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Theory of MRI contrast in the annulus fibrosus of the intervertebral disc

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Abstract

Objective—Here we develop a three-dimensional analytic model for MR image contrast of collagen lamellae in the annulus fibrosus of the intervertebral disc of the spine, based on the dependence of the MRI signal on collagen fiber orientation.

Materials and methods—High-resolution MRI scans were performed at 1.5 and 7 T on intact whole disc specimens from ovine, bovine, and human spines. An analytic model that approximates the three-dimensional curvature of the disc lamellae was developed to explain inter-lamellar contrast and intensity variations in the annulus. The model is based on the known anisotropic dipolar relaxation of water in tissues with ordered collagen.

Results—Simulated MRI data were generated that reproduced many features of the actual MRI data. The calculated inter-lamellar image contrast demonstrated a strong dependence on the collagen fiber angle and on the circumferential location within the annulus.

Conclusion—This analytic model may be useful for interpreting MR images of the disc and for predicting experimental conditions that will optimize MR image contrast in the annulus fibrosus.

Keywords

Intervertebral disc; Annulus fibrosus; Collagen; Image contrast; Dipolar relaxation

Authors contribution Wright: Protocol/project development, Data collection or management, Data analysis Yoder: Data collection or management Vresilovic: Protocol/project development Elliott: Protocol/project development

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standards The manuscript does not contain animal studies or clinical studies/patient data. Tissue specimens were obtained under IACUC and IRB approved protocols.

Introduction

The intervertebral disc is an avascular cartilaginous tissue between vertebrae that absorbs and redistributes mechanical forces during motion of the spine. Degeneration of the disc has been associated with lower back pain [1, 2], and attempts to understand this process and to devise new therapeutic strategies often rely on modeling the disc's anatomy and biomechanical properties [3–7]. The disc consists of at least three sub-structures (Fig. 1): the central nucleus pulposus (NP), the circumferential annulus fibrosus (AF), and the superior and inferior cartilaginous endplates (CEP) [8, 9]. These regions have different function, microstructure, and chemical composition. The AF is distinct in the high level of organization of its collagen fibers into contiguous lamellae (typically ~20), with fibers in adjacent lamellae oriented at approximately $\pm 60^\circ$ relative to the local spinal axis [5, 10, 11]. This alternation of fiber angle from one lamella to the next is believed to contribute to the complex mechanical behavior of the AF tissue as it supports multidirectional loads during normal activity [12, 13].

Computer-based models of the disc have become an important means for understanding its biomechanics and degenerative etiology, and for aiding the development of therapeutic strategies such as prosthetic device implants and engineered tissue [12, 14–18]. Image-informed models potentially have greater accuracy than purely theoretical ones, if, for example, detailed information about how the AF microstructure deforms in response to loads can be acquired. Magnetic resonance imaging (MRI) is ideally suited for this, since it is a non-destructive, non-perturbing, high-resolution tomographic modality that can achieve high contrast between tissues based on differences in T_1 and T_2 relaxation times [19]. In particular, for echo times $T_E \gtrsim 10$ ms and voxel sizes $\lesssim$ lamellar thickness, MRI can directly resolve the AF lamellae, displaying them as layers of alternating bright and dark intensity, though the physical origins of this alternation have not been examined in detail. In a study exploring diffusion tensor MRI for imaging the AF [20], this alternating pattern was attributed to the angular dependence of dipolar coupling between hydrogen nuclei of water associated with collagen fibers. This causes the MR signal intensity to depend on fiber orientation with respect to the static B_0 magnetic field of the MRI scanner, a phenomenon that has been extensively studied in other collagen-containing tissues and often referred to as the “magic angle effect” [21–28]. Another manifestation of the same phenomenon had been described previously [29], i.e., the azimuthal variation of image intensity within the AF when the disc spinal axis is not parallel to B_0 . However, in both cases the model used to represent fibers was essentially two-dimensional, assuming a central axial slice through the disc, and did not address the known curvature of the lamellae.

The relationship between the AF geometry and microstructure and its appearance on MR images is complex. Inter-lamellar contrast within the AF seen in MRI could be caused by unique local variations of the lamellar curvature and fiber angle, in addition to the expected alternation of fiber angle in adjacent lamellae. Such local variations also could give rise to incorrect apparent lamellar thickness due to partial volume averaging within each MRI voxel. To examine the effects of AF geometry and microstructure on MRI appearance, therefore, the AF model should be generalized to three dimensions. We present here such a model based on an idealized geometry that captures essential features of the AF and

excludes subvoxel irregularities such as fiber crimping [10]. We demonstrate that this model can account for the major features seen in MR images of the AF, and compare it to actual MRI data from disc specimens. Furthermore, we compute the expected AF inter-lamellar contrast under various conditions as a means to contrast optimization, with an immediate application to improved MRI data for biomechanical models. Finally, we discuss potential longer-range applications to in vivo MRI methods that may be sensitive to AF structural weaknesses and tears that could serve as early biomarkers for degenerative disc disease.

