Relationships among calcaneal backscatter, attenuation, sound speed, hip bone mineral density, and age in normal adult women

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Abstract

The present study was undertaken in order to investigate the use of calcaneal ultrasonic backscatter for the application of diagnosis of osteoporosis. Broadband ultrasonic attenuation (BUA), speed of sound (SOS), average backscatter coefficient (ABC), and hip bone mineral density (BMD) were measured in calcanea in forty-seven women (average age: 58 years, standard deviation: 13 years). All three ultrasound variables had comparable correlations with hip BMD (around 0.5). As reported previously by others, BUA and SOS were rather highly correlated with each other. The logarithm of ABC was only moderately correlated with the other two. The three ultrasound parameters exhibited similar moderate negative correlations with age. These results taken collectively suggest that ABC may carry important diagnostic information independent of that contained in BUA and SOS and therefore may be useful as an adjunct measurement in the diagnosis of osteoporosis.

Keywords

ultrasound; backscatter; osteoporosis; cancellous bone

Introduction

Ultrasound-based methods for bone assessment are less expensive, faster, simpler, and more portable than their x-ray counterparts: dual-energy x-ray absorptiometry (DEXA) and quantitative computed tomography (QCT). In addition, they produce no ionizing radiation. The diagnostic capability of ultrasound to predict fracture risk has been documented in many studies. Calcaneal broadband ultrasonic attenuation[1–4] (BUA) and speed of sound[2,3,5–11] (SOS) correlate highly with calcaneal bone mineral density (BMD) which is in turn an indicator of osteoporotic fracture risk in the hip.[12] Linear combinations of BUA and SOS are thought to have greater diagnostic capability than either parameter by itself and have been demonstrated to be predictive of hip and other fractures in women in prospective[13,14] and retrospective[15–18] studies.

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In general, ultrasonic backscatter is known to provide information regarding size, shape, number density, and elastic properties of scatterers.[19–23] In trabecular bone applications, trabeculae are likely candidates for scattering sites due to the high contrast in acoustic properties between mineralized trabeculae and marrow.[24–27] The diminished number and thicknesses of trabeculae within bone that are associated with increased fracture risk would be expected to reduce backscatter. Several preliminary studies have established diagnostic promise and/or clinical feasibility of this measurement.[28–34] A recent study has suggested that backscatter increases significantly upon decollagenization (with 7% sodium hypochlorite) and decreases or remains the same upon demineralization (with ethylenediaminetetraacetic acid, disodium salt dihydrate or EDTA).[35]

The present study was undertaken to further investigate the use of ultrasonic backscatter as a diagnostic measurement. This study is an extension to a larger population of subjects of an earlier preliminary investigation of 10 subjects. The initial study was performed using a clinical imaging system designed for abdominal applications. A center frequency of 2.25 MHz was used. In the present work a lower frequency (1 MHz, more suitable for highly attenuating bone) system, but without imaging capability, was employed and applied to a much larger set of subjects.

Methods

Forty-seven normal adult women (3 African American, 1 African European, 1 Asian, 1 Hispanic, and 41 non-Hispanic Caucasian; average age 58 years with a standard deviation of 13 years) were studied at the National Naval Medical Center (NNMC) in Bethesda, MD. These nonpregnant women were free of known disorders of skeletal metabolism, with no known history of nontraumatic bone fractures, and free of disorders whose treatment or medication promotes loss of bone such as diabetes, emphysema, and asthma. In addition, women with a history of bilateral hip replacement, Paget's disease of the bone, renal failure, hyperthyroidism, or treated hypothyroidism were excluded. All participants provided informed consent (approved by both FDA and NNMC).

Ultrasound measurements were performed on each subjects' left calcaneus. While sitting upright in a chair, the subject rested her left foot on her right knee as shown in Figure 1. A standoff pad (Cone Instruments, Solon, OH) was placed on the foot in order that data could be acquired in the focal zone of the transducer. The standoff pad also created a situation in which multiple reverberations between the transducer and the calcaneal surface were not received until well after the backscatter from the calcaneus and therefore could be excluded from the analysis.

Backscatter measurements were performed using a Panametrics (Waltham, MA) 5800 pulser/receiver and Panametrics V302 1" diameter, focussed (focal length = 2"), broadband transducer with center frequency of 1 MHz. Received signals were digitized (8 bit, 10 MHz) using a LeCroy (Chestnut Ridge, NY) 9310C Dual 400 MHz oscilloscope and stored on computer (via GPIB) for offline analysis.

