

# Simultaneous evaluation of long-lasting knee synovitis in patients undergoing arthroplasty by power Doppler ultrasonography and contrast-enhanced MRI in comparison with histopathology

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## Abstract Objectives

We simultaneously assessed ultrasonography (US) and magnetic resonance imaging (MRI) in comparison with histopathological changes in the knee joints of long-lasting arthritis patients.

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## Methods

We studied 15 patients with rheumatoid arthritis and 5 patients with osteoarthritis, who underwent total knee arthroplasty. On the day before surgery, the joints were examined by US and contrast-enhanced MRI. In US, synovitis was graded with 0–3 grey scale (GSUS) and power Doppler (PDUS). In MRI, synovitis was graded according to OMERACT-RAMRIS (grade 0–3). Synovial tissue samples were obtained during arthroplasty and evaluated on the basis of inflammatory cell infiltrates (grade 0–3), synovial lining layer thickness (grade 0–3) and vascularity (grade 0–3).

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## Results

Positive findings of PDUS and contrast-enhanced MRI were 45% and 85% of 20 operated joints, respectively. GSUS, PDUS and MRI synovitis were well correlated with overall histopathological grades of synovitis (Spearman correlation coefficients 0.48, 0.84 and 0.48,  $p < 0.05$ ,  $p < 0.01$  and  $p < 0.05$ , respectively). Moreover, positive PDUS findings were closely associated with all pathological compartments of synovitis including inflammatory cell infiltrates, synovial lining layer thickness and vascularity.

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## Conclusions

The present study revealed that positive PDUS findings more faithfully illustrated active synovitis than MRI, whereas contrast-enhanced MRI was more sensitive in detecting synovitis in patients with long-lasting arthritis. It is important to understand distinct features of the both modalities for clinical assessment of chronic joint diseases.

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## Key words

ultrasonography, magnetic resonance imaging, synovitis

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## Introduction

The accurate assessment of joint lesions is essential for the early diagnosis and evaluation of disease activity in inflammatory arthropathies such as rheumatoid arthritis (RA) and osteoarthritis (OA). In addition to physical findings and laboratory examinations, it is important to develop noninvasive imaging techniques that visualise inflammatory tissues in daily clinical practice. Histopathological findings of RA synovial tissues are characterised by marked hyperplasia of synovial cells, accumulation of various inflammatory cells, neovasculation, and subsequent destruction of the bone and cartilage by pannus, which consists of proliferated synovial cells. OA is widely regarded as being primarily a degenerative disorder of articular cartilage, which is associated with a considerable degree of synovial inflammation. Although conventional radiography (CR) essentially shows bone structural lesions, it hardly evaluates ongoing histopathological changes of inflammatory arthropathies in soft tissue lesions. Recent progression of treatment for RA in the biologic era further prompts us to establish more sensitive imaging techniques that evaluate individual joint lesions appropriately.

To meet the clinical demand as described above, ultrasonography (US) and magnetic resonance imaging (MRI) have been recently recognised as valuable imaging tools to evaluate individual joint lesions in inflammatory arthropathies (1, 2). Moreover, the imaging findings well represent pathological changes of synovial tissues (3, 4). Previous reports demonstrated that high Power Doppler signal in US is associated with pathological findings of active synovitis including neovascularisation and intensive infiltration of inflammatory cells such as macrophage-like synoviocytes and Th17 cells (5-7). Dynamic contrast-enhanced MRI visualises neovascularisation in the synovium in addition to bone marrow oedema, which represents infiltration of macrophages and osteoclasts and considered as an initial sign of RA (8-10). The assessments of synovitis by the two modalities are generally considered to be consistent (1, 2), though no study has simultaneously

compared histopathology of inflammatory joint lesions with imaging findings of both modalities.