Materials and methods

Intervertebral disc specimens

This study made use of non-degenerate human, ovine, and bovine disc specimens obtained according to IRB and IACUC approved protocols. Non-human disc specimens are routinely used as surrogates for human tissue due to their greater availability, uniformity, and health, while maintaining similar structure and mechanics [30, 31]. All disc specimens were fresh frozen, bone-disc-bone spinal segments. They were thawed and allowed to equilibrate at room temperature in phosphate buffered saline prior to imaging. In addition, they were wrapped in plastic during imaging to prevent dehydration and, in some cases, embedded in agarose to reduce the possibility of image artifacts that can occur due to magnetic susceptibility differences at tissue-air interfaces. The number of spines investigated by MRI for each species is 4 ovine lumbar spines, 3 bovine tails, and 20 human lumbar spines. The number of discs investigated by MRI for each species is 4 ovine lumbar discs, 3 bovine tail discs, and 40 human lumbar discs (at least 2 discs from each of the five lumbar levels).

MRI-based measurement of AF microstructure

High resolution MRI—The MRI scanners used were whole-body clinical systems: 1.5 T GE Signa and 7 T Siemens Magnetom. At each magnetic field strength the best available (i.e., closest-fitting) RF coils were used to maximize signal-to-noise ratio (SNR). At 1.5 T a planar 4 cm × 4 cm receive-only surface coil was used for the ovine disc, and a vertically oriented 12 cm diameter transmit-receive solenoidal coil was used for the human disc. At 7 T a Helmholtz-pair transmit coil with a four-channel receive array was used [32]. Ovine discs are smaller than bovine and human discs, so a smaller coil was used for imaging ovine discs. Different coils often have different spatial sensitivity profiles, which can create differences in intensity shading in the MR images. However, visibility of inter-lamellar contrast and azimuthal intensity variation in the annulus were not significantly affected by the coil sensitivity profile for all the MR images presented here.

To demonstrate the appearance of AF inter-lamellar contrast and azimuthal intensity variations, 2D and 3D MRI scans of disc specimens were acquired, with scan parameters shown in Table 1. Conventional spin echo (SE), fast spin echo (FSE), and turbo spin echo (TSE) sequences were used (FSE and TSE are commercial names for essentially the same sequence). Spin echo pulse sequences were chosen for their ability to refocus static spin dephasing due to magnetic susceptibility mismatches at tissue/air interfaces and to minimize other susceptibility-related effects. Repetition time (T_R), echo time (T_E), and number of signal averages (SA), were chosen to achieve sufficient SNR and image contrast at a given

resolution. For FSE and TSE sequences, the number of echoes per T_R (N_E) was kept small enough to avoid noticeable blurring. To avoid chemical shift artifacts from vertebral bone marrow, signal from fat was actively suppressed using standard methods. Resolution is listed in Table 1 for the MRI scans as the nominal voxel dimensions along the frequency/phase/slice encoding axes, and for the simulations as the final down sampled voxel dimensions. It should be noted that ultra-short T_E (UTE) sequences could be used if desired [33]. All fibrous soft tissues, not only intervertebral disc, contain some components having very short T_2 (e.g., hydrogen atoms in protein molecules), which are undetectable using conventional clinical sequences. However, as stated above, using a T_E of 10 ms or longer allows inter-lamellar contrast in the annulus to manifest. Such a T_E is well within the capability of SE and FSE/TSE sequences.

Magnetic resonance dipolar relaxation theory—Water molecules in most connective tissues, being loosely associated with collagen fibers, experience anisotropically restricted tumbling and hence are partially oriented on an NMR time scale [26, 27]. In tissues having oriented collagen fibers, such as the AF, the MR signal has been characterized by a dipolar term in the transverse relaxation rate R_2 ($=1/T_2$) for water ^1H nuclei that depends on the angle between the ^1H – ^1H molecular axis and the static magnetic field B_0 . The result is that MRI intensity, measured at echo time T_E , depends on the collagen fiber-to-magnetic field angle θ_{CB} according to

$$I(\theta_{CB}) = I_0 \exp(-T_E \cdot R_2(\theta_{CB})) \quad (1)$$

where

$$R_2(\theta_{CB}) = K \left(3\cos^2\theta_{CB} - 1 \right)^2 + R_2^0 \quad (2)$$

with I_0 the MRI intensity at $T_E = 0$, K a scaling factor of the dipolar term, and R_2^0 the contribution to the transverse relaxation rate that is not angularly dependent [26, 27, 34]. The angle θ_{CB} can be defined by the scalar product of the collagen orientation vector $\vec{C}$ with the magnetic field, i.e., $\vec{C} \cdot \vec{B}_0 = |\vec{C}||\vec{B}_0|\cos\theta_{CB}$. In the AF, however, the collagen fiber angle α typically is defined relative to the local spinal axis. This means that for a fixed orientation of a disc relative to B_0 , the relationship between θ_{CB} and α depends on the location in the AF. Furthermore, it implies that if $|\alpha|$ is constant throughout the AF (known from histology to be 50° – 60°), the variation of MRI intensity as a function of azimuthal angle $\mathcal{I}(\psi)$ can be calculated. This dependence of MRI intensity on position within the AF will be explicitly derived in the next section.

