LONG-TERM PRECISION OF QUANTITATIVE CARTILAGE ANALYSIS IN THE KNEE WITH MR IMAGING VS. INTERINDIVIDUAL VARIABILITY IN 100 VOLUNTEERS AND TISSUE LOSS IN OA PATIENTS

Introduction: Magnetic resonance (MR) imaging is the only non-invasive imaging modality that can delineate articular cartilage directly. It is therefore a promising tool for analyzing cartilage tissue loss in osteoarthritis (OA). Since cartilage degeneration and clinical symptoms are often weakly related, objective parameters of disease status are required for monitoring OA progression, defining the optimal stage for initiating therapy, selecting the most appropriate type of treatment, and evaluating the success of therapy. This is of particular interest since novel therapeutic strategies and structurally modifying compounds are emerging for treating cartilage disorders, the efficacy of which will have to be established in clinical trials. Other potential applications include epidemiologic studies into the risk factors of OA onset, and progression, and the study of functional adaptation of cartilage to its mechanical environment. In conjunction with image processing techniques, fat-suppressed gradient-echo MR sequences have been shown to provide mechanical resolution and fast imaging time to determine the long-term precision of quantitative cartilage analysis in the human knee. The precision will be related to both the variability in healthy volunteers (a measure of the precision of the technique in longitudinal investigations), and the estimated cartilage volume changes associated with OA.

Materials and Methods: To determine long-term precision, the knee joints of eight healthy volunteers (age 22 to 29 yrs; no history of knee affection) were imaged with a 1.5T magnet (Vision, Siemens, Germany). The reason for selecting this group was that the cartilageaguement, degeneration and wear assumed throughout the study period, whereas in OA patients long-term precision errors cannot be adequately separated from actual tissue loss. A sagittal, spoiled 3D gradient-echo sequence (TR = 17.2 ms, TE = 6.6 ms, FA = 20°) with selective water excitation was employed (5,6), with a resolution of 1.5 x 0.31 x 0.31 mm³ (imaging time = 9 min). Four data-sets of the right knee were acquired in the first session (with repositioning of the joint), and two further data-sets within the next 9 months. The MRI-data were transferred to a workstation (Octane Duo, SGI, CA), the cartilages were segmented interactively, and the volumes, mean thickness, and maximal thickness calculated, independent of the original section orientation, by 3D Euclidean distance transformation (4). From the four data-sets obtained in the first imaging session we determined the mean, standard deviation (SD), and coefficient of variation (CV%)) as a measure of the short-term precision. To estimate the long-term precision of the technique in healthy volunteers (a measure of the precision of the technique in cross-sectional studies), and to determine the estimated cartilage volume changes associated with OA, these data can provide a basis for study sample calculations of the power of the technique in longitudinal investigations.

Discussion: We have used a water excitation MR sequence with high spatial resolution and fast imaging time to determine the long-term precision of quantitative cartilage analysis in the knee. The short-term precision for the cartilage volume and mean cartilage thickness ranged from 2.0% to 3.3% (CV%) in the different knee joint regions. The values of repeated measurements (short-term conditions) being 36 mm³ (CV%=4.0%). The long-term precision errors in healthy volunteers, and the short-term precision errors in the patients cannot be adequately determined in OA patients, since errors resulting from scanner drift cannot be separated from actual tissue loss. In a first step, we therefore determined the long-term precision in healthy volunteers and patients with OA. The long-term precision was studied only in the volunteer (in which no change of cartilage volume is expected within the time frame of the study), and the results were then related to the short-term precision in the same sample. It is important to note that by computing the RMS average SD and CV%, a conservative estimate of the precision is given (7), the values being considerably lower when calculating the mean or median CV%.

Results: The long-term precision for the cartilage volume and mean cartilage thickness ranged from 2.0% to 3.3% (CV%) in the different knee joint surfaces (Tab. 1). The long-term precision was markedly lower in the patella and tibia (2.7 to 3.9%), but similar in the femur (Tab. 1). The interindividual variability between 100 healthy volunteers was substantially higher than the long-term precision errors (ratio 5:1 to 10:1). The OA patients displayed cartilage volumes of 620 to 1220 mm³ in the medial tibia, the SD of repeated measurements (short-term conditions) being 36 mm³ (CV%=4.0%). The volumes in the 50 healthy men were 2330 ± 570 mm³, and those in the 50 healthy women 1800 ± 440 mm³. The MR-based analysis in the OA patients underestimated the cartilage volume relative to postoperatively removed tissue by 13%, but there was a very high linear relationship between both measurements (r = 0.98; p < 0.01; SEE = 7%). Under short-term conditions, the standard deviation of repeated measurements in the medial tibia of the volunteers was 56 mm³, and under long-term conditions 93 mm³. These precision errors were small in view of an estimated average tissue loss of 110 mm³ in various OA patients (relative to healthy volunteers of the same gender).

Table 1: Short-and long-term precision (CV%) of quantitative cartilage analysis in the knee, related to interindividual variability in 100 volunteers

<table>
<thead>
<tr>
<th>Joint</th>
<th>Volume (mm³)</th>
<th>Thickness (mm)</th>
<th>Volume (mm³)</th>
<th>Thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patella</td>
<td>2.2%</td>
<td>2.0%</td>
<td>3.9%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Med. Tib.</td>
<td>2.4%</td>
<td>2.6%</td>
<td>3.6%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Lat. Tib.</td>
<td>3.3%</td>
<td>2.7%</td>
<td>3.5%</td>
<td>3.4%</td>
</tr>
</tbody>
</table>

Patellar cartilage volumes of 620 to 1220 mm³ in varus OA patients (relative to healthy volunteers of the same gender). The long-term precision errors were considerably smaller (ratio 30:1 and 12:1, respectively) than the short-term precision errors in healthy volunteers, and the estimated cartilage volume changes associated with OA therefore determined the short-term precision in healthy volunteers and patients with OA. The long-term precision was studied only in the volunteer (in which no change of cartilage volume is expected within the time frame of the study), and the results were then related to the short-term precision in the same sample. It is important to note that by computing the RMS average SD and CV%, a conservative estimate of the precision is given (7), the values being considerably lower when calculating the mean or median CV%.

The study shows that long-term precision errors are only slightly higher than those under short-term conditions, and that the errors are substantially lower than the interindividual variability in volunteers. This confirms a high discriminatory power of the technique in cross sectional studies. Quantitative cartilage measurements in OA are valuable against surgically removed tissue and were found to be highly accurate. The long-term precision errors in healthy volunteers, and the short-term precision errors in the patients were considerably smaller (ratio 30:1 and 12:1, respectively) than the estimated tissue loss in the medial tibia in severe OA.

Our results suggest that the long-term precision of quantitative cartilage MR imaging is sufficient to provide satisfactory discrimination in cross-sectional and longitudinal studies. Together with estimated rates of tissue loss in OA, these data can provide a basis for study sample calculations of pharmaceutical trials and longitudinal scientific investigations.


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