In vivo cartilage deformation after different types of activity and its dependence on physical training status

F Eckstein, B Lemberger, C Gratzke, M Hudelmaier, C Glaser, K-H Englmeier, M Reiser

Background: Knowledge of the deformatonal behaviour of articular cartilage in vivo is required to understand the pathogenesis of osteoarthritis and the mechanical target environment of prospective cartilage transplant recipients.

Objectives: To study the in vivo deformatonal behaviour of patellar and femorotibial cartilage for different types of physiological activities; and to test the hypothesis that in vivo deformation of cartilage is modified by intense physical exercise.

Methods: Magnetic resonance imaging and 3D digital image analysis were used to determine cartilage volume before and after physical activity in the patella of 12 volunteers (knee bends, squatting, normal gait, running, cycling). Deformation of femorotibial cartilage was investigated in 10 subjects (knee bends, static compression, high impact loading). Patellar cartilage deformation after knee bends was compared in seven professional weight lifters, seven sprinters, and 14 untrained volunteers.

Results: Patellar cartilage deformation was $-5.9\%$ after knee bends, $-4.7\%$ after squatting, $-2.8\%$ after normal walking, $-5.0\%$ after running, and $-4.5\%$ after cycling. The pattern of patellar cartilage deformation corresponded to the range of motion involved in the particular activity. Tibial cartilage deformation was greatest under high impact loading ($-7\%$), but small for other activities. No significant difference was found between athletes and non-athletic controls.

Conclusions: Patellar cartilage deformation shows a ‘dose dependent’ response, where more intense loading leads to greater deformation. Relatively little deformation was observed in the femorotibial joint, except during high impact activities. The findings provide no evidence that adult human cartilage properties are amendable to training effects in vivo.
There is a suggestion from several animal models that cartilage composition and mechanical properties depend on the level of physical training. Whether or not cartilage microstructure, composition, and mechanical properties are amendable to “training” effects and can functionally adapt to mechanical stimuli in humans is still an open question. The third objective of our study was therefore to test the hypothesis that athletes show less patellar cartilage deformation than non-athletic volunteers, because the mechanical stimulation causes an increase in the metabolic activity of the chondrocytes, the proteoglycan content of the cartilage matrix, and the stiffness of the cartilage.

**METHODS**

We examined three samples of healthy volunteers (50 in total), none of whom had a history of symptoms, signs, trauma, or surgery at the knee joint. Informed written consent was obtained from all volunteers and the study protocol was ratified by the local ethic committee.

All magnetic resonance (MR) images were acquired with a clinical 1.5T magnetic resonance scanner (Magnetom Vision, Siemens, Erlangen, Germany).

**Magnitude of patellar cartilage deformation after different types of exercise**

To determine the effect of various types of exercise on patellar cartilage deformation, we examined 12 healthy volunteers aged 23 to 30 years (six men and six women). In a first session, four axial scans of the patellar cartilage were acquired after 60 minutes of physical rest using a FLASH water excitation sequence \(^{11} 12 13 14 15 16 17 18 19 20 21\) (time of repetition (TR) = 17.2 ms, time of echo (TE) = 6.6 ms, flip angle = 20°, bandwidth = 120 Hz/pixel, slice thickness = 1.5 mm, in-plane resolution = 0.3 mm x 0.3 mm; acquisition time = 3 min 47 s). The knee was repositioned within the coil in between the four repeated scans. The volunteers were then asked to do 30 deep knee bends, as described previously. \(^{11}\) Another axial scan was then acquired starting at 90 seconds after the end of the knee bends. The same volunteers were re-examined over a period of six to 12 months. Upon re-examination one axial scan was acquired before and one after a specific activity. These activities included squatting at a 90° knee angle for 20 seconds, \(^{11}\) normal walking at ground level for five minutes, running 200 m, walking up and down 54 steps over a total time of four minutes, and cycling for 10 minutes on a training bike at 80 Hz frequency.

