QUANTITATIVE SUSCEPTIBILITY MAPPING (QSM) TO CORRELATE WITH HISTOLOGY AND QUANTITATIVE PARAMETRIC MAPPING IN SURGICALLY INDUCED JUVENILE OSTEOCHONDRITIS DISSECANS

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Target Audience: Scientists and clinicians interested in cartilage imaging, blood vessel imaging, susceptibility mapping, parametric relaxation mapping, novel pulse sequences, Osteochondritis dissecans.

Purpose: Osteochondritis dissecans (OCD) is a developmental orthopaedic disease occurring in active adolescents and several animal species. Previous studies have shown the OCD is closely associated failure of cartilage canal blood vessels in epiphyeal cartilage. We previously have shown the utility of traditional SWI for epiphyseal cartilage imaging [1] to detect differences in susceptibility of cartilage matrix and the cartilage canals, allowing direct visualization of the vasculature. Quantitative susceptibility mapping (QSM) provides another approach to quantitatively investigate susceptibility properties of local tissue. Nissi et al has shown that QSM could remove the doubling artifact present in SWI images used for visualization of cartilage canal blood vessels [2]. However, vascular degeneration has not been investigated in OCD lesions. The present study examined the correlation between quantitative MR relaxation times and histological changes in epiphyseal cartilage after surgical transection of cartilage canal blood vessels in young goats. Safranin O stained histological sections provided direct evidence of areas of ischemic necrosis in epiphyseal cartilage.The susceptibility properties of the cartilage canals in the epiphyseal cartilage were quantiatively assessed at different times after surgically-induced ischemia by using minimum intensity projections (MinIP) of the quantitative susceptibility map.

Methods: Distal femoral epiphyseal specimens were obtained from goats that underwent surgical induction of ischemia by transection of cartilage canal blood vessels at 4 days of age. Goats were euthanized 2, 3, 4, 5, and 6 weeks after surgery [3]. MRI scans were performed using a 9.4T Varian scanner (Agilent Technologies, Santa Clara, CA). Phase and magnitude data of the specimens were acquired using a 3D GRE sequence and the QSM images were subsequently calculated. Additionally, quantitative assessment of the epiphyseal cartilage was performed to identify the ischemic lesions by using two recently proposed magnetization preparation methods, adiabatic $T_{1\rho}$ [4] and relaxation along a fictitious field (RAFF) [5], with a 2D FSE readout sequence. The MRI protocol is detailed in Table 1. The MinIP of the QSM data was utilized to visualize the epiphyseal vasculature at about 1 mm thickness (10 slices) near the surgical site, closely matching the thickness of the MR relaxation maps. Safranin O staining of matching histological sections was conducted to evaluate proteoglycan (PG) content in the cartilage and to document induced necrosis of cartilage.

Results: Safranin O stained sections depicted regions of loss of stain near the incision site (outlined by a thin black line) (Figure 1). The adiabatic $T_{1\rho}$ and T_{RAFF} values of the necrotic cartilage near the incision were both higher than values in the surrounding epiphyseal cartilage, as indicated by the arrows in Figure 2. The lesion increased in size over time, reaching a maximum at 5 weeks following the surgery. By closely matching the thickness and location of the parametric MRI slices (Figure 2), with the corresponding 3D GRE images, the incision site (indicated by arrows) was clearly visible, though no significant signal difference was noted between the lesion area and the normal epiphyseal cartilage (Figure 3, left column). The MinIP images of the susceptibility map depicted the vasculature in the epiphyseal cartilage (Figure 3, right column). The areas matching the signal abnormalities near the incision site were magnified for improved visualization of the vasculature within the lesion (Figure 3, insets on the right). Although the vasculature within the lesion in close proximity to the incision appeared normal after (b) 2 and (d) 3 weeks, their contrast decreased compared to the vasculature within the surrounding normal epiphyseal cartilage, indicative of early vascular degeneration caused by surgical transection of the vessels. After (f) 4, (h) 5, and (j) 6 weeks, the vessels have degenerated and are not clearly delineated.

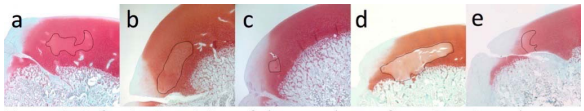

Figure 1. Safranin O staining of the goat knees from 2 to 6 weeks post surgery. Regions of necrosis are outlined in black.

