Specialty area: Sunrise Session MSK -Cartilage Structure & Function

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COLLAGEN STRUCTURE: DTI & T2 MAPPING

Highlights

- Articular cartilage is composed by a glycosaminoglycan (GAG) gel embedded on a structured collagen matrix.
- Early pathological changes in osteoarthritis (OA) involve loss of GAGs and disruption of the collagen architecture.
- T2 relaxation times are modulated by the interaction of water with the collagen matrix, and is thus used as an indirect marker for collagen integrity.
- Diffusion tensor imaging provide biomarkers specific to collagen (fractional anisotropy, FA) and proteoglycan content (mean diffusivity, MD)

TARGET AUDIENCE: MSK radiologist and MR physicists with interest in techniques for assessment of the integrity of articular cartilage

OBJECTIVE: After attending this lecture you will:

- Learn the basic biology and function of articular cartilage
- Recognize the importance of assessing the integrity of the collagen network
- Understand the value of T2 and DTI of articular cartilage to detect early pathological changes in the collagen network
- Have an up-to-date review of clinical use of T2 and DTI of articular cartilage

PURPOSE: To provide insight in the acquisition and clinical use of DTI and T2 as biomarkers for the integrity of the collagen network of the cartilage matrix.

METHODS: The hyaline cartilage is a thin layer (~3 mm) of connective tissue covering the articulating surface of the bones. The primary function of hyaline cartilage is mechanical: it provides low friction articulation of the bones and load transmission. Cartilage mechanical properties are a consequence of its composition. Cartilage is composed by water (~75%) and a solid matrix composed mainly of collagen (2/3 of the dry weight) and glycosaminoglycan (GAG, 1/3 of the dry weight)[1]. Collagen molecules are responsible for the tensile forces in cartilage, while GAG are responsible of the osmotic pressure [2].

During OA the cartilage matrix suffers an irreversible break down of its molecular constituents. Chondrocytes, the only cell found in articular cartilage, have a very low metabolic rate, and thus

very low ability to repair damage to the cartilage matrix. A comprehensive evaluation of the cartilage matrix requires assessment of both the collagen and the GAG content.

MRI offers many methods dedicated to the detection of the GAG content [3-9], however the assessment of collagen remain challenging. Direct measurement of collagen is difficult with magnetic resonance, since collagen molecules are large molecules with a very broad NMR spectra, and thus very short T2 values [7]. Nevertheless, there are possibilities for an indirect assessment of collagen structure with MRI. T2 and DTI are two methods that have shown potential to assess the integrity of the collagen network [5, 10].

T2 relaxation time in articular cartilage is heavily modulated by the interaction of water with the collagen molecules [11]. Collagen molecules induce a strong dipolar-dipolar interaction between water molecules that result in the low T2 relaxation times of articular cartilage and in the typical laminar appearance of cartilage in T2-weighted images. Quantification of T2 has thus been proposed as a biomarker for integrity of the collagen architecture [12].

The second biomarker is DTI of articular cartilage. DTI measurements can provide separate information of collagen and PG [10, 13-17]. The collagen network is organized in an arch-like architecture and favors the motion of water along the collagen fibers inducing anisotropy in the motion of water, so any measurement of diffusion anisotropy is a measurement of the collagen integrity. PG molecules, on the other hand, do not show a preferred orientation and therefore restrict the motion of water molecules equally in all directions and can be detected by the mean vale of diffusion.

RESULTS: *DTI:* Ex vivo studies of diffusion of articular cartilage demonstrated increase of the average diffusion after selective removal of the GAG [1]. More recently, ex vivo DTI studies showed that the orientation of the first eigenvector correlate with the arrangement of the collagen fibers as measured with polarized light microscopy and scanning electron microscopy [13, 15]. Depletion of GAG results in increase of the mean diffusivity (MD) but in no change in fractional anisotropy (FA) [16, 18]. In AC samples with early signs of osteoarthritis, DTI could identify the degraded samples with high accuracy (95%) [17]. The first in vivo DTI study including healthy and OA patients demonstrated an excellent accuracy (92%) in differentiation of healthy and OA subjects [9].

T2: The T2 relaxation time in articular cartilage depends on several factors like the water content [19, 20], the proteoglycan content [20], and the collagen orientation [11, 21, 22]. T2

relaxation time has shown correlation with the histological grade [23], although some ex vivo studies show that T2 might be insensitive to detect early stages of cartilage damage previous to cartilage fibrillation [23, 24]. T2 measurement can be performed in vivo with sequences that are available in most of the scanners and has good reproducibility (~5%), although influence of stimulated echoes and SNR need to be considered for an accurate T2 measurement [25-28]. Clinical studies have found slightly increased T2 values in OA subjects as compared with healthy controls, although T2 showed no difference between mild and advance OA subjects [29]. T2 maps of articular cartilage has been demonstrated to be more sensitive to de detection of focal lesions [30] and to significantly improve the sensitivity to detect cartilage lesions when combined with clinical sequences [31]. The osteoarthritis initiative (OAI) provided data to demonstrate the association of increased T2 in articular cartilage with Body Mass Index (BMI), higher activity levels and elevated pain levels [32].

CONCLUSION: Diffusion imaging and T2 are promising techniques to explore the integrity of the collagen integrity with potential for the early diagnosis of early OA.

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