Cartilage health in high tibial osteotomy using dGEMRIC: relationships with joint kinematics

Agnes G. d'Entremont^{a,b,c}, agnes.dentremont@mech.ubc.ca

Robert G. McCormack^c, robert.mccormack@ubc.ca

Kenard Agbanlog^{a,b}, kenard.agbanlog@gmail.com

Simon G. D. Horlick^c, shorlick@vbjc.ca

Trevor B. Stone^c, trevorstone@hotmail.com

Mojieb M. Manzary^{c,1}, mojieb@gmail.com

David R. Wilson^{b,c}, david.wilson@ubc.ca

^a Department of Mechanical Engineering, University of British Columbia

2054C - 6250 Applied Science Lane

Vancouver BC V6T 1Z4 Canada

^b Centre for Hip Health and Mobility, University of British Columbia

Robert H. N. Ho Research Centre

684-D - 2635 Laurel Street

Vancouver BC V5Z 1M9 Canada

^c Department of Orthopaedics, University of British Columbia

3114 - 910 West 10th Avenue

Vancouver, BC V5Z 1M9 Canada

¹ [Present address] John Hopkins Aramco Health Care Center, Dhahran, Saudi Arabia

P O Box 11348, Dhahran 31311 Saudi Arabia

Corresponding author:

Dr. Agnes d'Entremont

Department of Mechanical Engineering

University of British Columbia

2054C - 6250 Applied Science Lane

Vancouver BC V6T 1Z4 Canada

agnes.dentremont@mech.ubc.ca

1 604 827 1960

Running Title: dGEMRIC and kinematics in HTO

Keywords: High tibial osteotomy; dGEMRIC; joint kinematics; osteoarthritis; knee

Abbreviations:

dGEMRIC = Delayed gadolinium-enhanced MRI of cartilage

HTO = high tibial osteotomy

TF = tibiofemoral

PF = patellofemoral

GAG = glycosaminoglycans

IR = inversion recovery

SR = saturation recovery

TSE = turbo spin echo

UNCHGD = unchanged group (subjects with small decrease or increase in TF dGEMRIC score at 6 months)

DECRES = decreased group (subjects with large decrease in TF dGEMRIC score at 6 months)

1. Introduction

Opening-wedge high tibial osteotomy (HTO) is a procedure used to treat medial tibiofemoral (TF) osteoarthritis (OA) in knees with varus malalignment. This procedure is performed to change the alignment of the lower limb in an effort to shift load from the diseased medial compartment of the tibiofemoral joint to the lateral compartment. Young, active individuals with medial compartment osteoarthritis are not good candidates for total or unicompartmental knee arthroplasty and the most accepted surgical treatment option in this group is an HTO.

While there are clear guidelines for leg alignment correction in the literature, the correlation between correcting leg alignment to a specific target range and clinical outcome in HTO is not clear. Some studies have found a correlation between correcting leg alignment to a specified range and clinical success [1,2], and others have not [3,4]. Some authors report medial compartment cartilage repair following HTO [5-9], but evidence of further cartilage degeneration in the lateral TF compartment and on the patella has also been found by others [5,6]. It is not clear why cartilage may be protected, or restored, in some cases while in others it is not.

One potential reason that leg alignment is an inconsistent predictor of HTO outcome is that HTO changes many of the three-dimensional components of knee kinematics of the TF and patellofemoral (PF) joints [10]. The single two-dimensional measure used to quantify leg alignment and guide surgery does not capture the complex three-dimensional change to the movement of the knee in HTO [10].

A further limitation to understanding the links between cartilage health and joint mechanics (both in HTO and in OA in general) is that most techniques for assessing *in vivo* cartilage health require direct access to the cartilage through arthroscopic surgery or biopsy, which is invasive. Low glycosaminoglycan (GAG) content assessed with dGEMRIC is associated with early osteoarthritis (OA)[11]. Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC), a validated method for estimating GAG content of cartilage, *in vivo*, using T₁ mapping [12], represents a minimally invasive method to assess articular cartilage. Recent studies of cartilage health in HTO have applied dGEMRIC to TF cartilage before and after surgery [13,14], but have not been applied at the patella. In

each case, they found no significant difference in overall TF dGEMRIC score with HTO and found no correlation between changes in dGEMRIC score and changes in 2D leg alignment [13,14]. However, it is not clear whether there is a relationship between changes in cartilage health as assessed with dGEMRIC and changes in 3D knee kinematics following surgery. This is because, to our knowledge, there has been no simultaneous application of advanced measures of both cartilage health (dGEMRIC) and three-dimensional kinematics, in HTO or in any other population or joint.