Geometric model of AF dipolar relaxation—The microstructural anatomy of collagen fibers within the AF has been described [10]. In summary, collagen fibers in the AF have the following general characteristics: (1) fibers are arranged in roughly concentric cylindrical sheets (lamellae) around the NP, (2) fibers within each lamella are parallel, (3) fibers within

adjacent lamellae are oriented alternatively at $\sim +60^\circ$ or -60° relative to the local spinal axis at the central axial plane of the disc, and (4) lamellae exhibit z -axis curvature inward toward the spinal axis above and below the central axial plane of the disc (assumed here to be the xy -plane).

The 2D dipolar model for disc AF tissue [29], originally proposed to explain azimuthal intensity variation in the central axial plane, also can account for inter-lamellar contrast. In this model, each AF lamella is represented by a circle, the magnetic field vector $\vec{B}_0$ makes an angle ϕ_B relative to the local spinal axis vector $\vec{S}$ (parallel to the positive z -axis), and the collagen fiber unit vector $\hat{C} = \vec{C}/|\vec{C}|$ makes an angle α relative to $\vec{S}$. Thus by the scalar product $\hat{C} \cdot \hat{B}_0$, where $\hat{B}_0$ is a unit vector in the direction of $\vec{B}_0$, the angle θ_{CB} can be derived as a function of ϕ_B and azimuthal angle ψ around the circumference of the disc:

$$\theta_{CB} = \cos^{-1}(\sin\alpha \sin\phi_B \sin\psi + \cos\alpha \cos\phi_B) \quad (3)$$

This then allows one to compute the MRI intensity at a point in the AF via Eqs. 1–3. It can be seen that when the spinal axis is parallel to $\vec{B}_0$ ($\phi_B = 0^\circ$) there is no dependence on ψ , but that for other orientations of the disc there is an azimuthal intensity variation. Furthermore, when $\phi_B = 0^\circ$ it can be seen that by replacing α with $-\alpha$ there is no change in the resulting MRI intensity, however when $\phi_B \neq 0^\circ$ there is a $\pm \alpha$ -dependent change for most, but not all, ϕ_B . *Thus inter-lamellar contrast in an MR image of the AF can arise when $\phi_B \neq 0^\circ$ or when fibers within adjacent lamellae have different absolute orientations $|\alpha|$.*

A fully 3D dipolar model for disc AF tissue is needed to account for the z -axis curvature of the AF toward the spinal axis. Also, because the AF cross-section in the xy -plane is not circular but approximately elliptical, we have employed a set of concentric ellipsoids. Such a model is based on the equation for a tri-axial ellipsoid centered at the origin (Fig. 2):

$$\frac{x^2}{a^2} + \frac{y^2}{b^2} + \frac{z^2}{c^2} = 1 \quad (4)$$

that can be expressed as a surface $\vec{r}(x, y, z)$ in parametric form with $x = a \sin \phi \sin \psi$, $y = b \sin \phi \cos \psi$, and $z = c \cos \phi$. Here (a, b, c) are the semi-principal axes along the (x, y, z) -axes, ϕ is a polar angle measured from the positive z -axis and ψ is an azimuthal (equatorial) angle measured from the positive y -axis. Unit vectors can be defined on this surface in the equatorial and polar directions, respectively:

$$\begin{aligned} \hat{e} &= \frac{\vec{e}}{|\vec{e}|} = -\frac{\partial \vec{f}}{\partial \psi} \cdot \frac{1}{|\vec{e}|} = \frac{-(a \sin \phi \cos \psi, -b \sin \phi \sin \psi, 0)}{\sqrt{(a^2 \cos^2 \psi + b^2 \sin^2 \psi) \sin^2 \phi}} \\ \hat{p} &= \frac{\vec{p}}{|\vec{p}|} = -\frac{\partial \vec{f}}{\partial \phi} \cdot \frac{1}{|\vec{p}|} \\ &= \frac{-(a \cos \phi \sin \psi, b \cos \phi \cos \psi, -c \sin \phi)}{\sqrt{(a^2 \sin^2 \psi + b^2 \cos^2 \psi) \cos^2 \phi + c^2 \sin^2 \phi}} \end{aligned} \quad (5)$$

As a result, the collagen fiber unit vector can be expressed as $\hat{C} = \sin \alpha \hat{e} + \cos \alpha \hat{p}$. The magnetic field vector $\vec{B}_0$ is defined in three dimensions for arbitrary angles ϕ_B and ψ_B as

$$\vec{B}_0 = B_0 \hat{B}_0 = B_0 (\sin \phi_B \sin \psi_B, \sin \phi_B \cos \psi_B, \cos \phi_B) \quad (6)$$

