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Measurement of cartilage thickness in the human knee-joint by magnetic resonance imaging using a three-dimensional gradient-echo sequence

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Abstract We studied human specimens and compared data on cartilage thickness measurements with magnetic resonance imaging by using an image analysing system with corresponding histological sections in the middle of each sector. The findings are based on 768 measurements in 26 knee joints. Overall, there was very good magnetic resonance/anatomic correlation ($r=0.88$). The poorest correlation was in the sectors of the femur ($r=0.69$). The correlation seemed not to be dependent on the grade of osteoarthritic cartilage lesions. Despite good correlation rates, the mean magnetic resonance/anatomic difference (absolute values) was 0.41 mm (standard deviation (SD) 0.34 mm) or 18.08% (SD 18.9%). Imaging techniques need to be improved if the assessment of cartilage thickness by this means is to be of clinical relevance.

Résumé Nous avons examiné des spécimens humains et comparé les données des mesures de l'épaisseur du cartilage avec le MRI utilisant un système "image analysing" avec les sections histologiques correspondantes dans le centre de chaque secteur. Les résultats sont fondés sur 768 mesures de 26 articulations du genou. Tous ensemble, la corrélation magnétique résonance/anatomique était très bien ($r=0.88$). La corrélation plus petite dans notre exanination était dans les secteurs du fémur ($r=0.69$). La corrélation était apparemment indépendante du degré des lésions ostéoarthritiques du cartilage. En dépit des taux positifs

de corrélation, la différence moyenne magnétique résonance/anatomique (valeurs absolues) était 0.41 mm (écart-type (EC): 0.34 mm) ou 18.08% (EC 18.9%). Les techniques d'images ont besoin d'amélioration si les mesures de l'épaisseur du cartilage avec le MRI semble important pour les questions médicales. Il faut considérer les différences selon la localisation en évaluant l'épaisseur du cartilage avec le MRI.

Introduction

In the evaluation of cartilage lesions, arthroscopy is still the "gold standard". However, arthroscopy is invasive and is less informative about cartilage thickness. Ultrasonography has the potential to provide information on the cartilage layer but access to the knee joint is restricted. Techniques to assess cartilage thickness by arthrography and X-ray measurements have been described [4,8,12]; however, they mainly provide information on the joint space. These methods are of only minor value. By contrast, magnetic resonance imaging (MRI) provides a non-invasive image of the cartilage layer. It has been recommended that in cartilage imaging with MRI there should be high resolution, thin planar slices without gaps and with good discrimination of the cartilage relative to the surrounding tissue [9]. A sequence termed "fast imaging with steady state precession" (FISP) has proved to be very effective in the evaluation of knee disorders [7,24] and meets these criteria. The following study of human knee joints compares cartilage thickness measurements by MRI with corresponding histological sections.

Materials and methods

We removed 30 fully encapsulated human knee joints at autopsy. Gross deviation of the axis of the lower extremity and inflammatory joint disease were criteria for exclusion. Four of the 30 removed knee joints were excluded from the evaluation because air in the knee joints caused by undetected lesions of the joint capsule

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contaminated the MR images with artifacts. The findings are based on 26 knee joints. The patients ranged in age from 17 to 60 years (mean age 37.5 years); 17 of the 26 patients were males. Institutional review board approval was obtained before starting this study.

The knees were freshly frozen (-20°C) and thawed for the MRI investigation. We used a 1.5 Tesla imager (1.5 T Magnetom Siemens). The knees were positioned in the center of a commercially available surface coil designed specifically for MRI of the knee joint. The tibial tubercle was placed anteriorly. The first measurement was a short T1-weighted sequence in axial slice orientation. Then we used a three-dimensional gradient-echo sequence (FISP, TR=30 ms, TE=12 ms, field of view 170 mm $\times$ 170 mm, flip angle 40°) with an effective slice thickness of 1.6 mm (resolution 1.6 $\times$ 0.7 $\times$ 0.7 mm 3). The slice orientation was sagittal or parasagittal. The axial scout was used for positioning the slice orientation. The slice orientation was at right angles to a line defined by the posterior aspect of the femoral condyles. The axial scout with the femoral and the tibial condyles, and the three-dimensional sequence volume, and the slice orientation were printed as a guide for the bone cuts. Each MRI data set was stored on an optical disc for later investigations.

After MRI, soft tissue was removed. We then prepared 10 histological sections from each knee joint. We took 5-mm-thick bone blocks with one cutting border in the zone of the defined cutting planes. The bone was cut with a high-precision band-saw, using a 0.2 mm thick blade with a diamond surface (EXAKT). This device is specially designed for precision bone cutting with a minimum of tissue loss. It allows a controlled positioning of the rotation as defined in MRI by the posterior aspect of the femoral and tibial condyles. The cutting planes of the tibial plateau were defined by dividing the cartilage-covered area of the medial and lateral tibial plateau into four equal parts in sagittal slice orientation. Other planes were defined in the middle of the medial and lateral femoral condyle and in the middle of the medial and lateral patella facets, respectively. The planes were measured precisely in reference to the medial and lateral bony borders of the tibia, patella and femur, respectively. The geometric measurements defined the corresponding MR images. Controlling the rotation and the geometric measurements ensured that the histological section was within the corresponding magnetic resonance plane with a thickness of 1.6 mm. In addition, the shape of corresponding planes was matched.

