Diffusion Tensor Imaging as an Early Marker for Osteoarthritis

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INTRODUCTION

Articular cartilage is a heterogeneous, avascular tissue that coats the articulating surfaces of skeletal bone. Cartilage consists of three distinct anatomical zones (superficial, middle, and deep) each of which contains chondrocytes suspended in an extracellular matrix of collagen fibers and proteoglycan. The collagen fiber bundles differ in orientation, thickness and density in each of the three zones [1]. In the superficial zone, a highly ordered thin collagen fibers are organized parallel to the articular surface, while in the middle zone the fibers form a randomly oriented network, and in the deep zone the collagen fibers are ordered and perpendicular to the subchondral bone. High spatial resolution analysis of these layers is possible through diffusion tensor imaging (DTI), an MR based technique used for visualizing and characterizing anisotropic water diffusion in highly ordered tissue structures [2]. Recently several groups used DTI to investigate the microstructural properties of normal cartilage [3]. In this work, we use high resolution DTI at high field of human articular cartilage to evaluate potential markers for characterizing the early stages of degeneration in osteoarthritis (OA). Specifically, we measure the fractional anisotropy (FA) and the smallest eigenvalue (SEV) of the diffusion tensor (DT) matrix. Our hypothesis is that changes in FA will reflect disruption of the well-oriented collagen network during the initial stages of OA. Furthermore, we hypothesize that SEV can be correlated with bound water within collagen fibers (in the cartilage four-spin reservoir model [4]); hence the SEV will give an indication of collagen integrity.

MATERIALS AND METHODS

Human tali were obtained within 24 hours of death of the donor through the Gift of Hope Organ and Tissue Donor Network (with Rush university institutional approval), and frozen at -80 ^{0}C until experimentation. Just prior to experimentation, 10 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. The cartilage/bone cubes were placed in NMR sample tubes filled with physiologic saline. This initial gross morphological grading was carried out to insure variation in cartilage integrity. Three different sample types were identified, Grade 0 (intact cartilage morphology, or normal), Grade 1 (superficial fibrillation) and, Grade 2 (vertical fissure into mid zone). MR experiments were conducted using a 56-mm vertical bore 11.74 T (500 MHz for proton) magnet equipped with Bruker DRX Avance spectrometer. Three samples of each grade were loaded into the 5-mm diameter RF saddle coil and inserted into the Bruker Micro5 imaging probe equipped with a tri-axial gradient set with a maximum strength of 200 G/cm. Diffusion-weighted images were obtained using a standard spin-echo diffusion-weighted pulse sequence with the following parameters: TR = 1000 ms, TE = 30 ms, FOV = 0.6 cm, Δ = 18 ms, δ = 3 ms, NEX = 4, and 47 μm × 47 μm in-plane resolution for a slice thickness of 500 μm. For each sample, six diffusion weighted images were acquired with varying the direction of the diffusion sensitizing gradient along six non-collinear directions (*x*, *y*, *z*, *xy*, *xz*, and *yz*) at an effective b-value up to 1040 s/mm^2. A T_2-weighted image was acquired with the same TE and TR above for each sample. The DT matrix was calculated according to the procedure outlined in Basser *et al.* [5]. Finally, the eigenvalues and the FA were calculated.

RESULTS

The first row in Fig. 1 shows T_2-weighted images of articular cartilage for the three grades, G0=normal, G1=fibrillation and G2=fissuring conditions. The second and third rows in Fig. 1 show FA and SEV maps for the same samples, respectively. Regions of interest (ROIs) were manually selected by visual inspection for the three zones and the mean values for FA and SEV were calculated as shown in Table I. In summary, the FA decreases between G0 and G2 in the superficial zone while changes were statistically insignificant in the deep and middle zones. The SEV increases between G0 and G2 in the superficial and deep zones while changes were statistically insignificant in the middle zone as expected.