Our research questions were: how does opening-wedge high tibial osteotomy affect cartilage GAG content in the tibiofemoral joint and patella, and is there a relationship between tibiofemoral and patellofemoral joint kinematics and cartilage GAG content in HTO?

2. Methods

A cohort of 14 knees in 13 male subjects (mean age 48.3, SD 7.2) undergoing opening-wedge high tibial osteotomy for medial compartment osteoarthritis participated in this study (Table 1). All subjects gave informed consent and UBC Clinical Research Ethics Board approval was granted. Each subject was scanned using a 3T Philips Achieva scanner at three time points: within the month before surgery, 6 months after surgery, and 12 months after surgery. With some subjects unable to complete all scans, our final subject numbers were 13 at pre-operative baseline, 9 at 6 months, and 10 at 12 months.

[Table 1]

The primary participant inclusion criterion was that they were a patient undergoing opening-wedge high tibial osteotomy for treatment of medial tibiofemoral osteoarthritis. Exclusion criteria included previous surgery beyond arthroscopic lavage or debridement, and injury or disorder beyond varus deformity and medial tibiofemoral osteoarthritis (such as ligament rupture or insufficiency). This sample represents consecutive consenting participants available for recruitment in the authors' practices.

1.1. Surgical procedure

Pre-operative planning (using weight-bearing and flexed radiographs) was performed to change the mechanical axis to pass through the 62.5% width point on the tibial plateau. Using a medial approach, the osteotomy plane, proximal to the tibial tubercle, was marked with two k-wires, and the osteotomy was performed with osteotomes and a sagittal saw, leaving the lateral cortex intact. Alignment was checked with a three-foot rod, and fixation was performed with titanium hardware to minimize MR artifacts (plate and four locking screws, Puddu, Arthrex). The osteotomy was filled with autograft or calcium triphosphate wedges, and post-operative protocol consisted of no weight-bearing for 6-8 weeks followed by partial weight-bearing for 2-4 weeks.

1.2. MR imaging

We performed dGEMRIC scans on the tibiofemoral and patellofemoral joints of the operated knee of each subject to quantify cartilage GAG concentration. Each subject was first injected with an intravenous double dose (0.2 mmol/kg) of gadopentatate dimeglumine (Gd-DTPA²⁻, Magnevist, Bayer). Subjects then performed ten minutes of brisk walking following the injection and scanning began 90 minutes post-injection.

For each subject, we first obtained a dGEMRIC scan series of the tibiofemoral joint of the operated knee (coronal plane). Because the metal osteotomy plate near the cartilage can cause artifact that disrupts the T₁ map in the tibiofemoral cartilage [15], we used saturation recovery (SR) instead of inversion recovery (IR) to reduce metal artifact for scans of the tibiofemoral joint, as described in previous work [15]. We obtained a series of single-slice coronal plane saturation recovery turbo spin-echo (TSE) scans (Table 2) with two surface coils (SENSE Flex-M, Philips, Best, Netherlands) positioned one on either side of the joint.

[Table 2]

For each subject, we then obtained a dGEMRIC scan of the patella of the operated knee. This scan was started about two hours post-injection. The scan series consisted of a series of single-slice inversion recovery (IR) turbo spin-echo (TSE) scans in the axial plane (Table 2). We used the inversion recovery sequence at the patellofemoral joint because

the metal implant was sufficiently distant and the inversion recovery sequence has a higher signal to noise ratio than the saturation recovery sequence. The inversion preparation was achieved with a commercially available hyperbolic secant adiabatic pulse (amplitude and frequency modulated) which was designed to produce accurate inversion pulses even in presence of radiofrequency field (B_1) inhomogeneities [16].