The bone blocks were embedded in methyl methacrylate [3]. From the embedded block, a 6- μm section was cut off with a microtome (Polycut, Reichart-Jung). The sections were stained with Safranin-O. The cartilage-covered part of each section was divided into three sectors of the same size. The cartilage thickness measurement was taken at the middle of each sector. Cartilage thickness in MRI was determined by measuring the distance between two pixels. The MR images were shown on the monitor screen at two times magnification.

The histological sections were inducted into an image analysing system (Kontron) by a video camera (K 30, Siemens) connected to a microscope with a 1.25 $\times$ magnification lens (Planachromat, ZEISS). The cartilage thickness was measured interactively with a mouse board by determining the extension of the cartilage layer on the monitor screen and calculating the distance between the two given marks. In addition, the grade of osteoarthritis in each sector was determined according to surface irregularities in the histological sections: Grade 0=normal cartilage; grade 1=slight superficial fibrillations; grade 2=severe fibrillations not exceeding 50% of the cartilage layer; grade 3=severe fibrillations exceeding 50% of the cartilage layer; grade 4=full-thickness cartilage defect.

To obtain data on the reliability of cartilage thickness measurements we made 50 random measurements. The mean difference of intraindividual measurements on MRI was 14.3% (standard deviation (SD) 9.86%) or 0.39 mm (SD 0.31 mm). With the image analysing system the intraindividual difference was 1.4% (SD 1.25%). The values for the interindividual differences were 14.8% (SD 11.9%) or 0.39 mm (SD 0.33 mm) in MRI and 1.65% (SD 1.53%) or 0.034 mm (SD 0.03 mm).

Fig. 1 **a** Magnetic resonance image lateral compartment. **b** Sagittal slice orientation and corresponding histological section lateral proximal tibial articular surface, no surface irregularities

Results

We evaluated 768 out of 780 sectors (26 knee joints $\times$ 30 sectors). Six sectors had artefacts in the histological section. In six sectors, the measurement of cartilage thickness was impossible because of extensive full-thickness cartilage defects. Nearly 70% of the sectors ($n=534$) were grade 0. Nearly 20% of the sectors ($n=149$) were grade 1. Less than 10% of the sectors ($n=75$) were grade 2. There were only a few ($n=10$) grade 3 lesions.

The cartilage thickness in all sectors was 2.69 mm in the reference measurements of the histological sections (SD 1.09 mm). The cartilage thickness ranged from 0.5 mm to 7.4 mm. On MRI, the cartilage thickness ranged from 0.8 mm to 7.1 mm, the average thickness of the cartilage layer being 2.78 mm (SD 1.01 mm).

When comparing the two different systems of assessing the cartilage thickness, overall, a high correlation was found in all sectors ($r=0.88$, where r is the Pearson correlation coefficient). The poorest correlation was in the sectors of the femur ($r=0.69$). In the medial ($r=0.85$) and lateral ($r=0.88$) proximal tibial surface, and in the patella ($r=0.84$), there was reasonable correlation.

The correlation was not dependent on the grade of osteoarthritic cartilage lesions. For sectors without carti-

Table 1 Mean and standard deviation of cartilage thickness measurements for a range of grades of osteoarthritis

	Cartilage thickness – histology (mm)	Cartilage thickness – difference histo – MRI (mm) (absolute values)	Cartilage thickness – difference histo – MRI (%)
Total (<i>n</i> =768)	2.69±1.09	0.41±0.34	18.08±18.90
Grade 0 (<i>n</i> =534)	2.50±1.02	0.41±0.34	19.43±20.44
Grade 1 (<i>n</i> =149)	3.11±1.09	0.41±0.35	14.57±13.76
Grade 2 (<i>n</i> =075)	3.19±1.22	0.42±0.32	15.46±15.40
Grade 3 (<i>n</i> =010)	2.92±1.19	0.44±0.42	18.12±16.23

Table 2 Mean and standard deviation of cartilage thickness measurements according to the location

	Cartilage thickness – histology (mm)	Cartilage thickness – difference histo – MRI (mm) (absolute values)	Cartilage thickness – difference histo – MRI (%)
Total (<i>n</i> =768)	2.69±1.09	0.41±0.34	18.08±18.90
Medial tibia (<i>n</i> =228)	2.26±0.82	0.33±0.28	16.01±14.52
Lateral tibia (<i>n</i> =232)	2.89±1.10	0.42±0.33	16.65±15.37
Femur (<i>n</i> =155)	2.02±0.57	0.49±0.35	28.80±28.81
Patella (<i>n</i> =153)	3.72±0.99	0.45±0.38	12.48±11.34

lage surface irregularities, $r=0.86$; in sectors with grade 1 lesions, $r=0.87$; in sectors with grade 2 lesions, $r=0.90$; in sectors with grade 3 lesions, $r=0.86$.

