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Reversed Laminar Appearance of Articular Cartilage by T1-Weighting in 3D Fat-Suppressed Spoiled Gradient Recalled Echo (SPGR) Imaging

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Abstract

Purpose—To investigate the reversed intensity pattern in the laminar appearance of articular cartilage by 3D Fat-Suppressed Spoiled Gradient Recalled Echo (FS-SPGR) imaging in MRI.

Materials and Methods—The 3D SPGR experiments were carried out on canine articular cartilage with an echo time (TE) of 2.12 ms, a repetition time (TR) of 60ms, and various flip-angles (5°–80°). In addition, T1, T2 and T2* in cartilage were imaged and used to explain the laminar appearance in SPGR imaging.

Results—The profiles of T2 and T2* in cartilage were similar in shape. However, the T2 values from the multi-gradient-echo imaging sequence were about 1/3 of those from single spin-echo sequences at a pixel resolution of 26 μ m. While the laminar appearance of cartilage in spin-echo imaging is caused mostly by T2-weighting, the laminar appearance of cartilage in fast imaging (i.e., short TR) at the magic angle can have a reversed intensity pattern, which is caused mostly by T1-weighting.

Conclusion—Laminar appearance of articular cartilage can have the opposite intensity patterns in the deep part of the tissue, depending upon whether the image is T1-weighted or T2-weighted. The underlying molecular structure and experimental protocols should both be considered when one examines cartilage images in MRI.

Keywords

MRI; articular cartilage; laminar appearance; magic angle effect; FLASH/SPGR; T1 and T2 relaxation

INTRODUCTION

Degenerative joint diseases such as osteoarthritis currently affect a large proportion of the senior population, and have elicited extensive investigation through non-destructive imaging techniques such as magnetic resonance imaging (MRI). Current MRI procedures, however, cannot satisfactorily detect the subtle changes in the early stages of the tissue's degradation^{1,2}. One major factor preventing the successful development of early detection procedure in MRI is the complex structure of the tissue. In particular, the collagen fibril changes its spatial orientation significantly across the tissue thickness: parallel to the surface in the superficial zone, mostly random in the transitional zone, and perpendicular to the surface in

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the radial (deep) zone³. This depth-dependent organization of the collagen matrix in cartilage is the origin of tissue's anisotropic appearance as viewed by many imaging tools, such as magic angle effect in MRI, birefringence in polarized light microscopy, amide anisotropy in Fourier-transform infrared imaging, diffusion tensor imaging in MRI and anisotropic refraction angle in diffraction enhanced X-ray imaging.

The magic angle effect of articular cartilage in MRI^{4,5} refers to the disappearing of a laminar appearance of cartilage when the normal axis of the tissue surface is oriented at approximately 55° with respect to the static magnetic field B_0 . It has been well agreed that the laminar appearance of cartilage in spin echo MR images is caused by the T2 anisotropy in articular cartilage⁵, which is closely linked to the collagen matrix - the only known rigid and well-oriented network in the tissue. T2 anisotropy alone, however, cannot explain a slightly elevated signal lamina in the *deep* part of cartilage in images acquired by fast imaging sequences such as FLASH (Fast-Low-Angle-SHOT) or SPGR (SPoiled-Gradient-Recalled-echo)⁶⁻⁸. This phenomenon was commented by McCauley and Disler⁹ in a review article 10 years ago as, "a thin band of intermediate signal intensity is sometimes seen in the deep radial zone; the etiology of this band is uncertain." Since 3D FS-FLASH/SPGR sequences are efficient MRI protocols in clinical visualization of human cartilage, the objective of this project was to investigate the origin of this particular laminar phenomenon of articular cartilage by 3D FS-FLASH/SPGR sequences and compare them to the spin-echo images.