**Magnitude of femorotibial cartilage deformation after different types of exercise**

To determine the effects of various types of activities on femorotibial cartilage deformation, we examined 10 volunteers aged 18 to 37 years (five men and five women), employing the same sequence as described above but using a coronal section orientation (acquisition time seven minutes). Two coronal scans (with repositioning) were acquired after 60 minutes of rest in a first session, and then one coronal scan after 30 knee bends. The same volunteers were re-examined after a period of six to 12 months, before and after a specific activity. The activities included 30 knee bends done on one leg only, two minutes of static loading of the femorotibial joint of one leg at 15° flexion with 200% body weight, and 10 jumps from a chair (40 cm height) onto one leg.

**Digital image analysis of MR imaging data and reproducibility (precision)**

Cartilage volume and thickness were determined after segmentation, \(^{22}\) using three dimensional reconstruction and Euclidean distance transformation, \(^{23}\) as described previously. \(^{11} 12 13 17 19 20 21\) The magnitude of cartilage deformation was assessed by subtracting the cartilage volume determined after a specific activity from that obtained before the activity. This value was expressed by the percentage difference from the value before the activity.

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**Table 1** Short term and long term precision errors (RMS CV%) in the knee joint cartilage plates

<table>
<thead>
<tr>
<th></th>
<th>Patella</th>
<th>MT</th>
<th>LT</th>
<th>MFC</th>
<th>LFC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume short term</td>
<td>1.0%</td>
<td>0.0%</td>
<td>2.2%</td>
<td>3.8%</td>
<td>4.1%</td>
</tr>
<tr>
<td>Volume long term</td>
<td>1.6%</td>
<td>5.4%</td>
<td>3.9%</td>
<td>4.9%</td>
<td>4.1%</td>
</tr>
<tr>
<td>Mean thick short term</td>
<td>1.2%</td>
<td>1.6%</td>
<td>1.5%</td>
<td>2.5%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Mean thick long term</td>
<td>2.2%</td>
<td>3.2%</td>
<td>2.7%</td>
<td>5.1%</td>
<td>3.0%</td>
</tr>
</tbody>
</table>

LFC, lateral femoral condyle; LT, lateral tibia; MFC, medial femoral condyle; MT, medial tibia.
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involve a larger range of motion lead to more widespread deformation activities with a limited range of knee motion (squatting and walking) lighter areas are regions of low deformation. The results show that medial facet on the left). Dark areas are regions of high deformation and retropatellar surface from posteriorly (lateral facet on the right and different types of activities; average over all 12 volunteers. View on the Figure 2

Regional variation of deformation throughout the patella for different types of activities; average over all 12 volunteers. View on the retropatellar surface from posteriorly (lateral facet on the right and medial facet on the left). Dark areas are regions of high deformation and lighter areas are regions of low deformation. The results show that activities with a limited range of knee motion (squatting and walking) lead to deformation of some confined areas, whereas activities that involve a larger range of motion lead to more widespread deformation of patellar cartilage.

To determine the short term precision of the analyses of the various cartilage plates, we computed the root mean square coefficient of variation (RMS CV%) of repeated baseline measurements acquired in the first session, with image analysis also being done within a single session. To determine the “long term acquisition/resegmentation” precision of the measurements, we computed the root mean square coefficient of variation (RMS CV%) of all baseline measurements acquired over a period of six to 12 months, with image analysis being undertaken in different sessions also spread over a period of six to 12 months. In the latter case, the users were blinded to their previous segmentations.

In the patella, the short term precision error (four repeat scans during the first session; image analysis in one session) was 1.0% (RMS CV%) for cartilage volume and 1.2% for mean cartilage thickness (table 1). The long term acquisition/resegmentation precision error (five repeat (baseline) scans) was 1.6% for cartilage volume and 2.2% for mean cartilage thickness. These errors were random and not systematic, and there was no “drift” in the data (values becoming systematically smaller or larger with time). In the femorotibial joint the short term precision error (two repeat scans during the first session) ranged from 1.5% (mean cartilage thickness in the lateral tibia) to 3.8% (cartilage volume in the medial femoral condyle) (table 1). The long term acquisition/resegmentation precision error (four repeat (baseline) scans) ranged from 2.7% (mean cartilage thickness in the lateral tibia) to 5.4% (cartilage volume of the medial tibia), with again no drift being seen in the data (table 1).