Backscatter coefficients were measured using a reference phantom method.[36] Good agreement between experimental measurements using this method and theoretical predictions based on Faran's theory of scattering[19] for ultrasonic backscatter coefficients from phantoms consisting of glass spheres embedded in gelatin has previously been reported by this laboratory.[37] Over a band of frequencies corresponding to the system usable bandwidth (700 kHz to 1.5 MHz), backscatter coefficient vs. frequency data were least-squares fit to a power law relationship. The average backscatter coefficient (ABC) was computed from the midband (1 MHz) value of the fit. In order to compute backscatter coefficients it was necessary to compensate backscattered spectra for the effects of attenuation. For this compensation, the attenuation coefficient was taken to be linear with frequency and computed as the ratio of BUA (dB/MHz) and assumed constant value for calcaneal thickness for all subjects (3 cm).

A Lunar Achilles Plus bone sonometer was used for measurements of broadband ultrasonic attenuation (BUA) and speed of sound (SOS). The Achilles estimate of SOS was based on transit time of the *leading edge* rather than the *center* of the pulse propagating through the calcaneus and therefore provided an estimate closely related to *signal velocity* rather than *group velocity*.[38,39] This device also provided measurements of a parameter commonly (but not rigorously) referred to "stiffness" which is an linear combination of BUA and SOS and is thought to be a more robust indicator of bone status than either parameter by itself.

$$\text{"Stiffness"} = 0.68 * \text{BUA (dB/MHz)} + 0.28 * \text{SOS (m/s)} - 420$$

Based on a wealth of empirical data showing that BMD is positively correlated with both BUA and SOS, the first two coefficients in this equation were obtained by doing regression analysis to obtain those coefficients which make the contributions of the first two terms roughly equal in magnitude (on the average) over the range of clinical values. The constant term was designed to make the average value of "stiffness" for young normal adult women to be equal to 100. (This terminology should not be confused with the more standard and formal use of the term stiffness, which corresponds to the coefficient of proportionality between displacement and restorative force,[40] as in a spring, and may be expressed in units of N/m). The Achilles has been reported to yield estimates of BUA which are somewhat higher than those provided with comparable clinical calcaneal ultrasound devices.[41] In order to calibrate the Achilles, separate measurements of BUA were performed on two commercial phantoms using the Achilles and a laboratory apparatus previously described.[42] The phantoms were manufactured by CIRS Inc. (Norfolk, VA). One was designed to mimic normal bone (normalized BUA = 20.4 dB/cmMHz, SOS = 1562 m/s). The other was designed to mimic osteoporotic bone (normalized BUA = 14.2 dB/cmMHz, SOS = 1503 m/s). The normalized BUA values specified by the manufacturer were obtained over the frequency range from 250 kHz to 550 kHz. Six repeated measurements were acquired for each phantom for each measurement system. In the case of the laboratory system, each measurement was based on 8 RF lines. The average offset of the Achilles obtained from this comparison was subtracted from each of the clinical measurements of BUA.

A Hologic QDR-2000 DEXA scanner was used to measure BMD of the total hip, femoral neck, trochanter, and Ward's triangle. Only total hip BMD measurements are reported here.

Results

The average values and standard deviations for the measurements performed on the 47 subjects are given in Table I. The correlations between pairs of measurements are given in Table II. As reported by others, BUA and SOS were rather highly correlated with each other. The Alogarithm of the average backscatter coefficient was only moderately correlated with the other two. All three ultrasound variables had comparable correlations with hip BMD (around 0.5). The three ultrasound parameters exhibited similar moderate negative correlations with age. These results taken together suggest that ABC may carry important diagnostic information independent of that contained in BUA and SOS. Scatter plots of the three ultrasound parameters against Hip BMD and age are given in Figures 2 through 7.

The sharpest decline in BMD occurs shortly following menopause. The age related drop in BUA between subjects ranging in age from 45–54 and those ranging from 55–64 was 93.3 dB/MHz (average of 12 subjects) to 84.6 dB/MHz (average of 11 subjects). These values are quite similar to those reported by Cheng *et al.*,[43] namely 88.5 dB/MHz (average of 20 subjects) to 78.0 dB/MHz (average of 20 subjects) in the same age brackets. Similarly a drop in SOS from 1561 m/s to 1523 m/s was observed in the present study (Cheng *et al* did not measure SOS).

A linear regression between BUA and age was applied to the subset of subjects over 55, yielding a postmenopausal average annual rate of decline of 0.49 dB/MHz. This is similar to the value of 0.35 dB/MHz per year reported by Frost and co-workers.[44] The corresponding values for SOS are 0.30 m/s per year (present study) and 0.56 m/s per year (Frost *et al.).*

Discussion

This study indicates that calcaneal ultrasonic backscatter exhibits correlations with hip BMD and age that are comparable to those exhibited by BUA and SOS. The correlation between backscatter and the other two ultrasonic variables is only about 0.5, suggesting that backscatter may reveal substantial information not contained in the other two and therefore may have some potential value as a substitute or an adjunct for BUA and SOS for assessment of bone status. This study represents the first clinical evaluation of a contact-based (as opposed to water-bath based[30]) method for measurement of calcaneal backscatter near 1 MHz. The correlation between backscatter and hip BMD in these the contact-based and water-bath-based studies are essentially identical (0.50).[30]