Thus for a voxel (i, j, k) centered on point (x, y, z) within the AF, the MRI intensity $I(x, y, z)$ is given by Eqs. 1 and 2, with θ_{CB} replaced by θ_{CBijk} defined as

$$\theta_{CBijk} = \cos^{-1} ((A_{ijk}) \sin \phi_B \sin \psi_B + (B_{ijk}) \sin \phi_B \cos \psi_B + (C_{ijk}) \cos \phi_B) \quad (7)$$

where

$$\begin{aligned} A_{ijk} &= a_{ijk} \left(\frac{-\sin \alpha \sin \phi_{ijk} \cos \psi_{ijk}}{|\vec{e}|_{ijk}} - \frac{\cos \alpha \cos \phi_{ijk} \sin \psi_{ijk}}{|\vec{p}|_{ijk}} \right) \\ B_{ijk} &= b_{ijk} \left(\frac{\sin \alpha \sin \phi_{ijk} \sin \psi_{ijk}}{|\vec{e}|_{ijk}} - \frac{\cos \alpha \cos \phi_{ijk} \cos \psi_{ijk}}{|\vec{p}|_{ijk}} \right) \\ C_{ijk} &= c_{ijk} \left(\frac{\cos \alpha \sin \phi_{ijk}}{|\vec{p}|_{ijk}} \right) \end{aligned} \quad (8)$$

Also, $\phi_{ijk} = \cos^{-1}(z / \sqrt{x^2 + y^2 + z^2})$, $\psi_{ijk} = \cos^{-1}(y / \sqrt{x^2 + y^2})$, $a_{ijk} = x / (\sin \phi_{ijk} \sin \psi_{ijk})$, $b_{ijk} = y / (\sin \phi_{ijk} \cos \psi_{ijk})$, and $c_{ijk} = z / \cos \phi_{ijk}$. Note that $|\vec{e}|$ and $|\vec{p}|$ are defined in the denominators of Eq. 5, and that Eq. 7 reduces to Eq. 3 when $\psi_B = 0^\circ$, $\phi_{ijk} = 90^\circ$ (and/or $z = 0$), and $a_{ijk} = b_{ijk}$.

To mimic the lamellar z -axis curvature seen in real discs, a set of concentric ellipsoidal layers can be defined by ellipsoidal surfaces with anisotropic scaling, e.g., a and b increment by λ , the lamellar thickness in the central axial (xy -) plane, but c increments by $\lambda_z < \lambda$ along the z -axis (Fig. 2). The NP-AF interface is defined by the smallest ellipsoidal shell: $(a, b, c) = (a_0, b_0, c_0)$ in Eq. 4; and the lamellar surfaces are indexed from the NP outward by the number $n = \{0, 1, 2, \dots, N_\lambda\}$, where N_λ is the total number of lamellae. Lamellae are defined as layers of points (x, y, z) bounded by ellipsoidal shells:

$$\frac{x^2}{(a_0 + n\lambda)^2} + \frac{y^2}{(b_0 + n\lambda)^2} + \frac{z^2}{(c_0 + n\lambda_z)^2} > 1$$

and

$$\frac{x^2}{(a_0 + (n+1)\lambda)^2} + \frac{y^2}{(b_0 + (n+1)\lambda)^2} + \frac{z^2}{(c_0 + (n+1)\lambda_z)^2} \leq 1 \quad (9)$$

The collagen fiber direction is alternated in adjacent lamellae by setting α to $-\alpha$ (Fig. 3).

The above equations were implemented in IDL (Exelis Visual Information Solutions, Inc.). Using disc dimensions and orientations as measured on MR images, together with actual MRI pulse sequence parameters (T_E and resolution), simulated 3D MRI data sets were generated consisting of arrays up to $1080 \times 680 \times 200$ in size, as needed to span the disc dimensions with $50 \mu\text{m}$ isotropic voxels. Disc dimensions are given in Table 2 and were parameterized as follows: (LR, AP, SI) = left–right, anterior–posterior, and superior–inferior disc size along the (x , y , z)-axes, N_λ = number of lamellae, λ = thickness of lamellae in the central xy -plane, w = width of the AF in the central xy -plane ($=\lambda N_\lambda$), w_z = tapered width of the AF intersecting the z -axis, λ_z = tapered thickness of lamellae intersecting the z -axis ($=w_z/N_\lambda$), and $(a_0, b_0, c_0) = [(\frac{1}{2}LR - \Delta), (\frac{1}{2}AP - \Delta), (\frac{1}{2}AP - \Delta_z)]$. Note that the thickness of the ellipsoidal layers defined in Eq. 9 increases from λ_z to λ as ϕ varies from 0° to 90° .

Additional parameters were α , ϕ_B , ψ_B , K , and R_2^0 . In order to reproduce the lamellar z -axis curvature seen in MR images, the values of $(a_{ijk}, b_{ijk}, c_{ijk})$ were allowed to range from (a_0, b_0, c_0) to $(\frac{1}{2}LR, \frac{1}{2}AP, \frac{1}{2}AP)$, i.e., the outermost ellipsoidal shell was chosen to have circular cross-section in planes parallel to the yz -plane. This means that λ_z , which defines the smallest feature of the ellipsoidal layers, occurs at z -values external to the simulated array, and thus may be set smaller than the simulated voxel size without loss of information. In order to produce a peak SNR = 25 in the AF, each simulated data set was normalized to its maximum value, multiplied by 25, and added to an equal-sized 3D complex array of Gaussian noise (mean = 0, standard deviation = 1) before taking its absolute value. The simulated data sometimes were down sampled from $50 \mu\text{m}$ isotropic to a resolution equal to that in corresponding MRI data, using voxel averaging in ImageJ (NIH). Oblique image planes were generated from 3D data sets using the multi-planar reformatting feature of OsiriX (www.osirix-viewer.com).