We also collected three-dimensional knee kinematic data for these same subjects using a validated MR method [10]. Briefly, we obtained one high-resolution scan of the knee in a relaxed position, and six rapid scans of the knee loaded in simulated squats at flexion angles from 10 - 60°. These scans were segmented and registered, to obtain the full set of translations and rotations describing both the patella and the tibia with respect to the femur.

1.3. Data analysis

For each set of eight dGEMRIC scans, each image was manually aligned to the image with the highest inversion time (for the IR sequence) or the highest repetition time (for the SR sequence). The cartilage area of interest (tibiofemoral or patella) was segmented manually (MATLAB, MathWorks, MA, USA). Quantitative T_1 maps were obtained using in-house developed code (MATLAB, Mathworks, MA, USA, function `lsqcurvefit`) to fit the magnitude signal intensities versus inversion times (IR series - Equation 1) or saturation recovery times (SR series - Equation 2) by minimizing the sum of the squared residuals of signal intensity for each pixel of the image set.

$$SI = \left| S_0 \left(1 - f_{IR} e^{-\frac{TI}{T_1}} \right) \right|$$

Equation 1

$$SI = S_0 \left(1 - f_{SR} e^{-\frac{TR}{T_1}} \right)$$

Equation 2

Equation 1 is the fit equation for the IR series, and Equation 2 is the fit equation for the SR series. SI is signal intensity in the image, S_0 is the signal intensity at equilibrium

conditions, TI is inversion time, TR is repetition time and f_{IR} and f_{SR} are fit factors that account for imperfect inversion and excitation pulses. SI, TI, and TR are known values, and S_0 , T_1 , and f are calculated. The nominal f-factor values are $f_{IR} = 2$ for perfect inversion, and $f_{SR} = 1$ for perfect excitation; these values were allowed to vary to accommodate imperfect inversion or excitation. Twenty-five random initial values sets, centered around initial guesses (IR: $T_{1,initial} = TI(SI_{min})/\ln 2$, $S_{0,initial} = SI(TI_{max})$, $f_{IR,initial} = 1.9$; SR: $T_{1,initial} = 600$ ms, $S_{0,initial} = SI(TR_{max})$, $f_{SR,initial} = 1$) were used for each pixel and the result with the lowest residual was selected as the best result.

We defined two different groups based on the temporal pattern of TF dGEMRIC scores. We defined a “Decreased” group of subjects ($n = 3$) who had decreases in dGEMRIC score of 80 ms or more between pre-op and 6 months scans. We chose this threshold because a difference of 71 ms (at 1.5 T) between group means was associated with progression of OA at 6 years follow-up [17], which suggests that this magnitude of change may be clinically relevant. In all three subjects in the Decreased group, these decreases were recovered at 12 months. We examined kinematics changes in the Decreased group and contrasted those results with kinematic changes for all the other subjects who had both pre-operative and 6-month TF dGEMRIC data (Unchanged group, $n = 5$) (Table 1).

1.4. Statistical analysis

For each joint, we tested the null hypothesis that there was no difference in mean T_1 between the preoperative condition, 6 months after surgery, and 12 months after surgery using a linear mixed-effects model. All statistical analysis was performed using Stata 10.1 (StataCorp, Texas). We also examined differences within the TF joint between compartments (medial and lateral) and between groups (Decreased and Unchanged) at each timepoint, and within groups and compartments over time using linear mixed-effect models. A Bonferroni correction was applied to conservatively correct for multiple comparisons (Bonferroni alpha: $\alpha = 0.0015$).

Initial sample size calculations based on a paired t-test (the effect size estimated at 26 ms (1.5T) from differences between intact and damaged tibiofemoral compartments [18] and the underlying standard deviation in the tibiofemoral compartments estimated at 30 ms (1.5T) for a range of activity levels [19]) suggested a sample size of 13 to have adequate power (0.80) to detect clinically significant differences.

To explore relationships between knee kinematics and cartilage health, we applied linear mixed-effect models to the three timepoints within each group (Decreased and Unchanged) for each of 11 kinematic parameters (tibial internal rotation, tibial lateral translation, tibial proximal translation, tibial anterior translation, patellar flexion, patellar spin, patellar tilt, patellar lateral translation, patellar proximal translation, patellar anterior translation). We compared patterns of change between groups for each parameter. For simplicity, we focused on parameters where 6- and 12-month results were consistent within each group. As this aspect of the study was hypothesis generating, statistical comparisons are not presented.

