

dGEMRIC as a tool for measuring changes in cartilage quality following high tibial osteotomy: a feasibility study

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SUMMARY

Objective: The high tibial osteotomy (HTO) is an effective strategy for treatment of painful medial compartment knee osteoarthritis. Effects on cartilage quality are largely unknown. Delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) enables non-invasive assessment of cartilage glycosaminoglycan content. This study aimed to evaluate if dGEMRIC could detect relevant changes in cartilage glycosaminoglycan content following HTO.

Design: Ten patients with medial compartment osteoarthritis underwent a dGEMRIC scan prior to HTO, and after bone healing and subsequent hardware removal. A dGEMRIC index (T_1Gd) was used for changes in cartilage glycosaminoglycan content, a high T_1Gd indicating a high glycosaminoglycan content and *vice versa*. Radiographic analysis included mechanical axis and tibial slope measurement. Clinical scores [Knee Osteoarthritis Outcome Scale (KOOS), visual analogue score (VAS) for pain, Knee Society Clinical Rating System (KSCRS)] before, 3 and 6 months after HTO and after hardware removal were correlated to T_1Gd changes.

Results: Overall a trend towards a decreased T_1Gd , despite HTO, was observed. Before and after HTO, lateral femoral condyle T_1Gd was higher than medial femoral condyle (MFC) T_1Gd and tibial cartilage T_1Gd was higher than that of femoral cartilage ($P < 0.001$). The MFC had the lowest T_1Gd before and after HTO. Clinical scores all improved significantly ($P < 0.01$), KOOS Symptoms and QOL were moderately related to changes in MFC T_1Gd .

Conclusions: dGEMRIC effectively detected differences in cartilage quality within knee compartments before and after HTO, but no changes due to HTO were detected. Hardware removal post-HTO seems essential for adequate T_1Gd interpretation. T_1Gd was correlated to improved clinical scores on a subscore level only. Longer follow-up after HTO may reveal lasting changes.

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Introduction

In patients with medial compartment osteoarthritis of the knee, there is 'silver level evidence'¹ that the high tibial osteotomy (HTO) leads to reduction in pain and improvement in knee function. The goals of HTO, as first described by Jackson and Waugh in 1961², are

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realignment of the limb, resulting in a transfer of weight bearing load from the degenerative medial compartment to the relatively uninvolved lateral compartment. Ideally, the need for a total knee arthroplasty is thus delayed for several years or even abolished. Over the past decade, HTO has regained in appreciation due to improved indications and guidelines, a better understanding of knee biomechanics, improved surgical techniques and implant characteristics and higher numbers of young active patients with symptomatic osteoarthritis of the knee^{3,4}. In contrast to the uniform application of HTO in clinical practice and the substantial biomechanical evidence to support this, the effects of HTO on cartilage quality are still largely unknown.

A few *in vivo* studies have attempted to describe the effect of mechanical axis realignment on cartilage quality of the knee joint. During a 'second look arthroscopy' in 58 knees, partial or complete coverage with fibrocartilage was observed in 55% of the femorotibial joint surfaces 18 months after HTO⁵. A repair with 'white scattering fibrocartilage' was achieved in 34%, and three knees showed no regenerative change. In an earlier arthroscopic evaluation of 54 knee joints after HTO, it was observed that if adequate mechanical axis correction was obtained, repair of the ulcerated region was initiated by the surviving cartilage in the affected area and the cartilage bordering in the affected area⁶. At one and one-half to two years after osteotomy, the ulcerated region was completely covered with fibrous and membranous tissue. Histological biopsies taken after HTO in two other studies demonstrated mild safranin O and collagen type II staining^{7,8}.

However, performing a routine arthroscopy or taking intra-articular biopsies as a follow-up method is not a desirable method to determine cartilage quality after HTO. A non-invasive technique to quantitatively depict cartilage glycosaminoglycan content, and thus cartilage quality, is the delayed-gadolinium enhanced magnetic resonance imaging of cartilage (dGEMRIC) technique. Since its first description in 2001⁹, the dGEMRIC technique has been used successfully in orthopaedic and rheumatologic research as well as in clinical practice^{10–12}. The dGEMRIC technique is based on the electrical polarity of gadolinium [Gd(DPTA)²⁻ ions] and glycosaminoglycans in the joint. After intravenous injection of the gadolinium, the Gd(DPTA)²⁻ ions diffuse into the joint, and subsequently distribute between the negatively charged glycosaminoglycan side chains of the cartilage in an inverse relationship⁹. Due to electrical polarity, a high concentration of glycosaminoglycans results in a lower concentration of also negatively charged Gd(DPTA)²⁻ ions and *vice versa*. As the local concentration of Gd(DPTA)²⁻ ions within the cartilage is related to the longitudinal relaxation time (T₁, ms), the value of T₁ after administration of gadolinium (T₁Gd) is representative of local cartilage glycosaminoglycan content. A high T₁ relaxation time after Gd administration thus is indicative of high glycosaminoglycan content.

