Ultrasonographic evaluation of early knee osteoarthritis

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Abstract: Ultrasonography (US) is non-invasive, fast, easy-to-use and safe. The quality and resolution of US has been improved in recent years. Recently, in orthopaedics, US measurements have been used for the diagnosis of osteoarthritis (OA), which can provide the basis for proper early treatment. In this chapter, we review the published articles about US evaluation of knee OA, especially focused on cartilage, including probe selection, probe direction, evaluation site, knee position, measurement of thickness, echogenesis and superficial sharpness of cartilage with histological findings and accuracy to detect early OA changes.

Keywords: Ultrasound (US); cartilage; early osteoarthritis; knee

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Introduction

Knee osteoarthritis (OA) is common in elderly adults and is often seen in the outpatient clinic. The severity of clinical symptoms of knee OA is not reflected the radiological stage (1,2) and knee pain is associated with poor health status and psychological distress (3). However, OA is now diagnosed by radiological grading, which is based only on the joint space width. It is important to detect OA in its early stages to prevent it from progressing. However, a convenient method with rapid evaluation has not been reported.

Ultrasonography (US) is widely used in many medical fields and non-invasive US can be employed to evaluate cartilage, meniscus, tendon, joint effusion, bursitis and synovitis, as well as bony structures related to OA such as osteophytes and subchondral bone (4-23). US examination has been reported to be useful for evaluation of cartilage quantity, which cannot be detected by X-ray (4,5,9,11,21,23). It also has been reported that OA initiates superficially, and previous reports have shown the correlation between echoic superficial findings and histological score in the detection of early OA (8,10,11,13,17,19). However, optimization of the measurement protocol of US to detect early OA has not been established.

In this chapter, we review US evaluation of the cartilage and other components to reveal its potential to detect early knee OA. The aim of this review is to evaluate the effectiveness of US diagnosis of early OA, and to explore the associations between US findings such as echogenesis and superficial sharpness with histological findings in early knee OA.

Patients and methods

Study selection

We focused on US evaluation of the knee, especially cartilage and other OA characteristic findings, and chose 20 articles that provided the information about the sample site/species, sample number, probe selection, probe direction, knee position, evaluation site, assessment of the cartilage, and accuracy of the US diagnosis.

All items were reviewed in the selected articles and are summarized in *Table 1*.

Table 1 Summary of US examination of all articles

Author	Year	Sample	Number	Probe (MHz)	Probe direction	Knee position	Evaluation site	Assessment	Accuracy of US examination
Aisen (4)	1984	Bovine; Human (OA and RA)	20	7.5	Longitudinal; transverse	Full flexion	MFC; LFC; PG	Surface condition; cartilage thickness	Accurate measurement of surface characteristics and thickness
Mathiesen (5)	2004	Cadaver	11	10	Longitudinal; transverse	Full flexion	FC	Cartilage thickness; cartilage defect	Accurate measurement of cartilage thickness and depth of cartilage defects
Naredo (6)	2005	Patients (OA)	50	7–12	Transverse; longitudinal	Respective position in each compartment	FT space; posterior	Effusion; MRD; pain; Baker cyst	Significant correlation between MRD and effusion and pain
Kuroki (7)	2008	Patients for TKA (OA)	20	10, small transducer intraoperative (diameter 3 mm)	Not applicable	Not applicable	MFC; LFC; MTP; LTP	US findings; arthroscopic finding (ICRS classification)	Signal intensity helpful to differentiate ICRS grades, grade 0 from grade 1 cartilage
Lee (8)	2008	Patients (OA)	95	5–12	Horizontal	Full flexion	MFC; LFC	Grading of in vivo and in vitro US findings (margin sharpness, clarity and thickness); histological findings (Huang's criteria)	Significant correlation (both in vivo and in vitro)
Yoon (9)	2008	Patients (OA)	41	12.5	Longitudinal; transverse	Full flexion	MFC; LFC	Cartilage thickness measured by US and MRI	A good correlation between longitudinal US and MRI in cartilage thickness
Aula (10)	2010	Bovine osteochondral samples	10	5	Not applicable	Not applicable	MTP	Simultaneous measurement of cartilage and subchondral bone of US findings, biomechanical and histological (Safranin-O stain)	Weak relationship between US findings and properties of cartilage and bone
Wang (11)	2010	Fresh cylindrical mature bovine cartilage	20	40, small transducer (diameter 4.5 mm)	Not applicable	Not applicable	P	Cartilage degradation (stiffness, thickness, histological and scanning electron microscopy) and US findings	Significant association
Kaleva (12)	2011	Patient (OA)	7	40, small transducer (diameter 1 mm)	Not applicable	Not applicable	PG; P; T	Arthroscopic findings (ICRS classification); intra-articular US findings	Effectiveness of intra-articular US for quantitative imaging of the lesion
Niu (13)	2012	Rabbit	18	55, small transducer (diameter 4.5 mm)	Not applicable	Not applicable	MFC; LFC; MTP; LTP	URI, R; histological analysis (OARSI grade)	Correlation the change in URI and R with different OA grades