Predicted inter-lamellar MRI contrast based on AF fiber structure—In general, the absolute difference in MR image intensity (contrast) between two tissues arises primarily due to differences in relaxation rates. For tissues differing only in R_2 , Eq. 1 implies that contrast will vary with T_E , unless signal from one tissue falls below the noise level. For a disc in a fixed orientation relative to the magnetic field B_0 , and at a fixed T_E however, the difference in R_2 between adjacent lamellae and, hence, the contrast, will vary regionally throughout the AF due to the changing orientation of the collagen fibers relative to B_0 . Therefore, inter-lamellar contrast (κ) can be defined as the absolute difference in MRI intensity between adjacent lamellae at a given azimuthal angle ψ , and within an axial cross-section of the disc defined by height z . For example, consider the ellipsoidal shell between the first and second lamellae ($n = 1$), which intersects the (x , y , z)-axes at the points $(\pm(a_0 + \lambda), \pm(b_0 + \lambda), \pm(c_0 + \lambda_z))$. The intersection of this shell with a plane at constant z is an ellipse. For the set of points on this ellipse, the fiber angle α in Eq. 8 can be given either a positive value, corresponding to the outer surface of the first lamella, or its negative value, corresponding to the inner surface of the second lamella. Then, taking the difference of the intensities from Eq. 1, this would permit exploration of disc orientations relative to B_0 , i.e., (ϕ_B, ψ_B) values, that produce the most favorable contrast in terms of both magnitude and regional variation. Thus one can calculate:

$$\kappa_1(\psi, \alpha) = |I_{n=1}(\psi, \alpha) - I_{n=1}(\psi, -\alpha)| \quad (10)$$

to determine the contrast κ_1 as a function of two variables (ψ , α).

Equation 10 was plotted for two values of ϕ_B (5° and 60°), setting $T_E = 20$ ms, $\psi_B = 1^\circ$, and assuming the MRI slice plane is located 1 mm above the disc's central axial plane. Due to the right-left symmetry of the contrast, ψ was varied from 0° to 180° , corresponding to a change in azimuth from anterior to posterior, while $|\alpha|$ was varied from 0° to 90° . Here each $|\alpha|$ was held constant throughout the entire AF. Also note that ψ is a parametric angle of the ellipsoid and hence corresponds to the eccentric anomaly of lamellar ellipses in the MRI slice plane. To define the angular coordinate ψ_{path} of a point on an azimuthal path in the AF, ψ must be transformed according to: $\psi_{\text{path}} = \frac{\pi}{2} - \tan^{-1} \left[(b/a) \tan \left(\frac{\pi}{2} - \psi \right) \right]$. Finally, note that Eq. 10 does not include a noise contribution, but this easily could be added in order to calculate the contrast-to-noise ratio.

Results

MR images of the central axial plane of ovine and human lumbar disc specimens are shown in Fig. 4. By orienting the disc spinal axis approximately orthogonal to the magnetic field B_0 , i.e., $\phi_B \approx 90^\circ$, both inter-lamellar contrast κ and azimuthal intensity variation $I(\psi)$ were generated. The images are displayed in their original (non-rotated) format, because when $\phi_B = 90^\circ$ the azimuthal variation depends on the rotation angle ψ_B of the disc about its spinal axis due to the asymmetry of the AF. This was confirmed in simulations of an axial slice with $\phi_B = 90^\circ$, for which $\psi_B = 1^\circ$, 45° , and 90° produced different $I(\psi)$ (data not shown). This emphasizes the need for an ellipsoidal model rather than a spherical one, since circular lamellae would not produce such an effect.

An example simulated 3D MRI data set with $(\phi_B, \psi_B) = (90^\circ, 90^\circ)$ is shown in Fig. 5 as a volume rendering, generated in OsiriX. Both κ and $I(\psi)$ are evident, with the $I(\psi)$ azimuthal pattern having strong similarity to that seen in the MR images of Fig. 4.

As a means to more closely compare the 3D ellipsoidal model with actual MRI data, in Fig. 6 are shown both MR images and corresponding simulations of a bovine tail disc specimen, oriented at $(\phi_B, \psi_B) = (14^\circ, 45^\circ)$, and a human lumbar disc specimen (L4L5), oriented at $(\phi_B, \psi_B) = (4^\circ, 27^\circ)$. Axial, coronal, and sagittal MR images of each disc were obtained by double-oblique orientations either of the 2D MRI acquisition plane (bovine) or of the reformatted 3D MRI data (human). To more clearly see the lamellae, all MR images and simulated data in Fig. 6 were displayed using a Lanczos 5 sinc interpolation algorithm in OsiriX. To further aid comparison, the MR images in Figs. 6a and g were rotated to a horizontal position without loss of reference, because here $\phi_B < 45^\circ$. The 3D simulated data sets, displayed at cross-sectional planes matching those of the MR images, reveal strong similarities between the MR images and the simulated data, not only in terms of $I(\psi)$ and κ , but also in regards to the apparent thickness of lamellae. For example, $I(\psi)$ in both MRI and simulations appears relatively constant with ψ (Figs. 6a/d and g/j), while κ vanishes at