The correlation between backscatter and BMD observed here at 1 MHz (r = 0.50; 95% CI: 0.24 – 0.69) is smaller than previously reported at 2.25 MHz (r = 0.87).[29] In addition to the difference in center frequencies, there are numerous differences between these two studies that may account for this. Most importantly, the earlier study correlated calcaneal backscatter with *calcaneal* BMD (*volumetric* BMD, in g/cm^3, measured with QCT) while the current investigation correlated calcaneal backscatter with *hip* BMD (*areal* BMD, in g/cm^2, measured with DEXA). It is not surprising that choosing two different sites rather

than using the same site resulted in a decrease in the correlation. In addition, the orientation of the transducer relative to the calcaneus was different in the two studies. In the earlier study, the transducer was placed on the inferior surface of the foot, below the calcaneus, while in the present study, data were acquired in the mediolateral orientation. In addition, unlike the earlier study, the current study incorporated compensation for calcaneal attenuation. Finally, applying the method of Hoel,[45] the 95% CI for the correlation coefficient in the earlier study may be computed to be 0.54 – 0.97, indicating some overlap in the 95% CI's for the two studies.

Preliminary *in vitro* studies[28,29,32] have demonstrated that ultrasonic backscatter increases with BMD in human calcaneus. Variations in BMD accounted for 66% – 68% (correlation coefficient near 0.8) of variations in the backscatter coefficient, suggesting that backscatter measurements give some indication of BMD, but also may convey some structural information not already contained in BMD measurements. Another study in bovine tibia trabecular bone[34] reported "apparent" (not compensated for attenuation) integrated (averaged over a range of frequencies) backscatter to actually decrease with density in the mediolateral and superoinferior orientations and to show no change with density in the anteroposterior orientation. It is plausible that compensation for attenuation (which demonstrated a significant *increase* with BMD in the AP and ML directions) in this study[34] could have yielded backscatter results more similar to the two above mentioned *in vitro* studies on human calcaneus. Differences between human calcaneus and bovine tibia trabecular bone[46] as well as different frequency ranges of analysis (700 kHz to 1.5 MHz in the present study, 200 kHz – 600 kHz,[28] and 1 – 3 MHz[34]) may also partially account for some disparity in results.

Fracture risk, not BMD, is the fundamental clinical end-point in the diagnosis of osteoporosis. Ideally, the utility of any diagnostic measurement for the prediction of fracture risk should be compared in populations with and without fractures, either prospectively or retrospectively. However, such a study can be somewhat more difficult as individuals either with fractures or with high propensity for fracture can be harder to find and recruit than normals. The current study demonstrates feasibility and some clinical promise for the contact method.

Acknowledgements

Acronyms:

ABC	Average Backscatter Coefficient
BMD	Bone Mineral Density
BUA	Broadband Ultrasonic Attenuation
SOS	Speed of Sound