3. Results

Some subjects were unable to complete one or more of the follow-up scans: one subject had stainless steel hardware implanted at surgery, one subject had a non-union and an additional operation after the 6 month follow-up, two subjects missed the 6 month follow-up due to scheduling conflicts, and two subjects were lost to follow-up after pre-operative baseline. One subject's pre-operative scans were unusable due to data corruption. Final subject numbers were 13 at pre-operative baseline, 9 at 6 months, and 10 at 12 months, with 7 having all three timepoints.

Visible artifacts were present in post-operative tibiofemoral images despite the use of SR (Figure 1), though they did not appear to extend into cartilage and were not apparent in maps of the three fit parameters. None of the patellofemoral images had visible artifacts.

[Figure 1]

No statistically significant changes were found in overall tibiofemoral dGEMRIC score between the pre-op (598 ms) scan and the 6 month post-op (578 ms) scan ($p = 0.37$), between the pre-op scan and the 12 month post-op (607 ms) scan ($p = 0.67$) or between 6 months and 12 months post-op ($p = 0.21$) ($\alpha = 0.0015$, Table 3, Figure 2). We did, however, see a broad range of patterns of change in dGEMRIC across the individual subjects.

No statistically significant changes were found in patellar dGEMRIC score between the pre-op (664 ms) scan and the 6 month post-op (650 ms) scan ($p = 0.51$), between the pre-op scan and the 12 month post-op (674 ms) scan ($p = 0.66$) or between 6 months and 12 months post-op ($p = 0.30$) ($\alpha = 0.0015$, Table 3, Figure 2).

[Table 3]

[Figure 2]

In the tibiofemoral compartments, mean medial dGEMRIC scores were lower than mean lateral dGEMRIC scores at each timepoint (pre-op 56 ms, $p < 0.001$; 6 months 50 ms, $p < 0.001$; 12 months 66 ms, $p = 0.002$) ($\alpha = 0.0015$, Table 4, Figure 3). There was no significant change within either medial or lateral TF compartments over time ($p = 0.24$ to 0.87).

When dGEMRIC scores were divided by group (Decreased versus Unchanged), the TF Decreased results were statistically significantly different at 6 months from both pre-op ($p < 0.001$) and 12-month ($p < 0.001$) results ($\alpha = 0.0015$), and the 6-month results were significantly different between Decreased and Unchanged ($p < 0.001$), while not at pre-op ($p = 0.69$) or 12 months ($p = 0.50$). The Decreased group had decreases in patellar dGEMRIC compared to pre-op values at both 6 months ($p = 0.03$) and 12 months ($p = 0.004$), although they were not statistically significant (Table 3, Figure 2).

[Figure 3]

[Table 4]

The effect of HTO on kinematics was different in the Decreased and Unchanged groups. HTO changed tibial anterior translation, proximal translation, and patellar flexion at both 6 and 12 months follow-up by a different magnitude in one group than the other (Figure 4). However, for tibial proximal translation and patellar flexion, changes in the Decreased group were in the opposite direction to those in the Unchanged group (Figure 4). HTO shifted the tibia distally in the Decreased group but proximally in the Unchanged group, with a difference in mean change of 1.35 mm. HTO extended the patella in the Decreased group and flexed the patella in the Unchanged group, with a difference in mean change of 2.65° between the groups. In tibial anterior translation, the tibiae in

the Decreased group were positioned more anteriorly over the range of motion after HTO (both 6- and 12-month follow-ups) by a mean of 3.05 mm compared to the Unchanged group.

