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Abstract: Ultrasonic wave properties of human bone marrow obtained in the femur and tibia were measured using an ultrasound pulse technique. The measured frequency range was 4–10 MHz, and the temperature range was 30 °C–40 °C. The sound velocity was 1410 m/s, and the attenuation coefficient was 4.4 dB/cm at 36 °C (10 MHz). These values decreased with temperature. Site dependence and individual differences in elderly human bone marrow were negligible. The slopes of the attenuation coefficient were estimated by a power law. The values of the exponent *n* were 2.0 (30 °C–38 °C) and 2.3 (40 °C).

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1. Introduction

The number of persons with osteoporosis is expected to increase in aging societies. One of the common *in vivo* techniques for diagnosing osteoporosis is a quantitative ultrasonography (QUS) method in the megahertz range.[1,2] The conventional QUS technique allows to evaluate the speed of sound and broadband ultrasound attenuation (slope of linear frequency-dependent attenuation) in the calcaneus.[3,4] The longitudinal wave properties can give us information related to bone quality. Most conventional techniques, however, measure the averaged wave properties in the whole wave propagation path, which includes cortical bone, cancellous bone, bone marrow, and surface soft tissues. QUS is simpler and safer than techniques that require the use of x rays, but there is a problem of low reproducibility. Therefore, diagnostic criteria have not been standardized for the current clinical equipment.

Recently, new *in vivo* QUS techniques have been developed. One is for ultrasonic evaluation of cancellous bone in the radius.[5] Cancellous bone is an anisotropic porous medium composed of trabeculae and filled with viscous bone marrow. In this complex structure, it is well known that when ultrasound passes in the trabecular direction, it often separates into two waves called fast and slow waves.[6–8] The fast wave mainly propagates through trabecular bone (solid part), and the slow wave mainly propagates through the bone marrow (liquid part). Otani and Hosokawa[8] experimentally demonstrated this phenomenon in the megahertz range. Otani then succeeded in developing an *in vivo* technique to estimate the elastic properties and bone volume fraction of the cancellous bone based on the properties of these waves.[9,10] Most experimental studies of this phenomenon, however, were discussed in terms of water instead of bone marrow.[11–16] It is necessary, however, to be familiar with the ultrasonic wave properties in bone marrow to understand the precise characteristics of the slow wave.[17–21]

Bone marrow is a viscous soft tissue that fills the medullary cavity and space in cancellous bone. The bone marrow also affects the scattering phenomena occurring in trabecular bone.[22,23] There are two types of bone marrow, red or yellow, that have unique hematopoietic functions.[24–26] Red bone marrow is composed of 40% water, 40% fat, and 20% protein. It fulfills several functions during the production of new

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blood cells. Yellow bone marrow is composed of 15% water, 80% fat, and 5% protein.[26] In newborns, all bone marrow is red, but it gradually changes from red to yellow during the aging process. Therefore, yellow bone marrow is dominant in the limb bones of elderly people. Hence, for ultrasonic diagnosis of osteoporosis, sound waves are expected to propagate through yellow marrow.[24–26]

Ultrasonic wave properties of bovine bone marrow were investigated in previous studies.[27,28] Goss and colleagues reported properties of several mammalian tissues including human bone marrow.[29] However, these data were for acoustic impedance, not sound velocities or the attenuation coefficient. Therefore, the detailed temperature and frequency dependences of wave properties of human bone marrow have not yet been reported.

In the present study, the ultrasonic wave properties of the human bone marrow were experimentally observed using an ultrasonic pulse technique in the megahertz range. The temperature dependence and individual differences in bone marrow were also carefully observed.

2. Materials and methods

2.1 Bone marrow

Bone marrow samples from the distal femur and proximal tibia were obtained from seven patients (female, ages 63–84 yrs). These samples were placed in rectangular polystyrene cells (inner width 10 mm, outer width 12 mm) and degassed for 30 min to remove their bubble interiors. The Medical Ethics Committee at Doshisha University and Osaka Medical College approved the protocols.

2.2 Ultrasonic measurements

Ultrasonic pulse measurements were performed using self-made polyvinylidene fluoride planar transducers (diameter 3 mm).[30] The transmitter and receiver were placed coaxially at a distance of 15 mm, and a sample cell was placed between them. A function generator (33250A; Agilent, Santa Clara, CA) delivered electrical pulse signals to the transmitter, which were converted to ultrasonic waves. Several cycles of sinusoidal waves (4 to 6 waves) with the frequency of 4–10 MHz and the amplitude of 10 V_{pp} were applied to the transmitter.[27] The waves that passed through the sample were converted to an electrical signal by the receiver. The signal was amplified 40 dB by a preamplifier (BX-31; NF Corporation, Yokohama, Japan) and visualized by a digital oscilloscope (33250A; Tektronix, Portland, OR). Measurements were performed with the cell filled with bone marrow or water. Sound velocities of bone marrow were estimated according to arrival time differences. The reproducibility of sound velocity values was less than 1.0 m/s. The attenuation coefficient was estimated by comparing the amplitudes between the waves that propagated through the bone marrow and those that propagated through water. The measurement temperature range for all measurements was 30 °C–40 °C.

