Noninvasive Measurement of Stiffness and Density of Bone for Its Diagnosis Using Ultrasound

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Abstract

Because the acoustic and elastic properties of bone evaluated using ultrasound-based methods have proved so useful in the direct evaluation of bone characteristics, many workers have developed methods and systems based on the *in vivo* measurement of velocity, attenuation, or both, of ultrasound in bone. These include the acoustic emission (AE), apparent velocity of ultrasound (AVU), and speed of sound-broadband ultrasound attenuation (SOS-BUA) methods. Bone stiffness is accepted as an effective index in the diagnosis of such bone diseases as osteoporosis. The literature contains reports of the estimation of bone stiffness from velocity (speed of sound [SOS]) and attenuation (broadband ultrasound attenuation [BUA]). The physical explanation of the methods of evaluating stiffness from the obtained values of BUA and SOS is still not clear, however. Here we propose a new diagnostic method and system based on ultrasound measurement of the stiffness of bone. The proposed method determines stiffness from the velocity of the leaky surface skimming compressional waves (LSSCWs) obtained with the microdefocusing method and the acoustic impedance obtained with the reflectance method. Thus this method can evaluate stiffness without exposing the patient to X-rays; moreover, the physical basis of the calculation of stiffness from velocity and impedance is well understood. We applied this system to the human tibia *in vivo*: stiffness and density in a young volunteer were successfully evaluated at 24.9 GPa and 2.01×10^3 kg/m^3, respectively.

J Med Ultrasonics 2002; 29 (Autumn): 129-136.

Keywords

density, elastic constant, osteoporosis, microdefocusing method, reflectance method

1. Introduction

Ultrasonic diagnosis of bone is attracting attention because of its merit in evaluation of the elastic properties of bone and other bone characteristics without exposing patients to x-rays.

An array of ultrasonic diagnostic methods and systems have been devised to evaluate bone tissue: These include the acoustic emission (AE) method[1] and the apparent velocity of ultrasound (AVU) method[2], both of which measure acoustic velocity; the speed of sound-broadband ultrasound attenuation (SOS-BUA) method[3)4)], based on the measured acoustic velocity and the attenuation constant; and the impedance method[5], based on the measured acoustic impedance. However, values determined using these methods are not basic physical values, and associating these measured values with bone condition may prove difficult. Accordingly, we propose diagnosing bone by measuring stiffness and density, which are more-basic physical values.

Abendschein et al[6] measured acoustic velocity *in vitro* using 100 kHz ultrasound and calculated bone stiffness using the acoustic velocity thus obtained; the density of the human tibia of the cortical bone was measured separately. Stiffness calculated from acoustic velocity and density correlates closely with stiffness obtained by the three-point bend method. Stiffness has been shown to be less in patients with longterm diabetes mellitus or osteoporosis than in healthy individuals. Thus, if stiffness could be measured *in vivo*, the value could be used in the diagnosis of osteoporosis.

Stiffness and bone density can be determined using ultrasound by the measuring acoustic velocity

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Original article is cited in J Med Ultrasonics 1999; 26 (10): 1027-1033.

($\sqrt{\text{stiffness/density}}$) and acoustic impedance ($\sqrt{\text{stiffness} \times \text{density}}$) of the same local area. However, measurement of bone acoustic velocity, which is routinely carried out, employs a transmission technique and is difficult to combine with measurement of acoustic impedance.

Chubachi et al propose a method of measuring acoustic velocity in bone on the basis of reflectance, using leaky surface skimming compressional waves (LSSCWs), which propagate on the bone surface at a velocity close to that of longitudinal waves[9)-12)]. LSSCW is one of the elastic surface waves and is excited through a line focus-beam acoustic lens, as used in the ultrasonic microscope[7)]. Velocity can therefore be measured by analyzing the $V(z)$ curve[8)]. The system used to measure the velocity of LSSCWs, in which ultrasonic transmission and detection are performed from a direction oblique to the surface of the bone, can be combined with the system used to measure acoustic impedance, in which ultrasound signals are transmitted and received perpendicular to the surface of the bone. Because of the high level of attenuation in bone, however, obtaining a $V(z)$curve with a length sufficient for frequency analysis is difficult. To analyze the $V(z)$ curve, we thus developed[14)15)] a way to measure LSSCW velocity using the microdefocusing method[13)], which allows measurement of the phase velocity of LSSCW using a short moving distance δz of the sample (the defocusing quantity) that would be unlikely to produce sufficient length of $V(z)$ curve. This method uses a pair of focus-beam ultrasonic transducers to measure LSSCW velocity and is easily combined with the acoustic impedance measurement[16)]. Here we present both our method for measuring bone stiffness and density on the basis of the principle previously described and the results we obtained measuring the stiffness and density of the human tibia *in vivo*.

