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# Interphalangeal Joint Cartilage: High-Spatial-Resolution in Vivo MR T2 Mapping—A Feasibility Study<sup>1</sup>

The purpose of this study was to evaluate feasibility of magnetic resonance (MR) T2 mapping of the proximal interphalangeal joint of the index finger. Cartilage T2 maps with an in-plane resolution of 39  $\mu\text{m}$  were obtained from five asymptomatic subjects—four men and one woman, aged 24–45 years—by using a 3.0-T MR imager. Image acquisition time was 9.6 minutes. All cartilage T2 maps demonstrated spatial variation similar to that reported previously for knee cartilage, with T2 values increasing toward the articular surface. These results demonstrate the feasibility of acquiring cartilage T2 maps of small joints in the hand. Application of T2 mapping techniques to non-weight-bearing joints may provide a means for differentiation of local biomechanical and systemic factors that can affect cartilage T2 values.

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The pathophysiology of osteoarthritis is multifactorial and involves both biochemical and biomechanical factors (1). Systemic risk factors, such as inherited genetic mutations, patient sex, and nutrition, likely affect cartilage globally. Biomechanical risk factors, on the other hand, such as posttraumatic joint instability, obesity, or high-intensity exercise, are more likely to have local effects on specific joints. Because magnetic resonance (MR) imaging allows direct visualization of cartilage, it has the potential to become a valuable clinical research tool in the study of osteoarthritis (2). While clinical evaluation of

cartilage currently relies on anatomic imaging, there is growing interest in the application of MR parametric mapping techniques, such as cartilage T2 mapping for evaluation of biochemical composition and structure of the extracellular cartilage matrix (3).

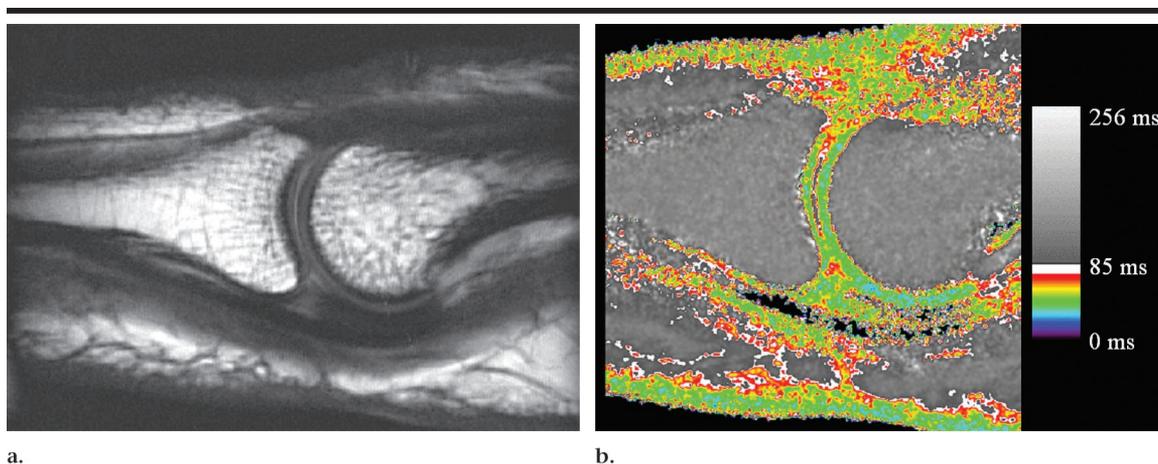
Thus far, human T2 mapping techniques have been limited to evaluation of articular cartilage of the knee (4–8). Cartilage damage in large weight-bearing joints reflects a combination of systemic and local biomechanical factors. Extension of MR imaging parametric mapping techniques to evaluation of small non-weight-bearing joints, such as the interphalangeal joints of the hand, could provide a means for comparing and differentiating effects of systemic factors from local biomechanical loading on early cartilage damage.