The aim of this study was to examine if changes in cartilage quality caused by a HTO, in patients with medial compartment osteoarthritis of the knee, were detectable with dGEMRIC and were correlated to changes in clinical parameters of osteoarthritis.

Methods

Patients

Ten patients with medial compartment osteoarthritis of the knee were included in the study. Medial compartment osteoarthritis of the knee was defined as clinical osteoarthritis symptoms [pain, morning stiffness, decreased range of motion (ROM)] in combination with radiographic features of medial compartment osteoarthritis [joint space narrowing of the medial articular facet, medial sclerosis on anteroposterior (AP) and/or lateral X-rays]. Patients with previous surgery of the knee, total meniscectomy or anterior cruciate ligament (ACL) lesions were excluded. The indication for HTO surgery was further based on weight bearing radiographs of the complete lower extremity, in which a varus leg axis was seen in all patients.

All included patients underwent a medial opening wedge HTO. In short, an osteotomy of the proximal tibia was performed, starting from the medial side. Next, the medial collateral ligament fibres were decompressed followed by realignment of the leg towards a slight valgus axis. The patient's body weight was thus shifted from the medial articular facet to the lateral facet, where the cartilage is presumed to be relatively unaffected¹³. The newly achieved

mechanical axis was maintained using a locking compression plate and screws. No bone graft was added. The HTO was followed by a standardized regime of limited load bearing with ROM exercises and subsequently controlled weight bearing. The study was performed at the University Medical Center Utrecht and the Sint Maartenskliniek Woerden, the Netherlands, according to the guidelines set out in the Helsinki declaration, approved by the local medical ethics committee (local reference: 07.117) and registered accordingly (NCT01269944). Written informed consent was obtained from all participants before inclusion in the trial.

Primary endpoint: change in cartilage quality after HTO

All patients underwent two dGEMRIC examinations. The first dGEMRIC was performed before HTO. The second dGEMRIC was performed after bone healing and subsequent removal of HTO hardware.

Hardware removal was required to obtain adequate image quality, to avoid overwhelming metal-induced artifacts [Fig. 1]. A minimum period of 9 months was chosen between HTO and removal of hardware, to allow for adequate bone healing. The 'post' MRI was made at a minimum of 1 month after removal of the hardware, to ensure an adequate period of full weight bearing between hardware removal and MRI.

dGEMRIC

Prior to the MRI, patients were injected intravenously with Magnevist® (Bayer HealthCare Pharmaceuticals Inc, Germany) at a dose of 0.2 mmol/kg body weight and were asked to walk a standardized route under supervision of a study investigator for at least 10 min. The walking route included several flights of steps, to facilitate uptake of the Magnevist® by the articular cartilage. After 90 min, MRI scanning of the affected knee joint was performed on a clinical 1.5-T MRI scanner (Achieva, Philips Healthcare, Best, The Netherlands) using a dedicated eight-element sense knee coil (Philips Healthcare, Best, the Netherlands) as a receiver. The pulse sequence used was a 3D sagittal transient field echo (TFE) with five different inversion times (50, 150, 350, 650 and 1650 ms), resembling a previously described protocol¹⁴. The acquired voxel size was 0.625 × 0.625 × 3 mm³, 36 partitions were acquired with an in plane acquisition matrix of 256 × 232, resulting in a field of view (FOV) of 160 mm (cranio-caudal) × 145 mm (anterior–posterior) × 118 mm (right–left). As a 3D acquisition was used, the acquired voxels were contiguous in the partition direction, so there was no gap between the slices as is often used with multiple 2D acquisition schemes. The repetition time was 10 ms with an echo time of 4.3 ms and a flip angle of 20°. Including survey scans and a reference scan to measure the receive coil sensitivity profile, the total examination time was about 25 min. The average T₁ after administration of contrast agent (T₁Gd) per ROI was calculated using voxel by voxel curve fitting with the Levenberg–Marquardt optimization method, using in-house developed software (imageXplorer).