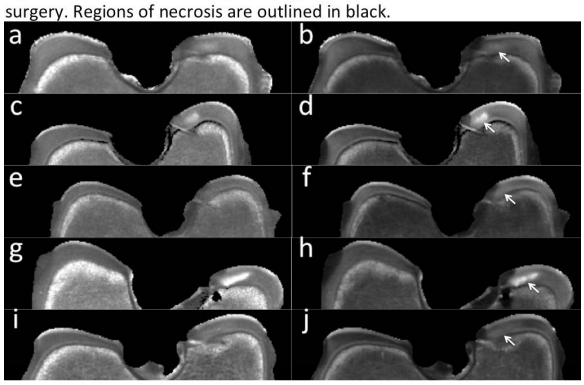

Figure 2. Adiabatic $T_{1\rho}$ and T_{RAFF} maps are presented in the left and right columns. Regions of necrosis are pointed by the white arrows.

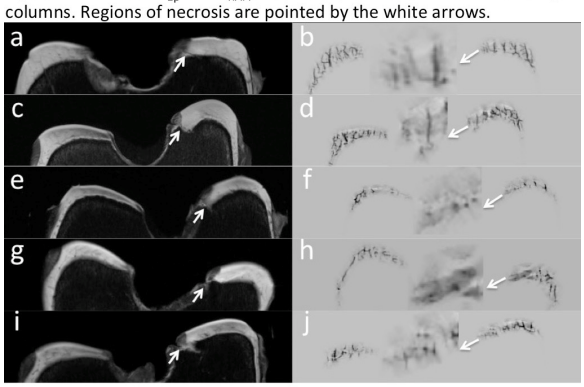

Figure 3. In the left column, the 3D GRE images are averaged in about 1 mm thickness. The corresponding MinIP images of blood canals are shown in the right column. The positions of Figures 2 and 3 are matched.

Table 1. List of MRI parameters

2D FSE Readout	TR/TE = 5s/10ms, ETL = 8, thk = 1 mm, FOV = 4^2 cm, 256^2, coronal
Adiabatic $T_{1\rho}$	Train of 0, 4, 8, 12, 16 AFP pulses, duration = 6 ms, γB_1^{max} = 2.5 kHz
T_{RAFF}	Train of 0, 8, 16, 24, 32 RAFF pulse, duration = 4.53 ms, γB_1^{max} = 625 Hz
3D GRE	TR/TE = 40/15 ms, α = 15°, FOV = 4^3 cm, 384^3, coronal

Discussion: Histologial sections stained with Safranin O are usually regarded as the gold standard to confirm the presence of OCD, but this method cannot be used for *in vivo* diagnosis. The adiabatic $T_{1\rho}$ and T_{RAFF} relaxation times are sensitive to the content of proteoglycan in the epiphyseal cartilage. As the amount of proteoglycan decreases after an ischemic insult, the MR relaxometry based methods demonstrated their ability to noninvasively detect lesions of OCD. However, the MR relaxometry results cannot be interpreted with certainty without combining them with histological results, and of these methods allowed to visualization of the vasculature in the epiphyseal cartilage. While the vasculature as depicted by the SWI may still be present, quantitative susceptibility mapping provides a direct map of local tissue magnetic susceptibility changes, possibly providing a reliable way to identify an area of chondronecrosis.

Conclusion: For the first time it is demonstrated that MinIP of the susceptiblity map of post-ischemic epiphyseal cartilage necrosis can identify changes in cartilage canal susceptibility while the vasculature is still intact. This novel and noninvasive approach provides a more sensitive method to directly visualize the tissue changes. These methods could potentially be utilized to detect early lesions of naturally occurring OCD in animals and humans.

Acknowledgement: We grateful acknowledge the financial support from NIH P41 EB015894 and R21 AR065385 grants and the WM KECK Foundation.

References: [1] Nissi, M. et al, Magn Reson Med. 2014:71(6):2197-205. [2] Nissi. M. et al. ISMRM 2014, abstract #3986, Milan, Italy. [3] Tóth, F. et al. Osteoarthritis and Cartilage. Accepted Manuscript: OAC1713R1. [4] Michaeli, S., et al. J Magn Reson, 2006. **181**(1):135-47. [5] Liimatainen, T., et al. Magn Reson Med, 2010. **64**(4):983-94.