CORRELATION BETWEEN QUANTITATIVE DELAYED CONTRAST-ENHANCEMENT IN MENISCUS AND CARTILAGE IN KNEE OSTEOARTHRITIS

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Purpose: Damage to the meniscus is known to play an important role in the development of knee osteoarthritis (OA) [1]. To assess the relation between meniscal damage and articular cartilage degeneration, quantitative analysis of delayed contrast-enhanced T1 values ($T1_{GD}$) was proposed to give insight in the degeneration of both structures within one MR examination [2-3]. It has been shown that there is a relation of $T1_{GD}$ of the meniscus and the adjacent cartilage in volunteers and self-reported knee OA patients (no OA diagnosed by a physician) [2]. This relation has, however, not yet been studied in patients diagnosed with OA. Therefore, the goal of this study was to explore the relation between $T1_{GD}$ values of the meniscus and the adjacent articular cartilage in knee OA patients.

Methods: We retrospectively analyzed data of 17 patients previously used to investigate the reproducibility of delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) [4]. All patients were diagnosed with early stage knee OA (knee complaints >3 months, NRS pain >2 and Kellgren and Lawrence (KL) grade 1 or 2 on radiography) and underwent dGEMRIC after a 1.5 hour delay. All examinations were performed on a 3T MRI scanner (Discovery MR750, GE Healthcare, Milwaukee, WI, USA) using a custom made open design 3-channel knee coil, enabling imaging of large diameter (>15 cm) OA knees. The dGEMRIC protocol consisted of a 3D FSPGR sequence with five different inversion times (TI = 2100, 800, 400, 200 and 100 ms) [5]. To correct for patient motion during MR acquisition, all scans with different TIs were rigidly registered in 3D using the TI=2100 images as fixed dataset. The femoral and tibial regions were registered independently, using an automatic method based on maximization of mutual information [6]. After registration, $T1_{GD}$ relaxation times in the anterior (antM) and posterior horn (postM) of the meniscus and in the adjacent weight-bearing femoral (wbFC) and tibial (wbTP) cartilage in the medial and lateral tibiofemoral compartment were calculated based on manually drawn regions of interest. $T1_{GD}$ values in all regions (meniscus and cartilage) in the medial and lateral compartment were compared using the Mann-Whitney test. In addition, the correlation coefficients between $T1_{GD}$ values of the meniscus and cartilage were calculated to assess the relation between degeneration of both structures.

Results: Median meniscus and cartilage $T1_{GD}$ values in the medial and lateral tibiofemoral joint are listed in *Table 1*. The correlation between $T1_{GD}$ values in the meniscus and adjacent cartilage regions was moderate in the lateral and strong in the medial tibiofemoral compartment (*Figure 1 and Table 2)*. Examples of a meniscus with adjacent cartilage with relatively low $T1_{GD}$ values and a meniscus with adjacent cartilage with relatively high $T1_{GD}$ values are shown in *Figure 2*.

Region	Lateral compartment	Medial compartment	p
antM $T1_{GD}$ (ms)	413 (375 - 435)	350 (315 - 485)	ns
postM $T1_{GD}$ (ms)	404 (330 - 441)	382 (314 - 355)	ns
wbFC $T1_{GD}$ (ms)	510 (466 - 574)	433 (410 - 506)	0.04
wbTP $T1_{GD}$ (ms)	607 (463 - 664)	465 (430 - 566)	0.04

Table 1. Median $T1_{GD}$ values with 25^{th} – 75^{th} percentile

Lateral compartment	wbFC	wbTP
antM	R = 0.78 95% CI = 0.48 - 0.92	R = 0.75 95% CI = 0.42 - 0.90
postM	R = 0.73 95% CI = 0.38 - 0.89	R = 0.73 95% CI = 0.38 - 0.90
Medial compartment	**wbFC**	**wbTP**
antM	R = 0.95 95% CI = 0.86 - 0.98	R = 0.88 95% CI = 0.68 - 0.95
postM	R = 0.88 95% CI = 0.69 - 0.96	R = 0.83 95% CI = 0.57 - 0.94

Table 2. Correlation between $T1_{GD}$ of meniscus and adjacent cartilage with 95% CI.