To visualise the pattern of cartilage deformation throughout the patella after different activities, we employed the matching algorithm described by Stammberger et al.25 Cartilage thickness difference maps for the 12 volunteers were displayed using grey value coding. Averages over the 12 volunteers (for each activity) were derived using commercial software (Adobe Photoshop 7.0, Adobe Systems Inc, San Jose, California, USA).

RESULTS

The cartilage deformation of the patella (mean (SD) was −5.9 (2.1)% after 30 knee bends, −4.7 (1.6)% after squatting, −2.8 (0.8)% after walking, −5.0 (1.3)% after running, and −4.5 (1.6)% after cycling (fig 1). These changes were significant at a 1% error level. Figure 2 shows the regional variation in deformation throughout the patella for the different activities. Whereas changes were confined to limited regions during squatting and walking, the deformation involved a more widespread area during activities that involved a larger range of knee motion, such as 200 m running (including 54 stairs), cycling, and knee bends.

In the non-athletic volunteers, the change in patellar cartilage volume after knee bends was −4.1 (2.6)%. Changes were −2.9 (1.9)% in the weight lifters and −3.9 (1.8)% in the bobsleigh sprinters. Changes were significant at a 1% error level in all groups, but differences in deformation between groups were not statistically significant at the 5% error level.

No significant change in cartilage volume was observed in femorotibial cartilage after two-legged knee bends (except in the lateral tibia) or one-legged knee bends (table 2). Highly significant changes were seen in the medial and lateral tibia after jumps from 40 cm height, but not in the medial or lateral femoral condyle (fig 3). Only changes of borderline significance were seen in the medial tibia and lateral femoral condyle after the static loading exercise (table 2).

DISCUSSION

One objective of this study was to determine the magnitude and distribution pattern of patellar cartilage deformation after various physiological activities with different load magnitudes and ranges of motion. The methodology employed to address this question has been shown to be valid17 26 and reproducible in vivo.17 21–23 25 Changes (deformation) measured in patellar cartilage were three to six times greater than the precision error (RMS CV%) of the method,
and the knee bend exercise used here produced very similar findings to two previous studies employing the same type of exercise.\textsuperscript{9, 10} Comparing different types of exercise with this technique we found that patellar cartilage shows a “dose dependent” response, more intense loading leading to greater in vivo surface to surface strains. The deformation pattern of the patellar cartilage corresponds to the range of motion involved in the particular activity. Activities with a small range of knee motion cause a confined deformation of relatively small regions of the joint surface, whereas those with a larger range of motion cause a more widespread deformation throughout the joint surface. It is interesting to note that the deformation patterns observed with this technique correspond closely with the patellar contact areas described by Hene\textsuperscript{27} for flexion angles of the knee involved in these various activities.

Another objective of this study was to explore femorotibial cartilage deformation after various activities in vivo. Deformation in the femorotibial cartilage was relatively small, even after intense loading. Among the different activities, high impact loading (jumping) caused the largest changes in tibial cartilage, with smaller (insignificant) changes being observed in the femoral condyles. The observation that tibial, and particularly femoral, cartilage deforms less than patellar cartilage is consistent with ex vivo measurement of cartilage mechanical properties.\textsuperscript{14} Froimson et al\textsuperscript{14} reported that femoral cartilage showed a 30% higher compressive aggregate modulus (p<0.001) and a 66% lower permeability (p<0.001) than patellar cartilage. Moreover, the water content of the femur was found to be lower (5%, \( p = 0.031 \)) and the proteoglycan content higher (19%, \( p = 0.030 \)) than that of the patella.\textsuperscript{14} The investigators hypothesised that the differences in biochemical and mechanical properties between the patella and femur may explain why patellar cartilage shows earlier and more severe fibrillation than the femoral cartilage clinically. Our results confirm that the mechanical properties of cartilage differ among cartilage plates and compartments of the knee, and are associated with the in vivo behaviour of human cartilage. These findings indicate that cartilage transplants with different properties may have to be generated ex vivo to be optimally suited to the mechanical environment of the patella and the femorotibial joint, respectively.

