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Direct Measurement of Speed of Sound in Cartilage *in situ* Using Ultrasound and Magnetic Resonance Images

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Abstract— **This study verified the accuracy of the speed of sound (SOS) measured by the combination method, which calculates the ratio between the thickness values of cartilage measured by using the magnetic resonance imaging (MRI) and the ultrasonic pulse-echo imaging, and investigated in vivo application of this method. SOS specific to an ultrasound imaging device was used as a reference value to calculate the actual SOS from the ratio of cartilage thicknesses obtained from MR and ultrasound images. The accuracy of the thickness measurement was verified by comparing results obtained using MRI and a non-contact laser, and the accuracy of the calculated SOS was confirmed by comparing results of the pulse-echo and transmission methods in vitro. The difference between laser and MRI measurements was 0.05 ± 0.22 mm. SOS values in a human knee measured by the combination method in the medial and lateral femoral condyles were 1650 ± 79 and 1642 ± 78 m/s, respectively (p < 0.05). The results revealed the feasibility of *in situ* SOS measurement using the combination method.**

I. Introduction

Osteoarthritis (OA) is a degenerative disease of cartilage that develops most commonly in weight-bearing regions. OA begins with a structural change in collagen and a decrease in proteoglycan and water content (Armstrong et al. 1982; Klussmann et al. 2008; Hennerbichler et al. 2008). In early stages of OA, water content increases with the relaxation of the collagen, often resulting in swelling and softening. As OA progresses, cartilage thickness decreases and mechanical properties deteriorate until the eventual destruction of cartilage (Koga et al. 2008).

Degeneration of cartilage can be assessed via biochemical testing, diagnostic imaging, and arthroscopy. However, all these techniques have some drawbacks. Biochemical testing is effective for a differential diagnosis, but it is invasive and not very effective. Further, diagnostic imaging by X-rays and magnetic resonance imaging (MRI) cannot identify early stages of OA. Finally, although arthroscopy can enable both diagnosis and treatment, its invasiveness is a drawback (Koga et al. 2008).

Some studies have used ultrasound to assess the degenerate cartilage; in particular, degenerative changes, surface roughness, and thickness changes have been assessed using high-frequency ultrasound (Kaleva et al. 2008; Wang et al. 2010; Chiang et al. 1994; Myers et al. 1995; Joiner et al. 2001; Aura et al. 2010). However, all studies performed the assessment in vitro over a relatively narrow area. In contrast, the pulse-echo method can enable high-resolution, real-time imaging of articular and periarticular structures. Using this method enables visualization of tissue boundaries such as that between the bone and cartilage as a high-intensity band image (Ohashi et al. 2012).

Evaluation of changes in the thickness and elasticity of cartilage is important for assessing its degeneration. Further, some studies have compared the measurement results of cartilage thickness using ultrasound with those obtained using optics, needles, microscopes in vitro (Jurvelin et al. 1995; Töyräs et al. 2003).

Conventional ultrasound elastography based on speckle tracking has been used as a noninvasive method for evaluating elasticity in several types of tissue, but the absence of any echoes inside cartilage makes it difficult to use in that setting (Lee et al. 2011; Park et al. 2010). As an alternative, the elasticity of cartilage can be measured through its correlation with the speed of sound (SOS), which is calculated from the thickness and propagation time measured for a given cartilage sample (Töyräs et al. 2003; Saarakkala et al. 2004). The theoretical reasoning behind the technique of evaluating the biomechanical properties of tissue based on the SOS (longitudinal wave velocity) in that tissue is based on the properties of the pulse-echo method.

In this paper, we propose the direct measurement method of SOS based on a combination of images acquired by ultrasonic pulse-echo method and MRI, which is referred to as the combination method in this study. The SOS is typically calculated from the propagation time in the pulse-echo method and the material thickness. On the other hand, in the pulse-echo imaging, the cartilage thickness corresponding to specific SOS value in the ultrasound imaging device is displayed. Therefore, the SOS of cartilage can be calculated using the SOS specific to the ultrasound imaging device and the ratio between the thickness values measured by MRI and the pulse-echo method. This study verified the accuracy of the SOS measured by using the combination method, and examined the applicability of this method to humans.

