Change in the DTI parameters of the articular cartilage with progressive proteoglycan depletion

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Introduction: The process of degradation of the articular cartilage during osteoarthritis (OA) involve a progressive loss of proteoglycan and a subsequently disruption of the collagen network. DTI has great potential for the early diagnoses of OA since it seems to be sensitive both to the PG content and the integrity of the collagen network [1–3]. The aim of our study was to investigate the effect of progressive proteoglycan (PG) depletion on the DTI parameters and to characterize the sensitivity of DTI parameters to detect early changes in OA.

Methods: Cylindrical bone-on-cartilage samples (n = 12) were drilled from healthy patellae (n = 4, (28±23) y) and halved. One halve underwent histology with Safranin-O staining to determine the PG content of the intact sample. The other halve was imaged on a 17.6-T MRI scanner (Bruker Advance, Bruker Biospin GmbH, Rheinstetten, Germany) using a 5-mm birdcage coil. For DTI measurement a diffusion-weighted spin-echo (SE) sequence was used (TR/TE=938/15.0 ms, b-values=0, 550 s/mm², 6 directions, 10 averages (avg), bandwidth (BW)=130.0 kHz, acquisition time (TA)=2:20 h). Since T2 is known to be primarily dependent on the collagen structure of the cartilage [4], T2 was also measured with a multiecho SE sequence (TR/TE=938/7 ms, echo spacing=7 ms, 20 echoes, BW=138.9 kHz, 16 avg, TA=20:00 min) to control that the collagen structure remained intact after PG depletion. Sequences used the same FOV of 12.8×12.8 mm², in-plane resolution of 50×100 µm², and slice thickness of 800 µm. Maps of T2, ADC, FA and the diffusion angle, θ (i.e. the angle of the first eigenvector with respect to the direction perpendicular to the articular surface) were calculated for each sample. In each imaging session three samples were examined. After the first MRI session two of the samples were immersed in a very diluted solution of trypsin (0.1 mg Trypsin/1 mg physiologic solution, i.e. between 100 and 250 fold more diluted than in other MRI experiments), whereas the third was kept as negative control in physiologic saline. All three samples were placed in an incubator at 37 °C for a distinct period of time (6, 48, 72 and 96 h) and subsequently measured again with MRI. Safranin-O-stained histological cuts were obtained from each sample after MRI. PG content was semiquantitatively assessed by digitizing the histological cuts with a microscope (Mirax-Midi, Carl Zeis, Jena, Germany). The intensity of staining, representing the PG content, was assessed as the Safranin-O index (SOi) after conversion of the images to a grey scale.

Results: The average change in each MRI parameter against the depletion time is represented in Fig 1.A. Fig 1.B represent the PG loss with increased incubation time as measured by the Safranin-O index. Figs. 1.A and B clearly demonstrate that the PG loss only has a significant effect on the ADC, which confirms previous results obtained with complete PG depletion [2,3]. Negative controls did not present significant changes in any parameter. Only the changes in ADC before and after PG depletion showed a significant correlation with the loss of PG as measured by the SOi (ADC: r^2 = -0.86, P<0.007 (Fig. 1.C), FA: r^2=0.62, P = 0.1; θ: r^2 = 0.06, P = 0.88; T2: r^2 = -0.11, P = 0.80). To analyze the depth dependent effect of PG depletion, 10 equally sized regions were defined in each sample covering the cartilage from the articular surface down to the bone-cartilage interface. For each region the correlation between mean change in the MRI parameters and the difference in SOi (i.e. proteoglycan loss) was calculated. Again, only the ADC changed with PG loss. Change in ADC was less pronounced in the superficial 20% of the cartilage and in the deep radial zone, where the changes in ADC per unit of SOi was around 60% of the changes in the rest of the cartilage (-3.1×10^{-5} mm^2/s/unit SOi).

Conclusions: Our results demonstrate that DTI represents a promising method for diagnosing early OA, since it can detect pathological changes in cartilage induced by a PG loss (ADC) and diagnose the integrity of the collagen structure (FA, diffusion angle). T2 did not show any difference with PG depletion, thus demonstrating the conservation of the collagen structure during depletion.

References:

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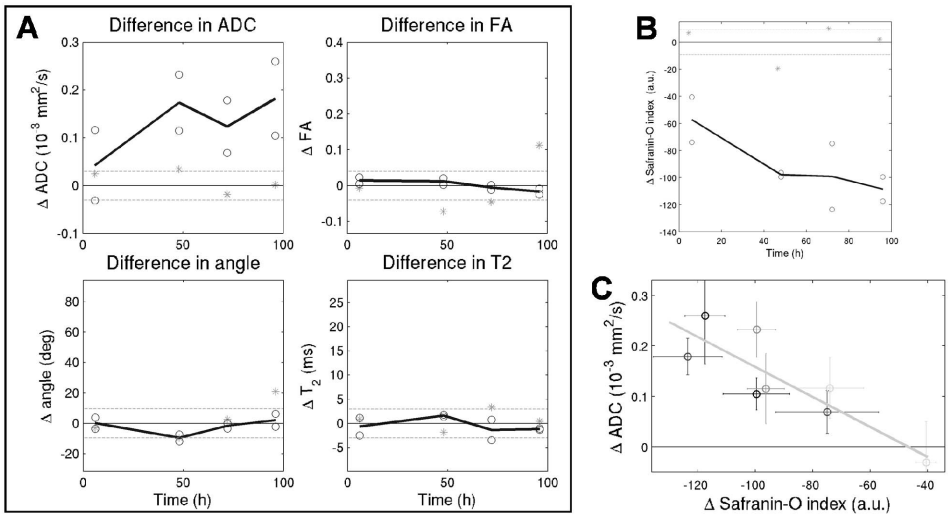

Figure 1. 1A. Mean change in ADC, FA, diffusion angle and T2 with increased depletion time. Circles represent depleted samples, stars negative controls. The dashed lines represent the standard deviation of the measurement errors, and black solid lines represent the mean of the two depleted samples. The negative control which underwent incubation during 96 h, was affected by artifacts, which diminished quality of the maps. **1B.** Change in Safranin-O index with the time of trypsin treatment. **1C.** Correlation between the change in ADC with the PG depletion as measured with the Safranin-O index. Only the changes in ADC showed a significant correlation with the change in Safranin-O index (r^2=0.86, P<0.007).