Population Average T2 MRI Maps Reveal Quantitative Regional Transformations in the Degenerating Rabbit Intervertebral Disc that Vary by Lumbar Level

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Introduction

Lumbar intervertebral disc degeneration has been implicated as a cause of low back pain as the natural, age-related degenerative process is closely related to deficiencies in disc function[1,2]. Magnetic resonance imaging (MRI) allows for the quantitative, non-invasive assessment of the disc and might be used to identify pathological changes associated with back pain. Clinical assessment of disc abnormalities is typically conducted through visual inspection of MR images or by qualitative evaluations on an integer scale, such as the Pfirrmann grading framework[3]. While these scoring systems provide some level of discrimination between degenerative states, they do not provide quantitative information on the MR signal or positional information regarding the location of compositional changes. Rigorous spatial quantification of T2 MR images may allow for improved discrimination between age-based sub-populations or degenerate sub-populations (populations with early versus advanced degeneration) by identifying changes in disc shape, structure and regional composition. The objective of this study was to spatially map changes in T2 relaxation time as a result of puncture-initiated degeneration in the rabbit lumbar spine. Rabbits were imaged before and after puncture to generate population average T2 maps of the healthy and post-injury state.

Methods

Surgical Procedure: New Zealand White rabbits (n = 20, age = 3mos.) underwent a procedure in which four lumbar discs (L3/L4 to L6/L7) were injured by needle puncture to induce degeneration[4,5]. Using a retroperitoneal approach, an 18G needle was inserted through the lateral AF to a depth of 5 mm. Rabbits were returned to normal cage activity after surgery.

MRI Acquisition In vivo: T2 mapping was performed on each rabbit pre-injury and 4 weeks post-injury with a 3.0 T MRI spectrometer (Figure 1a). Coronal T2 maps were generated with the following parameters: three 2mm-thick slices, 17 Echoes, TE/TR = 7.55ms/2000ms, FOV = 16.5x16.5cm^2, matrix = 384x384, 2 averages.

Population Average T2 Maps: Discs were manually segmented from coronal slices and mapped to a grid normalized to disc dimensions (Figure 1b). *Population Average T2 Maps* were developed by averaging the T2 values of discs from the Week 0 or Week 4 groups at each grid point. *T2 Difference Maps* were constructed by subtracting T2 values of individual or population average post-injury T2 maps from the pre-injury population average T2 map at each grid point.

NP Auto-Segmentation: An automatic procedure was developed to enable non-biased segmentation of the nucleus pulposus (NP) (Figure 1c). The area surrounding the NP was first manually segmented and then T2 values at each point were fit to a bimodal, bivariate Gaussian distribution function, given the natural bimodal distribution the T2 signal in the NP. NP boundaries were demarcated where 50% of the max NP T2 signal had dissipated, defined by the means/standard deviations of the Gaussian function. After segmentation, disc, NP and annulus fibrosus (AF) geometry were measured.

Results

Population average T2 maps showed quantitative differences in T2 values across healthy discs and revealed specific transformations following injury (Figure 2a–b). Before injury, T2 relaxation time was lowest in the AF and increased gradually towards the NP. The pre-injury map identified that the intranuclear cleft (bilateral T2 peaks at the center of the NP) is a consistent anatomical feature preserved across all discs. At Week 4, NP T2 values decreased and the T2 difference map showed that this reduction occurred at the periphery of the NP. The T2 relaxation time decreased in the NP but not in the AF. Between Weeks 0 and 4, the mean T2 decreased in the NP and the whole disc, while there was no change in the AF.

Needle injury also resulted in changes in disc shape (Figure 2c–e). Whole disc area remained

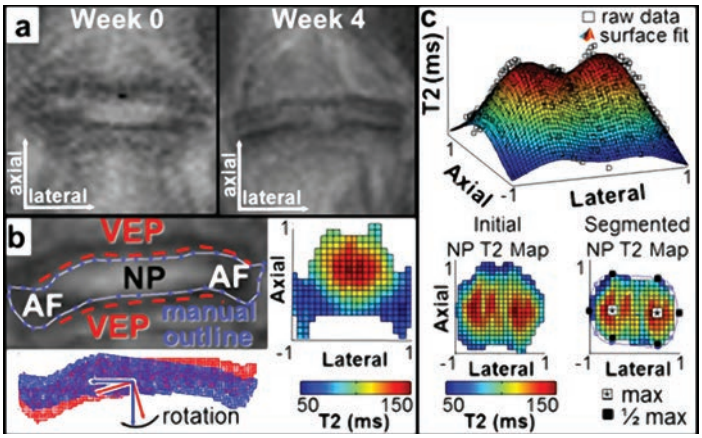

Figure 1. (A) Rabbit discs were punctured and T2 maps were generated pre- and 4 weeks post-injury. (B) Discs were segmented, principal axes were identified and discs were rotated and normalized to a grid. (C) NPs were segmented by fitting the T2 map with a Gaussian function. Fit parameters were used to demarcate the NP boundaries.

