DCEMRI shows slower wash-out in lumbar disc endplates to sustain diffusion of nutrients into the discs

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Target Audience: Clinicians and researchers interested in the pathophysiology of spinal disc degeneration

Introduction: The majority of chronic back pain is associated with degeneration of the intervertebral discs (IVD). The factors that lead to disc degeneration and its pathophysiology are still not completely understood. It has been suspected that poor nutrient delivery to discs is a major factor in the pathogenesis of IVD degeneration[1]. The IVD is avascular; nutrition is supplied (and waste is removed) via diffusion mechanism from the capillary beds of the cartilaginous vertebral body endplates (EP). Thus, disruptions in the capillary beds of disc EPs might cause poor nutrient delivery and lead to disc degeneration. However, this relation has not yet been demonstrated in humans. In the study presented here, we extended our previous dynamic contrast-enhanced MRI (DCEMRI) studies to characterize endplate (EP) perfusion. We anticipated that the characteristic DCEMRI signal would be different in the EP capillaries from those in bone marrow in vertebral bodies (VB) because of the different mechanisms of nutrient delivery to these two different systems. In order to sustain diffusion into the discs, higher concentrations should be maintained longer in the EPs, which should be different from capillary perfusion in the bone marrow.

Methods: The study was approved by the IRB and written consents were obtained from eight subjects (age: 27–61y; mean 43y). Dynamic Contrast Enhanced MRI (DCEMRI) was acquired in a 3T Philips Achieva scanner (Best, Netherlands) using a 3D gradient-echo sequence (TR/TE=3.4ms/1.2ms, flip-angle=30^o, 0.81×0.81mm^2 in-plane res. 22 frames/36.4s frame rate, 15-sagittal slices, thickness=3mm). The contrast (Gd-DTPA-BMA, 0.1 mmol/kg) was administered manually as a bolus via an antecubital vein at the start of the 3rd dynamic frame. A conventional T2 weighted (T2w) MRI was also acquired for anatomical reference and grading of disc degeneration using Pfirrmann classification[2]. Subjects were in supine position in the scanner. A trained operator drew regions of interest (ROI) on pre-contrast images of the DCEMRI set to segment out the 10 subchondral EPs in the lumbar area and a thin strip on the surface of the VB adjacent to the endplate (Fig.1). Since the EPs were very thin (~1mm), we chose to draw ROIs on pre-contrast DCEMRI images because even a slight misregistration with T2w image would lead to significant partial volume effects. The ROIs were inspected by other members of the research team to ensure accuracy. In each ROI, volume-averaged signal enhancement time course was calculated and percent enhancement curve were generated with respect to the baseline intensity before injection. DCEMRI signal enhancement in the EPs and VBs were compared and age related changes were investigated.

Results and discussion: Fig.2 shows DCEMRI signals averaged across all subjects. Signals from EPs above and below each IVD were averaged separately and shown in the plot. Error bars indicate standard deviation (either + or – bars for standard deviation are shown to avoid confusion). Although both signals reach the peaks simultaneously, inferior EPs have much slower wash-out, maintaining concentrations longer. Variability was also significantly smaller in inferior EPs. The area under each EP DCEMRI curve (AUC) was calculated and a t-test was run. The difference between superior and inferior EPs was statistically significant (p=0.018). Fig.3 shows average DCEMRI signals from the inferior EPs and adjacent VBs. The signals from the VBs show fast wash-in and fast wash-out characteristic compared to EPs. Relatively large variability was mostly caused by age effects. Pearson's correlation between age and the AUC was r= -0.56. Despite age effects, inspection of DCEMRI curves from each individual subject consistently showed these characteristic behaviors and only the overall enhancement was reduced with age. Subjects had varying degrees of degeneration (2-4 per Pfirrmann classification[2]), which might have also contributed to the variability. However it was not taken into account in these analyses due to the relatively small sample size. Another interesting finding was the strong correlation between AUC of VBs and EPs (r=0.69). Despite differences in their enhancement characteristics, overall magnitude of enhancement was similar. This is possibly due to the fact that both capillary networks are supplied through the same arteries and blood flow through those arteries modulated both systems. Fig.4 shows AUCs for EPs and VBs at different lumbar levels averaged across all subjects.

Conclusions: High spatial resolution DCEMRI was used to investigate the EP capillaries. Slower wash-out characteristics in the EP DCEMRI curves might indicate that those capillaries have slower clearance rate in order to maintain high concentration of nutrients to mediate diffusion into the discs. It was interesting to note that the EPs below the discs showed a slower wash-out compared to the EPs above the discs. This was not due to poor placement of ROIs and the findings were confirmed by inspection of DCEMRI curves at different lumbar levels for individual subjects. The signal enhancement decreased with age as expected, which might be contributing to the disc degeneration process associated with aging. Future studies with larger populations might help us understand deviations from these characteristic behavior and their association with disc degeneration.

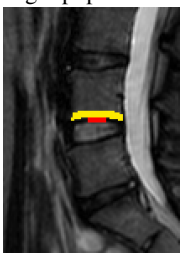

Fig.1. Example ROIs from the EP (red) and VB (yellow).

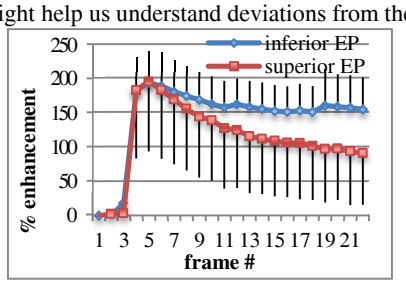

Fig.2. Average DCEMRI curves in endplates above and below the lumbar discs.

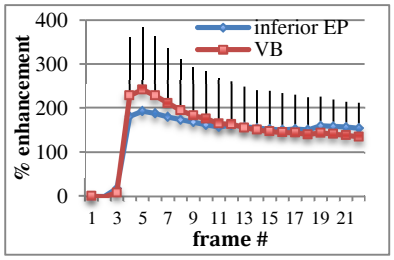

Fig.3. Average DCEMRI curves in inferior endplates versus lumbar vertebrae.

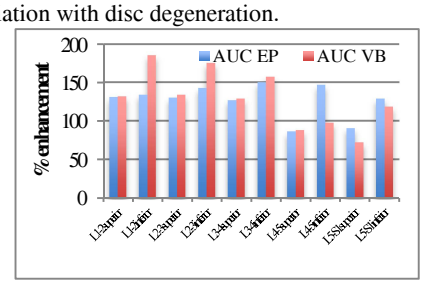

Fig.4. Area under curves in inferior endplates versus vertebrae at different lumbar levels.

References: 1) *N Boos, et al. Spine 2002, 27:2631–44*; 2) *Pfirrmann et al. Spine 2001, 26:1873-8*