T₁Gd measurement in femoral condyle and tibial plateau cartilage

The original 3D scan was used to draw four Regions Of Interest's (ROI's) of cartilage only. The sagittal slices of the 350 ms sequence were used as they provided optimal visual distinction between the cartilage and surrounding tissues (bone, meniscus, synovium). The following ROI's were distinguished: medial femoral condyle (MFC), lateral femoral condyle (LFC), medial tibial plateau (MTP) and lateral tibial plateau (LTP). Depending on the width of the knee, four or five adjacent sagittal slices, depicting a cartilage width of 12 or 15 mm within the selected femoral or tibial compartment, were

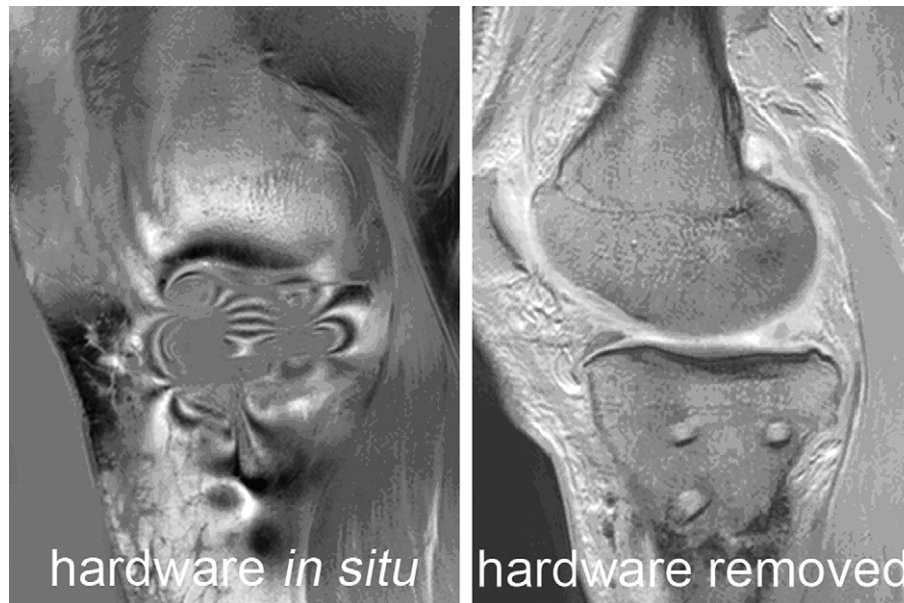


Fig. 1. Influence of HTO hardware artefacts on dGEMRIC scan result. Left: dGEMRIC scan of a HTO patient with hardware *in situ*. Gross artefacts are seen influencing T_1Gd measurements. Right: dGEMRIC scan in a HTO patient, in which hardware was removed prior to MRI. The right image is representative of all HTO patients, in whom hardware was removed.

selected to create the ROI [Fig. 2(A)]. Using these ROI's, a ' T_1Gd map' of the corresponding knee compartment was created [Fig. 2(B)]. The average T_1 of each ROI, and of all ROI's combined, was used to compare the glycosaminoglycan content in the different knee compartments before and after HTO. To assure that the ROI's were in the same area before and after HTO, in addition to positioning the knee in the same knee coil as the scan before HTO, the centre of the knee, defined as the slice depicting the sagittal crossing of the ACL and the posterior cruciate ligament (PCL), was used as anatomical reference. ROI measurements were performed by two different observers to enable reproducibility testing.

T_1Gd distribution throughout the femoral condyles

To distinguish smaller cartilage regions within the above-mentioned ROI's, the MFC and LFC ROI were divided in an anterior, a middle (load bearing) and a posterior sub-ROI. The anterior meniscus served as the border between the anterior and middle (load bearing) sub-ROI, the posterior meniscus served as a border between the middle (load bearing) and posterior cartilage sub-ROI¹⁵ [Fig. 2(C)].

Secondary endpoint: change in clinical scores

To evaluate clinical changes, all patients filled out the visual analogue score (VAS) for pain¹⁶, Knee Osteoarthritis Outcome Scale (KOOS)¹⁷ and the Knee Society Clinical Rating System (KSCRS)¹⁸ before HTO, 3 and 6 months after HTO, and after subsequent hardware removal. Correlation analysis between changes in clinical scores (KOOS, KSCRS and VAS) and changes in T_1Gd (MFC, LFC, MTP and LTP) after HTO were performed using the statistical analysis described below.

Radiographic analysis

AP and lateral views of the knee were acquired to depict the grade of knee OA. Weight bearing radiographs of the complete lower extremity were acquired to measure the pre- and

postoperative mechanical leg axis defined as the angle between the femoral and tibial mechanical axes. Furthermore, the posterior tibial slope (the angle between the slope of the tibial plateau and the line drawn perpendicular to the tibial anatomic axis, in lateral view) was measured semi-automatically as described earlier¹⁹ and compared before and after HTO. Measurements of femorotibial angle and tibial slope were performed using Philips Image Viewer Image Viewer R 11.4. Correlation analysis between the change in mechanical axis and tibial slope before and after HTO, and changes in T_1Gd within the MFC, LFC, MTP and LTP after HTO were performed using statistical analysis described below.