Table 1 (*continued*)

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Author	Year	Sample	Number	Probe (MHz)	Probe direction	Knee position	Evaluation site	Assessment	Accuracy of US examination
Wu (14)	2012	Patients (OA and healthy)	85 (symptomatic knee); 27 (asymptomatic knee)	6–13	Longitudinal; transverse	Respective position in each compartment	Suprapatellar effusion; osteophyte; medial meniscus protrusion; synovitis; baker cyst	US findings between the two groups	Positive correlation between suprapatellar effusion and medial compartment synovitis and pain at rest
Saarakkala (15)	2012	Painful patients	40	13	Transverse	Full flexion	MFC; LFC; PG	US findings (sharpness of superficial layer and cartilage) and arthroscopic findings (Noyes' grading)	Highest correlation in femoral cartilage
Kawaguchi (16)	2012	Patients (OA)	78	5	Longitudinal	Full extension	FT	MRD; radiological findings	Positive correlation between OA progression and MRD with weight bearing
Nishitani (17)	2014	Rabbit; Human (OA)	18; 20	10, small transducer (diameter 3 mm)	Not applicable	Not applicable	LFC	US findings (US signal intensity) and histological findings (Mankin score)	Positive correlation
Riecke (18)	2014	Patients (OA)	45	14	Transverse; longitudinal	0 and 90 degrees	14 positions	Validity, reliability and reproducibility of US findings in detecting OA	Relevant precision
Männicke (19)	2014	Human punched cartilage	19	40	Not applicable	Not applicable	FC	US findings (9 parameters); histological findings (Mankin score)	Good parameter of surface reflections and signals backscattered in very early degeneration of cartilage
Yanagisawa (20)	2014	Patients (OA)	81	12	Longitudinal	Full extension	FT	US findings (osteophyte, MRD and FT Joint space) with and without weight bearing between the OA and non-OA groups	A good tool to assess MRD, peripheral joint space and osteophytes
Bevers (21)	2014	Patients (OA)	55	8–15	Transverse	Full flexion	MFC LFC	US features in a cohort study (6 parameters: effusion, synovial proliferation, infrapatellar bursitis, meniscal protrusion, Baker cyst and cartilage thickness)	Stable futures of meniscal protrusion and Baker cyst
Yanagisawa (22)	2015	Patients (OA)	225	12	Longitudinal	Full extension	FT	US findings (osteophyte, MRD; and FT Joint space) with and without weight bearing between the ages	A high reliability and excellent diagnostic accuracy
Tuna (23)	2016	Patients (OA)	40	Not described	Transverse	Full flexion	MFC; LFC; PG	Cartilage thickness; muscle power	Positive correlation

US, ultrasound; TKA, total knee arthroplasty; OA, osteoarthritis; RA, rheumatoid arthritis; MFC, medial femoral condyle; LFC, lateral femoral condyle; T, tibia; MTP, medial tibial plateau; LTP, lateral tibial plateau; FT, femorotibial; PG, patellar groove; P, patella; MRD, medial radial displacement; URI, the surface roughness index; R, the ultrasound reflection coefficients of the cartilage.

Sample selection

All studies included animal and human subjects. Rabbit and bovine knees were widely used models in cartilage research. In human beings, OA patients who underwent total knee arthroplasty (TKA) were primary subjects. Fresh cadavers, osteochondral plugs or punched samples were also examined.

Results

US evaluation

Evaluation site

In the knee, the medial and lateral condyle, intercondylar notch area, and patellar cartilage were examined. In addition, medial meniscal displacement, synovitis and Baker cysts were checked.

Probe selection

Linear and spherical type probes were used in non-invasive US. The small transducer was used for intra-articular evaluation using US.

Probe frequency

In the orthopaedic area, 3–5 MHz frequency is used to assess the deep structures and 7–10 MHz frequency is used to evaluate more superficial areas under the skin. 0.1–1 MHz has been suggested as the most useful for bone characterization. The low frequency of conventional US may lack the resolution necessary for cartilage and has limited accuracy and sensitivity to detect cartilage degeneration. Previous reports have shown that higher frequencies have the potential to detect cartilage degeneration with ultrasound transducers arranged close to the cartilage (11-13,19). The drawback of using a high frequency probe is high attenuation, which inevitably prevents analysis of subchondral bone.

In this series, probe frequency was 5 to 55 and 5–15 MHz was most often used.

Internal or external US

External US is a safe and non-invasive approach to the knee joints, but minimization of the effect of overlying tissue layers is needed. Internal US is more accurate because there is no interference with soft tissues, but it is an invasive procedure.