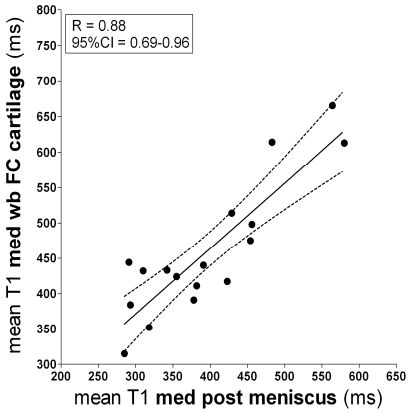

Figure 1. Correlation plot with 95% CI of med wbFC and med postM

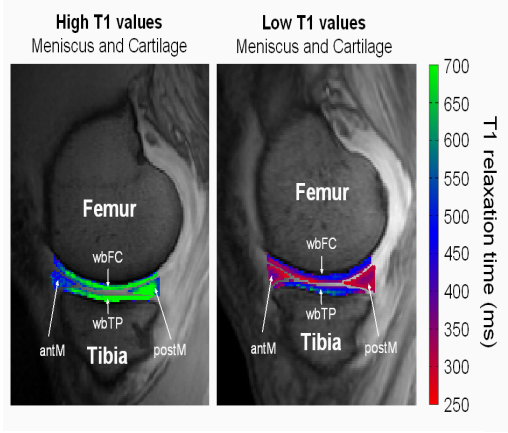

Figure 2. Example of meniscus with adjacent cartilage with relatively high and low $T1_{GD}$

Discussion: The results of the present study show a strong relation between meniscus and cartilage T1 values after intravenous injection of an ionic contrast agent. This finding is in agreement with previous research in which semi-quantitatively analyzed whole joint assessment of the knee shows an association between meniscal degeneration and cartilage loss in OA patients with KL grade > 2[1]. The correlation between meniscal and cartilage $T1_{GD}$ values is stronger compared to previously reported correlations in healthy volunteers and self-reported knee OA patients (weak to moderate) [2], which also suggest a strong relationship between degeneration of both structures in OA. However, unlike in dGEMRIC, contrast uptake in the meniscus is probably not determined by the glycosaminoglycan (sGAG) content and hence fixed charged density in the meniscus, but is rather based on the integrity of the collagen network [2, 7]. It has been shown that delayed contrast-enhancement of the meniscus can differentiate between OA and non-OA patients, both using non-ionic and ionic contrast agents [7]. The different factors which are thought to dominate contrast uptake in the meniscus and cartilage combined with the strong relation between ionic contrast uptake in the meniscus and cartilage found in our study, suggests that dGEMRIC may not be as sGAG specific as thought before: cartilage collagen integrity and/or orientation may also influence ionic contrast uptake in OA cartilage. This hypothesis is being supported by recent work of Salo *et al*. [8] and Stubendorf *et al*. [9]. Therefore, the interpretation of dGEMRIC $T1_{GD}$ outcomes in knee OA must be reevaluated in future investigations.

Conclusion: There is a strong relation between delayed contrast-enhancement in menisci and adjacent cartilage in OA patients. Since contrast uptake in both structures is thought to be dominated by different mechanisms (dependency on charge versus dependency on integrity of the collagen network), the results suggest that dGEMRIC $T1_{GD}$ values might not be as sGAG specific as thought before and that the interpretation of dGEMRIC $T1_{GD}$ outcomes must be reevaluated.

References: 1. Hunter et al. *Arthritis Rheum.* Mar 2006;54(3):795-801. **2.** Krishnan et al. *Arthritis Rheum.* May 2007;56(5):1507-1511. **3.** Mayerhoefer et al. *NMR Biomed.* Dec 2011;24(10):1210-1215. **4.** van Tiel et al. *Eur Radiol.* Aug 11 2012. **5.** McKenzie et al. *J Magn Reson Imaging.* Oct 2006;24(4):928-933. **6.** Bron et al. *Eur Radiol.* Aug 4 2012. **7.** Li et al. *J Magn Reson Imaging.* Mar 2011;33(3):731-735. **8.** Salo et al. *Osteoarthritis Cartilage.* Feb 2012;20(2):117-126. **9.** Stubendorff et al. *Osteoarthritis Cartilage.* May 2012;20(5):396-404.