3. Results and discussion

3.1 Temperature dependence of sound velocity and attenuation coefficient

Figure 1 shows typical sound velocity and the attenuation coefficient of bone marrow samples at 10 MHz as a function of temperature. The sound velocity was 1410 m/s, and the attenuation coefficient was 4.4 dB/cm at 10 MHz around body temperature (36 °C). These values decreased with increasing temperatures. The differences in the measured values for the samples were up to 2 m/s for sound velocity and up to 0.3 dB/

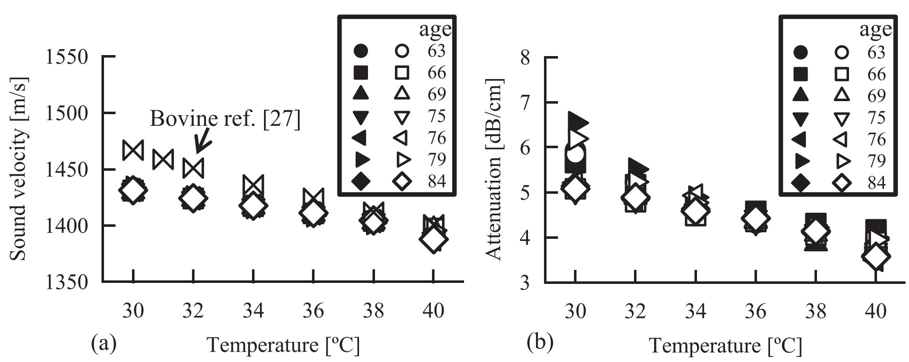

Fig. 1. Temperature dependences of sound velocity and attenuation coefficient at 10 MHz. Filled markers indicate data for femoral samples. Other markers indicate data for tibial samples.

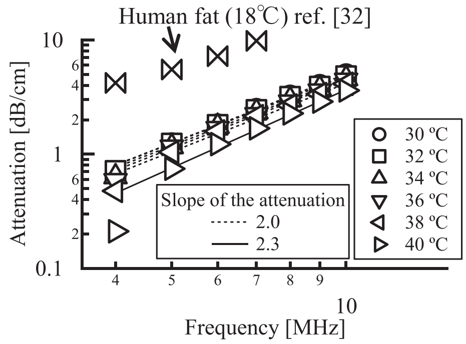

Fig. 2. Frequency dependence of the attenuation coefficient. This tibial sample was obtained from a 75-yr-old woman.

cm for the attenuation coefficient. These differences were within 10% of the measured values, indicating that site dependence and individual differences in elderly human bone marrow were negligible. One reason may be the narrow range in the ages of our patients, which could result in similar compositions of the bone marrow.

The decreasing tendency of the sound velocity and the attenuation coefficient were in good agreement with results from the bovine bone marrow studies.[27,28] The bovine bone marrow was in the same temperature range. These differences between human and bovine bone marrow seem to arise from their compositions of the bone marrow. Human bone marrow was a yellow, oily liquid, whereas the bovine bone marrow resembled a soft gel containing soft, and fibrous constituents.

3.2 Frequency dependent of the attenuation coefficient

Figure 2 shows the wave attenuation coefficient in the bone marrow samples as a function of frequency in the megahertz range. The attenuation coefficient values were less than 1.0 dB/cm at low frequencies but increased exponentially with frequency. The slopes of the attenuation coefficient were estimated by the power law ($\alpha = \alpha_0 f^n$). The values of the exponent n were 2.0 (30 °C–38 °C) and 2.3 (40 °C). The attenuation coefficient in human fat at 18 °C was higher than the attenuation coefficient in bone marrow.[31] In addition, the value of the exponent n was 1.6 in fat. Temperature differences seem to be mainly responsible for the differences between human fat and bone marrow. It is possible that the attenuation coefficient value for fat approaches that of bone marrow around body temperature because the attenuation coefficient decreases with increasing temperature.[32]

3.3 Two-wave phenomenon in cancellous bone filled with bone marrow

Using the bone marrow obtained from the total knee replacements, fast and slow waves in the cancellous bone were observed. Here, we used a bovine cancellous bone sample (cylindrical sample diameter 9.8 mm and length 2.5 mm) obtained from the femur of a 31-month-old bovine. The cancellous bone was filled with the bone marrow by degassing the inside air. Using the same experimental apparatus, we applied one cycle of sinusoidal waves at 0.8 MHz to the transmitter. Figure 3 shows the typical waveforms as a function of temperature. The slow wave was gradually delayed, and the amplitude increased because of the temperature increase. This means the decrease of slow wave velocity and decrease of slow wave attenuation with temperature. The

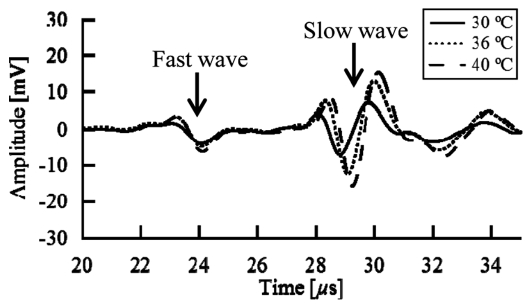

Fig. 3. Waveforms that were observed after passing through the cancellous bone filled with human bone marrow. The bone volume/trabecular volume ratio of the cancellous bone was 0.23. The wave passed through in the direction of the main trabecular alignment.

slow wave behaviors are in good agreement with the above-mentioned ultrasonic wave properties of bone marrow, indicating that the slow wave mainly propagates in the liquid part of cancellous bone. Lee pointed out that the replacement of marrow by water in cancellous bone led to increased phase velocity.[33] Because sound velocity in bone marrow was slower than that in water, we can expect better separation of fast and slow waves *in vivo*.

4. Conclusions

Ultrasonic wave properties of human bone marrow were investigated experimentally. Sound velocities and the attenuation coefficient decreased with increasing temperature. The slopes of the attenuation coefficient increased with the square of the frequency. In the samples from elderly people, there were few differences in the measured values in regard to site dependence and among individuals. These tendencies of the bone marrow were also found in the behavior of slow waves.

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