Probe direction to the knee

The direction of the probe to the femoral condyle is limited due to the patella. Suprapatellar, transverse or longitudinal sagittal plane approaches have been used.

The transverse direction is most often used to check the femoral cartilage.

The longitudinal sagittal approach to the distal end of the midline medial and lateral condyle is conducted when can be used with the patient sitting on the table in the deep flexed position. The ultrasound beam is kept perpendicular to the surface of the distal end of the femur along the midline (9).

There has been only one article that compared the suprapatellar transverse and longitudinal sagittal plane approaches to check the accuracy of cartilage thickness by validation with MRI (9). Yoon reported that the longitudinal sagittal plane of OA patients was more accurate than the transverse image in measuring cartilage thickness of the medial femoral condyle when compared to MRI.

Knee position

The knee position for cartilage measurement using US has been controversial because the shadow of the patella makes it difficult to determine the weight-bearing area of the cartilage. Therefore, it is important to assess how much of the weight-bearing femoral cartilage can be detected with US.

For the medial and lateral condyles and the intercondylar cartilage, the maximally flexed position was used most often by sweeping the cartilage from proximal to distal with the probe in transverse position in this series of studies. Lee reported that the correlation between *in vivo* and *in vitro* US grading of OA patients and maximum angle of knee flexion less than 120 degrees was not reliable, and they recommended the knee full flexed position in measurement by US (8).

Diagnostic study between arthroscopic or macroscopic and US findings

Three articles compared the US findings and arthroscopic or macroscopic findings of different characteristics of the articular surfaces of the human knee joint.

Kuroki reported that US signal intensity of cartilage, not signal duration or interval between signals, is most helpful to differentiate various OA grades of OA patients using the International Cartilage Repair Society (ICRS) scoring system. It is especially useful to distinguish grade 0 (normal) from grade 1 cartilage (nearly normal) (7).

Kaleva reported that the intra-articular arthroscopic US method (IAUS, 40 MHz) could provide a diagnostic method based on different characteristics of the articular surfaces of the human knee joint for evaluation of the severity of articular cartilage lesions, ICRS grade, and early osteoarthritic changes. There was no correlation between roughness index of the cartilage surface (URI) and ICRS grade. The IAUS score was one rank higher than the ICRS grade estimated during conventional arthroscopy. The IAUS method can distinguish ICRS grade 0 (normal) and grade 1 (almost normal) based on the characteristics of the cartilage surface. However, this method could only be performed invasively (12).

Saarakkala reported that US gradings based on interface sharpness and echogenicity of the cartilage in the transverse plane of the human femoral condyle in patients with pain had a strong correlation with arthroscopic changes of cartilage at least for the medial condyle and the sulcus area (15). The cartilage was subjectively evaluated using five classifications based on the US findings of the condition of the superficial layers (sharp interface or irregular interface) and the intensity of cartilage (monotonous anechoic or hyper echogenicity) as follows: grade 0 (sharp interface or monotonous echogenicity), grade 1 (loss of sharp interface and increased echogenicity), grade 2A (loss of sharp interface and increased echogenicity, less than 50% local thinning of cartilage), grade 2B (irregular interface and hyper echogenicity, more than 50% but less than 100% local thinning), and grade 3 (100% local loss of the cartilage).

The diagnostic accuracy of the cartilage surface of the medial and lateral condyles and sulcus area was evaluated. Sensitivity (83%) was good only in the medial femoral condyle. Specificity was good for the femoral sulcus and lateral condyle. A positive predictive value (88–100%) was strong at all sites. The negative predictive value (24–46%) was low. The diagnostic odds ratio and a general indicator of test performance of US varied between 5.0 and 13. They indicated that negative findings do not rule out degenerative changes.

From these findings it was concluded that *in vivo* intra-articular US examination could reflect more accurate macroscopic findings than that of being found with arthroscopy, indicating that US examination has the potential to detect early OA of the knee, especially changes to the superficial layer of the cartilage.

Diagnostic study between histological and US findings

Six articles compared US findings and histological findings.

Niu *et al.* reported that high frequency US measurements (55 MHz) can reflect changes in the URI and ultrasound reflection coefficients (R) of the cartilage samples from a rabbit model with different OA grades (OARSI grade), especially in early and mild OA (13). URI could be used to distinguish early OA and mild OA but had no ability to accurately distinguish grade 1 from grade 2. This study suggests that these two US acoustic parameters have the potential to become objective criteria in OA grading.

Nishitani *et al.* reported that ultrasound (10 MHz) can detect macroscopically undetectable changes in OA reflecting histological and biochemical degeneration in both rabbit and human OA samples, respectively (17). The URI was significantly different from nearly normal, early OA and moderate OA, and was correlated with Mankin scores. Parameters derived from fourier-transform infrared spectroscopy (FTIR) reflected collagen and proteoglycan content in the superficial zone.