MATERIALS AND METHODS

Cartilage Preparation

Canine humeral heads were harvested shortly after the sacrifice of several mature (1–2 year old) and musculoskeletally healthy dogs that were used for unrelated biomedical research. The Institutional Review Boards have approved the protocols handling the animal subjects. Tissue slices 1.75 mm thick were cut from the (relatively flat) loading part of the humeral head using a table diamond saw. Three or four cartilage-bone blocks (about $1.75 \times 2 \times 6$ mm) were cut from each slice. The specimens were frozen in saline at -20°C until imaging. Before MRI experiments, the specimen was thawed at room temperature, and sealed in a precision NMR tube that was filled with physiological saline with 1 % protease inhibitor (Sigma, Missouri). Three specimens from three animals were used in this investigation.

MRI Methods

MRI experiments were conducted at room temperature on a Bruker AVANCE II 300 NMR spectrometer equipped with a 7-Tesla/89-mm vertical-bore superconducting magnet and micro-imaging accessory (Bruker Instrument, Billerica, MA). A homemade 3mm solenoid coil was used for imaging, where the orientation of the cartilage block with respect to B_0 can be adjusted. The general parameters in imaging were kept constant for comparison in this report (unless noted individually): the field of view was $0.32\text{ cm} \times 0.32\text{ cm}$; the matrix size was 128×128 , corresponding to the in-plane pixel size of $26\text{ }\mu\text{m}$; the slice thickness was 1 mm; the repetition time (TR) of the spin echo imaging experiment was 2 seconds; the number of accumulation was 16; and the spectral bandwidth was 50 kHz.

T1 and T2 relaxations in cartilage were imaged quantitatively by the magnetization-prepared imaging sequences¹⁰, where all timings during the spatial mapping were kept constant regardless of the amount of relaxation weighting by an inversion-recovery and a CPMG sequence¹⁰⁻¹². Five T2-weighted images, corresponding to five echo-delays (at 0° : 2, 4, 10, 30, 60 ms; at 55° : 2, 14, 36, 60, 120 ms), were acquired for the calculation of an intrinsic T2 map. Similarly, five T1-weighted images were acquired for the construction of intrinsic T1

map, with five recovery times of 0, 0.4, 1.1, 2.2, 4 second respectively. In addition, the T2* imaging experiments of the same specimens were performed using a multiple gradient echo (MGE) sequence from Bruker, where twenty images, each from a different echo, were constructed (the echo spacing was 2.3 ms for MGE). Since the magnetization-prepared sequences acquire only one image at a particular T1 or T2 weighting, the use of multi-echoes enables significant reduction of the experimental time (80% in our experiments). All relaxation times were calculated by fitting of the magnitude images mono-exponentially on a pixel-by-pixel basis.

The intensity images of the cartilage specimens were acquired with multiple pulse sequences. In addition to the standard spin-echo images by the MSME sequence (only one slice and one echo were used), the same specimens were imaged with the 3D FS-FLASH sequence from Bruker, with a TR of 60 ms, a TE of 2.12 ms, and various flip angles (5° – 80°).

RESULTS

Fig 1 shows the representative intensity images and profiles of articular cartilage when the normal direction of its articular surface was at 0° and 55° (the magic angle) with respect to B_0 . The spin echo images were acquired using the 2D MSME sequence from Bruker (only one slice and one echo were used); the FLASH/SPGR images were the middle slices of the eight slices acquired using the 3D fat-suppressed FLASH sequence from Bruker. At the 0° specimen orientation, the spin-echo image of cartilage shows a strong trilaminar appearance (low-high-low, from the surface to the bone). The FLASH/SPGR mages of cartilage also showed a similar but weaker trilaminar appearance at 0° (cf. the profile in Fig 1a). If one excludes the first one or two data points around the 0 μ m depth of cartilage due to a number of experimental uncertainties (e.g., partial volume effect, surface roughness, slice tilting), the FLASH/SPGR images of cartilage at 0° could also be considered bilaminar (high-low). At 55° , the laminar appearance of the spin-echo images of cartilage nearly disappeared, which was consistent with previous observations and had been attributed to the minimization of the depth-dependent T2 anisotropy⁵. Interestingly, the intensity in the deep portion of cartilage by FLASH/SPGR at the magic angle was actually slightly higher than that in the other part of the tissue, resulting in a weak trilaminar appearance but in the reversed intensity pattern (high-low-high), which could not be explained by the influence of the T2 anisotropy alone.