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Figure 1.
Data Acquisition. The subject rested her left heel upon her right knee. A standoff pad was so that the region of interest coincided with the focal zone of the transducer. Coupling gel was used at the transducer/standoff-pad and standoff-pad/skin interfaces.
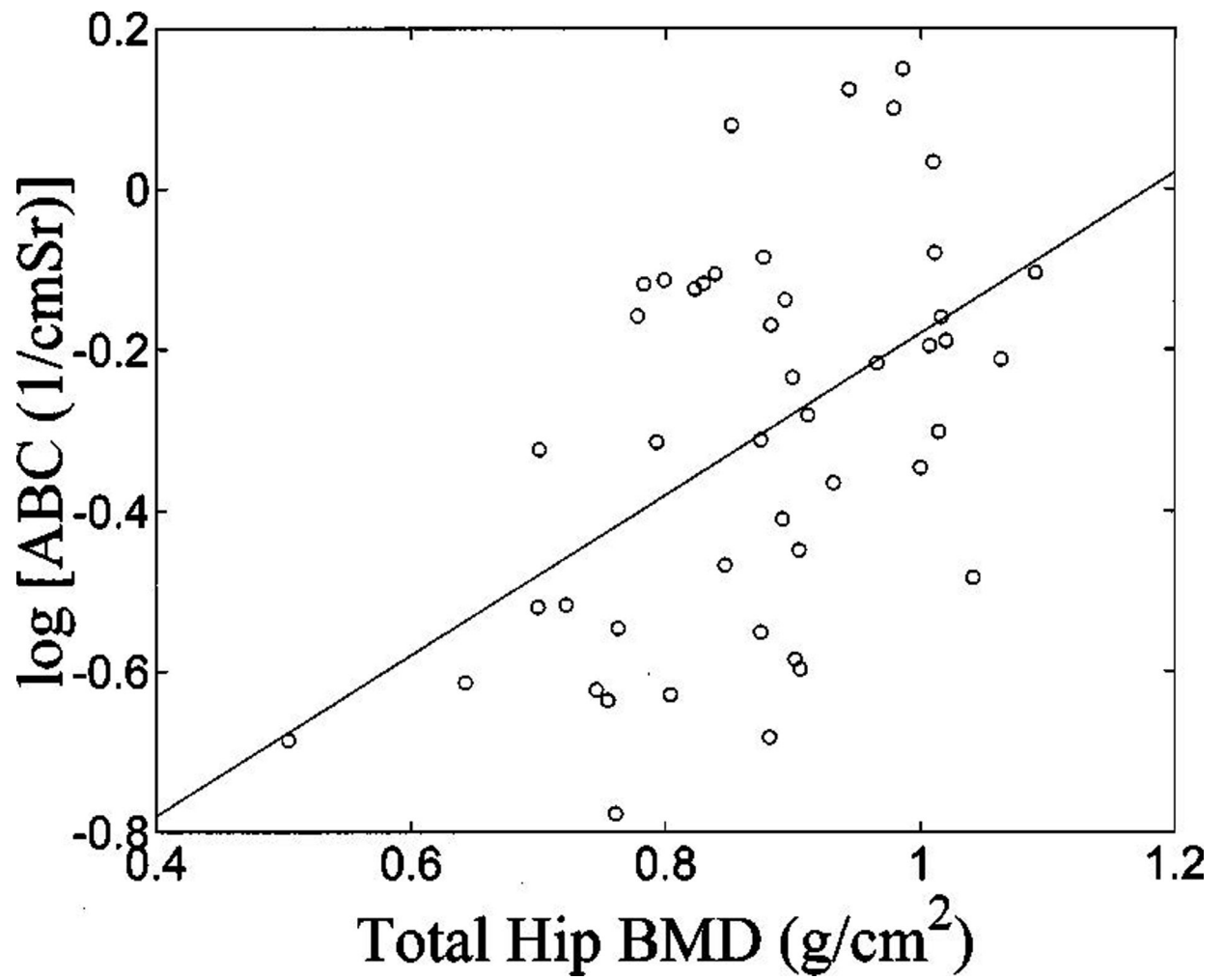
Figure 2.
Logarithm of average backscatter coefficient (ABC) vs. total hip bone mineral density
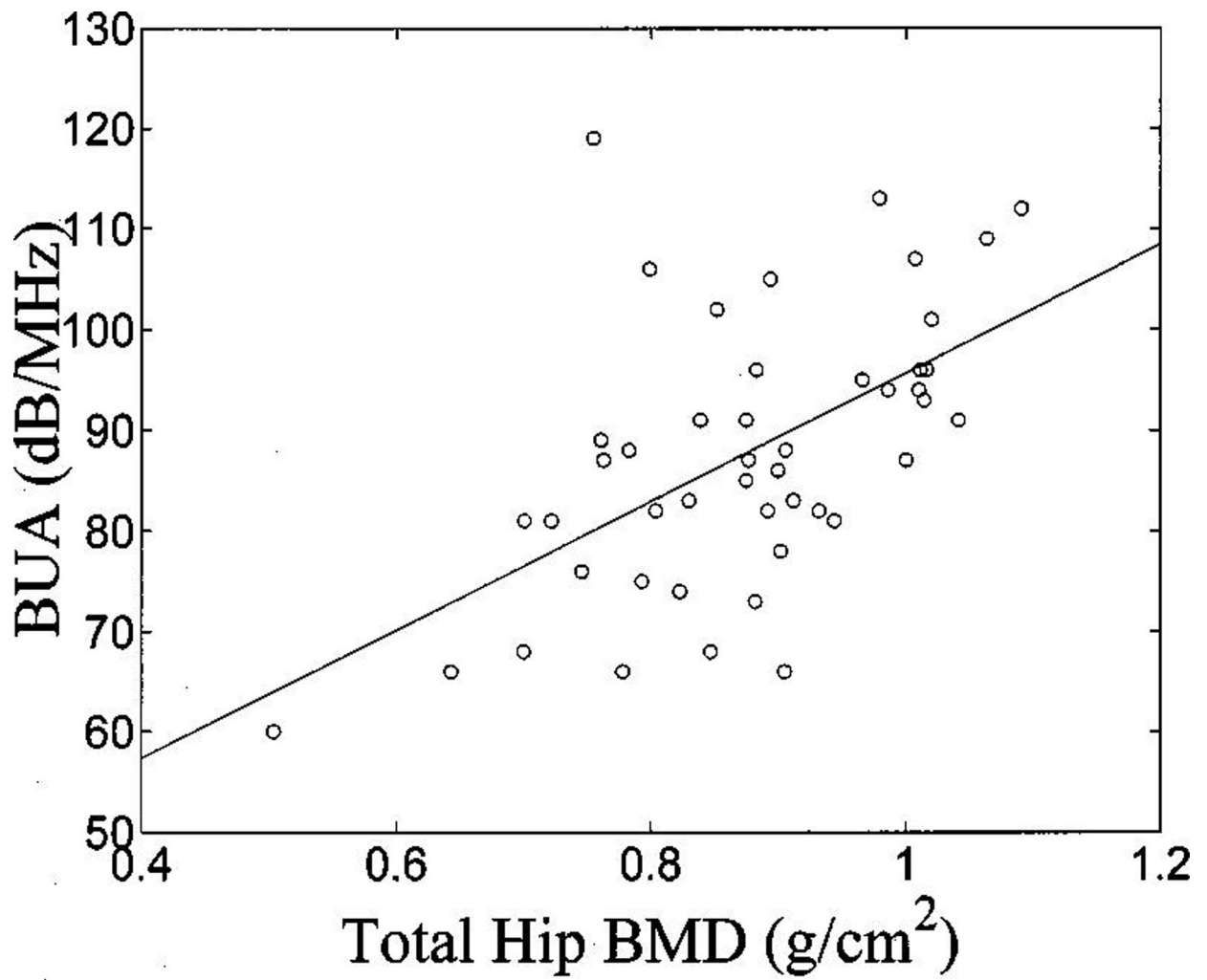(BMD).