2. The measuring system of stiffness and density

Fig. 1 shows the system used to measure stiffness by simultaneously measuring LSSCW velocity and acoustic impedance. The microdefocusing method[13)] is used to measure the acoustic velocity of LSSCWs[14)15)] with two focus-beam transducers: a transducer for transmitting (A) and a transducer for receiving (B). Acoustic impedance, on the other hand, is obtained using a focus-beam transducer (C) for transmitting and receiving. The ultrasound reflectance of the Pyrex glass used as a reference standard in this system is measured, and acoustic impedance is calculated[16)] using the acoustic impedance of water as the known value. The operating center frequency of transducers (A), (B), and (C) is 1 MHz, and the focal distance is 95 mm.

LSSCWs are elastic surface waves that propagate almost as fast as longitudinal waves on the bone surface. These waves are excited by projecting longitudinal waves at a critical angle on to the surface of the object. In the case of bone, longitudinal waves propagate at between 2700 and 4100 m/s[17)], forming a critical angle of 21 to 33 degrees. The use of LSSCWs to measure acoustic velocity in bone allows measurement without limiting the site of measurement, because there is no need to place the ultrasonic transducer on the far side of the bone, as required by the conventional method of measuring acoustic velocity using a transmission technique. Further, our method, by which ultrasound is transmitted and received from a direction oblique to the bone surface, is more easily combined with measurement of acoustic impedance, in which

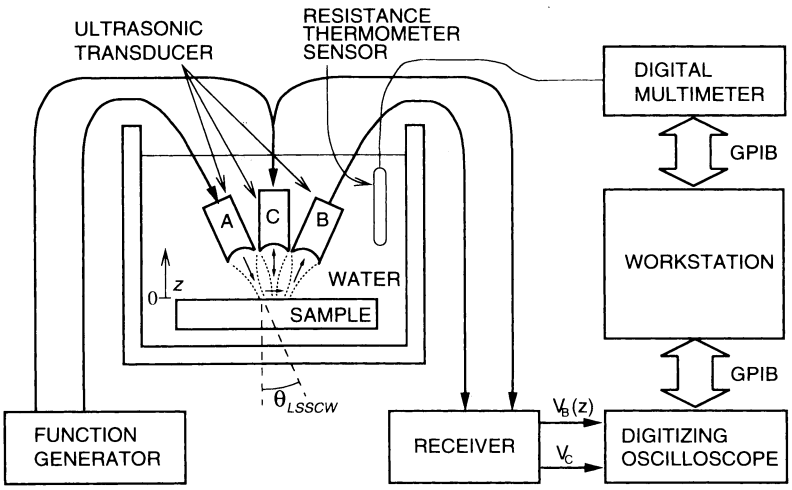

Fig. 1 Block diagram of the measuring system. The system can measure both LSSCW velocity and acoustic impedance of the same local area of a sample, and sample stiffness and density is calculated from the values obtained.

ultrasound is transmitted and received from the vertical direction.

3. Measuring method of LSSCWs

Analysis of the $V(z)$ curve, used in ultrasonic microscopy, is a method of measuring the phase velocity of LSSCWs. Because of the greater attenuation of bone, however, a $V(z)$ curve with a length sufficient for frequency analysis is difficult to obtain[9)-12)]. To analyze the $V(z)$ curve we therefore used[14)15)] a microdefocusing method[13)] that allows the measurement of the phase velocity of LSSCWs using a short moving distance δz of the sample (the defocusing quantity) and is thus unlikely to produce sufficient length for frequency analysis.