[Figure 4]

4. Discussion

We assessed three-dimensional kinematics and cartilage GAG content using dGEMRIC in patients before and after HTO to determine how opening-wedge high tibial osteotomy affected cartilage GAG content in the tibiofemoral joint and patella, and to explore relationships between tibiofemoral and patellofemoral joint kinematics and cartilage GAG content in HTO. We did not find a change in overall patellofemoral or tibiofemoral dGEMRIC score at 6 or 12 months after HTO. However, we did identify a pattern of reduction and recovery of tibiofemoral cartilage dGEMRIC score in some patients. We found differences in kinematics between these patients and those who did not show this pattern of dGEMRIC score reduction and recovery, and also found that patellar cartilage dGEMRIC score declined after HTO in this group of patients.

Our finding of no significant difference in overall patellar or tibiofemoral dGEMRIC score between pre-operative and 6 or 12 months post-surgery timepoints is consistent with previous work. Parker et al. studied tibiofemoral cartilage after opening-wedge HTO at 3T and found no statistically significant differences in tibiofemoral cartilage dGEMRIC score between the pre-op (medial 562 ms, lateral 628 ms; n = 10), 6 months (medial 507 ms, lateral 588 ms) and 1 year post-op (medial 516 ms, lateral 582 ms) states [13]. Rutger's study of opening-wedge HTO performed at 1.5 T found no significant differences between pre- and post-operative dGEMRIC (n = 10, pre-op 533 ms, post-op (~12 months) 466 ms) [14], although the values are not directly comparable to those measured at 3T. The dGEMRIC scores in our study were within with the range of 400-900 ms mean dGEMRIC T₁ value reported by McKenzie et al. in a study at 3T [20]. Large variability in dGEMRIC score between individuals, similar to that seen in this study, has been previously observed. Ranges of about 400-800 ms for OA patients and about 500-900 ms for normals at the TF joint at 3T have been reported [20]. Parker's study at 3T in HTO patients had a pre-operative range of 450-762 ms (medial and lateral), while

values 6 months post-operatively were 452-711 ms (medial and lateral) [13]. We observed similar ranges for dGEMRIC values in this study, with 540-712 ms (TF pre-operative) and 439-692 ms (TF 6 months).

Our finding that the medial tibiofemoral compartment had lower T_1 values than the lateral compartment at all timepoints (difference pre-op: 56 ms, 6 months: 50 ms, 12 months: 66 ms) is consistent with the indication for the operation, which is degeneration of the medial TF compartment cartilage due to varus malalignment. Our differences in TF dGEMRIC scores between medial and lateral compartments are consistent with an earlier study at 3T (side-to-side differences of 66 ms at pre-op, 80 ms at 6 months, and 70 at 12 months) [13].

Our findings suggest that patellar dGEMRIC scores are generally in the healthy range before HTO surgery. A study of ten normal volunteers at 1.5T found a mean patellar dGEMRIC score of 469 ms [21], which would scale to approximately 537 - 586 ms at 3T [20,22], somewhat lower than our preoperative mean of 664 ms [23]. A study of patients undergoing TKA found a preoperative mean dGEMRIC score of 321 ms ($n = 12$) at 3T over all regions, which is substantially lower than our finding. However, it is likely that these participants had more advanced patellar cartilage degeneration, on average, than the relatively young and active patients in the current study.

The decreases in TF dGEMRIC score of 80 ms or more at 6 months (mean -105 ms, -18%) in three out of eight individual participants (with recovery at 12 months) are likely clinically significant. A 71 ms (at 1.5T, equivalent to roughly 81 ms at 3T [20]) difference in dGEMRIC score is associated with development of radiographic OA by 6 years [17]. A pattern of substantial decline in TF dGEMRIC score 6 months after HTO in some patients is also evident in the raw data from a previous study [13], which had two subjects with a decrease of more than 100 ms in both compartments 6 months after HTO, and two additional subjects showing decreases of more than 100 ms in the lateral or medial compartment only (four out of ten subjects total) [13]. Apparent recovery of cartilage GAG content, as observed at 12 months in the Decreased group, was reported in a case study of posterior cruciate ligament (PCL) rupture, where overall pre-injury TF dGEMRIC score was decreased by 15% and 19% at 1 and 3 months post-injury respectively, but recovered to within 3% at 6 months post-injury [24]. It is not clear how changes in

intervention (type of osteotomy or rehabilitation) or particular patient characteristics may influence changes in TF dGEMRIC score.

