Feasibility of delayed anionic gadolinium enhancement in the intervertebral disc as a quantitative measurement of disc degeneration

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Intervertebral disc degeneration is often cited as a cause for lower back pain, a disabling condition which afflicts the majority of the population at some point in their lifetime. Currently, MRI is most effective at imaging disc degeneration in its later stages, when changes in T2 signal intensity are seen and disc bulging and cracking are evident[1]. While detection of early disc degeneration would be very useful clinically, it is currently difficult to diagnose degeneration before these signs are present. Using contrast agent and T1 weighted MRI, early degeneration of articular cartilage in the hip and knee has been quantitatively assessed with a technique known as dGEMRIC[2-] (delayed gadolinium enhancement of MRI in cartilage). The technique relies on the fact that degenerated cartilage is characterized by the degradation of negatively charged glycosaminoglycan (GAG) molecules. This consequently reduces the repulsive negative electrostatic force that usually prevents penetration of anionic contrast agent into healthy cartilage. Because the contrast agent lowers T1 of the tissue it accumulates in, regions of low T1 indicate regions of lower GAG concentration, and therefore cartilage degeneration. Because early disc degeneration, like early cartilage degeneration, involves loss of glycosaminoglycans, mapping T1 in discs after administration of negatively charged contrast agent may detect early degeneration. The objective of this study is to determine the feasibility of using this approach to map intervertebral disc degeneration.

Material and methods

We compared T1 maps of healthy and degenerated porcine discs, before and after contrast agent uptake.

Imaging: Discs were imaged using a 3D IR-TFE sequence on a 3.0T Phillips Intera MRI with a two element surface loop coil (Flex-S). Twenty axial slices were obtained per disc with a 0.5mm isotropic resolution, 200x200 acquisition matrix, TR/TE of 17/8.3 ms, FOV of 100x100 mm, and inversion times of 85, 150, 300, 500, 750, 1500 and 2500 ms.

Disc extraction: Intervertebral discs from 6-8 month old pigs were separated from each vertebra as close to the endplate as possible. In order to help contrast agent diffusion into the discs, the superior annulus was exposed using a diamond bit burring tool. Discs were immediately frozen after the extraction process.

Healthy discs: Three intervertebral discs were used as healthy specimens. After thawing the discs overnight, they were imaged to obtain pre-contrast T1 maps. Discs were then placed in a 0.2M solution of the contrast agent Gd-DTPA^{2-} (Magnevist; Berlex Laboratories, Wayne, NJ) and phosphate buffered saline (PBS). The discs soaked in the contrast agent for 8 hours which was determined, with prior dynamic testing, to be the necessary time to allow diffusion to equilibrium of the contrast into the disc.

Degenerated discs: Three discs were degenerated under controlled conditions by injecting 2.5 unit/μL Chondroitinase-ABC (ChABC) and 0.01M phosphate buffered saline solution into the nucleus pulposus and then soaking the discs in a PBS bath for 8 hours[3]. They were then imaged both before and after soaking in a contrast agent bath for 8 hrs as described for the healthy discs, above.

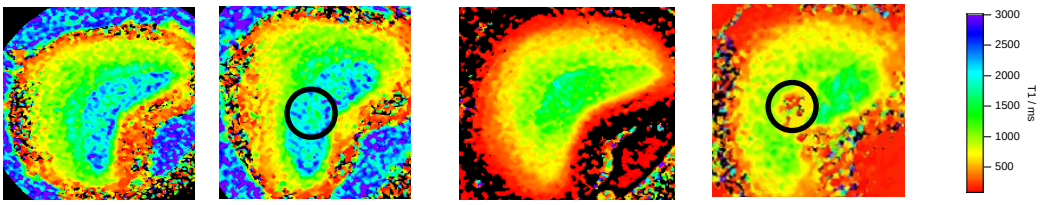
Image Analysis: T1 was calculated for each pixel to create T1 maps using Igor Pro Software (Wavemetrics, OR, USA). Mean T1 values were extracted from the central nucleus pulposus (CNP) and the anterior annulus fibrosus (AA), which were manually defined on T1 weighted images of the disc. The change in T1 times (ΔT1) between pre- and post contrast agent specimens was compared for healthy and degenerated discs, as were the actual T1 times.

Results

Soaking in Gd-DTPA^{2-} changed the mean T1 times in both the central nucleus pulposus and the anterior annulus fibrosus of healthy and degenerated intervertebral discs. Our measurements show that the change in T1 caused by soaking in Gd-DTPA^{2-} was higher in the degenerated discs (Table 1, Figure 1). Discs soaked in Gd-DTPA^{2-} show a clear decrease of T1 in the region where the degenerating chemical was injected (Figure 1), with degeneration reducing mean T1 by 700 (±170) ms in the CNP and 310 (±121) ms in the AA.

	Healthy disc average ΔT1 pre to post Gd-DTPA^{2-}	Deg. disc average ΔT1 pre to post Gd-DTPA^{2-}
CNP	634 (±60) ms	1001 (±95) ms
AA	114(±95) ms	295(±86) ms

Table 1: Changes in T1 times [mean (standard deviation)] between pre- and post Gd-DTPA^{2-} images. All values indicate a drop in T1 between from pre to post contrast images.



Healthy-no contrast *Degenerated-no contrast* *Healthy+ Gd-DTPA^{2-}* *Degenerated+ Gd-DTPA^{2-}*

Figure 1: T1 maps for one slice through healthy and degenerated discs without contrast agent (left) and after soaking in + Gd-DTPA^{2-} . The circled region in the degenerated disc is an area of large T1 difference between discs with and without + Gd-DTPA^{2-} .

Discussion

The results show that T1 mapping after administration of + Gd-DTPA^{2-} is sensitive to disc degeneration. It is not surprising to see lower T1 in the region where ChABC was injected because this chemical degrades GAGs, which reduces the regional negative charge density in the disc. This allows a higher accumulation of the negatively charged Gd-DTPA^{2-} contrast agent in these regions, and therefore a lower T1. GAG distribution is not uniform throughout the healthy disc which is why substantial differences in T1 exist in different regions of the healthy disc. Correlation of the T1 maps with histology is required to validate this method and is currently underway. *In vivo* application of this method to identify disc degeneration relies on complete diffusion of the contrast agent into the disc in a relatively short time, and although studies have shown in-vivo diffusion of contrast agent occurs[4], further studies will have to take place to assess the uptake of Gd-DTPA^{2-} *in vivo*.

References: 1. Thompson et al, Spine,1990; 2. Bashir et al, Magn Reson Med,1999; 3. Yerramalli et al, Biomechan Model Mechanobiol, 2007; 4. Ninnimäki et al, J Magn Reson Imaging, 2006.