

In vivo DTI of articular cartilage: A new set of biomarkers for the early diagnosis of osteoarthritis

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Introduction: Osteoarthritis (OA) is a major cause of chronic disability in most industrialized countries. In spite of intense research, the early diagnosis of OA, where pathologic changes may still be reversible, remains elusive. Articular cartilage is a key factor in the diagnostic workup of OA, since imbalance between cartilage degradation and repair is involved early in the pathogenesis of OA. Diffusion tensor imaging (DTI) has surged as a very promising technique for the early detection of OA, since DTI parameters are sensitive to both the proteoglycan content and the collagen architecture [1–3]. However, until now DTI of articular cartilage was only available ex vivo. The aim of this study was to assess the potential value of in vivo DTI of articular cartilage for the early diagnosis of OA as compared with a widely used proton-based non-contrast-enhanced MRI parameter: the T2 relaxation time.

Methods: The patellar cartilage of 16 healthy volunteers (mean age 30.7±2.3 y, no episodes of knee pain for three years, no history of trauma or surgery) and 8 OA-diagnosed patients (mean age 62.6±8.8 y) from the NYU-HJD cohort established in the department of rheumatology were imaged on a whole body 7-T scanner (Siemens Healthcare, Erlangen, Germany) with a dedicated birdcage transmit, 28-channel receive knee coil (QED, Cleveland OH). In order to obtain a sample of patients with early morphologic cartilage degeneration, patients were selected based on previous MRI examinations. Inclusion criteria were cartilage signal abnormalities and absence of visible cartilage defects or cartilage erosion. The MRI protocol included a high-resolution T2*-weighted FLASH sequence (TE/TR = 9.2/40 ms, flip angle = 15°, Matrix = 384×384×192, GRAPPA acceleration = 4, isotropic resolution = 0.5 mm, slice thickness = 2 mm, TA = 10:02 min), a Line Scan Diffusion Imaging (LSDI) sequence [4] (FOV = 154×77 mm², TE/TR/TR_{eff} = 46/180/2890 ms, matrix = 256×128, rotation angle (α) = 20°, in-plane resolution = 0.6×0.6 mm², 5 slices, slice thickness = 2 mm, slice gap = 5 mm, b-values = 0, 450 s/mm², 6 directions, bandwidth = 500 Hz/Pixel, acquisition time (TA) = 14:03 min) and a multi-slice multi-echo (MSME) sequence for T2 calculation [5] (TE/TR = 16/3800 ms, echo train length = 6, echo spacing 16 ms, Matrix = 256×256, in-plane resolution = 0.6×0.6 mm², slice thickness = 2 mm, 5 slices, slice gap = 5mm, TA = 13:40 min). The slice of the GRE sequence with the thickest patellar cartilage was selected as the central slice of the LSDI and MSME sequences. Cartilage was segmented in the first echo of the MSME sequence and maps were calculated: T2, ADC, FA and the diffusion angle, θ (i.e. the orientation of the first eigenvector relative to the vertical direction). In each of the 5 slices of each volunteer, the cartilage was automatically divided into 2 layers parallel to the bone-cartilage interface (BCI) and four consecutive sectors from medial to lateral. For each voxel at the BCI trajectories from the BCI to the articular surface (AS) were obtained and the profiles of each MRI parameter along these trajectories were calculated. Differences between the healthy and OA collectives were assessed with the non-parametric Wilcoxon test for each MRI parameter globally (averaged over all the slices), by layers, by sectors and for each point in the parameter profile.

Results: Fig. 1A shows representative parameter maps for an OA (top) patient and an example of a healthy volunteer (bottom). OA patients consistently showed increased ADC and reduced FA in at least one of the facets (Fig. 1A). Areas of abnormal ADC or FA values were larger and change was much more prominent than the areas of increased T2 values (Fig. 1A). This is illustrated quantitatively by the averaged profiles across cartilage in the healthy (5360 profiles) and OA (2678 profiles) collectives (Fig 1B). Healthy subjects showed the typical increase in T2 and ADC and a decrease of FA from the BCI to the AS. OA patients had significantly (P<0.05) increased ADC and reduced FA profile values across the complete cartilage depth. OA T2 profiles differed significantly from healthy T2-profiles only in the superficial 30% of the cartilage (Fig. 1C). The diffusion angle showed significantly reduced values in the upper 60% of the cartilage in the OA collective.

Globally, ADC and FA differed significantly (P<0.005) between the OA and the healthy collective, whereas for T2 and diffusion angle no such significant difference could be determined. A cutoff of $1.2 \times 10^{-3} \text{ mm}^2/\text{s}$ in ADC and 0.40 in FA for the differentiation of healthy and OA patients resulted in a specificity of 100% (16/16), a sensitivity of 87.5% (7/8), a positive predictive value of 100% (7/7) and a negative predictive value of 94.1% (16/17). In the two layers and the 4 sectors ADC was significantly higher and FA was significantly lower (P<0.05) in the OA population than in the healthy collective, whereas no difference could be assessed in T2 and the diffusion angle.

Conclusions: In vivo DTI of articular cartilage provides new proton-based non-contrast enhanced biomarkers for the early diagnosis of OA. Our data suggest that, upon confirmation in a larger trial, cutoff values for ADC and FA may be practical to differentiate healthy from OA subjects. In our population DTI appeared to reflect changes in articular cartilage more prominently than the T2 relaxation time.

References:

[1] Filidoro et al. MRM 2005;53:993–998; [2] Meder R et al. Osteoar. Cartil. 2006;14:875–883; [3] Deng X et al. JMRI. 2007;14:875–883; [4] Gudbjartsson H et al. MRM 1996;36:509–519; [5], Mendlik T et al. Invest Radiol. 2004;39:288–299.

Figure 1. **1A.** Representative ADC, FA, diffusion angle and T2 maps in an OA patient (60 y, top) and a healthy volunteer. Observe the increased ADC and reduced FA in the medial facet, whereas T2 shows markedly less pronounced changes. **1B.** Averaged profiles in volunteers (n=5360) and patients (n=2678) for ADC, FA and T2. ADC and FA showed significant differences across the complete cartilage depth, whereas T2 did so only in the most superficial 30% of cartilage. **1C.** Differences in averaged values between healthy and OA collectives. The dashed line represents the cutoff ($1.2 \times 10^{-3} \text{ mm}^2/\text{s}$ in ADC and 0.40 in FA), and + indicates the only OA patient presenting normal values.