Application of MR parametric mapping techniques to small joints is technically challenging. Because articular cartilage of the interphalangeal joints is thinner than 1 mm, specialized acquisition techniques are needed to generate high-spatial-resolution images, with pixel resolution less than 100  $\mu\text{m}$ . Such measurements require high signal-to-noise ratio, large gradient amplitudes with rapid rise times, and increased receiver bandwidths to minimize interecho times for accurate determination of T2 relaxation values without compromising spatial resolution. Thus, the purpose of our study was to evaluate the feasibility of MR T2 mapping of the proximal interphalangeal joint of the index finger.

## Materials and Methods

### Volunteers

The study population consisted of five volunteers—four men and one woman



**Figure 1.** (a) Representative sagittal source MR image (1500/19.4) and (b) sagittal T2 map of the proximal interphalangeal joint of the index finger. Images were acquired with pixel resolution of  $39\ \mu\text{m}$  and 1-mm section thickness (voxel volume,  $0.001\ 53\ \text{mm}^3$ ). There is spatial variation in cartilage T2, with values increasing from 39 msec in the midradial zone to 57 msec at the articular surface.

aged 24–45 years. All subjects were asymptomatic, as defined by a lack of pain, stiffness, or limited function of any joint. None of the subjects reported a history of prior trauma or surgery of the hand. After the nature of the procedure was explained, all participants provided informed consent to participate in the study, which was approved by the institutional review board of Penn State Milton S. Hershey Medical Center.

### MR T2 Mapping

Quantitative T2 mapping of the proximal interphalangeal joint was performed with a 3.0-T MR spectrometer (MedSpec S300; Bruker Instruments, Ettlingen, Germany) by using a home-built microimaging gradient coil with a 9.5-cm internal aperture and a maximum gradient strength of 1000 mT/m, combined with a slotted tube transmit-receive coil with a 2.5-cm internal diameter. The frequency-encoding axis was aligned with the long axis of the index finger. Magnitude and quantitative T2 maps were calculated from sagittal data sets obtained through the proximal interphalangeal joint of the index finger by using an 11-echo sequence with a repetition time msec/echo time msec of 1500/9.7–106.7, one signal acquired, four sections obtained with 1-mm section thickness, 384 (2) acquisition matrix zero-filled to 512 (2) matrix, and a  $1.5\text{-cm}^2$  field of view.

The repetition time and range of echo times were chosen specifically to allow direct comparison with T2 mapping results reported previously for the knee (6). This provided images with an acquired

in-plane pixel resolution of  $39\ \mu\text{m}$ . Total acquisition time to acquire the source images for quantitative maps was 9.6 minutes. The specific absorption rate was monitored throughout the study and was below the recommended limits of the Food and Drug Administration. None of the subjects experienced discomfort or symptoms of nerve stimulation that could be attributed to high magnetic field per unit time.

### Data Analysis

Magnitude images and T2 maps were calculated from 10 spin-echo MR images by means of linear least-squares curve fitting on a pixel-by-pixel basis with custom software (Cincinnati Children's Hospital Image Processing Software/Interactive Data Language; RSI, Boulder, Colo) (5). The first echo was excluded from the fit to reduce error that resulted from signal produced by stimulated echoes (8). Fitting of the signal intensity for the  $i^{\text{th}}, j^{\text{th}}$  pixel as a function of time,  $t$ , can be expressed as follows:  $SI_{i,j}(t) = SI_{0i,j} \cdot \exp(-t/T2_{i,j})$ , where  $SI_{0i,j}$  is the pixel intensity at  $t = 0$  and  $T2_{i,j}$  is the T2 time constant of pixel  $i,j$ . A magnitude image is generated from the pixel  $SI_{0i,j}$  data, and a T2 map is generated from the  $T2_{i,j}$  data.