Figure 3.
Broadband ultrasonic attenuation (BUA) vs. total hip bone mineral density (BMD).
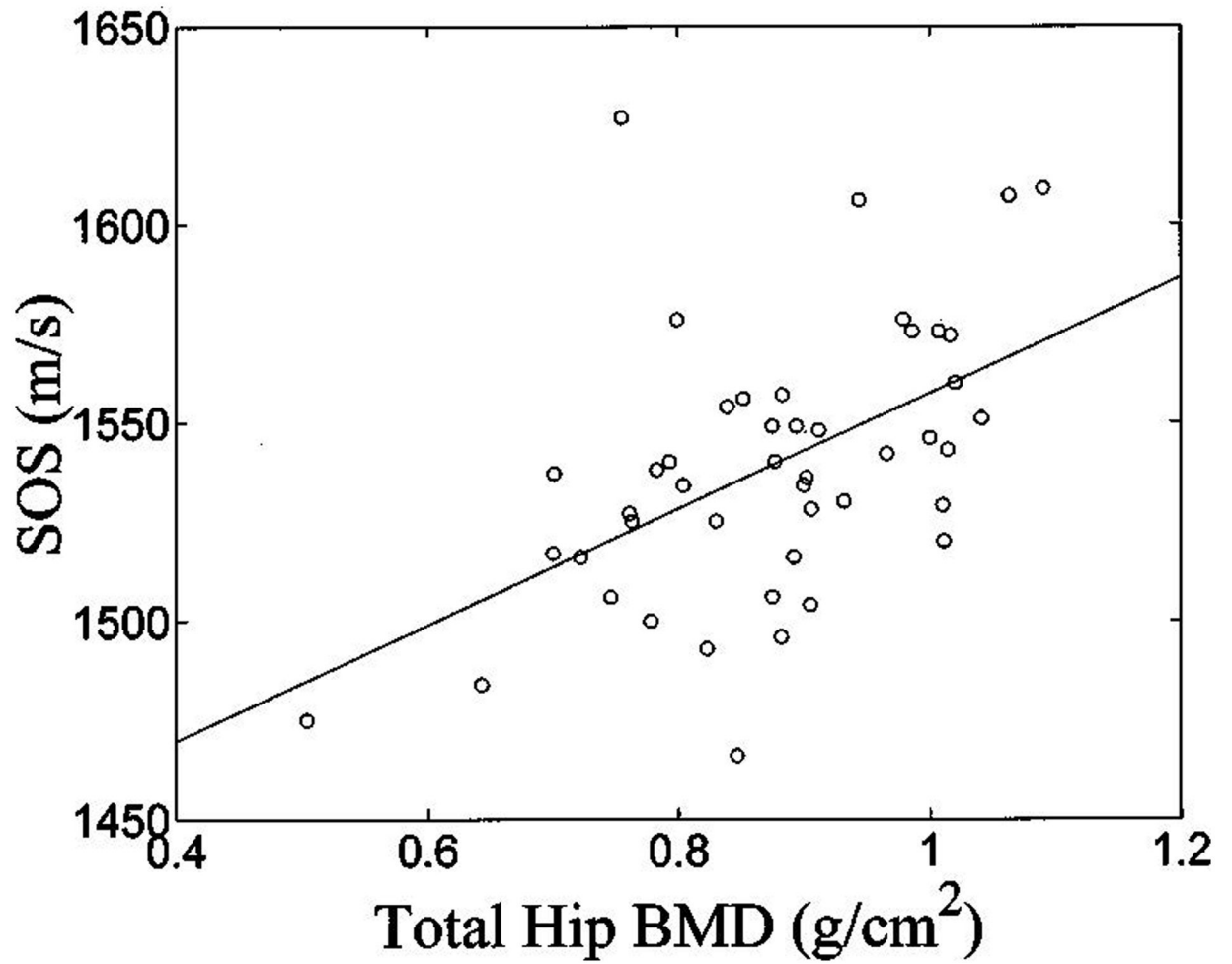
Figure 4.
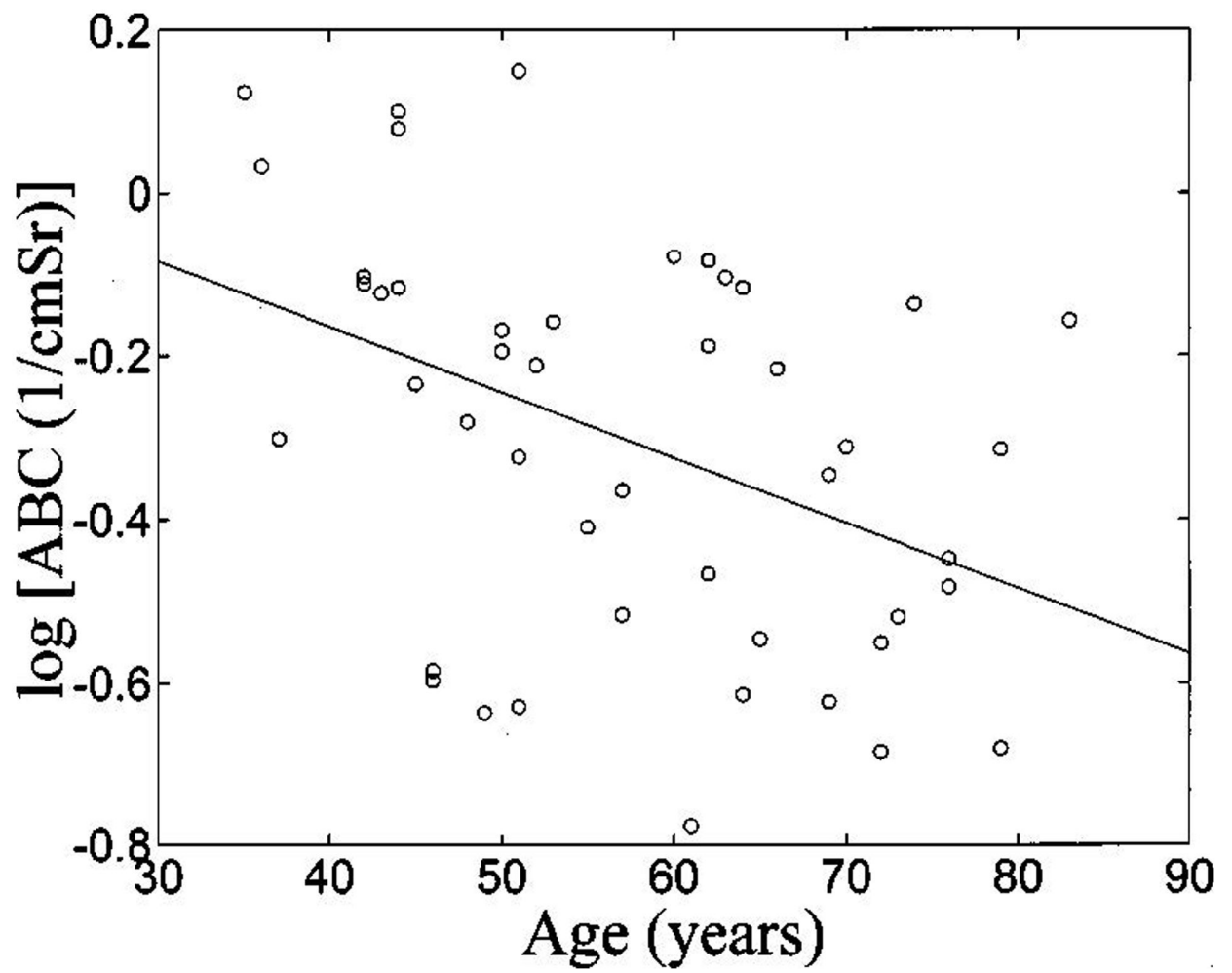Speed of Sound (SOS) vs. total hip bone mineral density (BMD).

