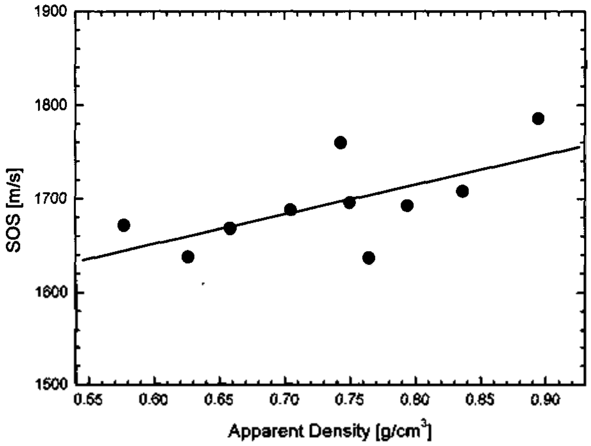

Figure 7. Correlation between SOS and the apparent density of the bone.

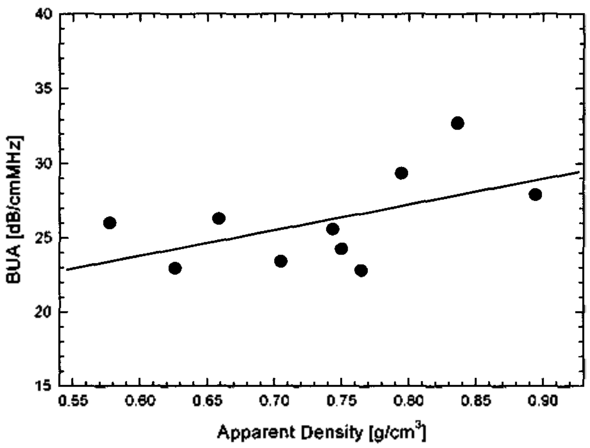

Figure 8. Correlation between BUA and the apparent density of the bone.

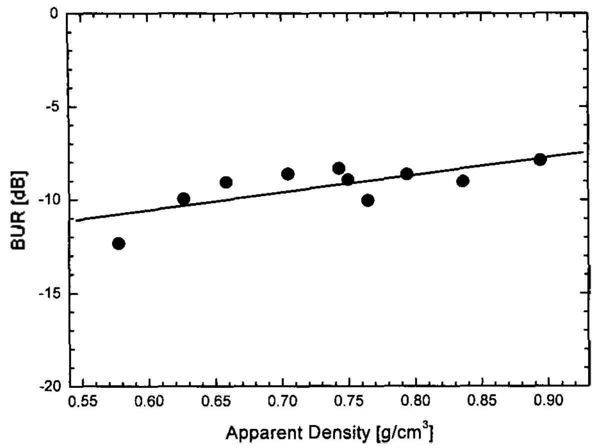

Figure 9. Correlation between BUR and the apparent density of the bone.

The multiple regression analysis summarized in Table 3 shows that the linear combination of all three ultrasonic parameters has a high correlation with the apparent density of the bone. The linear combination of BUA and BUR appeared to offer a significant improvement in the accuracy for predicting the apparent density. The final multiple regression model for predicting the apparent density is given by the following regression equation:

$$\text{apparent density} = (0.33164 \pm 1.17230) + (0.00031 \pm 0.00065)\text{SOS} + (0.01013 \pm 0.00791)\text{BUA} + (0.04243 \pm 0.02256)\text{BUR},$$

where the apparent density is measured in g/cm^3, SOS in m/s, BUA in dB/cmMHz, and BUR in dB. The standard errors of the estimates of the coefficients are presented in the regression equation.