Our finding of differences in tibial anterior translation and tibial proximal translation between the patients who had decreases at 6 months in TF dGEMRIC and the other patients suggests that the initial reduction in dGEMRIC score is a response to a mechanical change. While the mean TF dGEMRIC score recovered to pre-op values in the Decreased group at 12 months, the kinematic changes seen at 6 months remained at 12 months, which suggests that cartilage adapted to the mechanical change. Tibial slope increases have been associated with tibial anterior translation, and both groups had increases in tibial slope following HTO (as measured from the MR images). Mean increases in medial tibial slope of 6.4° (Decreased) and 4.5° (Unchanged) and in lateral slope of 4.0° (Decreased) and 5.2° (Unchanged) were found. It is unclear if these differences in tibial slope change between groups are related to differences in anterior tibial translation.

The reduced patellar dGEMRIC score in the Decreased group is also associated with a difference in patellar flexion, although this dGEMRIC reduction was not found to be statistically significant with our small numbers and conservative correction for multiple comparisons. We did not observe recovery in the reduced patellar dGEMRIC score in the Decreased group, which suggests that the patella may become a problem clinically in this group of patients.

One limitation of the kinematic aspects of this study is that the sample size was based on overall changes in dGEMRIC score. The study was not designed optimally to assess the difference between the two different groups (based on pattern of TF dGEMRIC score change) that we identified, and it is therefore possible that we have not identified all of the clinically significant differences between the groups due to insufficient power. Consequently, this aspect of the study should therefore be considered to be hypothesis generating. Nonetheless, our findings of significant differences in kinematics and patellar dGEMRIC score between the groups are important to report. Further follow-up may provide concrete relationships between changes in dGEMRIC and long-term outcomes.

Further limitations of this study relate primarily to the dGEMRIC methods. One limitation is that we had only one 2D slice of cartilage to evaluate dGEMRIC scores in each joint. Three-dimensional sequences would allow more complete coverage of the joint, although the single slice was defined through the weightbearing region, where changes in dGEMRIC score due to changes in mechanics would be expected. Matching slices between timepoints was also challenging, both due to typical difficulties in obtaining the same slice and to geometric changes in the joint as a result of surgery and healing, although we did establish protocols to minimize these potential errors.

5. Conclusions

Opening-wedge high tibial osteotomy did not consistently change overall dGEMRIC score in either the tibiofemoral joint or the patella. However, a number of subjects displayed a pattern of substantial reduction and then recovery of TF dGEMRIC score. These subjects had different three-dimensional knee kinematics from those who did not have such a decrease, and their overall patellar dGEMRIC score decreased substantially in the year after the operation. These results suggest that the effect of opening-wedge high tibial osteotomy on cartilage GAG concentration may be linked to specific changes in knee kinematics following surgery.

Acknowledgements

The authors wish to thank the UBC MRI Research Centre for assistance with methods implementation and data collection. This project was funded by a Canadian Institutes for Health Research (CIHR) Operating grant (DRW)(MOP - 106680), a Michael Smith Foundation Trainee Award (AGD), and a Natural Sciences and Engineering Research Council (NSERC) Post Graduate Fellowship (AGD). There was no involvement of study sponsors in study design, collection, analysis and interpretation of data; in the writing of the manuscript; or in the decision to submit the manuscript for publication.

