Cross-talk between Discs and Adjacent Bone, Implication for Vertebrogenic Pain
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Significance:
Annular tears may trigger bone marrow changes that are not detectable on MRI but may be a source of vertebrogenic pain.

Introduction:
A major obstacle in the development of new therapeutic interventions for patients with back pain is poor understanding of why some degenerated discs hurt while many others are asymptomatic. Ongoing studies suggest that cross-talk between the disc and adjacent vertebra influences both disc degeneration and pain. The bone marrow of the vertebra is normally separated from proinflammatory disc cytokines by a shared interface; the vertebral endplate. Endplate damage may cause bone marrow lesions (BML) marked by edema and neo-innervation [1], thought to be triggered by nucleus-secreted IL-1 [2]. The peripheral half of the annulus is firmly attached to the vertebral rim via Sharpey’s Fibers. Theoretically, tears of this interface (rim lesions) can expose underlying bone and initiate a bone marrow reaction. The present study investigates the relationship between the presence and nature of annular tears and marrow changes in the adjacent bone.

Methods:
Five cadaveric lumbar spines ages 50-63 were harvested after performing conventional T1- and T2-weighted MRI in situ. Spines were cut into 4 sagittal slabs that were fixed in formalin and decalcified. Each disc was cut into approximately 10 mm of the adjacent vertebra on either side, fixed in formalin, and decalcified. Sections were stained with Mallory Heidenhain for connective tissue and immunostained with PGP 9.5 as a nerve marker. Specimen MR images were assessed for BML (Modic changes), and histologic sections were graded for annular tears, and tissue changes in the adjacent bone.

Results:
Three types of annular tears were observed: concentric, radial, and rim lesions (Figure 1). Annular tears were present in 20/30 of the discs. Seven discs had concentric tears, 5 had radial tears, and 8 had rim lesions. Bone marrow lesions were associated with every annular tear with one exception, and these changes were often, but not always, accompanied by neo-nerveation (Figure 3). Seventy-seven percent of rim lesions and 100% of concentric tears occurred in the anterior annulus. Concentric tears were often associated with both rim lesions and radial tears. Some tears were associated with extensive neovascularization and sparse neo-nerveation in the outer annulus, but no nerve was observed in proximity to a tear. Interestingly, bone marrow elements were observed in annular fissures in 3 discs (Figure 2).

Rim lesions were observed primarily in Thompson Grade 2 and 3 discs, whereas the radial tears were seen primarily in Grade 4 discs. Within a spine, similar types of tears were seen at multiple levels. All 3 types of annular tears were associated with fatty or fibrovascular marrow changes that included neo-innervation (Figure 3), but only rim lesions were associated with ingrowth of fibrocartilage into the adjacent bone.

Discussion:
Annular tears are features of internal disc disruption (IDD) and are a putative pain generator [3]. However, their relationship to BML in adjacent vertebrae has not been described. This is important, since endplate BML are among the most specific of all MRI observations for predicting disc pain [4]. Our data suggest that IDD and BML are related, as annular rim tears may create a pathway for inflammatory cytokines from the nucleus to move into the vertebral body, inducing BML. The observation of bone marrow elements within the disc suggest hydraulic coupling, where disc pressure fluctuations characteristic of activities of daily living may cause mixing of disc and marrow tissues via endplate defects.

Less degenerated discs may be prone to rim lesions because the annulus is relatively intact, and the weak link may rather be its interface to bone. The fact that rim lesions and radial tears weren’t observed together suggests that once the annulus is compromised mechanically, injurious stresses don’t develop at the bone/annulus interface.

Acknowledgements:
NIH (RO1AR052811), Relievant Medsystems

References:

Conclusion:
Annular tears are closely associated with bone marrow changes in the adjacent vertebral body including neo-innervation and replacement of normal hematopoietic marrow by fatty and/ or fibrovascular marrow. These results suggest that annular tears may cause marrow changes not visible on MRI that could be a source of vertebrogenic pain.

Figure 1: A. Anterior to posterior radial tear (arrows) with associated areas of fatty marrow (right inset, arrow). B. Anterior concentric tear (red arrow) associated with fibrovascular marrow (right inset, red arrows) and posterior radial tear (black arrow). C. Rim lesions on anterior superior and anterior inferior surfaces with fibrocartilage ingrowth (right inset, black arrow).

Figure 2: Bone marrow elements including fibrotic marrow and necrotic bone (right inset) in a small concentric annular tear.

Figure 3: PGP 9.5 immunohistochemical stain of a rim lesion demonstrating fatty and fibrotic marrow containing abundant nerve (right inset, arrows).