Fig. 1 shows that the excitation of LSSCWs occurs on the surface of the sample when a radio frequency (RF) burst pulse with a frequency of 1 MHz and a pulse width of 50 μs is applied to transducer A. The LSSCWs propagate on the sample surface, reradiating leaky waves in the water. While maintaining the angle between the sample and the transducer, the distance z between the surface of the sample and the transducer is shortened, and the output waveform from transducer B at each z after A/D conversion using a digitizing oscilloscope is received by the workstation, in which the phase spectrum is calculated from the waveform at each z, using the fast Fourier transform (FFT). Water temperature at time of measurement is determined using a resistance thermometer sensor and a digital multimeter, and determination of acoustic velocity in water at the time of measurement is based on the temperature dependence[18)] of acoustic velocity in water. The change ($\delta\alpha$) in the phase of the transmitted signal when the sample is brought closer by δz to the pair of transmitter-receiver transducers is expressed by Snell's law as follows:

$$\sin\theta_{LSSCW}=\frac{v_w}{v_{LSSCW}}=\frac{k_{LSSCW}}{k_w} \tag{1}$$

$$\delta\alpha=2\,k_w\delta z\times\cos\theta_{LSSCW} \tag{2}$$

where θ_{LSSCW}, $v_w=2\pi f/k_w$, $v_{LSSCW}=2\pi f/k_{LSSCW}$, k_w, and k_{LSSCW} are the critical angle of LSSCW at the water/reference standard boundary, the acoustic velocity of the longitudinal wave in water, the phase velocity of LSSCW, the wave number of longitudinal wave in water, and the wave number of LSSCWs, respectively. Thus, obtaining the transmission signal at each z when the position z of the sample is moved closer to the transmitter-receiver transducers, the gradient ξ in phase (α) of the sample relative to the position (z) of the sample is determined as follows:

$$\xi=\frac{\delta\alpha}{\delta z}=2\,k_w\cos\theta_{LSSCW} \tag{3}$$

From Eqs. (1) and (3), the phase velocity of LSSCW, v_{LSSCW} is determined as follows:

$$v_{LSSCW}=\frac{v_w}{\sqrt{1-\left(\frac{\xi v_w}{4\pi f}\right)^2}} \tag{4}$$

4. Measuring method of acoustic impedance

Acoustic impedance is determined by measuring reflection coefficient at the surface of the bone. Using Medium 1 with the known acoustic impedance Z_1, the reflection coefficient R can be obtained by vertically projecting plane ultrasound on the plane boundary with Medium 2, of which the acoustic impedance Z_2 is unknown. These values are used to obtain Z_2 from the following equation.

$$Z_2=Z_1\times\frac{1+R}{1-R} \tag{5}$$

The reflection coefficient R is determined as the ratio between the amplitude of the incident wave and that of the reflected wave. In this system, instead of measuring the amplitudes of the incident and the reflected waves, the amplitude of the wave reflected from a reference standard of which the reflection coefficient is known and that from the measurement sample were determined[16)]. The Pyrex glass was used as the reference standard.

A 1 MHz center-frequency ultrasonic pulse is radiated from the focus-beam transducer (C). The wave $y(t)$ reflected from the measured object is detected by the same transducer (C) and transmitted to the workstation after A/D conversion using a digitizing oscilloscope. Frequency components distributed in a frequency bandwidth determined by the frequency characteristics of the measuring device and by the frequency dependence of the acoustic characteristics of the propagating medium are contained in $y(t)$. Thus the wave reflected from the reference standard of known reflection coefficient and the amplitude of the reflected wave from the measured sample are compared at each frequency. The calculated mean of the frequency bandwidths showing favorable signal-to-noise ratios (S/Ns) determine the reflection coefficient. First, for each of the waves reflected from the reference standard $y_r(t)$ and from the measurement sample $y_s(t)$, the power spectra $P_r(f)$ and $P_s(f)$, respectively, are obtained by fast Fourier transform (FFT). The reflection coefficient $R(f)$ at each frequency f is then calculated from Eq. (6) using an assumed value of R_0, the reflection coefficient of acoustic pressure at the water-reference standard boundary:

$$R(f)=\sqrt{\frac{P_s(f)}{P_r(f)}}\times R_0 \tag{6}$$

Further, Eq. (7) shows mean $R(f)$ at the frequency bandwidth B with favorable S/N calculated as the measured value of the reflection coefficient.

$$R=\frac{\int_B R(f)\,df}{\int_B 1\,df} \tag{7}$$

The center frequency of the transducer is 1 MHz, and the frequency bandwidth is approximately 1 MHz$\pm$ 0.2 MHz.