II. SOS Measurement

A. Thickness Measurement

Ultrasound device with a center frequency of 10 MHz (EUB-7500; Hitachi Medical Corporation, Tokyo, Japan) and

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MRI device (Intera Achieva; Philips Medical Systems, Best, Netherlands) were used for the thickness measurements.

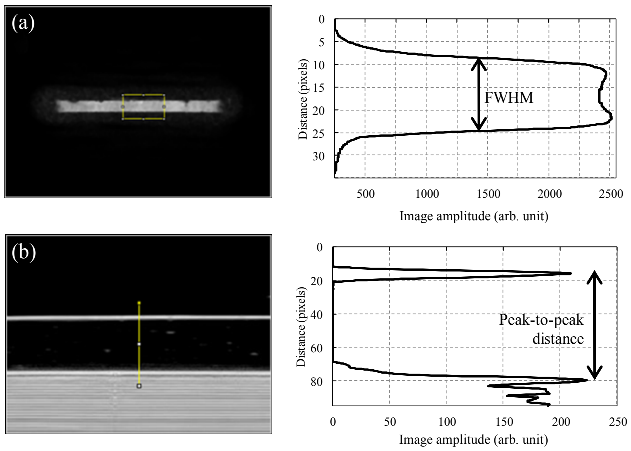

Figure 1. Thickness measurements using the full width at half maximum (FWHM) in MR image (a), and the peak-to-peak distance of the ultrasound image (b). The MRI image was interpolated and reconstructed using a 1024 matrix, and the mean value of the thickness in the region of interest (yellow line) was measured in three dimensions, whereas for the ultrasound image, the thickness was measured on the perpendicular line (yellow line).

MRI was performed using a 3.0-T whole-body clinical scanner with an 8-ch sensitivity encoding (SENSE) knee coil that employed a parallel imaging technique. Morphological isotropic voxel images were acquired using a three-dimensional (3D) fast-field echo (FFE) sequence with the following parameters: repetition time (TR)/echo time (TE1/TE2), 19/7.0/13.3 ms; field of view (FOV), 150 x 150 mm; zero filling interpolated matrix, 512 x 512 (acquired matrix: 256 x 256); voxel size, 0.3 mm^3; and number of excitations, 1; fat suppression was achieved using ProSet (total scan duration: 309 s). An advantage of the 3D scan with isotropic voxels is that the accuracy of image reconstruction is retained. Although the existence of synovial fluid made it difficult to identify the cartilage border, the outline extraction was carried out to measure the cartilage thickness directly. The thickness in the MR image was assumed to be the full width at half maximum (FWHM) (Fig. 1(a)), whereas the thickness in the ultrasound image was assumed to be the peak-to-peak distance of a profile (Fig. 1(b)).

B. SOS Measurement by Combination Method

Ultrasound imaging (USI) devices have a specific SOS. Therefore, the following relation is obtained when the MRI measurement gives the actual cartilage thickness.

SOS of cartilage/specific SOS of USI device

= thickness (MRI) / thickness (USI) (1)

Here, we used a nominal SOS of 1530 m/s for the ultrasound device. In the combination method, the SOS of cartilage can be calculated as follows.

SOS of cartilage

= 1530 × thickness (MRI) / thickness (USI) (2)

C. Verification of SOS Measurement

In the following experiments using phantoms and porcine knee cartilages, with the aim of verifying the accuracy of SOS measurement using the combination method, the transmission method was implemented using planar non-focusing transducers with a center frequency of 5 MHz and an aperture diameter of 0.25 inch (124-340, GE Inspection Technologies, Wichita, KS, USA) as shown in Fig. 2. Each phantom or cartilage was placed in a laboratory dish filled with saline solution, and the propagation time was measured without and with the phantom or cartilage at room temperature (18.4°C). Measuring and averaging the time between multiple echoes yields highly precise measurement of propagation time. In the transmission method, SOS of the agar phantom can be calculated as follows:

$$c = 1/\left((t_1 - t_0)/l_2 + 1/c_0\right) \qquad (3)$$

The round-trip propagation time of each phantom was measured using an oscilloscope. The actual SOS was calculated from the propagation time using Eq. (3).