References

- [1] Sprenger TR, Doerzbacher JF. Tibial osteotomy for the treatment of varus gonarthrosis: survival and failure analysis to twenty-two years. *J Bone Jt Surg Am* 2003;85:469.
- [2] Yasuda K, Majima T, Tsuchida T. A ten-to 15-year follow-up observation of high tibial osteotomy in medial compartment osteoarthritis. *Clin Orthop Relat Res* 1992;Sept:186-95.
- [3] Rinonapoli E, Mancini GB, Corvaglia A, Musiello S. Tibial osteotomy for varus gonarthrosis. A 10- to 21-year followup study. *Clin Orthop Relat Res* 1998;282:186-93.
- [4] González-Panisello MR, Hernández-Hermoso JA. Survivorship and prognostic factors of high tibial osteotomy in the treatment of arthritic genu varum. *Rev Esp Cir Ortop Traumatol (English Ed)* 2009;53:157-63.
- [5] Fujisawa Y, Masuhara K, Shiomi S. The effect of high tibial osteotomy on osteoarthritis of the knee: An arthroscopic study of 54 knee joints. *Orthop Clin North Am* 1979;10:585-608.
- [6] Hernigou P, Medevielle D, Debeyre J, Goutallier D. Proximal tibial osteotomy for osteoarthritis with varus deformity. A ten to thirteen-year follow-up study. *J Bone Jt Surg Am* 1987;69:332.
- [7] Odenbring S, Egund N, Lindstrand A, Lohmander LS, Willén H. Cartilage regeneration after proximal tibial osteotomy for medial gonarthrosis. An arthroscopic, roentgenographic, and histologic study. *Clin Orthop Relat Res* 1992:210-6.
- [8] Bergenudd H, Johnell O, Redlund-Johnell I, Lohmander LS. The articular cartilage after osteotomy for medial gonarthrosis. Biopsies after 2 years in 19 cases. *Acta Orthop Scand* 1992;63:413-6.
- [9] Koshino T, Wada S, Ara Y, Saito T. Regeneration of degenerated articular cartilage after high tibial valgus osteotomy for medial compartmental osteoarthritis of the knee. *Knee* 2003;10:229-36.
- [10] d'Entremont AG, McCormack RG, Horlick SG, Stone TB, Manzary MG, Wilson DR. Effect of opening-wedge high tibial osteotomy on the three-dimensional kinematics of the knee. *Bone Jt J* 2014;In Press.
- [11] Tiderius CJ, Olsson LE, Leander P, Ekberg O, Dahlberg L. Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) in early knee osteoarthritis. *Magn Reson Med* 2003;49:488-92.

- [12] Bashir A, Gray ML, Hartke J, Burstein D. Nondestructive imaging of human cartilage glycosaminoglycan concentration by MRI. *Magn Reson Med* 1999;41:857-65.
- [13] Parker DA, Beatty KT, Giuffre B, Scholes CJ, Coolican MRJ. Articular cartilage changes in patients with osteoarthritis after osteotomy. *Am J Sport Med* 2011;39:1039-45.
- [14] Rutgers M, Bartels LW, Tsuchida AI, Castelein RM, Dhert WJ, Vincken KL, et al. dGEMRIC as a tool for measuring changes in cartilage quality following high tibial osteotomy: a feasibility study. *Osteoarth Cart* 2012;20:1134-41.
- [15] d'Entremont AG, Kolind SH, Mädler B, Wilson DR, Mackay AL. Using the dGEMRIC technique to evaluate cartilage health in the presence of surgical hardware at 3T: comparison of inversion recovery and saturation recovery approaches. *Skeletal Radiol* 2014;43:331-44.
- [16] Norris D. Adiabatic radiofrequency pulse forms in biomedical nuclear magnetic resonance. *Concepts Magn Reson* 2002;14:89-101.
- [17] Owman H, Tiderius CJ, Neuman P, Nyquist F, Dahlberg LE. Association between findings on delayed gadolinium-enhanced magnetic resonance imaging of cartilage and future knee osteoarthritis. *Arthritis Rheum* 2008;58:1727-30.
- [18] Williams A, Sharma L, McKenzie CA, Prasad P V., Burstein D. Delayed gadolinium-enhanced magnetic resonance imaging of cartilage in knee osteoarthritis: findings at different radiographic stages of disease and relationship to malalignment. *Arthritis Rheum* 2005;52:3528-35.
- [19] Tiderius CJ, Svensson J, Leander P, Ola T, Dahlberg L. dGEMRIC (delayed gadolinium-enhanced MRI of cartilage) indicates adaptive capacity of human knee cartilage. *Magn Reson Med* 2004;51:286-90.
- [20] McKenzie CA, Williams A, Prasad P V, Burstein D. Three-dimensional delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) at 1.5T and 3.0T. *J Magn Reson Imaging* 2006;24:928-33.
- [21] Multanen J, Rauvala E, Lammentausta E, Ojala R, Kiviranta I, Häkkinen A, et al. Reproducibility of imaging human knee cartilage by delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) at 1.5 Tesla. *Osteoarth Cart* 2009;17:559-64.
- [22] Gold GE, Han E, Stainsby J, Wright G, Brittain J, Beaulieu C. Musculoskeletal MRI at 3.0 T: relaxation times and image contrast. *AJR Am J Roentgenol* 2004;183:343-51.
- [23] Kumahashi N, Tadenuma T, Kuwata S, Fukuba E, Uchio Y. A Longitudinal Study of the Quantitative Evaluation of Patella Cartilage After Total Knee Replacement by Delayed Gadolinium-enhanced Magnetic Resonance Imaging of Cartilage