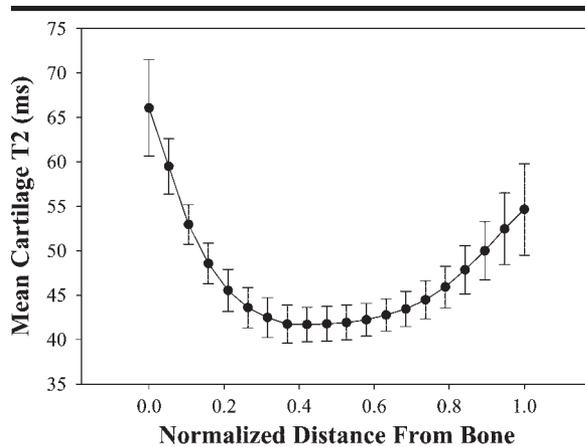
To generate regions of interest, segmentation of articular cartilage of the proximal phalanx was performed on each section of the T2 maps by using an interactive subroutine in the custom software. Segmentation of articular cartilage was performed by one investigator (H.E.S.) with 4 years of experience in analysis of cartilage T2 maps of the knee.

For the entire region of interest, the software automatically generates multiple T2 profiles by defining perpendicular tangents to the cartilage-bone interface that terminate at the articular surface.

For comparison of cartilage T2 values between volunteers, each profile was normalized for cartilage thickness such that cartilage at the subchondral surface has a normalized distance of 0.0, and cartilage at the articular surface has a normalized distance of 1.0. The T2 profiles for each individual were pooled to determine mean T2 values and standard deviations as a function of normalized distance from bone.

## Results

T2 MR imaging maps were obtained successfully in all five volunteers. A representative source image and T2 map of the proximal interphalangeal joint are shown in Figure 1. As observed in Figure 1b, there is spatial variation in cartilage T2 of the proximal interphalangeal joint, with longer values observed near the articular surface. This spatial variation in cartilage T2 was reproducible, as indicated by the small variation in T2 profiles of the proximal phalangeal cartilage presented in Figure 2. Long T2 values of  $66\ \text{msec} \pm 5$  are observed near the bone cartilage interface. With increasing distance from bone, cartilage T2 relaxation decreases to a minimum of  $42\ \text{msec} \pm 2$  at a normalized distance of 0.4 and subsequently increases monotonically to a value of  $55\ \text{msec} \pm 5$  at the articular surface.



**Figure 2.** Pooled cartilage T2 profiles (mean  $\pm$  standard deviation [bars]) as a function of normalized distance from bone. Normalized distance of 1.0 corresponds to the articular surface. Spatial variation in cartilage T2 is similar to that reported previously for the femoral tibial joint (6), with longer T2 values observed near the bone-cartilage interface and articular surface.

## I Discussion

Current clinical management of osteoarthritis relies on monitoring the progression of symptoms and plain radiographic findings that occur in response to loss of articular cartilage and reactive bone change. Arthroscopy is currently favored as the standard of reference for diagnosis of early intraarticular degenerative change, but the invasive nature of the procedure limits its feasibility as a clinical research tool for longitudinal studies in the asymptomatic population. A primary limitation in the study of osteoarthritis is lack of sensitive markers for monitoring of disease progression and response to therapy. There is growing interest in the development and validation of sensitive MR imaging techniques for study of *in vivo* articular cartilage physiology and early osteoarthritis (9).

New MR imaging parametric mapping techniques, such as cartilage T2 mapping (4), T1 $\rho$  mapping (10), and delayed gadolinium-enhanced MR imaging of cartilage (11), demonstrate sensitivity to biochemical and structural changes in the extracellular cartilage matrix and thus have the potential to serve as image markers of osteoarthritis. As a clinical research tool, it would be useful to apply image marker techniques to different joints within the same individual to differentiate systemic factors from biomechanical factors that may be localized to a specific joint.