several locations in the simulations (arrows in Figs. 6d and l) that appear to have correspondences in the MRI data. Furthermore, in the human disc MRI, the coronal image plane selected at an offset location (Fig. 6h) is tangential to AF lamellae and exhibits apparently thicker lamellae than those seen in the central axial view (Fig. 6g). This effect is reproduced in the simulated data in the offset coronal plane (Fig. 6k) compared to the central axial plane (Fig. 6j), thus confirming that it is caused by the 3D curvature of the lamellae. The effect was found to be even greater in the simulated bovine data, since the bovine geometry required increasing the z -axis curvature of the lamellae by decreasing α_0 and α_z (Table 2). However this is not visible in Fig. 6 due to the central location of all three planes.

Computed inter-lamellar contrast $\kappa_1(\psi, \alpha)$ (Eq. 10) is shown in Fig. 7 (top row) on a normalized linear color scale for two orientations of the magnetic field B_0 relative to the disc spinal axis: $(\phi_B, \psi_B) = (5^\circ, 1^\circ)$ and $(60^\circ, 1^\circ)$. Here the magnitude of κ_1 is clearly different for the two orientations, with maximum values of 0.58 and 1.0 for $\phi_B = 5^\circ$ and 60° , respectively. Given that AF fibers are typically found with $\alpha \sim 60^\circ$, maximum values along a horizontal line at $\alpha = 60^\circ$ are 0.35 and 0.88, respectively. This shows that κ_1 can be 2.5 times greater for $\phi_B = 60^\circ$, though it is less uniform within the AF. Note for $\phi_B = 5^\circ$ a horizontal null line occurs at $\alpha \sim 54.7^\circ$, i.e., the magic angle where the dipolar effect disappears. This can be seen from Eqs. 2, 7, and 8, where θ_{CB} is approximately equal to α under the conditions of the simulation. The null line becomes warped as ϕ_B increases. In Fig. 7 (bottom row) are shown single axial slices from the respective simulated data sets for $\alpha = 60^\circ$. No noise was added to these simulated data, and they were not down sampled. It can be seen that for $(\phi_B, \psi_B) = (60^\circ, 1^\circ)$ lamellae appear to start and terminate at certain positions in the AF, yet this is actually caused by the intensity of a lamella inverting. Thus what appear as discontinuities and lamellar terminations at azimuthal angles approximately $45^\circ, 135^\circ, 225^\circ$, and 315° are continuous lamellae that reverse intensity at these positions. This effect could give rise to similar features in MR images of the AF that might be mistaken for actual lamellar terminations.

Discussion

Summary of results

The theoretical model presented here is based on the dependence of the MRI signal on collagen fiber orientation and elucidates the origin of MR image contrast in the disc annulus. Inter-lamellar contrast and azimuthal intensity variation in the annulus were simulated using the 3D geometric model, demonstrating a qualitative similarity to MRI data from several discs. The simulation results of Figs. 5, 6, and 7 are validations of the model, in that they offer compelling evidence in support of the model's ability to account for specific contrast features in the MRI data of Figs. 4 and 6. The 3D nature of the simulation results is clearly seen in Fig. 6, particularly in Fig. 6k (the coronal plane) where the banding pattern of the lamellae is evident. This banding pattern is quite similar to that visible in the MR image of Fig. 6h, which has sufficient inter-lamellar contrast for comparison.

An important distinction should be made to avoid an over expectation of the model: the model is not intended to be used as a method to estimate the lamellar structure in the annulus of a real disc, rather the model approximates it by an analytically defined geometry, and in

so doing can account for specific contrast features seen in MR images of the annulus. This is consistent with the concept of a model, and distinguishes the model from an MR image, which does capture the true geometry of a real disc. By approximating the annular geometry using ellipsoids, the model demonstrates that MRI contrast features (inter-lamellar contrast and azimuthal intensity variation in the annulus) can be accounted for by such a simplified geometry. This is a very important result that is not obvious and illuminates the underlying mechanism of the image contrast.

Limitations of the model

An important limitation of the model is that the anatomy of AF lamellae often deviates from the geometry of an ideal ellipsoid, as in the well-known “bean” shape of human discs (although the cross-sectional annular geometry in some discs is very close to an ellipse, as seen for example in the bovine tail disc of Fig. 6a and in the human lumbar disc of Fig. 6g). In essence, the effect of a non-elliptical (bean shaped) cross-section of the annulus is to warp the azimuthal intensity pattern accordingly. This effect can be seen clearly in the MR image of the ovine disc in Fig. 4, where the disc’s shape can be thought of as arising from bending an ellipse around a pole located at point P . The ovine disc azimuthal intensity pattern is similar to that seen in the simulation of Fig. 5, although it has an asymmetry in the AP direction not matched by the simulation. The inability to account for this asymmetry, therefore, is a limitation of the model. Nevertheless, the same underlying mechanism is responsible for the warped asymmetric pattern as for the symmetric pattern, under the assumption of uniform lamellar structure and composition. While this assumption appears valid for the ovine disc in Fig. 4, in general the lamellar structure or composition in the posterior annulus often deviates from that found in the rest of the annulus.