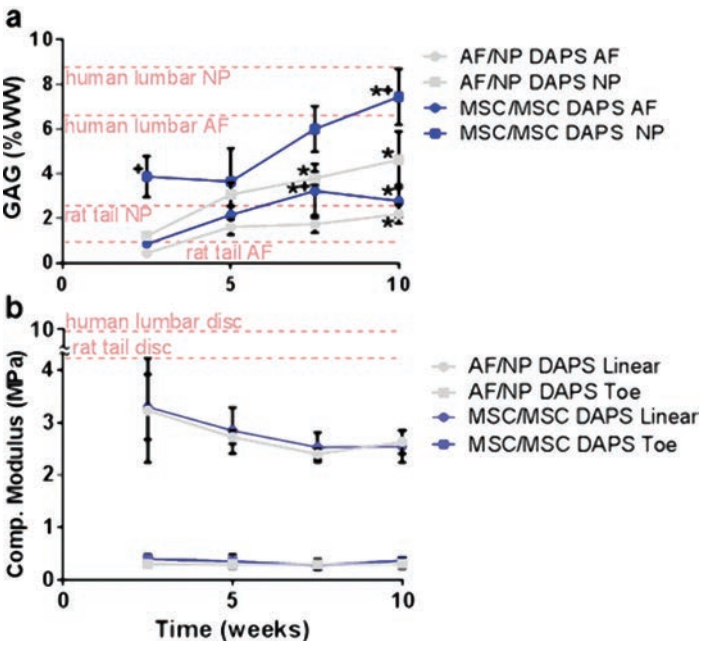

Figure 2. (A) Population average T2 maps revealed specific transformations following injury. At Week 4, NP T2 decreased and the T2 difference map showed that the reduction in signal occurred at the periphery of the NP. (B–E) Quantifying changes in T2 and disc geometry post- injury confirmed these findings. *, $p < 0.05$ vs. week 0.

constant from Week 0 to Week 4, while NP area decreased and AF area increased. Whole disc width increased, while NP width decreased and AF width increased. In addition, whole disc and AF heights decreased, while there was no change in NP height. While MRI measurements showed a disc height decrease in the coronal plane, radiographs demonstrated that disc height decreased in the sagittal plane.

T2 difference maps revealed how discs at different lumbar levels responded to injury (Figure 3). With progression along the spine, the T2 difference in individual discs decreased in magnitude and increased in variability, indicating that the response to injury was not only less severe, but was less repeatable at these lower levels. The mean NP T2 signal in the

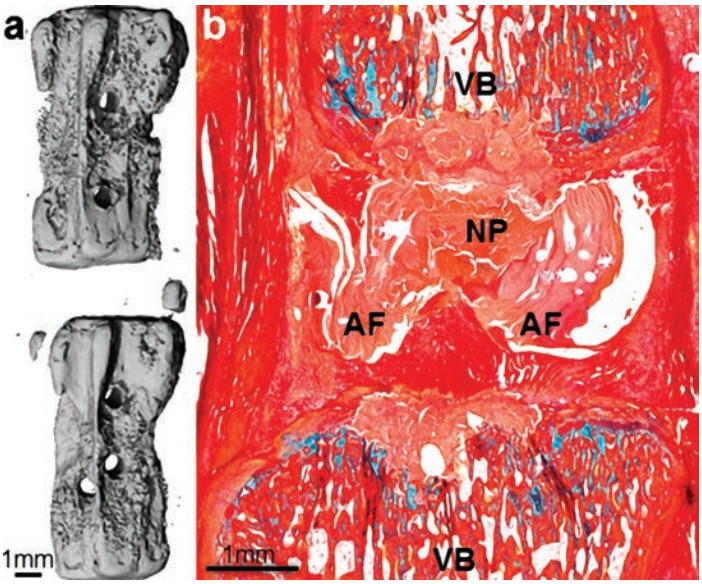

Figure 3. (A) Population average T2 difference maps illustrate variability by level. (B) Level differences were confirmed by calculating the mean T2 difference of individual discs, a single numerical quantity representing the response to puncture injury. (C) The pre-injury AF width of L5/L6 and L6/L7 discs was greater than L3/L4 discs, a possible explanation for variations by level. *, $p < 0.05$ vs. L3/L4.

L3/L4 and L4/L5 discs decreased significantly between Weeks 0 and 4, while the mean NP T2 value in both the L5/L6 and L6/L7 discs did not change over the same time period, and was significantly greater than the L3/L4 NP T2.

Discussion

Rabbit lumbar discs were injured by needle puncture, a standard model for inducing degeneration. We generated population average T2 maps before and after injury that demonstrated that the reduced T2 signal occurred primarily in the NP. Geometric changes following needle puncture included decreases in disc height and NP width. Additionally, the increase in the coronal disc width following puncture supports the idea that disc bulging occurs in this model, a common finding in human epidemiological studies. The heterogeneity in response to injury by anatomic location suggests that, to produce a consistent degenerative response, puncture depth should be adjusted as a function of disc level. Future work will determine whether these population average T2 and corresponding T2 difference maps are useful in a clinical population to assess the degree of degeneration, to predict pain/disability, and to quantify adjacent segment degeneration.

Significance

This study outlines a method for analyzing T2 MRI maps to improve clinical diagnosis of intervertebral disc disease. Heterogeneity in the rabbit needle injury model, a standard disc degeneration model, must be considered when planning future studies.

Acknowledgement

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