

## **TARGET AUDIENCE and OUTCOME/OBJECTIVES**

This objective of this course is to introduce clinicians to the new emerging techniques in characterizing articular cartilage. At the conclusion of the talk, the audience will be able to analyze the role of these imaging techniques in unraveling the underlying pathophysiology of cartilage changes, and challenges to their clinical dissemination will be clear.

## **PURPOSE**

Hyaline cartilage consists of a low density of chondrocytes and a large extracellular matrix (ECM). The ECM is composed primarily of water (~75% of cartilage by weight), and a mixture of proteoglycans and collagen fibers (mainly type II). Although the etiopathogenesis of OA is not fully understood, it is believed that osteoarthritis (OA) results from an imbalance between predominantly chondrocyte-controlled anabolic and catabolic processes, and is characterized by progressive degradation of the components of the extracellular matrix of the cartilage<sup>1-3</sup>. During early stage of OA, the increased synthesis of the ECM components (the attempt to repair by cartilage chondrocytes) is exceeded by their degradation due to increased synthesis and activity of proteases. Collagen breakdown is characterized by thinning of the collagen fibrils and loosening of the tight weave of the collagen network. However, it has been suggested that neither the content nor the type of collagen is altered in early OA<sup>2</sup>. The proteoglycan, which are no longer constrained (or less constrained) by the tension of the collagen network, are able to bind increased amounts of water, resulting in increased water content in early OA. There is also loss of proteoglycan during early OA. As the osteoarthritic process progresses, the proteoglycans, which were captured underneath the intact articular surface, diffuse into the synovial fluid. This loss of proteoglycans results in a decreased water content of the cartilage and a subsequent loss of its biomechanical characteristics, such as compressive stiffness. The collagen network becomes more disorganized. Late stage of OA is characterized by extensive fibrillation of the cartilage. The purpose of this presentation is to review emerging techniques that hold promise for quantifying cartilage ECM changes.

## **METHODS**

The methods that will be discussed are high-field magnetic resonance imaging, primarily focused on 3T imaging, but with some focus on the recent advances in 7T imaging. Particularly,  $T_{1\rho}$ ,  $T_2$ , diffusion, gagCEST, ultra-short TE (UTE), dGEMRIC, sodium and other MR imaging techniques will be discussed.

## **RESULTS**

Studies demonstrating the role of each of these imaging techniques will be reviewed. For example:

- In vivo studies show increased cartilage  $T_{1\rho}$  values in OA subjects compared to controls<sup>4-10</sup> and were found to be moderately age-dependent<sup>8</sup>.
- Elevated  $T_{1\rho}$  has also been correlated with lesions evaluated with arthroscopy<sup>11, 12</sup>, especially when a small region of interest was used for  $T_{1\rho}$  quantification<sup>12</sup>.
- In vivo  $T_2$  quantification using data from the Osteoarthritis Initiative<sup>13</sup> showed significantly elevated  $T_2$  and higher heterogeneity parameters of  $T_2$  in subjects at risk for OA than controls, although there was no significant difference in the prevalence of knee abnormalities.
- The spatial correlation between  $T_2$  and  $T_{1\rho}$  in cartilage has also been explored in vivo<sup>14</sup>. Although the average  $T_{1\rho}$  and  $T_2$  values correlated significantly, the pixel-by-pixel correlation between  $T_{1\rho}$  and  $T_2$  showed a large range in both controls and OA patients.
- Decreased dGEMRIC index was observed in cartilage with early degeneration as detected by arthroscopic evaluation<sup>15</sup> and in compartments with radiography joint space narrowing compared to other compartments<sup>16</sup>.

- At 7T, a strong correlation ( $r = 0.701$ ) was found between ratios of signal intensity from native cartilage to signal intensity from repair tissue obtained with gagCEST<sup>17</sup>.
- In vivo diffusion-weighted MRI been applied in monitoring tissue integrity after cartilage repair<sup>18, 19</sup>.
- At 7 T, sodium concentrations were reduced significantly in OA subjects compared to controls by approximately 30%-60%, depending on the degree of cartilage degeneration<sup>20</sup>.
- Mean normalized sodium signal intensities were significantly lower in the cartilage transplant after matrix-associated autologous chondrocyte transplantation (MACT) compared to healthy cartilage<sup>21</sup>.

## DISCUSSION and CONCLUSION

Many new quantitative methods have emerged but their use in clinical practice remains elusive. The challenges will be discussed and solutions proposed.

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