Statistics

Statistical analyses were performed using the statistical software SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Data were tested for normality using the Kolmogorov–Smirnov test and for homogeneity of variances using Levene's test of equality of variances. Assuming normality and equal variances, T_1Gd values before and after HTO were compared using paired *T*-testing. Clinical scores were compared using repeated measurement testing. Pearson's correlation coefficient was used for correlation analysis of changes in MFC, LFC, MTP and LTP T_1Gd (% of T_1Gd before HTO) with changes in clinical scores (% of score before HTO), mechanical axis and tibial slope. Inter-observer and intra-observer agreement of T_1Gd within the ROI's were evaluated by two observers in three knee joints using intra-class correlation (ICC) testing. Data were expressed as means \pm 95% confidence intervals (CI). $P \leq 0.05$ (*) was considered statistically significant.

Results

Patient characteristics

Eight male patients and two female patients with medial compartment osteoarthritis of the knee were included. Mean age was 53 years (range, 43–64 years), all patients were Caucasian.

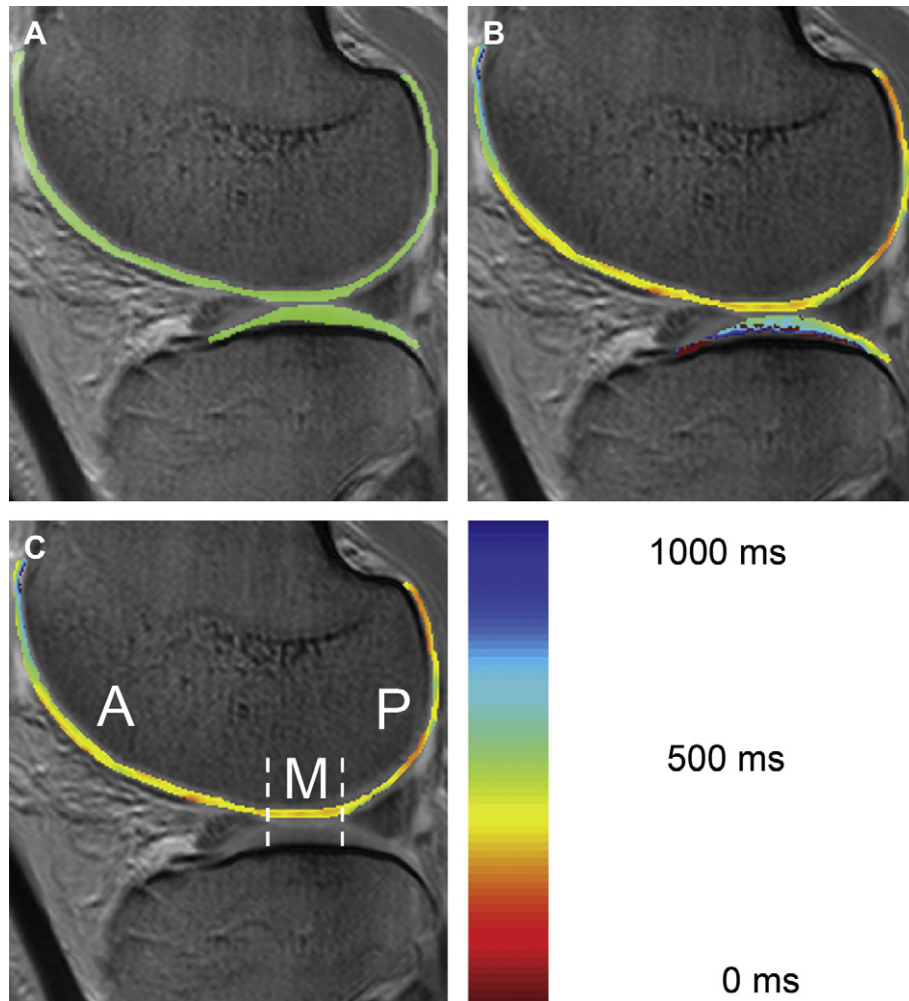


Fig. 2. 3D ROI's were generated of various sections of the knee and used for T₁Gd comparison before and after HTO. (A): Designation of the cartilaginous area on a sagittal slice of the LFC and tibial plateau. Depending on the width of the knee, four or five adjacent sagittal slices were used to create the separate 3D ROI's: the MFC, the LFC, the MTP and the LTP. (B): T₁-mapping was performed in each ROI. This section demonstrates T₁Gd distribution throughout a sagittal slice, used for creation of the LFC and LTP ROI. Using these sagittal slices, a mean T₁Gd could be calculated for each ROI. (C): A sagittal slice, used for creation of the LFC ROI is demonstrated. The MFC and LFC ROI's were divided into three different sub-ROI's, using the anterior and posterior meniscal border as anatomical landmark: Anterior (A), Middle load bearing (M) and Posterior (P) femoral cartilage.