There are also known variations of lamellar thickness in a real disc annulus that may affect its biomechanical behavior, and that are not implemented in the current model. A generalized model might be constructed by assigning a unique lamellar thickness to each (x, y, z) position within the annulus. However, this would be done at the expense of simplicity and with the loss of analytically defined ellipsoidal shells. A less extreme generalization might be made in a straightforward way by introducing the parameters (λ_x, λ_x) and (λ_y, λ_y) , similar to (λ_z, λ_z) already used in the model. This would allow for continuously varying lamellar thickness from anterior to lateral to posterior regions. Nevertheless, even using lamellae of constant thickness, the presented model can simulate the dominant features seen in MR images, namely the inter-lamellar contrast and azimuthal intensity variation in the annulus.

Potential applications

The primary application intended for the model is in optimizing MR image contrast, especially when imaging disc specimens for the benefit of image-informed biomechanical modeling of the disc. Integrity of the collagen fiber microstructure of the AF is important for disc health, and loss of this integrity is associated with a cascade of disc degeneration, symptoms of pain, and reduced spinal mobility [1]. Biomechanical models of the disc, currently being developed to better understand this process, can be improved by studying the AF microstructure using a non-perturbing method such as MRI [2], given sufficient SNR,

resolution, and contrast. Direct MR imaging of collagen fibers in the AF is difficult to achieve, and diffusion tensor MR imaging of fiber angles is severely SNR-limited, meaning only small samples or sections of the AF can be scanned [20] and thereby precluding biomechanical studies of the entire disc [35], or the evaluation of clinical procedures such as nucleus decompression [36]. The model presented here, however, could be used to interpret intensity patterns in the AF even for relatively low resolution images, and to predict experimental conditions for which $I(\psi)$ and $\kappa(\psi, \alpha)$ are most favorable. For example, one could minimize induced azimuthal variation in the AF by orienting the spinal axis parallel to B_0 ($\phi_B \sim 0^\circ$), as seen in Figs. 6j and 7(bottom left). Furthermore, this model also may provide insight into how the contrast varies with MRI-specific and tissue-specific parameters. In the most general case, the tissue-specific parameters I_0 , K , R_2^0 , λ , and $|\alpha|$ could be made to vary with position (x, y, z) within the AF, rather than fixed as global constants. Physical conditions under which these tissue-specific parameters could change include compression and/or degeneration of the disc. Thus, this 3D geometric model incorporating dipolar relaxation may prove useful for predicting MRI intensity changes in the AF induced by disc compression, bending, or torsion. This would have implications for tracking disc deformations under load and for computation of 3D strain maps [35]. Another opportunity exists in that by acquiring MRI data sets from a large number of human lumbar disc samples at different disc levels one could possibly explore human anatomical variability. For example, the model could be used to generate simulations corresponding to each MRI data set, or corresponding to the average disc geometry for each disc level.

There is also a potential for in vivo clinical applications, specifically the identification of abnormal azimuthal intensity variations in the annulus. The model may be useful for detecting disruptions in lamellar structure associated with tears and degeneration, which would be clinically relevant as a potential early biomarker of disc degeneration. Using a clinical spine RF coil, SNR is known to fall off sharply from the skin surface of the patient's back toward the interior of the body, thus limiting both image resolution and contrast. Nevertheless, with appropriate pulse sequence parameters, it is possible to visualize azimuthal intensity variation in the annulus. However the azimuthal variation will be more pronounced when the magnetic field of the scanner is approximately orthogonal to the spine, as is in so-called "open" MRI scanners. For such in vivo studies, a rapid MRI technique would be needed. However, high resolution MRI of the AF often is not feasible during a clinical exam because the scan time, being proportional to $1/(\text{voxel volume})^2$, would be too long. This suggests a potential role for "indirect" MRI methods that can characterize AF microstructure even in images with larger voxels in which lamellae are not directly resolved. As results presented in Figs. 4, 5, 6 and 7 demonstrate, spatial variation of $I(\psi)$ can be on the order of centimeters, much larger than typical in vivo voxel sizes. Thus disruptions of the AF fiber structure may be identifiable by deviations from the calculated MRI intensity pattern. In addition, the model may provide insight for the interpretation of so-called high intensity zones (HIZ) seen in the posterior AF of lumbar discs on MRI [37]. Future studies are envisioned that will investigate the model's usefulness for detecting these and other disc changes due to age, injury, disease, and therapeutic interventions.

Conclusion

The AF model developed here for azimuthal variations in intensity $I(\psi)$ and inter-lamellar contrast $\kappa(\psi, \alpha)$ may be useful for interpreting MR images of the disc, and has potential for predicting experimental conditions for acquiring MR images of the disc that are optimal for a particular study. The model provides insight into the origins of inter-lamellar MRI contrast by employing a simple analytic form of concentric ellipsoids, and can reproduce many contrast features observed in the disc due to changes of the lamellar fiber angle α relative to the magnetic field of the MRI scanner. Within the geometric limitations of the model, the convenience of an analytic form for predicting the magnitude and spatial pattern of inter-lamellar MRI contrast potentially could benefit both high-resolution mechanical modeling of the disc as well as the clinical diagnosis and management of disc-related pathology.