The relaxation profiles of T1 and T2 in cartilage were shown in Fig 2, which were measured by the magnetization-prepared T1 and T2 imaging sequences respectively. These quantitative profiles agree well with previous quantitative measurements reported in the literature^{10,12–14}. Since the T1 profile is independent of the orientation of tissue in the magnet¹⁰, the measurement of T1 can be carried out at any orientation. The profiles of T2* relaxation in cartilage (Fig 2c) were acquired by a standard multi-echo sequences (2D MGE sequence), which had the same shape as in Fig 2b. However, the T2* values by the gradient echo sequence at the same pixel size were only about 1/3 of the T2 by the magnetization-prepared sequence¹⁰.

The intensity patterns of the laminar appearances of cartilage by 3D FS-FLASH/SPGR imaging were examined in detail at various flip-angles (5° – 80°) and the fixed TR/TE (60 ms/2.12 ms). When the flip angle was larger than 20° , the tissue had a weak but clear reversed intensity pattern in its trilaminar (high-low-high) appearance. The experimental profiles of the image intensity at 5° and 40° were shown Fig 3a.

The effects of T1 and T2* relaxation on the depth-dependent signal intensity in cartilage were calculated using the following equation¹⁵

$$\widehat{\rho}(\theta, TE) = \rho_0 \sin\theta \frac{(1 - E_1)}{(1 - E_1 \cos\theta)} e^{-TE/T_2^*} \quad (1)$$

where $E_1 = \exp(-TR/T_1)$. The measured profiles of T1 and T2* cartilage at 55° (Fig 2a and 2c) and the imaging parameters (TR = 60ms, TE = 2.12ms) were used in the calculation of the MRI intensity of cartilage as a function of the flip angles. Two calculated profiles are shown in Fig 3b. Also shown in Fig 3b is the signal intensity profiles by a constant T2* of 20 ms. Two features should be noted. First, under these experimental conditions, the cartilage intensity profile by a constant T2* (the heavy lines) is nearly identical to that created by the actual T2* values (the symbols). Second, these calculated cartilage profiles were remarkably similar to the actual experimental profiles of cartilage as shown in Fig 3a at 55°, not only in its relationship to the flip angles but also the slight increase in intensity in the deep tissue, which was caused directly by the small decrease of T1 in the deep tissue (e.g., from 400μm to 600μm tissue depth in Fig 2a) at short TR (60ms).

DISCUSSION

To better diagnose the subtle changes in cartilage degradation, it is important to understand the complex appearances of articular cartilage in MR images. While it is true that “the direct cause of the laminar appearance of articular cartilage is the T2 relaxation anisotropy in the tissue, which is closely linked to the structure of the collagen fibers, their orientation in the magnetic field, and the water-proteoglycan interaction that amplifies the prevailing orientation of the collagen fiber network”⁵, this statement is applicable only to the situations where the tissue is strongly T2-weighted (e.g., in spin-echo experiments). The T2-weighting alone cannot explain the **higher** intensity in the **deeper** part of the tissue, as seen in the images by FLASH/SPGR sequences in this project (e.g., Fig 1b and Fig 3a) as well as in previous studies^{6–8}.