IV. Discussion

In the present study, the ultrasonic parameters of the bone, SOS, BUA, and BUR were measured in 10 defatted bovine cancellous bone specimens *in vitro*. A linear regression resulted in that SOS showed a significant positive correlation with the apparent density. However, a comparable correlation between BUA and the apparent density was observed in the bovine cancellous bone of high density. In recent years, the relation between the ultrasonic parameters and the bone density has been extensively studied *in vitro*. Many studies[14-18] have reported a strong correlation between BUA and the apparent density in human cancellous bone. Serpe *et al*[15]. showed strong correlations between the apparent density and both SOS and BUA in the low density cancellous bone from the bovine tibiae. In a dense bovine cancellous bone, however, the correlation is much weaker or even completely absent, and both positive and negative regression slopes have been reported[14-16,19]. These results suggest that the relation between BUA and density over a wide range of the density of the cancellous bone may not be linear. Similar trends have been also reported in bone phantom materials, suggesting that this nonlinear behavior is a general feature of fluid-saturated porous media[20].

BUR showed a significant correlation with the apparent density, and the correlation was higher compared to SOS and BUA. The correlations between BUR and the two parameters of SOS and BUA are 0.23 and 0.62, respectively, suggesting that BUR may reveal substantial information not contained in SOS and BUA. Therefore, BUR may have a potential as an alternative ultrasonic parameter to the existing parameters of SOS and BUA for assessing the bone status. The combination of all three ultrasonic parameters in a multiple regression model was more predictive of the apparent density.

Future studies may be raised by addressing some limitations of the present study. First, this study was carried out for the small number of specimens. In order to get the orientation of the trabecular specimens be the same, we used only one bovine tibia. Ten specimens were obtained from the proximal ends of one bovine tibia so that all specimens could be oriented in the same direction (ML). The most significant limitation may be that all measurements were performed using the specimens of the bovine cancellous bone with relatively high mineral densities. For the high density bovine cancellous bone, ultrasonic absorption and scattering may be characteristically different from the human cancellous bone with low density. Further study using a similar procedure would be valuable on specimens of the human cancellous bone.

V. Conclusions

Correlations between the acoustic properties and the bone density have been investigated in the bovine cancellous bone. SOS, BUA, and BUR were measured in 10 defatted bovine cancellous bone specimens *in vitro*. SOS showed a significant correlation with the apparent density. However, a comparable correlation between BUA and the apparent density was observed in the bovine cancellous bone with high density. BUR showed a significant correlation with the apparent density, and the correlation was higher compared to the parameters of SOS and BUA. SOS and BUA were only moderately correlated with each other. BUR showed a significant correlation with SOS, but a weak correlation with BUA. A linear combination of all three ultrasonic parameters of SOS, BUA, and BUR in a multiple regression model led to a significant improvement in predicting the apparent density. These results suggest that the parameter BUR can provide important information that may not be contained in SOS and BUA and, therefore, can be useful as an alternative diagnostic parameter of osteoporosis.

Acknowledgments

This work was supported by a Korea Research Foundation grant (KRF-2000-015-DP0178) and the BK21 Program of the Ministry of Education.