(dGEMRIC) and T2 Mapping at 3.0T: Preliminary Results. *Osteoarth Cart* 2012;1-10.

- [24] Young AA, Stanwell P, Williams A, Rohrsheim JA, Parker DA, Giuffre B, et al. Glycosaminoglycan Content of Knee Cartilage Following Posterior Cruciate Ligament Rupture Demonstrated by Delayed Gadolinium-Enhanced Magnetic Resonance Imaging of Cartilage (dGEMRIC). *J Bone Jt Surg Am* 2005;87-A:2763-8.

Figure Captions

Figure 1: Patellar and tibiofemoral dGEMRIC maps for all timepoints for sample subject (subject 6). Colourmap represents T_1 values in ms.

Figure 2: Overall mean dGEMRIC score models and individual results for all subjects ($n = 14$) at pre-operative, 6-month and 12-month timepoints for (a) tibiofemoral and (b) patellar cartilage. Mean dGEMRIC models for both groups (Decreased ($n = 3$) and Unchanged ($n = 5$)) for (c) tibiofemoral and (d) patellar cartilage. Individuals with drop in overall TF dGEMRIC score at 6 months indicated by darker, dashed individual lines in plots. ** indicates $p < 0.001$, $\alpha = 0.0015$.

Figure 3: Tibiofemoral dGEMRIC results divided by compartment. Medial dGEMRIC values are lower than lateral values at each timepoint. ** indicates $p < 0.001$, $\alpha = 0.0015$.

Figure 4: Three-dimensional kinematic results divided by group based on TF dGEMRIC results. Tibial anterior translation models for three timepoints for (a) Decreased group ($n = 3$) and (b) Unchanged group ($n = 5$); tibial proximal translation models for three timepoints for (c) Decreased group ($n = 3$) and (d) Unchanged group ($n = 5$); and patellar flexion for three timepoints for (e) Decreased group ($n = 3$) and (f) Unchanged group ($n = 5$). Arrows indicate direction of parameter change with HTO and numerical values indicate the mean change between pre-op and both post-op timepoints for the group for that parameter.

Figures

Figure 1: Patellar and tibiofemoral dGEMRIC maps for all timepoints for sample subject (subject 6). Colourmap represents T₁ values in ms.

Figure 2: Overall mean dGEMRIC score models and individual results for all subjects ($n = 14$) at pre-operative, 6-month and 12-month timepoints for (a) tibiofemoral and (b) patellar cartilage. Mean dGEMRIC models for both groups (Decreased ($n = 3$) and Unchanged ($n = 5$)) for (c) tibiofemoral and (d) patellar cartilage. Individuals with drop in overall TF dGEMRIC score at 6 months indicated by darker, dashed individual lines in plots. ** indicates $p < 0.001$, $\alpha = 0.0015$.

Figure 3: Tibiofemoral dGEMRIC results divided by compartment. Medial dGEMRIC values are lower than lateral values at each timepoint. ** indicates $p < 0.001$, $\alpha = 0.0015$.

Figure 4: Three-dimensional kinematic results divided by group based on TF dGEMRIC results. Tibial anterior translation models for three timepoints for (a) Decreased group (n = 3) and (b) Unchanged group (n = 5); tibial proximal translation models for three timepoints for (c) Decreased group (n = 3) and (d) Unchanged group (n = 5); and patellar flexion for three timepoints for (e) Decreased group (n = 3) and (f) Unchanged group (n = 5). Arrows indicate direction of parameter change with HTO and numerical values indicate the mean change between pre-op and both post-op timepoints for the group for that parameter.