# Effect of Joint Loading on T2 relaxation and dGEMRIC of Knee Cartilage in Marathon Trainers

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## INTRODUCTION

Previously, in animal studies moderate exercise has been shown to increase proteoglycan (PG) content and stiffness of articular cartilage [1,2]. Rigorous training, however, may lead to site dependent depletion of PGs, deterioration of collagen network and elevation of cartilage water content, i.e. alterations resembling degenerative changes [3,4]. Quantitative MRI techniques provide means to indirectly study the macromolecular status of cartilage. Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) reflects the PG concentration of cartilage in vivo [5], while T2 relaxation time mapping is sensitive to the integrity and arrangement of the collagen network [6] and water content [7].

Human marathon trainers were studied to investigate the effect of six-month intensive running exercise, as controlled by biomechanical joint loading measurements, on the macromolecular status of cartilage as measured by qMRI.

## METHODS

Initially, 41 male volunteers (24-46 years) were enrolled. Exclusion criteria included history of competitive sports within 5 years, running more than 30 km/week within 2 years and operations or acute symptoms on the knee to be followed. Twenty trainers and 9 controls participated at baseline, 16 trainers and 8 controls at 6-months follow-up. For biomechanical measurements, loading rate (LR) and the maximum vertical component of the ground reaction force of lower extremity (F) were determined at baseline, aerobic threshold level (AT) both at baseline and follow-up. The mean number of foot contacts/impacts (IMP) per week at training level of aerobic threshold was determined at follow-up. Quantitative MRI of the knee cartilage was performed at 1.5T at baseline and follow-up. T2 was measured (multi echo spin echo sequence with TR/TE=1500ms/15, 30, 45, 60ms; 5-mm slice thickness; 0.27x0.27mm in-plane resolution) in the sagittal plane covering the central weight-bearing area of lateral and medial femoral condyles. This was followed by the dGEMRIC-experiment, i.e. T1 measurement (inversion recovery fast spin echo sequence (TR/TE/TI=1800ms/16ms/50, 100, 200, 400, 800, 1600ms; 5-mm slice thickness; 0.27x0.27mm in-plane resolution) 90min after i.v. administration of 0.2mM/kg Gd-DTPA(2-). BMI-correction was applied on dGEMRIC data [8]. The weight bearing areas of femoral and tibial cartilage were divided into several regions of interest (ROIs) and separately into superficial and deep half of the tissue (Fig. 1). The mean T2 and dGEMRIC index were determined for each ROI.

Mann-Whitney U-test was used to compare trainers and controls, Wilcoxon test to evaluate change from baseline to follow-up, and Pearson correlation analysis to assess the relationship between MRI and biomechanical measurements in pooled data of controls and trainers.

## RESULTS

At baseline, trainers had a higher AT than controls (T:9.5±1.7km/h, C:8.0±0.7km/h; p=0.05), however, the difference increased at follow-up (T:11.1±1.5km/h, C:8.2±0.8km/h; p<0.001). At follow-up, trainers had more contacts per week (IMP) than controls (T:48400±16200, C:7400±7600; p<0.001).

At baseline, the T2 relaxation time at cLTs showed longer values for trainers as compared to controls (T:30.2±3.3ms, C:27.5±1.7ms, p=0.02). At follow-up, T2 was systematically higher in six ROIs of the tibia for trainers as opposed to controls (Table 1). However, when comparing T2 between baseline and follow-up measurements, a decreasing trend in T2 was seen at three ROIs for trainers and at five ROIs for controls (Table 2). Significant correlations for pooled data were observed at baseline between T2 and AT at cLTs, cMTs and pMTd (r=0.43-0.50), and between T2 and LR at aLTs and cLTs (r=-0.39). Significant correlations were observed at follow-up between T2 and AT at cMTs and pMTs (r=0.49-0.68), between T2 and IMP at cLTs, pLTd, pLTs, cMTs and pMTs (r=0.46-0.61).

At baseline, the dGEMRIC index at cLTs showed longer values for trainers as compared to controls (T:512±33ms, C:471±72ms, p=0.04). At follow-up, trainer and control groups did not differ. During training dGEMRIC increased at three ROIs and decreased at one ROI for trainers, and increased for three ROIs for controls (Table 2). Statistically significant correlations were observed between dGEMRIC and AT at pLFd (r=0.47), and between dGEMRIC and F at cMFd (r=-0.44) and pMTs (r=-0.37). At follow-up, a statistically significant negative correlation was observed between dGEMRIC and AT at cMTs (r=-0.45).