In patients with long-lasting knee arthritis such as RA and OA, joint swelling can be caused by mixture of various degrees of joint fluid, synovitis and synovial hypertrophy due to fibrotic change. Because elderly RA patients often complicate with OA that modulates pathological changes in a single joint, it is often difficult to assess ongoing active inflammation in a preoperative condition (11, 12). In this study, we simultaneously examined US, MRI and histopathology of the knee joint lesions in RA or OA patients who required surgical operation due to advanced joint destruction.

## Patients and methods

### Patients

We studied 15 patients with rheumatoid arthritis (12 female, 3 male; age range, 39-85 years) and 5 patients with osteoarthritis (4 female, 1 male; age range, 66-78 years) who underwent total knee arthroplasty with synovectomy due to severe knee pain and the impaired joint function. Fifteen patients fulfilled the American College of Rheumatology (ACR) 1987 classification criteria for RA (13) and the remaining 5 patients met the 1986 ACR classification criteria for idiopathic OA of the knee joint (14). The severity of knee joint pain was calculated as an average of pain VAS (visual analogue scale). The study was approved by the ethics committee of our institute, and all subjects in the study gave their written informed consent.

### Conventional radiography

Preoperative radiographs of standard anteroposterior (AP) knee were taken in all patients within 1 month before surgery and were scored for the severity of RA and OA, using the Larsen score and Kellgren-Lawrence scale, respectively.

### Ultrasonography

All ultrasonographic examinations were conducted one day before surgery by a single experienced rheumatologist (KT). All recorded images were re-evaluated by the same examiner later without any other clinical information.

Competing interests: none declared.

Our former study revealed that the assessment of GSUS and PDUS showed a good intraobserver agreement with  $\kappa$  values of 0.85 and 0.92, respectively. Knee joints were examined by suprapatellar longitudinal and transverse, lateral longitudinal and medial longitudinal scanning at the neutral supine position using a 10 MHz electronic linear transducer (Logiq 7, GE Healthcare). The findings of synovitis in US were assessed by gray scale (GSUS) and power Doppler (PDUS) with the standard setting according to recommendations (15-18). Grey scale was scored from 0 to 3 by synovial thickness as follows; score 0: absent (<2 mm), score 1: mild synovial hypertrophy (<5 mm), score 2: moderate synovial hypertrophy ( $\geq 5$  mm), score 3: intense synovial hypertrophy (>8 mm). The synovial thickness of the suprapatellar recess was determined by scanning the zone between the prefemoral (posterior suprapatellar) fat pad and the upper margin of the femoral cartilage. At the level of the lateral and medial recesses, the vertical edge along the medial and lateral margins of the knee cap (biceps femoris contracted) was identified by scanning. Nodular vegetations, when present, were measured in their entire thickness. Each knee was evaluated as a whole, and the worst area of thickening detected between the three recesses was measured (19). Pulse repetition frequency was 800 Hz, Doppler frequency 7.5MHz and Doppler gain to avoid random noise was used. PD signal, which represents vascularity in the synovial tissue, also scored from 0 to 3 as follows; score 0: normal (undetectable power Doppler vessel signals in ultrasonographic synovial thickening area), score 1: mild (intrasynovial power Doppler flow signal distribution was detectable over <25%), score 2: moderate (<50%), score 3: marked (>50%). The highest grade throughout the knee joint was adopted (20). Positive PD signal at quadriceps and or patellar entheses were excluded.

#### *Magnetic resonance imaging*

MRI was also performed one day before surgery using a 1.5 Tesla scanner (MAGNETOM Avanto). For MRI, the