Despite the good correlation between cartilage thickness measurements by MRI (Fig. 1) and the corresponding measurements in histologic sections as reference, there was an overall average difference of 0.41 mm (absolute values) or 18.08% (Table 1). Depending on the grade of osteoarthritis, the values varied between 15% and 20%. The average cartilage thickness in histological sections seemed to increase with the severity of osteoarthritis. This difference may be because the grading of cartilage lesions was according to the maximum cartilage defect in the sector whereas the cartilage thickness measurement was taken in the middle of the sector. In many cases, the maximum cartilage defect did not cover the whole area in the sector but rather was very small in extent.

The lowest values for the thickness of the cartilage layer were in the femur. However, in this location there was the greatest difference between MRI measurements and the reference values (nearly 30%). In the patella, medial and lateral tibia, the average difference ranged between 12% and 16% (Table 2).

Discussion

The results of our study show a high correlation between measurements of cartilage thickness by MRI and the reference method in histological sections. These data confirm the results from Karvonen et al., who found no significant differences between MRI and specimens in over 200 sites in four knees [13]. Chandnani et al. compared cartilage thickness measurements by MRI with gross sections in six cadaveric knees. In 30 measurements, differences ranged from 0.1 mm to 2.9 mm [2]. The corre-

lation rates were better in isolated proximal tibial articular surfaces [14]. This may be because in MRI the discrimination of the hyaline cartilage in different locations within a knee joint is more difficult to obtain than in an isolated part of the knee joint. If there is no effusion, the articular surfaces are in close contact with each other. Two sequences may be required to define articular cartilage accurately [15,18]. The assessment of articular cartilage can be improved by contrast material, but even then, the mean magnetic resonance/anatomic difference was 0.37 mm for gradient-echo images of the humeral head [11].

By measuring cartilage volume and defining cartilage thickness intervals in MRI information on local changes is lost despite good reproducibility [6,22]. In the patella specimen, less than 17% of the image points deviated more than 0.5 mm when comparing MRI and histological sections. Between 50% and 90% were within an interval of 0.5 mm [19]. In our study, a difference of 0.5 mm would have led to a possible difference of about 20% for the average cartilage thickness of 2.69 mm.

The same applies to the dependency on pixel-based measurements in MRI. This dependency on the pixel size may account for the lower correlation and the higher deviation between the two methods used in our study to measure cartilage thickness in the femoral areas.

Eckstein et al. found no significant difference between areas of thin and thick cartilage in six human patellae [5]. In our study, we have very good correlation in the patellar cartilage. However, the mean cartilage thickness in the patella was the greatest of all the locations and, therefore, pixel-based errors of measurement that occurred in thin cartilage areas would not be expected in the patella. Another reason for the poor correlation in the femur may be that the geometry of a round contour is much more complex than that of the patella or the tibia plateau in the sagittal planes. The geometry of the hip

joint may account for differences that make MRI of this joint unsuitable for clinical practice [10].

In our study we compared thickness measurements. The volume of the cartilage was not calculated. There are reports that MRI with three-dimensional reconstruction and measurement techniques can accurately and reproducibly measure the volume of articular cartilage [15,17]. In osteoarthritis, topographical changes are significant. Data on local changes are lost in volumetric calculation. Considering the transition zone of cartilage, the mean value for underestimation of the talus cartilage thickness was 14.1%, ranging from 6.7% to 21.5% in a fat-saturated three-dimensional gradient-echo sequence [23]. These data are comparable with our results and it is therefore assumed that volumetric calculation offers no advantages.

Trattnig et al. state that accuracy can be improved if the transition zone is included [23]. Calcified cartilage makes up to 10% of the total cartilage thickness [1,16]. With this in mind, the limiting factor is not the calcified tissue, which is difficult to delineate by MRI in commonly used sequences [21], but the resolution in plane.

We used a three-dimensional gradient-echo sequence (FISP). So far there has been no clear consensus on which technique is best for cartilage imaging. Three-dimensional sequences [21] with thin slices [15] provide better results in the assessment of hyaline cartilage thickness and hyaline cartilage volume. Fat-suppressed sequences may improve the discrimination of cartilage [20,21].

Cartilage thickness measurements are possible in MRI. Imaging techniques, however, need to be improved, especially the resolution in plane, if the assessment of cartilage thickness by MRI is to be of clinical relevance.

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