Kellgren–Lawrence score was grade II (one patient), grade III (seven patients) and grade IV (two patients). Mean change in knee alignment after HTO was 10.0° (range, 7.8°–15.3°). The posterior tibial slope increased by 1.3° (from 8.7° to 10.0°). In one patient, hardware was removed 22 months after HTO due to delayed bone healing as seen on X-rays, followed by the dGEMRIC [Table I].

Table I
Patient characteristics

Patients	Eight males, Two females
Age	53 years (range; 43–64 years)
Weight	85.8 kg (range; 72.0–110 kg)
Length	1.78 m (range; 1.66–1.95 m)
Body mass index	28.2 (range; 25.5–32.1)
Osteoarthritis grade (Kellgren–Lawrence)	One grade II, seven grade III, two grade IV
Time HTO – hardware removal	12 months (range; 10–22 months)
○ Varus before HTO	7.1° (range; 2.0°/13.8°)
○ Varus after HTO	–3.6° (range; –5.0°/1.0°)
○ Change in mechanical axis after HTO	10.0° (range; 7.0°/15.3°)
○ Posterior tibial slope before HTO	8.6° (range; 5.1°/12.0°)
○ Posterior tibial slope after HTO	9.9° (range; 6.5°/15.3°)
○ Change in posterior tibial slope	1.3° (range; –0.3°/3.4°)

Differences in T₁Gd before and after HTO

ICC reliability analysis for inter-observer agreement in T₁Gd was 0.934 (95% CI 0.816–0.977), for the intra-observer agreement it was 0.960 (95% CI 0.885–0.986), demonstrating an excellent reproducibility. Following HTO and hardware removal, the mean T₁Gd of all ROI's combined was lower than before HTO (before: 533, 95% CI 474–632; after: 466, 95% CI 399–533; $P = 0.11$) [Fig. 3(a)]. Similar mean lower values were observed for the individual compartments (MFC $P = 0.148$, LFC $P = 0.532$, MTP $P = 0.118$, LTP $P = 0.197$). Interestingly, the postoperative femoral cartilage T₁Gd values seemed to resemble their pre-operative values to a greater extent (95% medial, 97% lateral) than the tibial cartilage values (85% medial, 84% lateral) [Fig. 3(b)]. Within the MFC, posterior cartilage T₁Gd decreased following HTO ($P = 0.047$). No correlation was detected between changes in T₁Gd within MFC, LFC, MTP or LTP and changes in mechanical axis or tibial slope (MFC $P = 0.73$ $r = -0.13$, LFC $P = 0.30$ $r = -0.39$, MTP $P = 0.38$ $r = -0.32$, LTP $P = 0.48$ $r = -0.27$).

Regional differences in T₁Gd distribution

Before HTO, T₁Gd of medial femoral cartilage (mean 379, 95% CI 332–426) was lower than that of lateral femoral cartilage (mean

