Mapping MR Parameters of Human Articular Cartilage Degeneration Using Magnetic Resonance Microscopy

S. F. Othman[1], J. Moinness[1], J. Li[2], H. Xu[1], C. Muehleman[2], R. L. Magin[1]

[1]Bioengineering, University of Illinois at Chicago, Chicago, IL, United States, [2]Department of Biochemistry, Rush university Medical Center, Chicago, IL, United States

Introduction

Assessment of articular cartilage deterioration and degeneration is an important step in the staging of joint disease. MRI could play a bigger role in diagnosis if we can better understand the relationship between tissue structure and MR relaxation. MR imaging of articular cartilage reflects the colligative properties of the water in each tissue layer through local variation in its MR properties. The variation of water content in the articular cartilage arises from the hydrophilic nature of proteoglycan. Water content varies throughout the cartilage, increasing in concentration from 65% near the subchondral bone to 80% at the articular surface (1). The water content of cartilage changes with the onset of diseases such as osteoarthritis, which progressively alter its composition and structure. MRI can be used directly to monitor changes in water content and indirectly measure changes in the MR relaxation parameters and the apparent diffusion coefficient. In this work, using an 11.74 T (500 MHz for proton) magnet we correlated tissue structure through different stages of human articular degeneration with the MR relaxation times and apparent diffusion coefficient. We mapped the T2 relaxation times and apparent diffusion coefficient (ADC) on a pixel by pixel basis from the radial to the tangential zones with an in-plane resolution of 47 µm x 47 µm . In addition, the T2 relaxation time as a bi-exponential and its behavior is investigated in different regions of interest. Finally, our MR finding were correlated with histological examination of the tissue.

Methods

Human tali were obtained through the Gift of Hope Organ and Tissue Donor Network with institutional approval, and frozen at -20 ^{0}C until experimentation. Prior to experimentation, ten mm cubes containing full thickness cartilage with subchondral bone were harvested from the talar dome using a band saw with a diamond tip blade. To eliminate any saw blade artifacts, the samples were then trimmed, with a sharp scalpel blade, to 3 mm width cubes. Three grades of cartilage degeneration were examined G0 = normal, un-degenerated; G1 = shallow, superficial fibrillation, and G2 = fissuring. Three samples were tested for each stage of degeneration. MR experiments were conducted at 11.74 T (500 MHz for proton) in a 56-mm vertical bore magnet equipped with Bruker DRX Avance spectrometer controlled by a Silicon Graphics SGI2 workstation (Mountain View, CA, USA). MR images were acquired using a Bruker Micro 5 imaging probe with triple axis gradients (maximum strength 200 G/cm). A 5 mm diameter RF saddle coil was used to transmit/receive the nuclear magnetic resonance signals. The T_2 relaxation time was measured by applying a standard spin-echo imaging sequence to acquire 32 echoes with a 7 msec echo spacing (TE) from the chosen axial slice containing the full depth of the cartilage (TR = 4 sec, TE = 7 msec, matrix = 128 x 128, and NEX = 1). The ADC was measured using a standard diffusion weighted imaging (DWI) spin echo imaging sequence. The diffusion gradient was applied along the read direction by varying the "b" values in 16 steps corresponding linearly to diffusion weighted gradient strength ranging from 0 to 30 G/cm (TR = 1 sec, TE = 30 msec, δ = 3 msec, Δ = 18 msec, matrix = 128 x 128, NEX =1, and 16 corresponding "b" values up to 1513 sec/mm^2). The T_2 data were modeled using both a mono-exponential and a bi-exponential for all stages of degeneration. The bi-exponential decay was fit to the equation: $SNR = A_1 e^{-TE/T_{2f}} + A_2 e^{-TE/T_{2s}}$, where T_{2f} and T_{2s} are the extracted "fast" and "slow" T_2 relaxation components while A_1 and A_2 indicate the apparent size of the two compartments. The T2 relaxation times and ADC were measured for a specific region of interest and mapped for the entire image on a pixel by pixel basis. After MR imaging, the samples were fixed in 10% formalin and processed for histology. Histological sections were stained with Safranin-O/fast green.