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Fig. 1.

Diagram of the vertebrae of the human lumbar spine and an intervertebral disc (L2/L3). The local spinal axis is $\vec{S}$. The disc consists of nucleus pulposus (NP), annulus fibrosus (AF), and cartilaginous endplates (CEP). Collagen fibers in adjacent lamellae of the AF point in direction $\hat{C}$ at angles $\pm\alpha$ relative to $\vec{S}$

Fig. 2.

Tri-axial ellipsoidal coordinate system used to define the disc's anatomical dimensions (*left*), and the orientation of its collagen fibers $\hat{C}$ relative to the B_0 magnetic field of the MRI scanner (*right*). In the central xy -plane, the thickness of lamellae and the width of the AF are defined by λ and Δ , respectively. R right, A anterior, and $\vec{S}$ points in the superior direction

Fig. 3. Illustration of lamellar shell index n and fiber angle α sign alternation in the AF. Lamellar shells intersect the x -axis in the central xy -plane at the x values indicated

Fig. 4.

MRI of lumbar disc specimens: (*left*) ovine, (*right*) human L2L3. Discs were oriented with spinal axes $\sim 90^\circ$ to the magnetic field (B_0 is horizontal in the images). L/R/A/P = left/right/anterior/posterior. *Scale bars* 1 cm

Fig. 5.
A 3D MRI simulation of a disc oriented at $(\phi_B, \psi_B) = (90^\circ, 90^\circ)$, reproducing the alternating intensity pattern of adjacent lamellae in the AF

Fig. 6.

Direct comparison between the simulations and the MRI data: **a–c** MRI of a bovine tail disc specimen, oriented at $(\phi_B, \psi_B) = (14^\circ, 45^\circ)$, showing axial, coronal, and sagittal planes of the disc as indicated by reference lines (online version in color), and **d–f** the corresponding simulated 3D data. **g–i** MRI of a human lumbar disc specimen (L4L5), oriented at $(\phi_B, \psi_B) = (4^\circ, 27^\circ)$, and **j–l** the simulated 3D data. *Arrows* indicate regions of reduced inter-lamellar contrast in the simulations that appear to match the MRI data. Disc dimensions are given in Table 2

Fig. 7.

(*Top row*) Computed inter-lamellar contrast as a function of azimuthal angle ψ and collagen fiber angle α (Eq. 10), at two orientations of the disc in the magnetic field: (*left*) $(\phi_B, \psi_B) = (5^\circ, 1^\circ)$; (*right*) $(\phi_B, \psi_B) = (60^\circ, 1^\circ)$. *Side bar* indicates the normalized linear scale (online version in color). (*Bottom row*) Single axial slices from simulated 3D MRI data sets of discs oriented in the magnetic field as in the *top row*, and for $\alpha = 60^\circ$

Table 1

MRI parameters for images and simulations shown in Figs. 4, 5, 6 and 7

Figs.	Type	B_0 (T)	Sequence	T_R/T_E (ms)	N_E	SA	Scan time (h:min:s)	Resolution (μm)
4	Ovine lumbar	1.5	2D SE	3000/13	1	1	0:13:24	$313 \times 313 \times 3000$
4	Human L2L3	1.5	2D FSE	1000/17	4	4	0:04:18	$313 \times 313 \times 3000$
5	Simulation	-	-	-/20	-	-	-	$50 \times 50 \times 50$
6a-c	Bovine tail	7	2D TSE	3000/14	7	1	0:02:00	$234 \times 234 \times 2000$
6d-f	Simulation	-	-	-/14	-	-	-	$234 \times 234 \times 2000$
6g-i	Human L4L5	7	3D TSE	3000/34	7	1	2:58:15	$297 \times 297 \times 300$
6j-l	Simulation	-	-	-/34	-	-	-	$300 \times 300 \times 300$
7	Simulations	-	-	-/20	-	-	-	$50 \times 50 \times 50$

Table 2

Disc dimensions and orientations for simulations shown in Figs. 5, 6 and 7

Figs.	Type	LR, AP, SI (mm)	a_0, b_0, c_0 (mm)	N_λ	λ (mm)	λ_z (μ m)	(mm)	z (mm)	α ($^\circ$)	K (ms $^{-1}$)	R_2^0 (ms $^{-1}$)	ϕ_B ($^\circ$)	ψ_B ($^\circ$)
5	Human	50, 34, 10	17, 9, 16	20	0.4	50	8	1	60	0.025	0	90	90
6	Bovine	24, 22, 10	7.2, 6.2, 10.4	16	0.3	37.5	4.8	0.6	60	0.025	0	14	45
6	Human	54, 34, 10	19, 9, 16	20	0.4	50	8	1	60	0.025	0	4	27
7	Human	50, 34, 10	17, 9, 16	20	0.4	50	8	1	0-90	0.025	0	5, 60	1