The interphalangeal joints of the hand are a common site for osteoarthritis, with risk factors that differ from those of large

weight-bearing joints, such as the hip or knee (1,12,13). Thus far, there has been limited application of MR imaging techniques in the evaluation of articular cartilage in small joints of the hand, and these have been limited to anatomic imaging techniques for the evaluation of tissue morphology. An initial feasibility study by Fry et al (14) demonstrated the potential of MR imaging to depict cartilage of the interphalangeal joints of the fingers. By using a highly optimized 2.4-T MR imaging system, Hodgson and co-workers (15) developed a method for obtaining anatomic images of cartilage of the distal interphalangeal joint of the finger with an in-plane spatial resolution of 75  $\mu\text{m}$  by 150  $\mu\text{m}$ . Peterfy et al (16) were able to obtain accurate reproducible quantification of articular cartilage volume in the metacarpophalangeal joints of the hand by using a clinical 1.5-T MR imager with a home-built receiver coil. When compared with the study of knee cartilage, the relative paucity of studies that involve MR imaging in the evaluation of the small joints of the hand reflects the substantial technical limitations when current techniques are applied with existing MR imaging systems.

### Technical Considerations

Technical requirements are even more substantial for application of MR imaging parametric mapping techniques, such as T2 mapping, in the evaluation of articular cartilage in the hand. Thus far, T2 mapping techniques have been lim-

ited to evaluation of knee cartilage. The major limitation in the evaluation of phalangeal cartilage of the hand is the small volume of tissue ranging from 34 to 86  $\mu\text{L}$  for phalangeal cartilage of the metacarpophalangeal joint (16). Obtaining reproducible *in vivo* T2 maps of the hand with a quality similar to that reported previously for knee cartilage requires data acquisition techniques currently used in ultra-high-field-strength MR microscopy studies of excised cartilage plugs.

*In vivo* cartilage T2 maps with an in-plane resolution of 250  $\mu\text{m}$  have been used in the evaluation of femoral tibial cartilage (6,17). If the average thickness of femoral cartilage is assumed to be 1.5 mm, the T2 map comprises approximately 6 pixels across the cartilage. To obtain similar effective resolution in phalangeal cartilage, pixels of less than 100  $\mu\text{m}$  would be required, which necessitates methods to optimize signal-to-noise ratio. In our study, signal-to-noise ratio was optimized through the use of a 3.0-T imager and a specialized radiofrequency transmit-receive coil with a high filling factor.

Because cartilage has short T2 values that range from 20 to 60 msec, the signal from cartilage will decay rapidly with long TE values. To characterize the T2 decay curve of cartilage accurately, it is necessary to minimize interecho spacing of the multiecho pulse sequence (18). The simultaneous need for high spatial resolution and short interecho spacing necessitates large receiver bandwidths, which further decreases signal-to-noise ratio and requires large magnetic field gradient amplitudes, rapid gradient switching, fast digitizers, and small transmit radiofrequency coils to minimize duration of the 180 $^\circ$  refocusing pulses.

For the present study, we used a home-built gradient insert capable of generating 1000 mT/m, with a rise time of less than 50  $\mu\text{sec}$ . With the 2.5-cm transmit-receive coil and a 2.5-kW radiofrequency amplifier, the duration of the refocusing pulse was 2000  $\mu\text{sec}$ . By using a receiver bandwidth of 80 kHz, the interecho spacing could be reduced to approximately 10 msec while an in-plane pixel resolution of approximately 40  $\mu\text{m}$  was obtained.

### Cartilage T2 Maps

Prior studies have demonstrated that the T2 of articular cartilage is sensitive to differences in water content (19), collagen content (20), and collagen fiber ori-

entation in the extracellular matrix (21). Early studies by Xia et al (22) involving excised cartilage plugs demonstrated spatial variation in cartilage T2, with longer values observed near the articular surface. This observation was confirmed later with an *in vivo* study by Dardzinski et al (4) on the evaluation of patellar cartilage.

Despite substantial differences in acquisition methods, magnetic field strength, and hardware, the pattern of spatial dependency of *in vivo* cartilage T2 of phalangeal cartilage observed in the present study is similar to that reported in prior *ex vivo* studies of cartilage plugs (21,23–25) and *in vivo* measurements of femoral and/or tibial (6,17) and patellar cartilage (5,7,8). The range of spatial variation in cartilage T2 values of proximal phalangeal cartilage is less than that reported by Smith et al (6) for patellar cartilage (45–67 msec) and is similar to that observed in femoral cartilage (46–56 msec).