Figure 5.
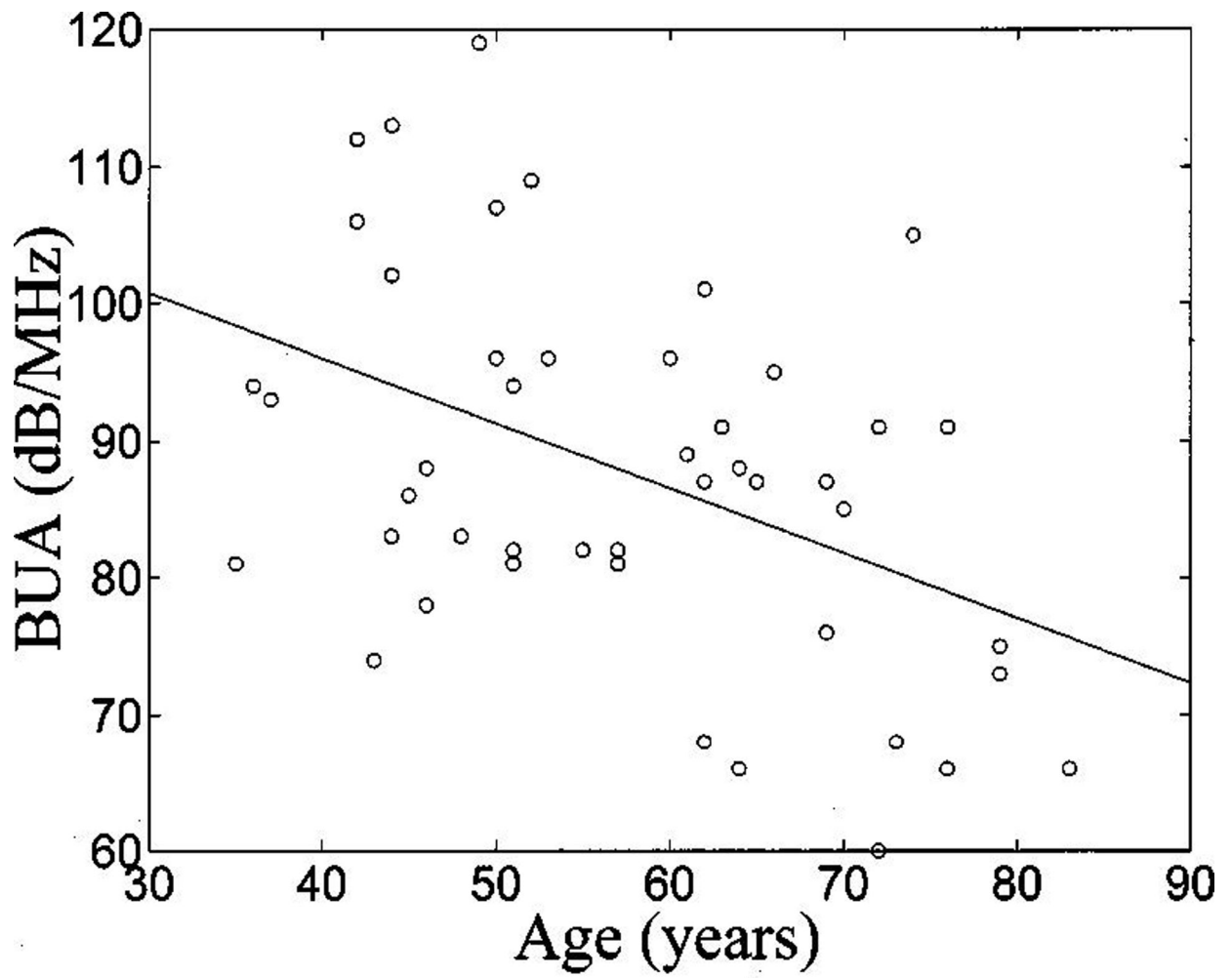Logarithm of average backscatter coefficient (ABC) vs. age.

