



## Original article

# How precisely does ultrasonographic evaluation reflect the histological status of the articular cartilage of the knee joint?



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## ABSTRACT

The thickness and the grade of the articular cartilages of the knee of 34 patients who underwent total knee arthroplasty were evaluated by ultrasound (US) and by histology. The US grade correlated with the histological grade and the thickness of the articular cartilage measured by US. The thickness measured by US was significantly correlated with that measured by histology for the medial condyle. The US thickness was significantly less than the histological thickness for thicker articular cartilages. US grading and the thickness of the articular cartilages evaluated by US is sufficiently reliable to indicate their histological status.

## 1. Introduction

In degenerative joint disorders such as osteoarthritis (OA) and rheumatoid arthritis (RA), articular cartilages wear down and become thinner over time, and patients with severe degeneration eventually require total joint replacement. It is widely accepted that the state of the articular cartilage is well correlated with the symptoms and severity of the joint degeneration.<sup>1</sup> X-ray and magnetic resonance imaging (MRI) are commonly used to reliably evaluate the status and the severity of joint degeneration. However, ultrasonography (US) of the joint has been recently developed and has gradually gained wide acceptance as an advanced technology capable of observing subtle changes. Of these three modalities, however, X-ray cannot directly assess cartilages, and MRI is time-consuming and costly. Therefore, the advantages of US, including its low cost, lower demands for processing, and the lack of radiological exposure, have been widely appreciated.

US evaluation of the joints has gained credibility, especially for assessment of joint inflammation and destruction. Previous studies have shown a correlation between US features and pain or arthroscopic features.<sup>2,3</sup> In particular, it has been shown that knee US performs excellently compared with arthroscopic grading for detection of degenerative changes in the articular cartilage.<sup>4</sup> However, its concordance with direct histological evaluation has not been confirmed. It is crucial to know how the femoral articular cartilages have degenerated because this reportedly represents accurately the status of all the articular cartilages.<sup>2,3,5</sup> Lee et al. reported that the histological grading was weakly

correlated with the US grading.<sup>6</sup> However, that study evaluated the articular cartilages in a transverse plane, which in practice is not easily scanned by US, and moreover, did not compare the thickness of cartilages evaluated by US and histology. We have previously shown in an *in vitro* study using a specific US system to detect early changes in the articular cartilage that US grades correlate well with histological grades.<sup>7</sup> However, we did not evaluate *in vivo* changes or analyze degenerative changes or the thickness of the articular cartilages.

Thus, the purpose of this study was to assess the reliability of US for evaluation of articular cartilage thickness and grades *in vivo* in patients with degenerative knee changes who underwent total knee arthroplasty.

## 2. Patients and methods

### 2.1. Patients

The protocol for this study was approved by the Institutional Review Board before the start of this study (Approval no. E1490). Informed consent for the study was obtained from all participating patients in accordance with the World Medical Association Declaration of Helsinki. Sequential patients undergoing total knee arthroplasty because of RA or OA were recruited for this study. The diagnoses of OA and RA were established based on the diagnostic criteria of the American College of Rheumatology<sup>8</sup> and the European League Against Rheumatoid Arthritis/ACR,<sup>9</sup> respectively. A total of 35 knees in 34 patients were

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**Table 1**  
Demographic data.

parameters	
number of specimens (patients)	35 (34)
age $\pm$ SD (min-max)	72.3 $\pm$ 7.8 (61–87)
females (%)	27 (77.1)
OA / RA	31 / 4
BMI $\pm$ SD (min-max)	25.0 $\pm$ 4.0 (18.2–34.1)

OA; osteoarthritis, RA; rheumatoid arthritis, BMI; body mass index.

enrolled. The average age of the patients was 74.5 years (61–87 years) and 27 patients (77%) were women (Table 1). The demographic information for all patients was collected from their medical records.

## 2.2. Clinical evaluation

Knee joint symptoms were evaluated using the Knee Society Score (KSS), which was developed and revised for patients who undergo total knee arthroplasty.<sup>10–12</sup> An X-ray of the knee joint was taken using a standardized protocol,<sup>13</sup> and the level of joint destruction was graded using the Kellgren–Lawrence grading system<sup>14</sup> by two experienced orthopedic surgeons (MF, HI), both of whom were board members of the Japanese Orthopaedic Association and were blinded to the US and histological findings for the articular cartilages.