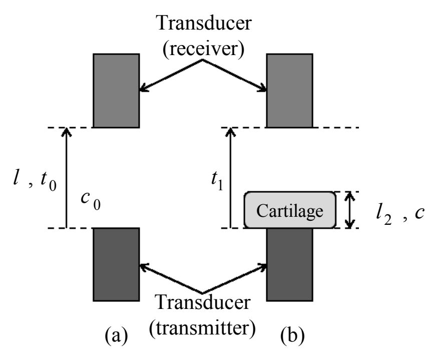

Figure 2. SOS measurement by the transmission method. (a) a setup for SOS measurement of surrounding saline solution, and (b) SOS measurement of cartilage using SOS of saline solution measured in (a).

III. RESULTS

A. Accuracy of Thickness Measurement Using MRI

In order to assess the accuracy of thickness measurement using MRI, true thickness obtained by a non-contact laser (spot diameter of 70 µm; LK-G35, LKGD500, Keyence, Japan) was compared with that measured using MRI. As the result, the difference between MRI and laser measurements was 0.05 ± 0.22 mm ($p < 0.05$). Most of the MRI measurements were in agreement with those obtained using the laser.

B. Assessment of Resolution of SOS

The resolution of the SOS using ultrasound and MR images was evaluated using agar-based phantoms. These were made from 3 % (W/v) of agar powder (010-15815, Wako Pure Chemical Industries, Japan), which was dissolved in deionized water, and then glycerin was added in concentrations ranging from 10 % to 60 % by 5 % (w/v) (075-00611, Wako Pure Chemical Industries, Japan). The amount of glycerin changes the SOS of the phantom. The resolution of SOS was evaluated by measuring the SOS in phantoms with different concentrations of glycerin.

Figure 3 shows the correlation between SOS values measured in the agar-based phantoms with glycerin obtained by the combination method and the transmission method. The figure shows a high correlation ($R^2 = 0.98$, $p < 0.05$) between the transmission and combination methods.

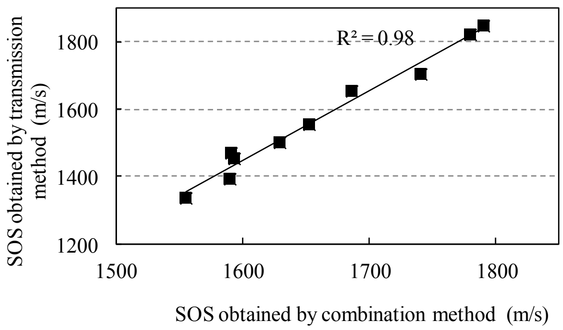

Figure 3. Assessment result of resolution of SOS measurements using agar-based phantoms.

C. SOS measurement with porcine knee cartilage

Next, the SOS values obtained using the transmission and combination methods were compared using the porcine knee cartilage specimen. Fresh porcine knee joints (n = 6) were obtained from a local abattoir (ZEN-NOH Central Research Institute for Feed and Livestock, Ibaraki, Japan). In each specimen, disks 12 mm in diameter (n = 24) were harvested from four sites on the medial and lateral femoral condyles. The subchondral bone was removed from each specimen using a punch and a razor. All specimens were encased in agar after the transmission method measurement, and the US and MR images were acquired. Specimens were examined by a MRI equipment using the above-described scanner with a 4-ch SENSE wrist coil; morphological isotropic images were acquired using the previously described 3D-FFE sequence.

As the results, the mean thicknesses obtained using MRI were 2.96 ± 0.95 and 3.03 ± 0.96 mm, respectively ($R^2 = 0.92$, $p < 0.05$). The difference between these values was not significant. The mean SOS values measured using the transmission method and combination method were 1629 ± 74 and 1575 ± 119 m/s, respectively. Again, the difference between these values was not significant ($p < 0.01$).

D. In vivo application

This study was approved by the committee for human research at the institution, and prior informed consent was obtained from all subjects.

Eleven healthy female volunteers (ranging in age from 24 to 54) underwent MRI, using the above-described scanner with an 8-ch SENSE knee coil; morphological isotropic images were acquired using the previously described 3D-FFE sequence. Sagittal MR images were acquired along a plane perpendicular to the line that passes through both the medial femoral condyle and the lateral femoral condyle. The 3D-FFE sagittal image was reconstructed from the section perpendicular to the cartilage at the center of the femoral condyle, in order to measure the thickness accurately. The cartilage thickness was measured by manual outline extraction (Cohen et al. 1999; Stammberger et al. 2000).

