Assessment of Cartilaginous Endplate Morphology and Damage Using Ultrashort Echo Time (UTE) MRI

Aaron J. Fields, Ph.D.1, Britta Berg-Johansen, B.S.1, Brandon Lim, B.S.1, Misung Han, Ph.D.1, Ellen C. Liebenberg, B.S.1, Cigdem Gunduz-Demir, Ph.D.2, Galateia J. Kazakia, Ph.D.1, Roland Krug, Ph.D.1, Jeffrey C. Lotz, Ph.D.1.

1University of California, San Francisco, San Francisco, CA, USA, 2Bilkent University, Ankara, Turkey.

Disclosures:

Introduction: The cartilaginous endplate is a thin layer of cartilage whose biomechanical and transport functions play an important role in intervertebral disc health [1,2]. In addition to compromising disc health, endplate damage associates with painful bone marrow lesions [3]. Despite its important role, cartilaginous endplate morphology and the extent and nature of endplate damage are poorly characterized. This is because visualizing the cartilaginous endplate currently requires destructive techniques, as the cartilage has short T2 values and thus its signal is not captured by standard MRI sequences with long echo times. Ultrashort echo time (UTE) MRI was recently demonstrated to capture the signal of the cartilaginous endplate [4,5]; however, it remains unclear whether UTE MRI is capable of accurately quantifying endplate morphology and damage. The goal of this study was to validate UTE MRI-derived estimates of endplate thickness and damage fraction by comparing the estimates with site-matched histologic measurements.

Methods: Five lumbar motion segments (3 L1-L2 and 2 L4-L5; Pfirrmann grades 2 and 3) were harvested from human cadaver spines (ages 51, 57, and 66 years). Each motion segment was attached to a rigid alignment guide that served as fiducial marker for aligning subsequent HR-pQCT and UTE MR image prescriptions [6]. MR imaging was performed on a Discovery MR 750W 3T scanner (GE Healthcare, Waukesha, WI) using an eight-channel phased-array wrist coil (Invivo, Gainesville, FL). The 3D UTE sequence (TE = 75 µs, TR = 12 ms, 15° flip angle, 8.0 x 8.0 x 7.0 cm³ field-of-view, and 0.5 x 0.5 x 0.5 mm³ voxels) included a radial acquisition and nonselective excitation pulse [7]. Fat suppression was applied every five radial-spoke acquisitions to minimize blurring from fatty components of the bone marrow. HR-pQCT imaging was performed with an XtremeCT scanner (Scanco Medical AG, Bruttisellen, Switzerland) using settings to yield a 41 µm voxel size [6]. After imaging, the motion segment was sectioned into para-sagittal slabs for histology (see below). The alignment guide was used during sectioning to ensure the slabs were co-planar with the HR-pQCT and UTE MR image slices.

The para-sagittal slabs of the motion segments were fixed, decalcified, and sectioned for histology. Sections were stained with a tri-chrome stain that contains aniline blue, orange G, and acid fuchsin. Cartilaginous endplate thickness was measured on photomicrographs at 50 evenly spaced positions from anterior to posterior. Damage fraction was calculated as the length with no visible cartilage divided by the total length of the cartilaginous endplate.

Following reconstruction, UTE MRI data were processed using a custom, automated Matlab code (Mathworks; Natick, MA). The code identifies the endplates, thresholds the images, and calculates endplate thickness at each of the same 50 anterior-posterior positions identified on histology. Individual UTE MRI slices (n = 20 slices, 2 endplates/slice) were matched to their corresponding histology sections (Fig. 1) by finding the precise location of the histology section in the HR-pQCT datasets, which had been co-aligned with the UTE MRI slices.
Several comparison metrics were used to evaluate the agreement between UTE MRI-derived estimates of endplate thickness and damage fraction and their respective gold-standard histology measurements (Fig. 2). For each endplate section, the systematic bias and noise in the thickness estimates were determined by calculating the mean difference and root-mean-square deviation (RMSD) for the 50 anterior-posterior positions (Fig. 2A). The proportional bias was determined from Bland-Altman plots for each endplate (Fig. 2B). Also, general agreement between the two measurement techniques was assessed using

**Figure 1**: Typical sagittal histology sections (7 μm-thick) showing endplates without damage (top left) and with damage (top right, arrowhead). Matching UTE MRI slices with cartilaginous endplate signal (middle row) and conventional T2 MRI slices without cartilaginous endplate signal (bottom row). In all panels, the left side is anterior.
correlation analysis (Fig. 2C). The mean ± SD of the metrics is given for all 40 endplates. Damage fraction was compared using a paired t-test.
Figure 2: (A) Typical comparison of anterior-posterior variation in cartilaginous endplate thickness between UTE MRI and histology for a single endplate section. Endplate thickness was evaluated at 50 evenly spaced positions from anterior to posterior.
Results: UTE MRI systematically underestimated endplate thickness (systematic bias = -0.033 ± 0.160 mm, n = 40 endplate sections), although the magnitude of the underestimation was not significantly different from zero (p = 0.19). Bland-Altman plots indicated that there was a significant proportional bias in 33/40 endplate sections, and the mean proportional bias, 0.279 ± 0.735, was significantly greater than zero (p = 0.02). Whereas UTE MRI tended to underestimate endplate thickness, it overestimated endplate thickness variation: correlation analysis showed that variation in UTE MRI-derived estimates of endplate thickness correlated significantly with variation in the gold-standard histology measurements in 32/40 endplate sections, and the mean regression slope, 0.33 ± 0.29, was significantly less than 1 (p < 0.0001). The noise of the UTE MRI estimates (RMSD = 0.278 ± 0.093 mm) was significantly greater than zero (p < 0.0001). Amongst the 14/40 histology sections with endplate damage, there was no significant difference between UTE MRI-derived estimates of damage fraction and the histology measurements of damage fraction (11.2 ± 4.7% vs. 12.0 ± 7.8%, p = 0.66 paired t-test), and the UTE MRI-derived estimates of damage fraction correlated significantly with the histology measurements (p < 0.05).

Discussion: In this study we sought to validate UTE MRI-derived estimates of endplate thickness and damage fraction by comparing the estimates with site-matched histology measurements. Results from the Bland-Altman analysis indicated that UTE MRI estimates had no systematic bias and a small but significant proportional bias. This means UTE MRI overestimates thickness where the endplate is locally thick and underestimates thickness where the endplate is locally thin and suggests that adaptive thresholding of UTE images could enhance the overall agreement with histology. Correlation analysis revealed that UTE MRI thickness estimates were weakly, although significantly, correlated with histology measurements (r = 0.25-0.71). This could result from a combination of factors. Most likely, the weak correlations reflect the small intra-endplate thickness range coupled with the limited precision in individual UTE MRI estimates. The limited precision, which is apparent from the modest RMSD, can be improved in future studies by increasing the signal-to-noise ratio. Nevertheless, comparison of damage fraction between UTE MRI and histology showed promising results, since there was no significant difference in damage fraction estimates between the two techniques. Taken together, these findings indicate that the current UTE MRI sequence provides accurate estimates of cartilaginous endplate thickness and damage fraction, although individual estimates may have poor precision.

Significance: The morphology of the cartilaginous endplate and the extent of cartilaginous endplate damage have not been well characterized, yet endplate morphology and damage are known determinants of disc degeneration and discogenic low back pain. Here we demonstrate that UTE MRI can accurately quantify endplate thickness and damage fraction, which suggests that UTE MRI may be useful for non-invasively assessing cartilaginous endplate structure.

Acknowledgments: Study supported by NIH Grant AR063705, Relievant.