## 2.3. US evaluation

Patients underwent US in the operating room just before total knee arthroplasty or one day before the operation at their bedside. Transverse scans of the intercondylar notch and sagittal longitudinal scans of the distal femoral condyles medially and laterally to the patella were performed with the patient lying supine with a fully flexed knee.<sup>4, 15, 16</sup> The thickness of the cartilages was measured at three points on the images, and the cartilage thickness was defined as the average of the three measurements. As a reference, the thickness of the femoral cartilage of the patellofemoral joint was also recorded.<sup>17</sup> The degree of degenerative change in the cartilages was classified into five grades using the grading system reported previously.<sup>4</sup> The US machine used for this study was a NOBLUS (Hitachi Aloka, Tokyo, Japan) with a 5 MHz linear transducer.

## 2.4. Histological evaluation

The articular cartilage fragments attached to the subchondral bone of the distal femoral condyles were resected during the operation. During the placement of the US probe, lines were drawn with a marker pen to indicate the femoral articular cartilage medial and lateral to the patella with the knee fully flexed; the outlined portion was collected after the femoral resection for arthroplasty and used for the histological evaluation (Fig. 1). These specimens were first cut into approximately 3-mm-wide sections in the sagittal plane, corresponding to the plane used for US imaging. The specimens were fixed in 4% paraformaldehyde and decalcified in Morse's solution for 2–3 days. After decalcification, the tissue was embedded in paraffin wax, and 7- $\mu$ m sections were made. These sections were stained with 0.1% Safranin O and 0.06% fast green. Cartilage thickness was measured at three points of each section, similar to the measurement of cartilage thickness by US, and the cartilage thickness was defined as the average of the three measurements. In addition, the histological features were graded using the Osteoarthritis Research Society International grading system.<sup>18</sup> The measurements and grades were independently evaluated by two researchers (KM, MF) and were strongly correlated (data not shown).

## 2.5. Statistical analyses

Statistical analyses were performed by an independent researcher (YM) who was blinded to the intraoperative findings and who did not assess any of the US, radiological, or histological grades or measure the thickness of the cartilage. Continuous data are expressed as means, standard deviation (SD), and ranges, whereas categorical data are presented as absolute numbers and percentages. Spearman's rank correlation coefficient was used to determine correlations between two grades. We also calculated Spearman's rank correlation coefficient to compare the values of the thickness measured by the two methods. The intraclass correlation coefficient (ICC) was also calculated for the values measured by the two methods. A *p* value < 0.05 was considered significant.

## 3. Results

The average cartilage thicknesses of the patellofemoral joint, and medial and lateral condyles measured by US were 1.18  $\pm$  0.72 (0–2.76) mm, 0.49  $\pm$  0.35 (0–1.47) mm, and 0.75  $\pm$  0.45 (0.10–1.60) mm, respectively (Table 2). The knee function evaluated by KSS was weakly but significantly correlated with the histological grade for the medial femoral condyle but not with that for the lateral femoral condyle (data not shown), which is consistent with other reports.<sup>2</sup> Importantly, the US grades were strongly correlated with the histological grades for the femoral medial condylar cartilages (Fig. 2a), while there was no significant correlation for the femoral lateral condyles (data not shown). However, the US grades were significantly correlated with the thickness of the articular cartilage measured by US for both the medial and the lateral condyles (Fig. 2b).

Next, the cartilage thicknesses assessed by US and histology were compared. Fig. 3 shows that there was a significant correlation between the two evaluation methods for the medial condyle ( $\rho = 0.42$ ,  $p = 0.02$ , ICC = 0.751), but not for the lateral condyle ( $\rho = 0.15$ ,  $p = 0.42$ , ICC = 0.204). In addition, Fig. 4 shows that many specimens came from the area under the center line, especially those with thicker cartilages. The subtracted difference between the value measured by histology and that by US showed significant positive correlation with the thickness of the articular cartilage measured by histology (Fig. 4). Therefore, the thickness of the cartilages in this thick group appeared significantly thinner by US evaluation than by histological evaluation (Fig. 4).

## 4. Discussion

This study identified several important results concerning the measurement and grade of the articular cartilage of the knee joint evaluated by US. First, the US grades were strongly correlated with the histological grades, which also supports the validity of the standardized US grading system currently used. Second, the measurements of cartilage thickness showed that knee symptoms were also correlated with the thickness of the medial but not of the lateral femoral condyle as measured by US. Third, for the medial but not the lateral condylar cartilage, there was a significant correlation between the thickness of the articular cartilage as measured by US and the histological evaluation. Lastly, as a practically important point, the thickness of the thickest cartilages appeared thinner on US than on histological evaluation.

The grading system for articular cartilages aims to indicate the overall degree of degeneration with sufficient reliability. Both the radiological Kellgren–Lawrence grading and the US grading have been frequently reported to have excellent practicality and reliability.<sup>2, 19</sup> However, the correlation between the US and histological grading may not have been adequately demonstrated. This study shows that the US grading system correlates well with histological grading. Although each system has its own weaknesses, the three systems seem to complement each other. Although we did not have the opportunity to obtain MRI for

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