5. Measuring method of stiffness and density

Equations (8) and (9) show the relationship among acoustic impedance Z, acoustic velocity of longitudinal wave v_{long}, stiffness c, and density ρ.

$$Z=\sqrt{\rho\times c} \tag{8}$$

$$v_{long}=\sqrt{\frac{c}{\rho}} \tag{9}$$

Therefore, using the ratio K between LSSCW velocity v_{LSSCW} and the velocity of longitudinal wave v_{long}, stiffness c, and density ρ are obtained from Eqs. 10 and 11, with acoustic impedance Z and acoustic velocity of the longitudinal wave v_{LSSCW}.

$$c=\frac{Z\times v_{long}}{K} \tag{10}$$

$$\rho=\frac{Z\times K}{v_{long}} \tag{11}$$

6. Noninvasive measurement of the stiffness and density of human tibia

The tibia was chosen as the site of measurement because of its thin soft-tissues and relatively plane surface. **Fig. 2** shows a block diagram for measurements of stiffness and density of bone.

The effect on the soft tissues surrounding the bone must be investigated for measurements *in vivo*.

To measure LSSCW velocity after exciting LSSCWs on the surface of the bone, the excitation and detection of LSSCWs has to be carried out from outside the body via the soft tissues around the bone. In this measurement, the phase velocity of LSSCWs is likely to vary with acoustic velocity and density of the soft tissue. Also, refraction may occur at the boundary between water and soft tissue, and the refraction angle will vary with acoustic velocity of the soft tissue. Here, we investigated the effect of soft tissues surrounding bone on measurement method using LSSCW using the model shown in **Fig. 3**. The refraction angle at the boundary between water and soft tissue shown in **Fig. 3** is determined by Snell's law. Setting the θ_w and θ_{LSSCW} as shown in the figure, Snell's law can be described as follows:

$$\frac{\sin\theta_w}{v_w}=\frac{\sin\theta_{LSSCW}}{v_t}=\frac{1}{v_{LSSCW}} \tag{12}$$

v_w, v_t, and v_{LSSCW} indicate the velocity of the longitudinal wave in water, the velocity of the longitudinal wave in soft tissues, and the velocity of LSSCWs propagating through the soft tissue-bone boundary, respectively. The gradient of the phase relative to distance of the measurement signal is expressed as follows:

$$\xi=\frac{2k_w}{\cos\theta_w}-2k_{LSSCW}\tan\theta_{LSSCW} \tag{13}$$

$$=\frac{4\pi f}{v_w\sqrt{1-\left(\frac{v_w}{v_{LSSCW}}\right)^2}}-\frac{4\pi f}{v_{LSSCW}^{\,2}}\frac{v_t}{\sqrt{1-\left(\frac{v_t}{v_{LSSCW}}\right)^2}} \tag{14}$$

The difficulty of obtaining LSSCW velocity v_{LSSCW} by transforming the equation, required us to repeat the calculation to find the value of V_{LSSCW} at which