knees were positioned neutrally rotated in a dedicated knee coil. Continuous coronal and sagittal T1-weighted spin-echo images (repetition time/echo time/slice thickness, 500 ms/12 ms/5 mm) were obtained. While the patient remained in the same position in the MR unit, 0.1 mmol Gd-DTPA/kg body weight was injected into a cubital vein. The T1-weighted spin-echo images were repeated: the coronal images first (5–10 minutes after Gd-DTPA injection), then the sagittal images (10–15 minutes after Gd-DTPA injection). The MRI images were assessed according to OMERACT-RAMRIS (21, 22). Slices selected for grading of synovial membrane inflammation corresponded to the first and the last sagittal slices in which the patella was still visible. Synovial membrane inflammation was investigated in the 3 recesses (suprapatellar and lateral and medial parapatellar). Synovitis was defined as an area in the synovial compartment that showed above normal post-gadolinium enhancement of the thickness greater than the normal synovium. Severity of synovitis was graded from 0 to 3; grade 0: normal, grade 1: mild, grade 2: moderate, grade 3: severe. The synovitis score of the region of interest among the 3 recesses was adopted. MRI scans were scored independently by two radiologists with musculoskeletal reading experience (KS, UT). When there was a difference in the score of synovitis, these cases were discussed until consensus was reached. The interreader agreement for synovitis was good, with  $\kappa=0.85$ .

#### *Histopathology*

At operation, specimens of the synovial tissue were taken from the site, which was determined as the region of interest by US, were served for pathological studies. Synovial tissues were fixed in 20% formalin and embedded in paraffin according to standard practice. Ten serial sections were cut for each specimen. Sections were cut at a 4  $\mu$ m thickness. Sections 1 to 2 and 9 to 10, 3 and 6, 4 and 7, 5 and 8, were stained with haematoxylin and eosin, anti-CD68 antibody, anti-Ki-67 antibody, and anti-CD31 antibody, respectively.

#### *Histopathologic analysis*

The degree of inflammatory cell infiltrates, synovial lining layer thickness and vascularity was evaluated in the haematoxylin and eosin stained section. The synovial samples were all examined under blinded conditions by the histopathologist (YN). Three histological parameters of the specimen were determined separately. Each parameter was graded according to the amount of the character. Parameters were scored as 0 (normal), 1 (mild change), 2 (moderate change) and 3 (severe change). Finally, the total histopathological synovitis score was calculated as follows: inflammatory cell infiltrates score + synovial lining layer thickness score + vascularity score. As inflammatory changes are heterogeneous by nature, analysis was done at the site showing the strongest histopathological alterations. The degree of inflammatory cell infiltrates was analysed under low magnification (100x), on the other hand, synovial lining layer thickness and vascularity were evaluated at higher magnification (400x) according to recommendations (23).

#### *Immunohistochemical analysis*

To further analyse the individual pathological factors in synovitis, we assessed macrophage, cell proliferation and vascularity by immunohistochemical studies using anti-CD68 (DAKO, Glostrup, Denmark), Ki-67 (DAKO, Glostrup, Denmark) and CD31 (DAKO, Glostrup, Denmark) antibodies, respectively. For staining, the sections were dewaxed, rehydrated, and autoclaved in 10 mmol/L citrate buffer, pH 6.0 (121°C for 15 minutes), for antigen retrieval. Then intrinsic peroxidase activity was quenched with 0.3% hydrogen peroxide. Immunostaining was performed overnight at 4°C with optimally diluted anti-CD68, Ki-67 and CD31 antibodies by using the Vector M.O.M. immunodetection kit (Vector Laboratories, Burlingame, CA). The labelled antigens were visualised with the Histofine-PO kit (Nichirei Pharmaceutical, Tokyo, Japan), followed by 3,3'-diaminobenzidine reaction. The sections were counterstained with haematoxylin.

**Table I.** Patient characteristics\*.

Characteristic	RA patients n=15	OA patients n=5
N. of female/male	12/3	4/1
Age, years	70 (39–85)	70 (66–78)
Disease duration, years	6 (0.5–33)	2 (1–10)
Serum CRP, mg/dl	2.15 (0.36–6.66)	0.128 (0.03–0.30)
VAS pain score (range 0–100)	50 (10–90)	35 (10–75)
Disease Activity Score in 28 joints	3.57 (2.78–4.70)	–
Medication, no.		
None	2	4
NSAID	7	1
Prednisolone	7	0
DMARDs	10	0

\*Except where otherwise indicated, values are the median (range). RA: rheumatoid arthritis; OA: osteoarthritis; CRP: C-reactive protein; VAS: visual analogue scale; NSAID: non-steroidal anti-inflammatory drug; DMARD: disease-modifying antirheumatic drug.