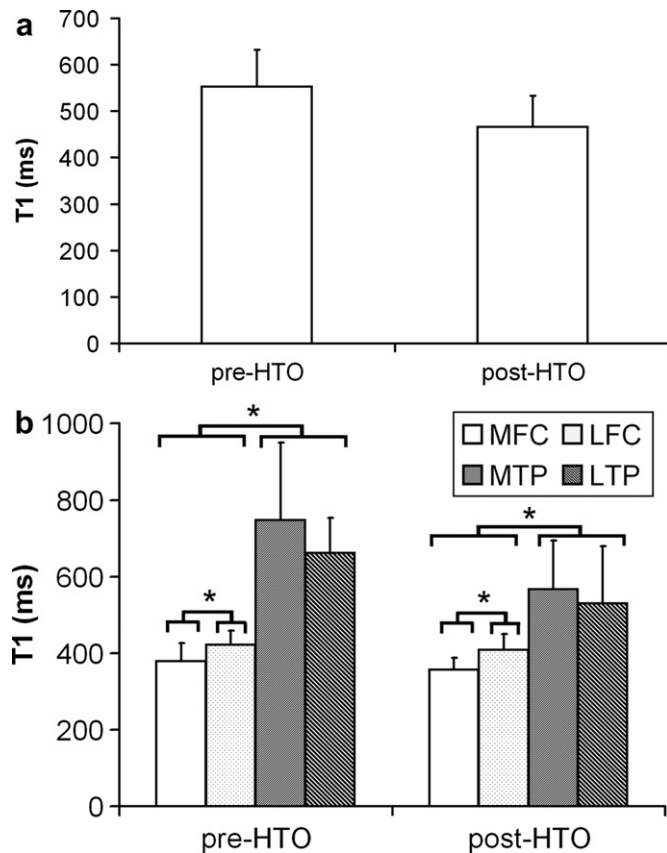


Fig. 3. (a) Mean T₁Gd values of all compartments combined, before and after HTO in 10 patients (before vs after, $P = 0.11$). Bars represent means \pm 95% CI. (b) Mean T₁Gd values of the ROI's before and after HTO in 10 patients. The decrease in T₁Gd was higher in tibial (15% decrease in MTP T₁Gd, 16% decrease in LTP T₁Gd) than in femoral cartilage (5% decrease in MFC T₁Gd, 3% decrease in LFC T₁Gd), although the differences were not significant within the separate ROI's. Before and after HTO, medial femoral cartilage had a lower T₁Gd than lateral femoral cartilage (before HTO $P = 0.007$; after HTO $P = 0.015$). Tibial cartilage had a consistent higher T₁Gd than femoral cartilage in the medial as well as lateral compartment ($P < 0.001$). Bars represent means \pm 95% CI.

423, 95% CI 387–459; $P = 0.007$). Femoral cartilage had a lower T₁Gd than the opposing tibial cartilage (MTP mean 748, 95% CI 547–909, LTP mean 662, 95% CI 571–753; $P < 0.001$). Within the MFC surface, cartilage of the anterior aspect of the femoral condyle (mean 371, 95% CI 330–412) had a lower T₁Gd than the posterior femoral cartilage (mean 407, 95% CI 461–453) ($P = 0.036$). Middle (load bearing) cartilage had the lowest T₁Gd in the medial (mean 364, 95% CI 304–424) as well as LFC surface (mean 412, 95% CI 380–444).

After HTO, medial femoral cartilage T₁Gd (mean 356, 95% CI 325–387) was lower than that of the lateral femoral cartilage

(mean 409, 95% CI 369–449; $P = 0.015$) and femoral cartilage had a lower T₁Gd than tibial cartilage (MTP mean 567, 95% CI 440–694; LTP mean 531, 95% CI 383–679; $P = 0.008$), similar to before HTO [Fig. 3(b)]. In the MFC, anterior cartilage T₁Gd (mean 365, 95% CI 334–396; $P = 0.001$) and posterior cartilage T₁Gd (mean 376, 95% CI 333–419; $P = 0.001$) were greater than middle (load bearing) femoral cartilage (mean 306, 95% CI 276–336). In the LFC, no significant differences between the sub-ROI's were observed post-HTO.

Improvement of clinical scores

Clinical scores improved significantly following HTO; the VAS for pain, the KSCRS and KOOS scores for pain, symptoms, ADL and Quality of Life (QOL) all improved ($P < 0.01$) except for KOOS sports ($P = 0.15$). A moderate correlation existed between improvement in KOOS subscore for Symptoms ($r = 0.63$, $P = 0.05$) and KOOS QOL ($r = 0.69$, $P = 0.05$) with % change in MFC T₁Gd, and a weak correlation existed for improvement in KOOS overall score ($r = 0.35$, $P = 0.03$) with % change in MFC T₁Gd [Table II]. No significant correlations were present for clinical scores and changes in LFC, MTP or LTP T₁Gd.

Discussion

Although the HTO seems to have regained popularity⁴ as treatment for medial compartment osteoarthritis of the knee due to effectiveness in pain reduction, its effect on cartilage quality is still largely unknown. In the current study, dGEMRIC was used to detect changes in cartilage quality before and after HTO, however no changes due to HTO were detected. Pre-existing differences between medial and lateral compartment cartilage remained and in all investigated knee compartments cartilage degradation continued despite HTO.

In the study of Parker *et al.*²⁰, dGEMRIC was also used to evaluate changes following HTO. Interestingly, several findings are similar to ours. Lateral femoral cartilage had a higher T₁ than medial femoral cartilage pre and postoperatively, and changes following HTO varied per patient but overall a decrease in T₁ was observed. Similar to the observation of Parker *et al.*, the MTP had a slightly higher T₁Gd than the LTP.