	Superficial		*Middle*		*Deep*	
	FA [A.U.]	**SEV [10^{-4} mm^2/s]**	**FA [A.U.]**	**SEV [10^{-4} mm^2/s]**	**FA [A.U.]**	**SEV [(10^{-4} mm^2/s]**
G0	0.4 ± 0.01	3.3 ± 0.5	0.28 ± 0.01	5.7 ± 0.5	0.42 ± 0.02	2.4 ± 0.5
G1	0.36 ± 0.04	3.7 ± 0.8	0.32 ± 0.05	5.0 ± 0.6	0.42 ± 0.03	2.5 ± 0.3
G2	0.33 ± 0.03	5.9 ± 0.7	0.29 ± 0.06	5.7 ± 0.5	0.40 ± 0.03	3.2 ± 0.1

Table I: FA and the SEV changes in cartilage at different cartilage grades: G0 (normal), G1 (fibrillation) and G2 (fissuring). Three samples of each grade were studied

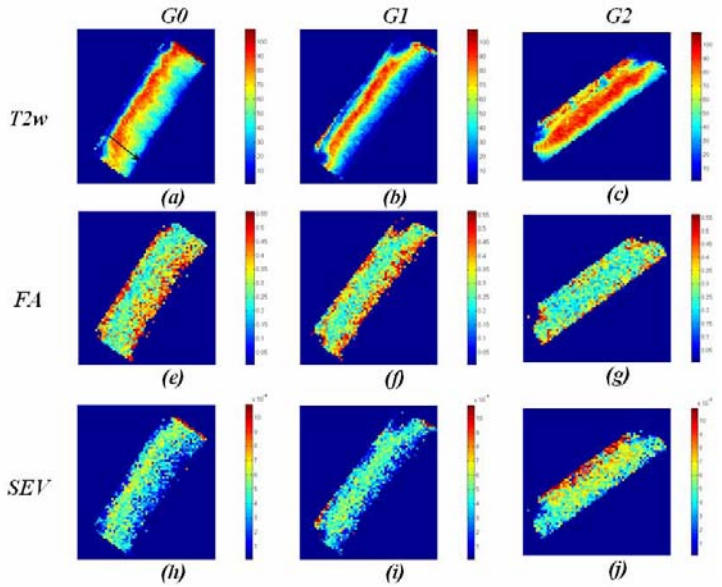

Figure 1. (a-c) T_2-weighted images of different cartilage grades **(d-f)** FA maps and **(g-i)** SEV maps. The arrow in (a) points to the subchondral bone.

DISCUSSION AND CONCLUSION

The three cartilage zones can be distinguished by the T_2-weighted images shown in Fig. 1. These T_2-weighted images serve as a reference for identifying the ROIs used in calculating the FA and the SEV values for each zone. For example, the superficial zone in G0 can be determined from the low signal intensity in the T_2-weighted image and, hence, can be identified in the FA map. The high anisotropy index observed in the superficial zone for G0 reflects the ordered collagen fibers. This observation is consistent with the fact that this zone contains a highly ordered fibrous network, unlike the middle zone where fibers are randomly oriented. The same argument can be applied to the deep zone. Predominantly, degradation in collagen integrity is reflected in the FA maps as shown in the second row of Fig. 1. Starting with the superficial zone, the thin layer of high FA values at G0 begins to merge with the middle zone reflecting loss of the ordered collagen network until is completely absent in G2. This observation is supported by the SEV maps, which show relatively low values in the superficial zone, reflecting restricted water, at G0 and much higher values in G2 which suggests that fiber anisotropy no longer limits water mobility. Neither FA nor SEV exhibit any significant changes in the middle zone, perhaps due to the lack of oriented collagen fibers in this zone. Finally, in the deep zone, no significant changes appear from G0 to G1. However, in this zone the FA was unchanged but the SEV increase suggests a disruption of collagen fibers. In conclusion, the FA and SEV of the DT matrix were found to correlate with the progression of OA in articular cartilage. However, only SEV was able to track changes in the deep zone.

REFERENCES

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