*Digital image analysis of histology samples*

Immunohistochemically stained slides were quantified using digital image analysis. The size of the image was 340×250 pixels. The numbers of sublining CD68 or Ki-67 expressing cells per high power field (400x) were determined in 5–12 fields per specimen by automatic cell counting. The total CD31 expressing areas were automatically calculated. And the average percentage of blood vessels proliferating

areas in relation to the whole area of the tissue sample was measured.

*Statistical analysis*

Spearman correlation and Mann-Whitney U-test analyses were performed to determine their statistical significance. *p*-values less than 0.05 were considered significant.

**Results**

*Preoperative profiles of the patients*

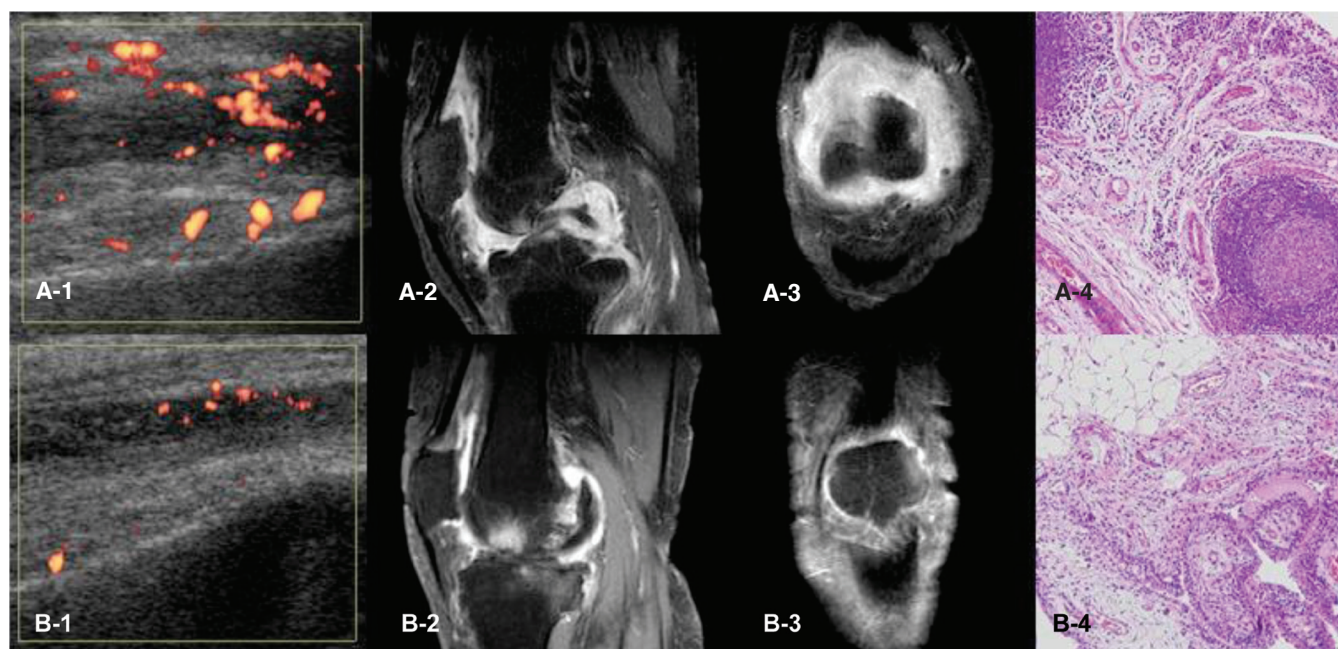
Table I summarises preoperative clinical