Results

T2 relaxation time maps for the three stages of articular cartilage degeneration are displayed in Fig. 1 (a, b, and c) on top of the MR magnitude images. In normal cartilage, the T2 value was not constant along the cartilage depth. The T2 relaxation time was measured for three regions corresponding to upper, lower, and middle zones of the cartilage, for both normal and diseased tissue and the values are displayed in Table 1. The bi-exponential model for measuring T2 showed no difference from the mono-exponential model. Fig. 1 (d, e, f) also displays the ADC map for cartilage in the three stages of degeneration where the ADC increased when moving from grade 0 to grade 2. In the ADC map, loss of structure can be noticed for grade 2. The corresponding histologic findings are displayed in Fig 1 (g, h, and i).

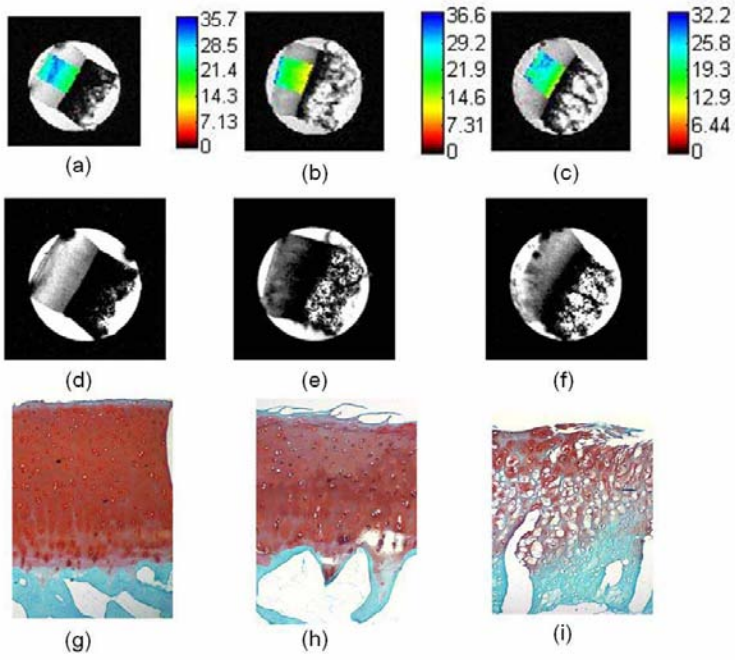

Fig. 1 Three stages of cartilage degeneration displayed by various contrast and imaging mechanisems. (a, b, c) T2 maps for grades 0, 1, and 2 respectively, (d, e, and f) ADC maps for grades 0, 1, and 2 respectively, (g, h, i) Safranin-O/Fast green-stained histologic sections (40x) of the three cartilage with the same order

Table 1. T2 values for different stages of cartilage degeneration based on a selected ROI. Three regions were selected to represent the deep, transitional, and artificial zones, respectively.

	Grade 0	Grade 1	Grade 2
Deep Zone	24.4 ± 0.86	16.7 ± 2.5	26.0 ± 0.53
Middle Zone	30.8 ± 1.64	23.9 ± 2.52	26.0 ± 0.53
Superficial Zone	29.8 ± 2.29	23.5 ± 1.95	26.0 ± 0.53

DISCUSSION and CONCLUSION

This study examined the changes that occur with articular cartilage degeneration. The disease was not artificially induced to the cartilage by an enzymatic depletion of proteoglycan, like the use of chymopapain; this might explain the inconsistency in the T_2 relaxation values. In normal cartilage, the T2 value was not constant along the cartilage depth reflecting the known structure of the tissue (1). For degenerated cartilage, the T2 values were almost constant along the cartilage depth suggesting the washing of the proteoglycan. The ADC, as a contrast parameter was better able to characterize the tissue compared to the T_2 relaxation time. The MR images, specially the ADC maps, correlated well with histology. The normal cartilage displayed a variation in the parameters in a consistent way, while the values for the diseased cartilage displayed larger variation. This variation can be attributed to the fact that they are not in the same disease stages. For grade 2, the cartilage was severely damaged and no zonal variations were noticed. The bi-exponential model for measuring the T2 relaxation times showed no difference from the mono-exponential model. The slow compartment relaxation time was close to the mono-exponential value, however the bi-exponential model for investigating the diffusion coefficient under low and high b values is needed. Future studies should include the study of other MR parameters such as the diffusion tensor and *q*-Space analysis.

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