Figure 6.
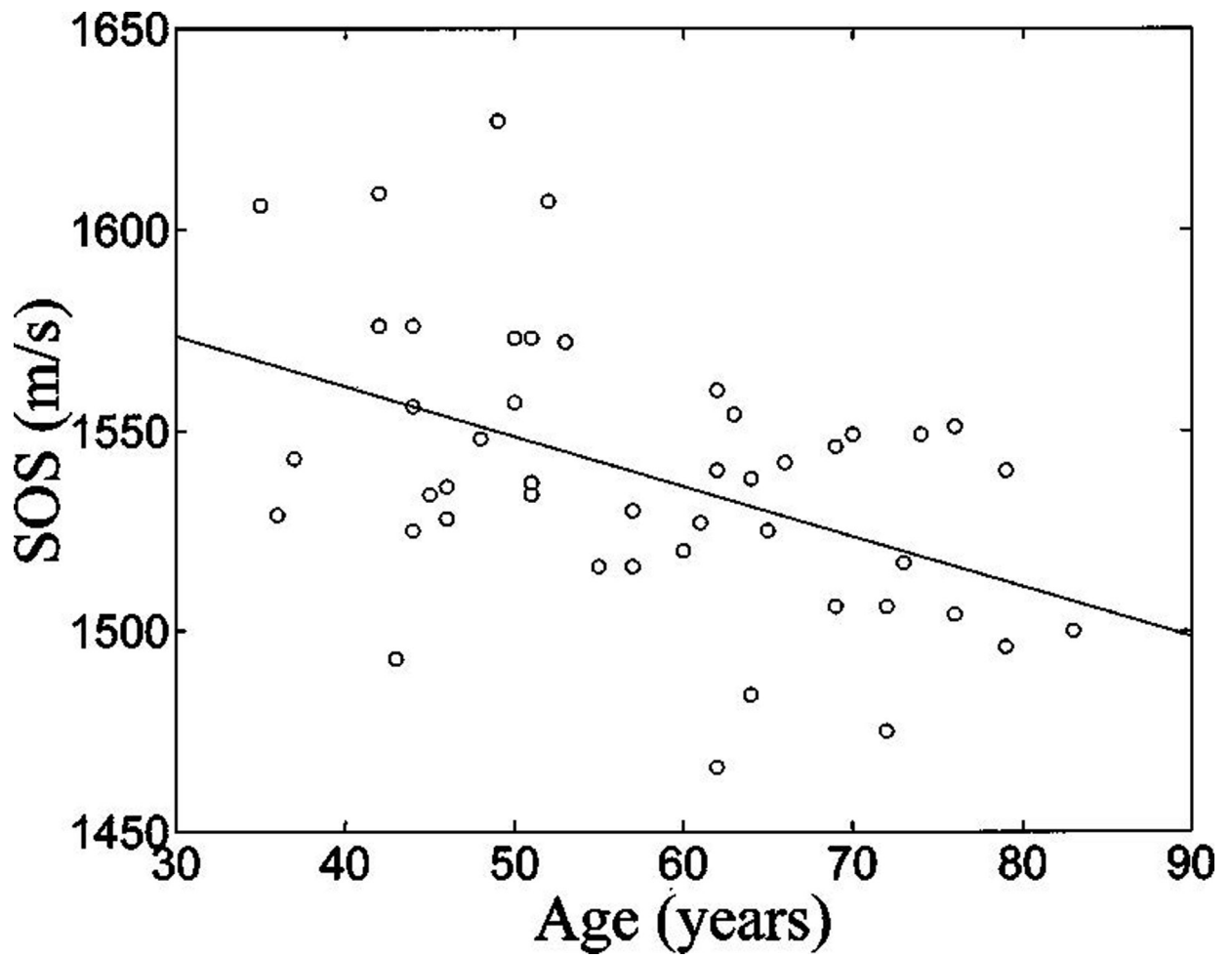Broadband ultrasonic attenuation (BUA) vs. age.

