Imaging Markers for Early Matrix Depletion

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The hyaline articular cartilage is composed of a few chondrocytes surrounded by a large extracellular matrix (ECM). The ECM is composed primarily by water and two groups of macromolecules: proteoglycan (PG) and collagen fibers. These macromolecules in the ECM restrict the motion of water protons. Changes to the ECM, are said to precede morphological changes in articular cartilage and may prove to be early biomarkers of osteo-arthritis. ECM changes such as PG loss, therefore, may be reflected in measurements of: 1) T1ρ of water protons, 2) Delayed Gadolinium Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC). Collagen content and orientation changes can be probed using T2 relaxation time measures. In vitro studies and validation of these methodologies have been widespread, and more recently in-vivo studies utilizing these tools have also confirmed the potential for quantitative imaging for monitoring changes in the ECM.

In vitro studies have evaluated the relationship between T1ρ relaxation time and the biochemical composition of cartilage (1-3). In vivo studies showed increased cartilage T1ρ values in OA subjects compared to controls (4-7). In addition to evaluating cartilage in patients with OA, T1ρ quantification techniques have been applied to cartilage in patients with acutely injured knees, who have a high risk of developing OA (8, 9).
Delayed gadolinium enhanced MRI studies validated that regions of cartilage degeneration (from trypsin or interleukin) showed histological differences, as well as differences in the post-contrast (Gd-DTPA2-) signal intensity and T1 relaxation time (10, 11). The application of this technique has been evaluated (12) and specifically in OA, the dGEMRIC index is associated with joint space width, Kellgren Lawrence (KL) grading scale and malalignment. A recent longitudinal study reported that a low dGEMRIC index at baseline was significance associated with the development of radiographic OA at six years follow-up (13). dGEMRIC studies have evaluated potential therapies in OA, demonstrated that moderate exercise can improve knee cartilage GAG content in patients with high risk of OA (14), and showed that dGEMRIC can be used to monitor GAG content in autologous chondrocyte transplantation and microfracture (15-17).

Changes in collagen in degenerating cartilage increases the mobility of water, thus increasing its signal intensity on T2-weighted images (18). In vitro imaging studies have evaluated the relationship between biochemistry of cartilage and T2 measurements (19, 20). A recent in vitro study (21) has shown that T2 relaxation time in human patellar cartilage is significantly correlated to Young's Modulus, suggesting that T2 quantification may predict the mechanical properties of cartilage. In vivo imaging studies have measured T2 relaxation time to evaluate the effects of gender, age (22, 23), disease (24-29), activity level (30-32). Studies have measured T2 relaxation time to assess cartilage following cartilage repair techniques including chondrocyte transplantation and microfracture (33-37). Studies have shown an inverse relationship between cartilage T2 and cartilage thickness (27, 38) and that higher medial cartilage T2 results in greater loss of medial cartilage volume at twelve months, demonstrating a relationship between cartilage T2 and cartilage volume (27).

With these techniques and other emerging methodologies including Sodium imaging (39-42), and Glycosamin Concentration by Chemical Exchange Dependent Saturation Transfer gagCEST (43), the role of quantitative imaging in assessing early cartilage changes has tremendous clinical potential. Translating these methodologies to the clinic clearly requires standardization of imaging, analysis protocols, commitments from the vendors for long term support of the acquisition sequences. Multi-center trials

and testing of these tools in specific populations will enhance the role of MR imaging in Osteoarthritis and related disorders.

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