In the study of Parker, the greatest decrease in T₁ was observed at 6 months, when patients had just resumed weight bearing. Loss of GAG due to the immobilisation was mentioned as a plausible cause. In the current study, we removed the hardware after bone healing prior to the second MRI, which in our opinion decreases the risk of inadequate T₁ measurements due to metal-induced artifacts [Fig. 1]. The postoperative scan was made at a minimum of 9 months after HTO, when the patients had resumed full weight bearing of their knee joints. T₁Gd was calculated of medial and lateral femoral and tibial cartilage, as well as of multiple sub-ROI's,

Table II
Clinical scores (KOOS, KSCRS, VAS) of HTO patients ($n = 10$), and correlation of change in clinical scores to change in MFC T₁Gd. The clinical scores are displayed as mean \pm 95% CI

	Before high tibial osteotomy (HTO)	3 months after HTO	6 months after HTO	After hardware removal (>9 months)	P-value	Pearson's r (Δ clin. score vs Δ MFC T ₁ Gd)
KOOS pain	48 (37–58)	59 (52–66)	76 (68–85)	82 (72–91)	$P < 0.001$	n.s.
KOOS Symptoms	56 (45–66)	62 (52–72)	74 (63–84)	79 (68–89)	$P = 0.002$	$r = 0.63$, $P = 0.05$
KOOS ADL	58 (47–70)	67 (57–76)	75 (66–85)	83 (73–92)	$P = 0.008$	n.s.
KOOS sports	34 (11–58)	36 (19–52)	42 (27–57)	55 (37–73)	$P = 0.157$	n.s.
KOOS QOL	31 (24–39)	32 (22–41)	47 (32–62)	58 (44–73)	$P = 0.004$	$r = 0.69$, $P = 0.03$
KOOS overall	46 (35–57)	51 (45–57)	63 (53–72)	71 (60–83)	$P = 0.001$	$r = 0.35$, $P = 0.04$
KSCRS	76 (68–83)	75 (66–85)	90 (84–96)	90 (83–99)	$P = 0.008$	n.s.
VAS	63 (52–74)	37 (27–47)	20 (11–29)	11 (6–17)	$P < 0.001$	n.s.

which provides additional information about the sub-regional T₁Gd distribution on sagittal slices throughout the femoral surface. In addition, correlations were measured between T₁Gd and clinical scores, mechanical axis and tibial slope.

In contrast to expectations, clinical scores improved without similar improvement in T₁Gd, except for a moderate correlation of MFC T₁Gd with the KOOS subscores for 'Symptoms' and 'Quality of Life'. In an earlier HTO study, clinical improvement was also shown not to correlate with repair tissue quality²¹. It is unclear why a low correlation often exists between clinical symptoms of OA and histological^{22,23}, radiographic²⁴ or MRI^{25,26} parameters of cartilage quality. The clinical importance of cartilage quality is well documented in longitudinal follow-up series, in which the prevalence of knee pain is shown to correlate with cartilage volume decrease²⁷ and radiographic severity of OA²⁸. In this study, clinical symptoms may have been influenced by changes in serum markers of cartilage metabolism²⁹. Mere placebo effects of the HTO seem unlikely, as improvements in pain and knee function following HTO have been described in systematic review of several clinical trials¹.

It can be stated with reasonable certainty that following HTO the medial compartment is covered with (a thin layer) of fibrocartilage^{5,7,8,30}, which has inferior biomechanical properties in comparison to hyaline cartilage^{31,32}. The low T₁Gd values currently observed can well be seen in the light of these findings. However, it remains difficult to explain why T₁Gd actually decreases. The intra-articular environment may be of influence, and at the time of osteotomy contains a variety of chondrodegradative cytokines³³. Following osteotomy, increases in proteoglycan epitopes²¹, FGF-2³⁴ as well as procollagen peptides³⁵ have been observed, which would be in favour of cartilage regeneration^{33,36}. Nevertheless, chondrodegradative cytokines present in the subchondral bone of the osteoarthritic knee³⁷ are still present and may continue to inhibit cartilage regeneration and overrule regeneration. Further, the femoral chondrocytes may have become hypertrophic during the development of osteoarthritis³⁸ and thus produce lower amounts of glycosaminoglycans, or no glycosaminoglycans at all. It may thus take longer for the non-hypertrophic chondrocytes to compensate for the loss in GAG production and resume matrix formation.

