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CONTRAST-ENHANCED MRI AS A MEANS TO STUDY CARTILAGE STRUCTURE

L. Dahlberg*, L. E. Olsson**, P. Leander***, O. Ekberg***, C. J. Tiderius*.
*Departments of * Orthopaedics **Radiation Physics ***Radiology, Malmö University Hospital, Sweden*

Introduction: A major issue in OA research has been the fact that cartilage changes develop over decades, however, our ability to identify such changes before severe joint cartilage disease occur has been limited. Since treatments attempted at restore the functional properties of the joint cartilage likely is more successful if initiated before such severe matrix changes develop, we must be able to identify the earliest phases of disease changes. Magnetic resonance imaging (MRI) has become the most accurate method to image articular cartilage structure as well as to provide information about surrounding soft tissues and subchondral bone non-invasively. However, in earlier stages of cartilage pathology, conventional MRI sequences have shown limitations in providing a detailed assessment of the matrix. In OA research, it would be more valuable to be able to image and quantify macromolecules in the matrix, particularly those that are altered early in the OA disease. A method to study cartilage GAG content is delayed contrast enhanced MRI of cartilage (dGEMRIC). This technique is based on the principle that the negatively charged contrast agent (Gd-DTPA^{2-}) distributes in the cartilage in an inverse relationship to the GAG content. In normal cartilage Gd-DTPA^{2-} is repelled by the abundant negatively charged GAG, whereas in conditions of GAG loss, more Gd-DTPA^{2-} will be distributed within the cartilage matrix. To address the issues of the *in vivo* dose-response distribution in cartilage as well as the time window for MR imaging after contrast injection we examined the temporal pattern of Gd-DTPA^{2-} distribution in knee cartilage at three different doses in healthy volunteers. It was shown that dGEMRIC has a linear dose-response distribution in femoral weight bearing cartilage with the highest concentration between two and three hours post-contrast (1,2,3).

To explore the potential of dGEMRIC, we compared Gd-DTPA^{2-} distribution in femoral knee joint cartilage in sedentary and physically active subjects after an intravenous injection of Gd-DTPA^{2-}. This to test the hypothesis that cartilage is an adaptive tissue, as suggested from animal studies. Moderately exercising dogs have shown an increased proteoglycan content in their knee cartilage (4).

Methods: 28 healthy volunteers (age 21-30 years) were included in this cross-sectional study. Obesity (BMI>30 kg/m^2) and previous knee injury were exclusion criteria. The subjects were divided into two groups according to their level of physical activity during the previous two years, no regular activity (n=12), and exercise 2-4 times a week (n=16). The most common activities were jogging and workout at a gym.

Gd-DTPA^{2-} was administered intravenously at the dose of 0.3mmol/kg.bw (triple dose). After the injection, subjects walked in stairs during approximately seven minutes in order to optimize the distribution of the contrast medium into the cartilage. MRI examinations were performed two hours post-contrast using a 1.5 T machine (Siemens Magnetom Vision). Quantitative relaxation rate (R1) measurements were made in regions of interest (ROI's) in the femoral cartilage using a single slice sagittal turbo inversion recovery sequence with different inversion times. All ROI's were drawn by one single investigator and positioned in the central weight-bearing medial femoral cartilages (ROI size: 150-250 pixels). Student's t-test was used for the statistical analyses.

Results: Subjects with no regular physical exercise had significantly higher distribution of the contrast medium in the weight-bearing medial femoral cartilage, approximately 15%, (p<0.01) (table). higher R1 than both groups of exercising individuals.

Exercise level	1 (n=12)	2 (n=16)
R1 medial (mean±SD)	2.8±0.3	2.4±0.2

Table. R1 (mean±SD) in medial femoral weight-bearing cartilage.

Discussion and Conclusions: Results suggest a higher proteoglycan content in the cartilage of regularly exercising individuals. To our knowledge this is the first human study to indicate that cartilage, in similarity to other skeletal tissues, may have the capacity to adapt to physical demand.

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