References

1. C. M. Langton, S. B. Palmer, and R. W. Porter, "The measurement of broadband ultrasonic attenuation in cancellous bone," *Eng. Med.*, **13**, 89-91, 1984.
2. R. Strelitzki and J. A. Evans, "An investigation of the measurement of broadband ultrasonic attenuation in trabecular bone," *Ultrasonics*, **34**, 785-791, 1996.
3. S. Han, J. Medige, and I. Ziv, "Combined models of ultrasound velocity and attenuation for predicting trabecular bone strength and mineral density," Clin. Biomech, **11**, 348-353, 1996.
4. J. Toyras, H. Kroger, and J. S. Jurvelin, "Bone properties as estimated by mineral density, ultrasound attenuation, and velocity," *Bone*, **25**, 725-731, 1999.
5. C. F. Njeh, D. Hans, T. Fuerst, C. C. Gluer, and H. K. Genant, Quantitative *Ultrasound: Assessment of osteoporosis and bone status*, Martin Dunitz, London, 1999.
6. S. R. Cummings et al., "The study of osteoporotic fractures research group: Bone density at various sites for the prediction of hip fractures," *Lancet*, **341**, 72-75, 1993.
7. D. Hans, P. Dargent-Molina, A. M. Schott, J. L. Sebert, C. Cormier, P. O. Kotzki, P. D. Delmas, J. M. Pouilles, G. Breart, and P. J. Meunier, "Ultrasonographic heel measurements to predict hip fracture in elderly women: The EPIDOS prospective study," *Lancet*, **348**, 511-514, 1996.
8. M. Schott, S. Weill-Engerer, D. Hans, F. Duboeuf, P. D. Delmas, and P. J. Meunier, "Ultrasound discriminates patients with hip fracture equally well as dual-energy x-ray absorptionmetry and independently of bone mineral density," *J. Bone Min. Res*, **10**, 243-249, 1995.
9. K. A. Wear, A. P. Stuber, and J. C. Reynolds, "Relationships of ultrasonic backscatter with ultrasonic attenuation, sound speed and bone mineral density in human calcaneus," *Ultrasound Med. Biol*, **26**, 1311-1316, 2000.
10. K. A. Wear and D. W. Armstrong III, "Relationships among calcaneal backscatter, attenuation, sound speed, hip bone mineral density, and age in normal adult women," *J. Acoust. Soc. Am*, **110**, 573-578, 2001.
11. C. Roux, V. Roberjot, S. Kolta, R. Porcher, J. Fechtenbaum, and P. Laugier, "Broadband ultrasound backscattering (BUB) measurements at the os calcis in osteoporosis," *J. Bone Min. Res*, **14**, S375, 1999.
12. K. A. Wear, "Ultrasonic attenuation in human calcaneus from 0.2 to 1.7 MHz," *IEEE Trans*, Ultrason, Ferroelectr, Freq. Control, **48**, 602-608, 2001.
13. G. W. C. Kaye and T. H. Laby, *Table of Physical and Chemical Constants*, Longman, London, 1973.
14. S. Han, J. Y. Rho, and I. Ziv, "Ultrasound velocity and broadband attenuation over a wide range of bone mineral density," *Osteoporosis Int*, **6**, 291-296, 1996.
15. L. Serpe and J. Y. Rho, "The nonlinear transition period of broadband ultrasound attenuation as bone density varies," *J. Biomech*, **29**, 963-966, 1996.
16. J. M. Alves, W. Xu, D. Lin, R. S. Stiffert, J. T. Ryaby, and J. J. Kaufman, "Ultrasonic assessment of human and bovine trabecular bone: a comparison study," *IEEE Trans, Biomed, Eng*, **43**, 249-258, 1996.
17. P. H. F. Nicholson, M. J. Haddaway, and M. W. J. Davie, "The dependence of ultrasonic properties on orientation in human vertebral bone," *Phys. Med. Biol*, **39**, 1013-1024, 1994.
18. P. Laugier, P. Droin, A. M. Laval-Jeantet, and G. Berger, "In vitro assessment of the relationship between acoustic properties and bone mass density of the calcaneus by comparison of ultrasound parametric imaging and quantitative computed tomography," *Bone*,

20, 157-165, 1997.
19. K. I. Lee, H. S. Roh, and S. W. Yoon, "Correlations between acoustic properties and bone density in bovine cancellous bone from 0.5 to 2 MHz," *J. Acoust. Soc. Am.*, 113, 2933-2938, 2003.
20. R. Strelitzki, J. A. Evans, and A. J. Clarke, "The influence of porosity and pore size on the ultrasonic properties of bone investigated using a phantom material," Osteoporosis Int., 7, 370-375, 1997.

[Profile]

• Kang Il Lee
The Journal of the Acoustical Society of Korea Vol. 19, No. 1E, 2002.

• Bok Kyoung Choi
The Journal of the Acoustical Society of Korea Vol. 22, No. 4, 2003.

• Suk Wang Yoon
The Journal of the Acoustical Society of Korea Vol. 22, No. 4, 2003.