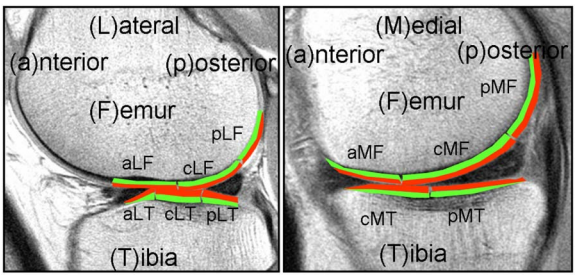


**Figure 1**: Division and nomenclature for ROIs. Suffix "s" and "d" are used in text for superficial and deep cartilage, respectively.

**Table 1**: T2 at follow-up for ROIs with significant differences between trainers and controls (Mann-Whitney U test)

| ROI | trainers | controls | p-value |
|---|---|---|---|
| cLTd | 23.4±1.6 | 22.0±1.3 | 0.03 |
| cLTs | 30.1±3.1 | 27.3±1.6 | 0.02 |
| pLTd | 28.6±3.0 | 25.8±3.3 | 0.03 |
| pLTs | 35.6±2.5 | 32.8±2.9 | 0.03 |
| cMTs | 36.8±2.4 | 33.2±2.1 | 0.002 |
| pMTs | 36.7±2.9 | 32.8±3.1 | 0.005 |

**Table 2**: T2 and dGEMRIC values for ROIs with significant differences between baseline and follow-up (Wilcoxon test)

| | ROI | baseline | follow-up | p-value |
|---|---|---|---|---|
| **T2** | | | | |
| Trainers | pLFd | 34.3±3.2 | 33.7±2.5 | 0.06 |
| | aLTs | 36.2±5.3 | 31.3±8.5 | 0.02 |
| | pLTd | 26.5±2.9 | 28.6±3.0 | 0.03 |
| | cMTd | 25.0±1.8 | 24.1±1.5 | 0.03 |
| Controls | pLFd | 32.5±4.4 | 31.5±3.9 | 0.05 |
| | pLFs | 38.1±5.4 | 35.7±3.9 | 0.04 |
| | aLTs | 34.4±6.0 | 31.8±4.5 | 0.01 |
| | cLTd | 24.0±2.2 | 22.0±1.3 | 0.02 |
| | cMTd | 25.6±2.2 | 23.3±2.4 | 0.01 |
| **dGEMRIC** | | | | |
| Trainers | pLFs | 437±58 | 479±71 | 0.04 |
| | cMFd | 508±55 | 486±50 | 0.04 |
| | cMFs | 494±71 | 538±40 | 0.03 |
| | pMFs | 440±62 | 482±55 | 0.01 |
| Controls | cMFs | 482±50 | 538±24 | 0.04 |
| | pMFs | 441±53 | 489±50 | 0.01 |
| | cLTd | 490±54 | 526±36 | 0.02 |

## DISCUSSION

To our knowledge this is the first MRI study to report the response of human articular cartilage to intensive long-term running training. Our results here show that training results in subtle but significant local changes in T2 and dGEMRIC in the femoral and tibial load bearing compartments. The T2 results show a trend towards prolonged values after intensive training but also when the quality of loading is stressful for the joint. Previously, prolonged T2 values have been related to a degenerative change in collagen properties and/or an increase in cartilage hydration [6-7].

**REFERENCES:** [1] Kiviranta I et al. J Orthop Res 1998;6:188-195. [2] Jurvelin JS et al. Int J Sports Med 1986;7:106-110. [3] Säämänen AM et al. Connective Tissue Res 1994;30:191-201. [4] Arokoski J et al. Arthritis Rheum 1993;36:1451-1459. [5] Bashir A et al. Magn Reson Med 1999;41:857-865. [6] Nieminen MT et al Magn Reson Med 2000;43:676-681. [7] Lüsse S et al. Magn Reson Imaging 2000;18:423-430. [8] Tiderius C et al. Osteoarthritis Cartilage 2006;14:1091-1097.