The cartilage thickness in a weight-bearing region cannot be measured by the USI in the same posture as that in MRI. Therefore, during thickness measurement by the USI, the knee was placed in the maximum flexure position. Because different imaging postures are used in the MRI and the USI, it becomes challenging to identify the same position. The agreement between the measurement regions in the two modalities was checked using one volunteer. MRI of the knee of a young healthy volunteer (female aged 25) was performed in the mild flexure position and the maximum flexure position by using the above-described scanner with a two-element SENSE Flex coil, and morphological isotropic images were acquired as explained above. One volunteer was subjected to real-time virtual sonography (RVS) only once. The system used for RVS comprised the digital ultrasound EUB-8500 and Workstation RVS (Hitachi Medico Co., Tokyo, Japan), which generate real-time multiplanar reconstruction (MPR) images (Nakano et al. 2009). The RVS device, a revolutionary real-time MPR imaging machine that supports ultrasonography diagnosis, consists of a small magnetic sensor attached to a linear probe. This magnetic sensor precisely and consistently captures changes in magnetic fields generated by the generator placed on the knee of a subject and detects the changes in the location, direction, and rotation of the probe while scanning the subject. The RVS device instantaneously processes changes in positional information detected by the magnetic sensor and generates real-time MPR images matching cross-sectional images of the cartilage captured by the probe. MRI in the maximum flexure position is not typically performed because it is spatially difficult. For this reason, it was performed only once in the present study. The positions of the medial (a, b) and lateral (c, d) condyle areas were confirmed by RVS (Fig. 4).

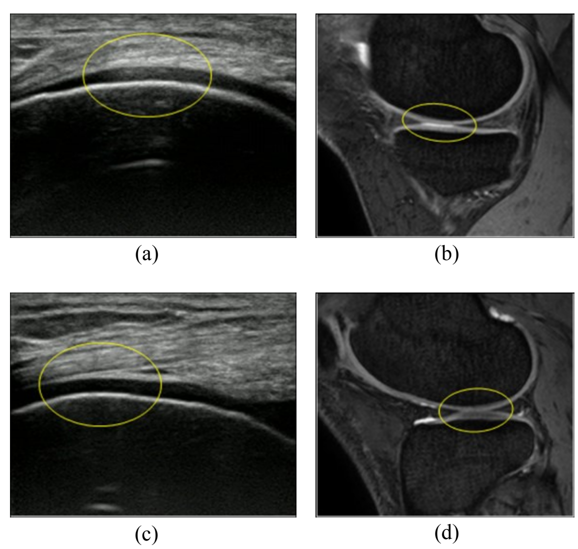

Figure 4. The position relations between the ultrasound images (a)(c), and the MR images (b)(d). The weight-bearing region of the medial condyle is slightly displaced forward from the center (a,b), and the weight-bearing region of the lateral condyle is slightly displaced backward from the center (c, d).

As the results, the mean thicknesses of the medial and lateral condyles obtained using the USI were 1.59 ± 0.29 and 1.69 ± 0.42 mm, respectively. There was no significant difference between these thicknesses ($p < 0.05$). The mean thicknesses of the medial and lateral condyles obtained using MRI were 1.75 ± 0.30 and 1.86 ± 0.40 mm, respectively. Again, there was no significant difference between these two thicknesses ($p < 0.05$). The SOS values in the medial and lateral femoral condyles obtained by the combination method were 1649.9 ± 78.5 m/s (range: 1539.2–1785.6 m/s) and 1641.9 ± 77.9 m/s (range: 1526.3–1793.6 m/s), respectively. There was no significant difference between these SOS values ($p < 0.05$). These SOS values measured by using the proposed combination method were in accordance with the results reported in the other literatures (Myers et al. 1995; Suh et al. 2001; Joiner et al. 2001).

IV. Conclusion

The direct measurement method for the SOS in cartilage *in situ* was presented and referred to as the combination method in this study, which is performed using a combination of two noninvasive modalities: MRI and ultrasound. The high accuracy of the combination method and good correlation with true SOS were verified in the phantoms and porcine specimens. In addition, in vivo measurements for human articular cartilage revealed the feasibility of combination method. In future work, clinical investigations should be conducted.

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