It is tempting to speculate that in vivo cartilage deformation may represent a more responsive marker in early osteoarthritis than macro-morphological variables such as cartilage volume and thickness, because cartilage loss and swelling may occur in parallel in early osteoarthritis.\textsuperscript{1} The technique used here may be employed to detect changes in cartilage composition in early osteoarthritis, or even to monitor the effect of structure modifying osteoarthritis drugs (SMOADs) in early stages of the disease. High impact loading exercises are inappropriate for patients with osteoarthritis, but the static loading exercise used here may be suitable for investigating patients with early osteoarthritis. As cartilage has been reported to become less stiff and display higher permeability in osteoarthritis,\textsuperscript{26} in vivo deformation of femorotibial cartilage may be greater and become statistically significant in patients. However, this will have to be examined and verified in future studies.

The third objective of our study was to test the hypothesis that the in vivo deformation of patellar cartilage is smaller in athletes than in non-athletic volunteers. This hypothesis was based on the finding that cartilage composition and mechanical properties adapt functionally to mechanical stimulation in animal experiments.\textsuperscript{15} However, in our study no difference in patellar cartilage deformation was observed between athletes and non-athletic volunteers, and at least one previous animal study has shown that training of dogs did not alter the morphological, compositional, or mechanical properties of articular cartilage, even though the animal had been training throughout life.\textsuperscript{29} These different outcomes of animal models may have to do with differences in the maturity of the cartilage, and in susceptibility to mechanical stimuli at different stages of skeletal maturity.

One in vivo study has shown substantial and significant differences in the deformational behaviour of cartilage of young and elderly volunteers, using the same in vivo technique employed here.\textsuperscript{12} These differences have been attributed to differences in cartilage composition, specifically an increase in collagen crosslinks. The results of this study have thus indicated that age dependent changes in cartilage composition and mechanical properties have potential to be measured in vivo. However, our current study provides no evidence that intense physical training modulates cartilage composition and mechanical properties in articular cartilage of athletes than in non-athletic volunteers. This hypothesis was examined and verified in future studies.

In vivo deformation of femorotibial cartilage may be greater and become statistically significant in patients. However, this will have to be examined and verified in future studies.

Table 2: Cartilage deformation (cartilage volume change) in the femorotibial compartment after various exercises

<table>
<thead>
<tr>
<th>Exercise</th>
<th>MT (%±\text{}SD)</th>
<th>LT (%±\text{}SD)</th>
<th>MFC (%±\text{}SD)</th>
<th>LFC (%±\text{}SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee bends (2 legs)</td>
<td>0.1 (4.2%)</td>
<td>-2.8 (4.0%)</td>
<td>-3.9 (9.4%)</td>
<td>-3.3 (6.1%)</td>
</tr>
<tr>
<td>Knee bends (1 leg)</td>
<td>0.1 (2.4%)</td>
<td>0.0 (2.8%)</td>
<td>-3.2 (8.7%)</td>
<td>0.1 (4.7%)</td>
</tr>
<tr>
<td>Jumps (40 cm height)</td>
<td>-6.1 (3.5%)***</td>
<td>-7.2 (4.2%)***</td>
<td>-1.1 (8.3%)</td>
<td>0.2 (5.2%)</td>
</tr>
<tr>
<td>Static exercise</td>
<td>-3.1 (4.5%)*</td>
<td>-2.4 (5.2%)</td>
<td>0.0 (6.6%)</td>
<td>-3.3 (6.2%)</td>
</tr>
</tbody>
</table>

Values are mean (SD). *Borderline significance (p<0.1); **significant at 5% error level (p<0.05); ***significant at 1% error level (p<0.01).

MT, medial tibia; LT, lateral tibia; MFC, medial femoral condyle; LFC, lateral femoral condyle.

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