

## T2 Mapping as a Potential Biomarker in a Rabbit Model of Intervertebral Disk Damage and Degeneration

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**Introduction:** Intervertebral disk degeneration is a source of pain and disability for millions of people. Disk degeneration is believed to correlate with changes in its water-binding properties. With aging there is fragmentation of proteoglycans and an overall decrease in both proteoglycan and water content of the nucleus pulposus. The collagen fibrils undergo increased cross-linking, which further inhibits matrix turnover and repair, and retards the biomechanical properties of the annulus in its role of constraining the nucleus pulposus. The biomechanical efficacy of the intervertebral disk is believed to correlate with both the water-binding properties of the nucleus pulposus, as well as the constraint of the nucleus pulposus by the surrounding annulus fibrosus. As water molecules are forced through the extracellular matrix with compression, the compressive energy is dissipated as frictional drag of the water molecules. The  $T_2$  relaxation rate has been shown to correlate directly with the water-binding properties of tissue. The use of  $T_2$  as a potential imaging biomarker has been studied in articular cartilage (1), and preliminary work has suggested  $T_2$  mapping may also be more sensitive to disk degeneration than traditional imaging classification systems (2). Here we apply  $T_2$  mapping in a well-established model of disk degeneration in rabbits to assess sensitivity to pathologic changes in the disk space.

**Materials and Methods:**  $T_2$  mapping was performed *in vivo* on 4 intervertebral disks at three time points (baseline, 3 weeks after injury, and 7 weeks after treatment) in 18 male New Zealand White rabbits (total of 72 disks, three timepoints/disk.) To accomplish imaging with adequate SNR, a quadrature birdcage coil just large enough for the rabbit torso (highpass, 12 elements, 12 cm diameter, 12 cm length) was constructed. Imaging was performed on a 3T whole-body Bruker MRI system.  $T_2$  mapping was accomplished with exponential fit to decay of signal intensity (excluding signal from first echo) as measured on a multi-slice, multi-echo acquisition (three 2mm-thick slices, 17 Echoes, TE/TR=7.55ms/2000ms, FOV=16.5x16.5cm<sup>2</sup>, matrix=384x384, 2 averages). Injury consisted of puncture of the intervertebral disk with an 18 gauge needle. Treatment consisted of injection of either 1) Umbilical Cord Blood-derived (UCB) mesenchymal stem cells, 2) UCB stem cells transduced with bone morphogenic protein AdBMP-7 or growth factor protein AdGFP, 3) rabbit articular chondrocytes, 4) rabbit articular chondrocytes transduced with AdBMP-7 or AdGFP, or 5) saline as a control. This injury and treatment model is fairly well established, and some of the treatments have shown improvement in the disks at both a histologic level and in size of the intervertebral space (3). All procedures were approved by our Institutional Animal Care and Use Committee and Biohazard Committee.

**Results:** Figure 1 shows an anatomical image acquired with rabbit-sized body coil. Figure 2 shows  $T_2$ -weighted images of healthy and damaged intervertebral disks. Figure 3 shows  $T_2$  decay curve at one location in disk. Figure 4 shows quantitative  $T_2$  maps in healthy and damaged disks.

**Discussion:** The lumbar disk injury model for degeneration produces significant changes in the  $T_2$  maps. These changes likely represent the loss of the more mobile water compartment from the nucleus pulposus as a result of disk degeneration. The heterogeneous zone of  $T_2$  values seen at the border of the nucleus pulposus may represent a zone of fragmented proteoglycans. The quantitative nature of  $T_2$  mapping facilitates accurate, reproducible, and non-invasive characterization of the tissue properties of the intervertebral disk.  $T_2$  mapping may have applications to longitudinal studies of disk degeneration, as well as in assessing the efficacy of treatment modalities for disk degeneration. At the time of preparation of this abstract, evaluation of  $T_2$  and histology in rabbit intervertebral disks after treatment is being performed.

### References

1. Harvey E. Smith *et al.*, J Magn Reson Imaging 2001;14:50-5
2. Watanabe Atsuya *et al.* AJR 2007; 189:936-942
3. YeJia Zhang *et al.*, Am J Physical Medicine and Rehabilitation 2008;87:649-702

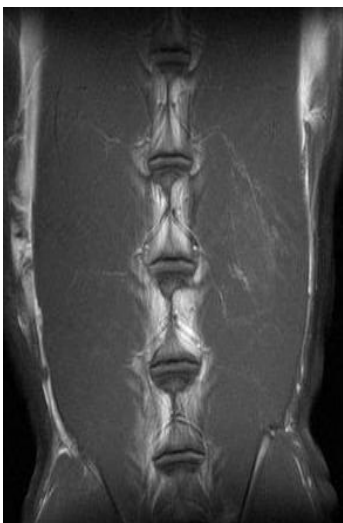


Figure 1. Anatomical image of Rabbit Spine



Figure 2. Conventional  $T_2$ -weighted images of healthy intervertebral disk (top) and damaged disk (bottom)

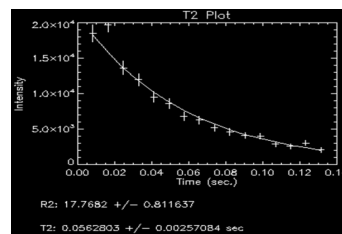


Figure 3. Exponential Fit to Signal Intensity of 25 echoes at one location to determine  $T_2$

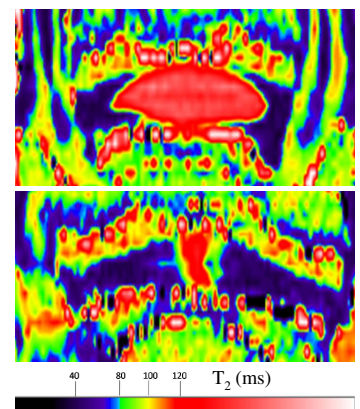


Figure 4.  $T_2$  map of healthy intervertebral disk (top) and damaged disk (bottom)