Minimum duration before hardware removal was 10 months, with an average of 12 months in our study. One patient had hardware removed at 22 months owing to doubtful bone healing on radiography. Time to bony healing is reported to vary from 12 weeks³⁹ to 1 year, assessed by radiographs, CT, and MRI imaging⁴. Although in theory complete remodelling of the medial cortex may not yet have occurred, full weight bearing was initiated early in all patients and no adverse events after hardware removal were observed.

The mean mechanical leg axis in this patient group was in accordance with the recommended valgus leg alignment post-HTO^{40,41}. The mean change in femorotibial angle was 10° which seems to be large enough to expect significant changes in cartilage loading patterns represented in the dGEMRIC measurements. Nevertheless, a correlation between change in mechanical axis and change in T₁Gd was not detected. Possibly, the variation in degrees of axial realignment outweighs the subtle changes in T₁Gd. In any case, it can be assumed that the medial knee compartment was adequately decompressed by releasing the distal fibres of the medial collateral ligament¹³.

The increase in tibial slope after HTO is in agreement with previous observations⁴². One would expect that an increase in tibial slope decreases forces directed to the posterior femoral cartilage⁴³, leading to at least steady or increased T₁Gd, instead of a decrease as observed in the current study. Possibly, as the entire medial condyle was unloaded, the regional changes were greater than changes due to unloading of the posterior cartilage, caused by decreased contact pressure as a result of the increase in tibial slope.

Differences between medial and lateral compartment T₁Gd are not unique to osteoarthritic knees or those with a varus or valgus axis. Healthy subjects with varying activity levels⁴⁴, medial meniscectomy patients 1–6 years after meniscectomy⁴⁵ and ACL-deficient patients¹¹ have been reported to have a lower medial compartment T₁Gd. While studying osteoarthritis patients, Williams *et al.*⁴⁶ found a lower T₁Gd in the compartment with the narrowest joint space width. The lowest T₁Gd was observed medially in knees with a varus mechanical leg axis, while a lower lateral T₁Gd was observed in knees with a valgus mechanical leg axis. As the lowest T₁Gd values were currently observed medially before and after HTO, considering the influence of altered cartilage stress due to an axial realignment⁴⁷, changes in T₁Gd may possibly occur during longer follow-up.

There are several limitations to this study. First, this study focuses on relatively short term effects of mechanical axis change after HTO. Ideally, a control cohort with longer follow-up of non-operatively treated osteoarthritis of the medial knee compartment would have been included to evaluate the natural progress of cartilage degeneration. Although the patient number of this feasibility study is relatively small, this is the first study in which the hardware was removed before performing a post-HTO dGEMRIC. From our experience [Fig. 1] it seems advisable to take hardware artifacts into account when using dGEMRIC for follow-up. The general consensus is that osteotomy provides best results in mild to moderate unicompartmental osteoarthritis^{4,41}. Although out of 10 patients two had radiological grade IV osteoarthritis, the remaining population was representative for the general HTO population. In future studies, an interesting control group may be formed by patients undergoing joint distraction in late stage osteoarthritis. Recently, Intema *et al.*⁴⁸ demonstrated that joint distraction during 2 months resulted in an increase in joint space width and cartilage thickness assessed by MRI, while clinical scores increased, similar to the HTO. Due to the characteristics of the MRI method used, cartilage quality was not evaluated.

dGEMRIC as a tool to evaluate cartilage changes has gained attention during the past decade and is increasingly being used to gain fundamental information about cartilage-related disorders, formerly requiring invasive procedures as arthroscopy¹¹ and histological biopsies. From this feasibility study it can be concluded that dGEMRIC can effectively be applied to assess cartilage quality of HTO patients, provided the hardware is removed after consolidation of the osteotomy. Although unaffected by HTO, this study confirms that the cartilage glycosaminoglycan content of the MFC is lower than that of the lateral condyle, and that femoral cartilage glycosaminoglycan content is lower than that of the tibial plateau. Further, differences in T₁Gd between anterior, middle (load bearing) and posterior femoral cartilage are demonstrated. Although dGEMRIC should be further investigated and its value for assessment of cartilage quality compared to other techniques such as T1 Rho⁴⁹, dGEMRIC seems a valuable method to longitudinally evaluate changes in cartilage quality following cartilage related surgery^{12,50}. This feasibility study is valuable for future studies, in which dGEMRIC will be used to compare effects of knee distraction versus HTO versus total knee replacement.

Contributions

All authors have made substantial contributions to (1) conception and design of the study, data acquisition or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be submitted. Responsibility for the integrity of the work as a whole, from inception to finished article, is taken by M. Rutgers, MD and DBF. Saris, MD, PhD.

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Conflict of interest

The authors declare that no conflict of interest exists.

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