Wang reported the feasibility of high frequency (40 MHz) ultrasound for simultaneous assessment of the surface condition, acoustic parameters, thickness and mechanical properties of articular cartilage of fresh bovine cartilage *in vitro* (11). They showed a significant relationship between the surface integrity and URI. The ultrasound reflection intensity is sensitive to early histological changes of OA *in vitro*.

Lee *et al.* reported significant correlations between both *in vivo* US findings (5–12 MHz) and *in vitro* gradings (sharpness of the superficial margin, and clarity and thickness of the cartilage band) with histologic gradings of distal medial and lateral femoral condyles according to Huang's criteria (8).

Aula *et al.* showed that 5 MHz ultrasound could provide diagnostically valuable information on both cartilage and bone (10). They showed the feasibility for simultaneous measurement of the acoustic properties of articular cartilage and subchondral bone of bovine osteochondral samples by pulse-echo ultrasound at 5 MHz, which could quantify both cartilage and subchondral bone changes. The relationship between the US parameters (backscattered signal from the internal cartilage and from subchondral bone) and properties of cartilage and bone were not as strong as earlier studies focusing only either on bone or cartilage.

Männicke *et al.* reported that the combinations of high frequency and US-based parameters derived from surface reflections and signals backscattered from the cartilage matrix (40 MHz) exhibit potential to characterize the very early degeneration stages of articular cartilage of human punched samples evaluated by a modified Mankin score (19). The surface parameters [integrated reflection amplitude (IRC) and URI] used in this study are related to cartilage softening and surface fibrillation. They suggested that both minimally invasive arthroscopic US and high frequency transcutaneous US could conceivably be used for *in vivo* application.

Based on these findings, US examination, especially high frequency US *in vitro*, correlates with histological change and can detect superficial microscopic histological changes that cannot be detected macroscopically. Further studies are needed for optimization of the ultrasound frequency and measurement geometry in clinical application.

Diagnostic study between other findings of knee OA and US findings

There were seven reports about critical US findings reflecting OA changes.

Radiological assessment

Naredo *et al.* reported the comparative study with clinical and radiographic assessment that knee effusion and protrusion of the medial meniscus with displacement of the medial collateral ligament measured with US were associated with knee mechanical pain and pain at rest between the symptomatic and asymptomatic OA patients (6). In addition, protrusion of the medial meniscus may contribute to the radiologic medial FT space narrowing.

Riecke *et al.* reported that five separate domains including morphological changes and inflammation in the medial and lateral compartment, and effusion were examined with US and US score displayed substantial reliability and reproducibility in comparison with standing radiographs of the knees (18).

Pain assessment

Wu *et al.* reported that medial meniscus compartment synovitis and suprapatellar effusion measured with US were positively linearly associated with knee pain at motion with equal radiographic grades of OA in both knees (14).

Medial meniscal and other assessment

Kawaguchi *et al.* reported that medial meniscus displacement (MRD) measured with US increased with weight bearing, with a close association between extraarticular displacement of the medial meniscus and progression of OA (16).

Yanagisawa *et al.* reported that the longitudinal US image in knee extension in both the standing and supine positions had a high reliability and excellent diagnostic accuracy for OA of the knee based on the joint space, peripheral osteophytes and MRD, and could accurately detect the early degeneration of the knee joint (20,22).

Bevers *et al.* reported the prospective and explorative study that six US features including effusion, synovial proliferation, infrapatellar bursitis, meniscus displacement protrusion, Baker's cyst and cartilage thickness were investigated in 55 OA patients receiving standardized multimodal treatment for 1 year. The prevalence of inflammatory features like effusion and synovial hypertrophy show a fluctuating pattern in time in contrast to meniscus displacement protrusion, Baker's cyst (21).

Clinical relevance between US findings and muscle power

Berger *et al.* reported that KL grade was limited and not significant as a severity stratification method to show differences in knee extension force. The KL radiological classification has not been associated with OA symptoms and muscle power (1). On the other hand, there has been one report of the relationship between cartilage thickness measured by US and muscle power showing that femoral cartilage thicknesses were positively correlated with isometric quadriceps and hamstring muscle strength at baseline and after three months of a muscle strengthening program (23).

Conclusions

The US evaluation of knee cartilage has the potential to detect both *in vitro* and *in vivo* superficial cartilage abnormalities and characterize very early degenerative stages of articular cartilage before macroscopic changes. US is a promising technique for clinical screening of degenerative changes of articular cartilage and detection of the early stages of OA *in vivo*. Further studies are needed to elucidate the diagnostic value and potential limitations of US and to reveal the most appropriate combination of invasive or non-invasive probe selection with other conditions when used clinically.

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Footnote

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