Although the T1 profile in articular cartilage was considered to be isotropic and relatively uniform^{10,16}, the T1 value in cartilage does decrease modestly towards the deeper tissue (Fig 2a), from about 1.2 s in most of the upper tissue to about 0.8 s in the very deep tissue. When the imaging experiments are strongly T2-weighted at long repetition times (e.g., ~2000 ms), this modest variation of T1 has little effect on the laminar appearance of cartilage in MRI. When the imaging experiments are strongly T1-weighted as in FLASH/SPGR, however, this same variation of T1 value can cause notable intensity variation in cartilage MRI, resulting in a **higher** signal intensity in the deep part of the tissue just above the cartilage-bone interface, and consequently the reversal of the laminar pattern in articular cartilage from a low intensity to a high intensity above the interface. This conclusion is confirmed by the simulation result in Fig 3b.

Note that there could be other sources for some complex patterns of laminar appearances in MRI of articular cartilage. For examples, a cartilage tissue with a uniform intensity **can become** reversely laminated when the tissue is imaged under static loading^{17,18}, which signals the load-induced structural adaptation of the collagen matrix in cartilage. Articular cartilage can also have a ‘natural appearance’ of multiple layers in spin-echo imaging, depending upon the age and source of the cartilage tissue⁵. The aim of this project was to investigate under what experimental conditions, the same articular cartilage could change

from a ‘conversional’ laminar appearance (i.e., the deep tissue was the darkest) to a reversed laminar appearance (i.e., the deep tissue became brighter).

In conclusion, this study demonstrated that (1) the values of T2 from multi-gradient-echo imaging sequence could be about 1/3 of those from single spin-echo sequences at high pixel resolution – due to the adverse effect of imaging gradients^{19,20}, and (2) the laminar appearance of articular cartilage can have the opposite intensity patterns in the deep part of the tissue, depending upon whether the image is T1-weighted or T2-weighted. If the tissue is imaged by a standard spin-echo sequence, the cartilage image is essentially T2-weighted because of relatively long TE and long TR in the experiment. A strong low-high-low trilaminar appearance should be found at the 0° orientation. This trilaminar appearance would largely disappear at the magic angle because the minimization of the dipolar interaction restores the T₂ relaxation to be approximately isotropic. (Another possible appearance of cartilage at 0° is bilaminar (high-low) if one excludes the first one or two pixel(s) at the tissue surface *or* if the resolution is limited.) In contrast, if the tissue is imaged by fast sequences such as FLASH/SPGR with very short TR, the image is essentially T1-weighted. While the same laminar pattern could be seen in cartilage at 0°, articular cartilage *at the magic angle* could have a reversed intensity pattern, i.e., the tissue having a higher intensity just above the tissue/bone interface. This reversed intensity pattern should be equally observable at high field (e.g., 7T in this report) as well as at common clinical fields (as commented by McCauley and Disler⁹ 10 years ago). In any case, the underlying molecular structure in cartilage and the imaging methodology should both be considered when one examines the appearance of cartilage in MRI.

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Fig 1.

The intensity images and profiles of a cartilage-bone specimen by the spin-echo (SE) and FLASH (SPGR) sequences when the normal axis of the tissue surface was 0° and 55° from the direction of B_0 (vertically upwards). The thickness of the cartilage tissue was about $600\ \mu\text{m}$. The saline and saline/tissue interface from -100 to $0\ \mu\text{m}$ were also shown in the profiles.

Fig 2.

(a) The T1 profiles of cartilage by the T1-weighted magnetization-prepared imaging sequence. (b) The T2 profiles of cartilage by the T2-weighted magnetization-prepared imaging sequence. (c) The T2* profiles of cartilage by the MGE imaging sequence. The pixel size and slice thickness were the same for all experiments.

Fig 3.

(a) The experimental intensity profiles of cartilage by a 3D FS-FLASH/SPGR imaging sequence, acquired at the fixed TR/TE (60ms/2.12 ms) and the flip angles of 5° and 40° . (b) The calculated intensity profiles of cartilage based on the measured T1 and T2* in Fig 2 (the symbols) and on a constant T2* of 20ms (heavy lines).