Figure 7.
Speed of Sound (SOS) vs. age.

Table I.

Means and standard deviations of measurements. Acronyms are BUA (broadband ultrasonic attenuation), SOS (speed of sound), ABC (average backscatter coefficient), and BMD (bone mineral density).

Parameter	Mean ± Standard Deviation
BUA (dB/MHz):	87.7 ± 13.6
SOS (m/s):	1539.1 ± 34.2
"Stiffness":	89 ± 18
Log(ABC):	-0.3 ± 0.24
BMD (g/cm^2):	0.873 ± 0.120
Age (years):	58 ± 12.8
Height (inches):	64.8 ± 2.8
Weight (lb.s):	148.6 ± 27.3

Table II.

Correlation matrix for measurements and age. Acronyms are BUA (broadband ultrasonic attenuation), SOS (speed of sound), ABC (average backscatter coefficient), and BMD (bone mineral density).

Parameter	BUA	SOS	"Stiffness"	ABC	BMD	AGE	HGT	WGT
BUA	1.00	0.81	0.95	0.43	0.56	−0.44	0.17	0.19
SOS	0.81	1.00	0.96	0.46	0.51	−0.46	−0.06	−0.04
"Stiffness"	0.95	0.96	1.00	0.47	0.56	−0.47	0.05	0.08
ABC	0.43	0.46	0.47	1.00	0.50	−0.42	0.17	0.08
BMD	0.56	0.51	0.56	0.50	1.00	−0.31	0.06	0.30
Age	−0.44	−0.46	−0.47	−0.42	−0.31	1.00	−0.29	0.03
Height	0.17	−0.06	0.05	0.17	0.06	−0.29	1.00	0.35
Weight	0.19	−0.04	0.08	0.08	0.30	0.03	0.35	1.00