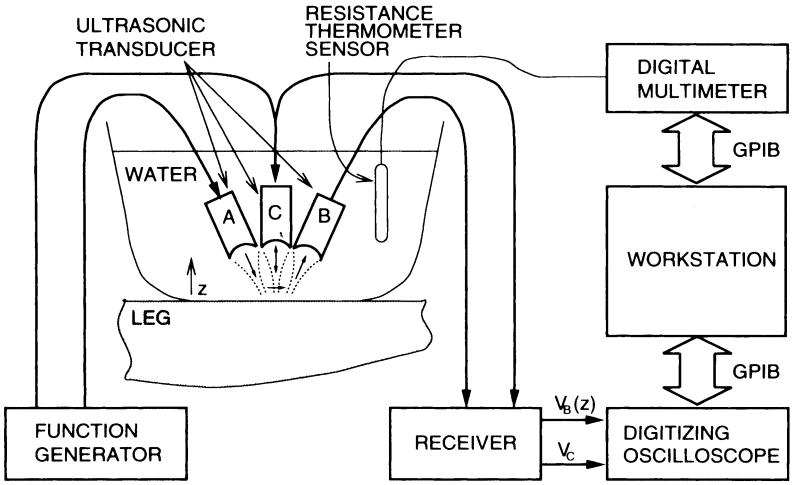

Fig. 2 Block diagram showing the system used to measure the tibia.

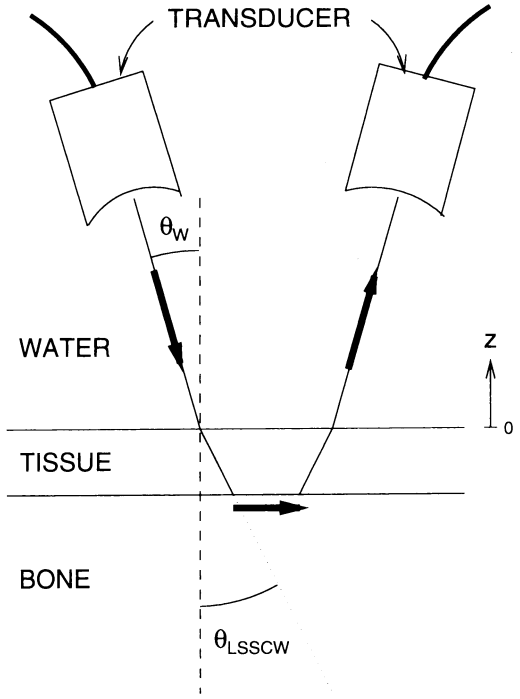

Fig. 3 A refraction model for measuring LSSCW velocity in bone *in vivo*.

percent change in phase calculated from Eq. (14) is equal to the measured value, in order to determine v_{LSSCW} from the gradient in phase, taking into consideration the effect of refraction. The acoustic velocity of the soft tissue must be measured or assumed.

Reflection on the surface of soft tissue and attenuation in soft tissue must be considered when measuring acoustic impedance. To reduce the effects of these factors, we have proposed[16] a method to estimate the acoustic impedance taking ultrasonic reflection and attenuation into account by using an expression of the site of measurement using the propagation model, and measuring the refrection waves from both the surface of the soft tissue and the surface of the bone. In the tibia, chosen in this study as the site of measurement, however, discrimination between the reflected waves from the soft tissue surface and those from the bone surface is complicated by the thinness of the soft tissue around this bone. Thus, this method could not be applied in the present study.

Anisotropy of bone must be considered when calculating stiffness and density. Katz et al[19] have indicated that anisotropy of human bone can be expressed in a hexagonal model using the long axis of bone as the Z-axis. The direction of ultrasonic-wave propagation in the measurement of acoustic impedance is the radial direction of the bone (11 Direction), and is therefore expressed as follows, using density ρ and stiffness c_{11} of the radial direction:

$$Z_{11}=\sqrt{\rho\times c_{11}} \tag{15}$$

Assuming that the direction of propagation in the measurement of LSSCW velocity is the axial direction of bone (33 Direction), taking the actual measurements into consideration, LSSCW velocity to be measured is expressed by Eq. (16), using density ρ and stiffness c_{33} of the axial direction:

$$v_{L_{33}}=K_1\times v_{c_{33}}=K_1\times\sqrt{\frac{c_{33}}{\rho}} \tag{16}$$

K_1 is the ratio between the velocity of axial longitudinal wave $V_{c_{33}}$ and the axial LSSCW velocity $v_{L_{33}}$.