As has been described previously by Smith et al (6), high T2 values are observed near the bone-cartilage interface. By using high-spatial-resolution MR imaging, T2 maps, and histologic findings of bovine cartilage plugs, Nieminen et al (26) found that this zone of high T2 values corresponded to a zone of cartilage that contained an accumulation of chondrocytes. While the elevated T2 value in this zone may be a result of longer T2 values of intracellular water and the higher water content of the pericellular matrix surrounding the chondrocyte, this location is also subject to artifact from volume averaging, with bone and chemical shift artifact making interpretation ambiguous. Similarly, volume averaging with synovial fluid will result in error near the articular surface. This may be one reason why we did not observe low T2 values from the superficial lamina splendens, as has been observed with excised cartilage plugs (26).

### Study Limitations

There are inherent limitations in the use of MR imaging techniques for quantitative determinations of T2 (27). Nonuniformity of the B1 field generates stimulated echoes in multiecho pulse sequences. Maier et al (8) showed that T2 is overestimated when a multiecho sequence is used, compared with measurements obtained by using a series of single-echo acquisitions with differing echo times. This error is reduced by excluding the first echo, as was done in the present study (8,27). The use of multisection acquisition produces off-resonance ir-

radiation and incidental magnetization transfer (28) that can lead to an underestimation of T2 (8).

Fortuitously, positive error resulting from signal contribution of stimulated echoes is partially negated by negative error that results from incidental magnetization transfer (8). These errors arise from different factors, however; thus, it cannot be assumed that this effect will improve accuracy. Likewise, these systematic biases will vary with hardware and acquisition parameters and thus may contribute to differences in absolute T2 values acquired from knee cartilage and those acquired from the hand. Careful validation studies and methods for quality control are necessary (*a*) prior to implementation of these techniques in multicenter trials or (*b*) following technical modifications at individual sites.

At the bone-cartilage interface and articular surface, partial volume averaging with cortical bone and synovial fluid produces error in cartilage T2 measurements. With a pixel resolution of 39  $\mu\text{m}$  and an average cartilage thickness of 500  $\mu\text{m}$ , approximately 13 pixels are acquired across articular cartilage. With regard to the normalized T2 profiles, the relative resolution is a normalized distance of approximately 0.08. Additional factors can result in error in T2 measurement near the bone-cartilage interface. At the tidemark zone, differences in magnetic susceptibility between calcified bone and cartilage produce local magnetic field gradients that lead to rapid T2 decay, which is not measured accurately with the echo time values used in the acquisition protocol in the present study (18). Chemical shift artifact is increased at 3.0 T; however, this can be reduced with the use of large frequency-encoding gradients. In this case, use of a 80-KHz bandwidth produced a chemical shift of approximately 2 pixels. With regard to T2 profiles, chemical shift artifact from bone would be limited to the region of 0.0 to 0.16 normalized distance.

The results of the present study demonstrate the feasibility of acquiring cartilage MR T2 maps of small joints in the hand with an acquisition time of less than 10 minutes. With clinical implementation of 3.0-T MR imagers, it is likely that these techniques could be applied with relatively minor modifications to commercially available systems. Similar combined gradient and radiofrequency coil inserts have been used to obtain cartilage T2 maps of patellar samples with a 1.5-T clinical MR imager (29).

Cartilage T2 mapping of the hand may

have clinical research applications in the study of hand arthritis and may provide novel information that improves understanding of the pathophysiology of generalized osteoarthritis. While biochemical changes in cartilage physiology can be modeled in animal studies, it is difficult to simulate the biomechanical loading conditions of the human joint. The ability to obtain cartilage T2 values in the same individual from both weight-bearing and non-weight-bearing joints provides a potential method to differentiate local biomechanical effects from systemic effects.

This information would be useful in understanding the effect of conditions such as exercise, body habitus, and prior trauma on the composition and organization of the extracellular cartilage matrix.

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