MRI Measurement of Collagen Orientation in Whole Intervertebral Discs

A. C. Wright[1], D. M. Elliott[2], W. Johannessen[2], E. J. Vresilovic[2], F. W. Wehrli[1]

[1]Laboratory for Structural NMR Imaging, Department of Radiology, University of Pennsylvania, Philadelphia, PA, United States, [2]McKay Orthopaedic Research Laboratory, Department of Orthopaedic Surgery, University of Pennsylvania, Philadelphia, PA, United States

Introduction

Lower back pain is associated with loss of structural integrity of collagen fibers composing the annulus fibrosus (AF) of the intervertebral disc (1). The etiology of disc degeneration and injury, as well as new therapeutic strategies, can be modeled in animals by examining changes in the AF microstructure (2), typically via histological sectioning. Recently, however, Hsu, et al., used diffusion tensor MR microscopy (μ-DTI) to measure collagen fiber orientation in the AF, and showed fibers at ~60° relative to the spinal axis can give rise to bright and dark regions in the AF on an MR image, consistent with a theory of anisotropic ^{1}H-^{1}H dipolar relaxation of water oriented by the collagen fibers (3). While μ-DTI directly provides fiber angles, it is severely SNR-limited, meaning only small samples or sections of the AF can be scanned and thereby precluding biomechanical studies of the entire disc. Sheep disc, for example, is commonly used to model human disc disease and therapy, as it shares many relevant microstructural features with human discs (4), but it is too large for high resolution DTI in a reasonable scan time. To quantify AF collagen orientation in whole discs, therefore, we implemented a technique based on the dipolar relaxation of water, and compared its results from both sheep and human discs.

Materials and Methods

MRI intensity in anisotropic tissue with oriented collagen has been characterized by a T_2 relaxation mechanism for water protons (5) that depends on the angle between the ^{1}H-^{1}H axis and static magnetic field B_0 as $(3\cos^2\theta - 1)$. For a fixed orientation of a disc relative to B_0, the angle θ varies in a predictable manner along a path in the AF. The collagen fiber angle, however, is measured from the longitudinal spinal axis, known from histological studies of the disc to be in the range 50°-60°. Therefore, to extract collagen orientation from an MR image, intensity variation along a circle in the AF can be measured and fit to a relaxation model as described below.

Images were acquired on a 1.5 T clinical MRI scanner (GE Medical Systems) with standard spin echo sequences. Both a sheep spinal motion segment (L3-L4) and a human cadaveric lumbar spine (L2-L3) were imaged with their spinal axes oriented orthogonal to B_0 to assure intensity variation with azimuthal angle in the disc AF.

The analysis technique, implemented in IDL (Research Systems, Inc.), involved tracing MRI intensities along a circle in the AF and fitting them to a relaxation model (6) given by $I(\psi) = I_0 exp(-TE \cdot R_2) + I_1$, where $R_2 = K(3\cos^2\theta - 1)^2 + R_2^0$ is the transverse relaxation rate with two terms: oriented water (θ-dependent) and free water, and $\theta = \cos^{-1}[(-\cos\alpha \cdot \cos\phi) \pm (\sin\alpha \cdot \cos\psi \cdot \sin\phi)]$ is the angle between the static field B_0 and the collagen fibers in the AF. Here, α is the angle the collagen fibers make with the longitudinal spinal axis, ϕ is the polar angle (here 90°) between the spinal axis and B_0, and ψ is the azimuthal angle in the image plane along the circle, shown drawn on the image of each disc in Fig. 1. Intensity along each circle, $I(\psi)$, is plotted next to each image, normalized to maximum values.

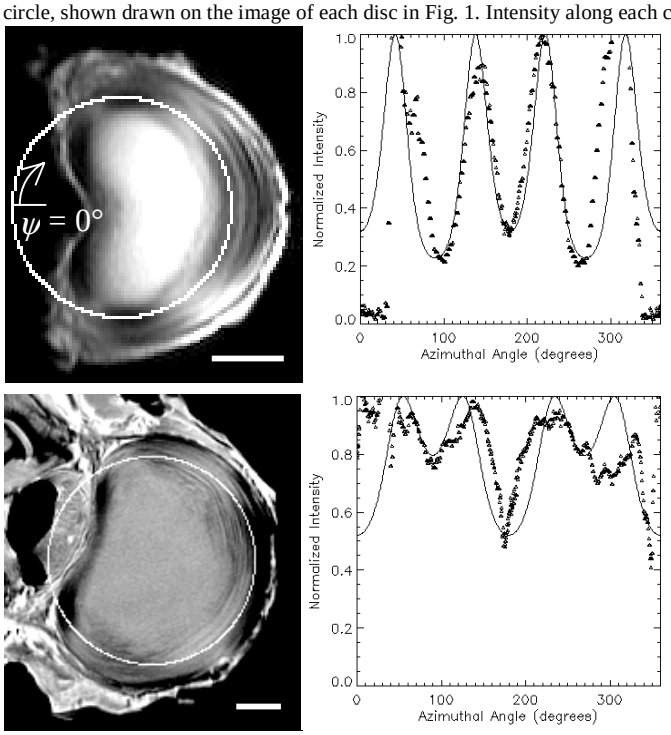

Fig. 1 (left) MR image sections through sheep (top) and human (bottom) lumbar spine, ex vivo. Images show $I(\psi)$ variation, with high intensity at ψ likely corresponding to the magic angle ($\theta = 54.7°$) between collagen fibers and B_0. Scale bar in each image = 1 cm.
Sheep: Spin Echo, matrix = 256x256, FOV = 8x8cm^2, TE=13 ms, TR=3 s, NEX = 1, scan time = 13.4 min, voxel = 313x313x3000 μm^3.
Human: Fast Spin Echo, matrix = 256x256, FOV = 8x8mm^2, TE=17 ms, TR=1 s, NEX = 4, scan time = 4.3 min, voxel = 313x313x3000 μm^3.

(right) Graphs of intensity variation $I(\psi)$ in the AF, along the circle drawn on the images next to each graph. The solid lines are approximate fits to the data points using the above equation for $I(\psi)$. General features of the data vary slightly for circles of different radii on each image. Fitted parameters were:
Sheep: I_0=0.89, I_1=0.11, K=0.17, R_2^0=0.05 ms^{-1}, α=60°
Human: I_0=0.70, I_1=0.30, K=0.17, R_2^0=0.05 ms^{-1}, α=45°

Results and Conclusions

For the circles drawn in Fig. 1, α was 60° in sheep disc and 45° in human disc. While these values are averaged along a circle in the AF, the fiber angles are consistent with those measured on histological sections (4). In addition, since $I_0 + I_1 = 1$, where I_1 is the isotropic water fraction, a relative anisotropy of the AF is given by I_0, the coefficient of the anisotropic term in $I(\psi)$. As shown, I_0 was 89% in the sheep disc and 70% in the human disc. As the circle radius was increased from the edge of the nucleus to the outer lamellae in the AF, best-fit values for fiber angle (α) and relative anisotropy (I_0) increased for both the sheep and human discs, as expected from the known radial dependence on structure and composition (4).

The technique presented here provides a means to rapidly and non-invasively quantify disc microstructure. Future studies will investigate its ability to detect changes due to age, injury, disease and therapeutic interventions. Non-invasive measurements of fiber angles in whole discs and disc motion segments will help guide formulation of biomechanical models of the disc, since the intact disc is required when performing in vitro mechanical testing and when evaluating the outcome of clinical procedures such as nucleus decompression.

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References

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