RELATIONSHIP BETWEEN EPIDEMIOLOGIC OA RISK FACTORS AND CARTILAGE QUALITY ASSESSED BY dGEMRIC

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INTRODUCTION
In knee osteoarthritis (OA), exogenous factors such as previous meniscus injury, obesity and reduced lower extremities muscle strength often precede radiographic knee OA. With the advent of delayed Gadolinium-Enhanced Magnetic Resonance Imaging of Cartilage (dGEMRIC) it has become possible to examine the relationship between the quality of the joint cartilage and OA risk factors in order to understand more of the aetiology of OA. dGEMRIC, that specifically measures the in vivo fixed charge density comprised by the glycosaminoglycans (GAG), has shown reduced GAG content in patients with early knee OA, hip dysplasia and after knee anterior cruciate ligament injury (Tiderius 2003, 2005; Kim 2003), whereas exercising subjects show increased cartilage GAG content (Tiderius 2004; Roos 2005).

It has been suggested that GAG loss with impaired matrix viscoelastic properties may compromise the fibril network and eventually result in the overt cartilage destruction in OA. To find support for such a hypothesis we studied the relationship between obesity, reduced knee extensor strength and function, and joint cartilage GAG content in meniscectomized patients assessed by T1(Gd).

METHODS
45 patients (age 35-45, 16 women) at risk for OA due to arthroscopic meniscectomy were included. Cartilage was intact in 23 subjects, had surface lesions in 19 and minor localized full thickness lesion in 4 subjects. Subjects with cruciate ligament injury, severe cartilage changes, steroid medication, depression, sick leave/sick pension caused by knee dysfunction, lack of outdoor walking ability or competitive athletes, were excluded.

MRI was performed by a standard 1.5 T MRI-system (Magnetom Vision; Siemens Medical Systems, Erlangen, Germany) approximately two hours after injection of the contrast agent (Gd-DTPA) at 0.3 mmol/kg. To optimize the contrast agent distribution into the joint, subjects exercised fifteen minutes on a bicycle for ergometer tests starting within 10 minutes after injection. Sets of six sagittal turbo inversion recovery images with different inversion times were acquired, TR=2000 ms, TE=15 ms, Fov=120 x 120 mm2, matrix=256 x 256, TI=50-1600 ms. In each set of images, a region of interest (ROI) was positioned in a central slice in the weight bearing cartilage of the medial femoral condyle. The ROI was chosen to include the full thickness of the femoral cartilage where OA lesions appear first. Quantitative T1(Gd) relaxation time calculations were performed using the mean signal intensity from each ROI as input to a three-parameter fit.

Isokinetic muscle strength (Nm) was calculated in percentage of body weight (Biodex®). Body Mass Index (BMI kg/m2) was calculated and self-reported disease-specific questionnaire Knee injury and Osteoarthritis Outcome Score (KOOS) was used to assess knee-related symptoms and pain (Roos 1998). Functional performance was assessed by one leg hop (Tegner 1986) and one leg rising tests (Larsson 1998). Using regression analyses, muscle strength, BMI, pain and function were correlated to T1(Gd). The study was approved by the institutional review board.

RESULTS
There were no differences between men and women in age (p=0.21), BMI-level (p=0.69), strength (p=0.12-0.86), functional performance (p=0.28-0.98) or self-reported outcome (p=0.3-0.8). The mean BMI value (kg/m2) for the group was 26.5 (20.0-34.3). Thirty-one patients had BMI>25, and 9 patients BMI>30. The meniscectomy was performed 4.4 years prior to investigation (median).

T1(Gd) relaxation time of the study group was 355±65ms (mean±sd). There were no T1(Gd) difference between men and women and no relationship between T1(Gd) and age or time from meniscectomy.

There was a positive relationship between T1(Gd) and knee extensor strength relative to body weight (r = 0.34, r² = 0.20, p=0.002) (Fig 1) and to the functional performance test one leg hop (r = 0.38, r² = 0.14, p=0.010) (Fig 2) as well as between T1(Gd) and self-reported symptoms (r = 0.32, r² = 0.10, p=0.033) but not between T1(Gd) and self-reported pain (r²=0.07, p=0.072) (Fig 3) and not with one leg rising (r = 0.22, r² = 0.05, p=0.149). A negative correlation was found between T1(Gd) and Body Mass Index (r = -0.48, r² = -0.23, p = 0.001) (Fig 4).

The multivariate analyse showed that lower BMI, higher knee extensor strength and better symptom score predict higher T1(Gd).

DISCUSSION
The increased risk to develop knee OA in middle-aged subjects previously meniscectomized because of a degenerative tear enables us to study cartilage matrix features related to cartilage disease in these subjects. The present study indicates that the recognized OA risk factors meniscectomy, corresponds to a decreased content of GAG, since T1(Gd) in a previous study in healthy volunteers was 10-15 % longer than in the diseased compartment in the present subjects (Tiderius et al. 2004). Furthermore, knee extensor strength and overweight are inversely related to T1(Gd). Interestingly, there was a trend to a relationship between pain and T1(Gd), as previously suggested in hip OA (Kim YJ et al. 2003).

The study’s cross-sectional design does not allow conclusions about causality. However, reduced knee extensor strength and obesity may precede radiographic knee OA and exercise relieves knee symptoms and has the potential to increase knee cartilage GAG content. Accordingly, it seems possible that one molecular mechanism in OA development is that inactivity causes lower GAG content which impairs cartilage capacity to resist load. Obesity and muscle weakness further increases the stress and strain forces on the joint. Eventually, this may trigger degenerative processes causing molecular cleavage and overt cartilage damage.

REFERENCES