Using $K_2^2=c_{33}/c_{11}$ as the ratio between c_{11} and c_{33}, K_2 can be calculated from the data obtained in the in vitro measurement. With the value reported by Katz et al[20], K_2 is calculated at approximately 1.17. Stiffness c_{11} and c_{33} and density ρ are determined using the following formulas.

$$c_{11}=\frac{Z_{11}\times v_{L_{33}}}{K_1\times K_2} \tag{17}$$

$$c_{33}=\frac{Z_{11}\times v_{L_{33}}\times K_2}{K_1} \tag{18}$$

$$\rho=\frac{Z_{11}}{v_{L_{33}}}\times K_1\times K_2 \tag{19}$$

"Stiffness" is used as an index alternative to stiffness (c_{11}, c_{33}), determined[21] at the Achilles, the transmission diagnostic equipment for osteoporosis by Lunar Corporation.

$$\text{Stiffness}=0.67(\text{BUA}-50)+0.28(\text{SOS}-1380) \tag{20}$$

Broadband ultrasound attenuation (BUA) is defined as the ultrasound attenuation coefficient, and the speed of sound (SOS) is the apparent velocity of the ultrasound transmitted through the calcaneal region. The physical explanation of the Stiffness value calculated from Eq. (20) remains obscure, however; on the other hand, stiffness, c_{11}, c_{33} and density ρ calculated from Eqs. (17), (18), and (19) has a physical basis.

7. Experiments and results

LSSCW velocity and acoustic impedance were measured and stiffness and density were calculated using phenolic resin (Risholite; Risho Kogyo Co, Ltd) and acrylic resin (Acrylite; Mitsubishi Rayon Co, Ltd), as samples. Estimated values were compared with separately measured acoustic velocity of the longitudinal wave using the ultrasound transmission method and with the density calculated from the mass and volume. **Table 1** shows the results. Stiffness and density estimated by this method are

Table 1 Experimental Results of the Measurement of the Stiffness and Density of Phenol Resin, Acryc resin, and the Human Tibia

	Proposed Method			Transmission Method			
	Z_{11} kg/m^2•s	$v_{L_{33}}$ m/s	$Z_{11}/v_{L_{33}}$ kg/m^3	$Z_{11}\times v_{L_{33}}$ GPa	v_{11} m/s	ρ kg/m^3	$\rho\times v_{11}^2$ GPa
Phenol resin	5.31×10^6	3515	1.51×10^3	18.7	3718	1.36×10^3	18.8
Acryc resin	3.31×10^6	2696	1.22×10^3	8.92	2727	1.21×10^3	9.02
Tibia (a)	7.08×10^6	3522	2.01×10^3	24.9			
(b)	7.08×10^6	3638	1.95×10^3	25.8			

almost equal to those measured by the transmission method, making the proposed system useful in estimating stiffness and density.

This method was used for *in vivo* measurement of LSSCW velocity and reflection coefficient of the right tibia of a 25-year-old man to estimate stiffness and density. Values in columns (a) of the table exclude the effect of refraction in the calculation of the LSSCW velocity; those in column (b) include it. Acoustic velocity of the soft tissues was assumed to be 1540 m/s. Estimates of LSSCW velocity, stiffness, and density obtained excluding the effect of refraction caused by the presence of soft tissues did not differ substantially (approximately three percent) from those including it.

Estimates of stiffness and density obtained using the proposed method were compared with the following results obtained from in vitro measurement of the tibias of healthy volunteers by Abendschein et al[6]: LSSCW velocity, 3526 m/s; density, 1.97×10^3 kg/m^3; and stiffness calculated from these values, 24.5 GPa. Thus the proposed method also produced reasonable estimates in the tibia.

8. Conclusion

A noninvasive ultrasonic diagnostic method for determining stiffness and density of bone by measuring the LSSCW velocity and acoustic impedance in almost the same local area of a sample is described, and the method produced reasonable results when applied in human tibia. Further studies must determine the accuracy and detectability of the measurements obtained by accumulating data from individuals in a broad range of age groups before this method can be used to diagnose osteoporosis and other bone diseases. The method will also have to be modified to reduce the effect of the soft tissues around the bone.

We are grateful to the Nikka Densoku Company for their support regarding the experimental equipment. This study was partially supported by the Fellowship Grant in Aid for Scientific Research of the Ministry of Education (Japan).

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