profiles of the patients before surgery. The median disease duration was 6.0 years with a range from 0.5 to 33 years. Ten of 15 RA patients had received nonbiologic DMARD with or without NSAID and prednisolone, while biologic DMARD had never used in any patient. All patients had mild to moderate disease activity (DAS28 score 2.8–4.7). The Larsen score of the impaired knee joints of RA patients ranged from 2 to 5, whereas the Kellgren-Lawrence scale in OA patients ranged from 2 to 4 (Table II). The findings indicated that all patients had an advanced knee joint lesion with bone and cartilage destruction. Clinical activity prior to operation was evaluated by serum CRP levels and patient’s visual analogue scale (VAS) of pain (Table I, II). Serum CRP level showed a marginal correlation with GSUS and PDUS (Spearman correlation coefficients 0.53 and 0.56, *p*<0.05 and *p*<0.05, respectively), but not MRI synovitis score (Spearman correlation coefficients 0.27). VAS also showed a moderate correlation with GSUS (Spearman correlation coefficients 0.45, *p*<0.05), but neither PDUS nor MRI synovitis score (Spearman correlation coefficients 0.13 and 0.20, respectively).

**Table II.** US, MRI, Histopathology, CR and clinical features.

Diagnosis	US		MRI		Histopathology	CR	
	Grey scale (range 0–3)	Power Doppler (range 0–3)	Synovitis (range 0–3)	Synovitis score (range 0–9)	Larsen score (range 0–5)	K/L scale (range 0–4)	CRP (mg/dl)
RA	2	2	3	7	3		2.23
RA	2	2	3	6	2		6.66
RA	2	2	1	6	4		6.52
RA	3	2	3	6	3		4.72
RA	2	2	2	6	4		0.53
RA	2	2	3	5	2		2.13
RA	1	2	3	5	4		0.36
RA	1	2	3	4	4		3.56
RA	1	2	2	4	4		0.74
RA	2	1	3	4	3		2.90
RA	2	1	2	4	3		0.65
RA	1	1	1	3	3		5.44
RA	2	1	2	3	4		1.56
RA	3	1	2	1	5		1.73
RA	1	1	2	0	3		0.67
OA	1	1	2	3		4	0.11
OA	1	1	2	3		3	0.03
OA	1	0	1	3		2	0.30
OA	1	0	2	2		3	0.13
OA	1	0	2	1		3	0.21

K/L scale, Kellgren-Lawrence scale.



**Fig. 1.** Distinctive features of different scores of haematoxylin and eosin stained synovial tissues (1:100) and power Doppler images and T1-weighted post-contrast fat-suppressed images.

**A.** Rheumatoid arthritis patient.

**A-1.** Power Doppler signal score: 2 (Anterior suprapatellar longitudinal lateral scan).

**A-2, A-3.** MRI-determined synovitis score: 3 (A-2: Coronal image, A-3: Sagittal image).

**A-4.** Synovitis score: 6 (Inflammatory cell infiltrates: 3, Synovial lining layer thickness: 1, Vascularity: 2).

**B.** Osteoarthritis patient.

**A-1.** Power Doppler signal score: 1 (Anterior suprapatellar longitudinal lateral scan).

**A-2, A-3.** MRI-determined synovitis score: 2 (A-2: Coronal image, A-3: Sagittal image).

**A-4.** Synovitis score: 3 (Inflammatory cell infiltrates: 1, Synovial lining layer thickness: 1, Vascularity: 1).

### Histopathological assessment of synovial tissues

Synovial tissues were obtained from the site, which was determined by US, during the operation in individual patients. The histopathological analysis was focused on inflammatory cell infiltration, synovial cell proliferation, and neoan-

giogenesis, all of which were characteristic for pathological findings in RA, rather than OA.

Whereas hyperplasia of the synovial lining layer was found in both RA and OA, infiltration of inflammatory cells such as lymphocytes and plasma cells, and vascularisation were more prominent in the

synovium tissues from RA than those from OA. The total synovitis score, which as determined by sum-up of individual scores of the three components, was correlated with serum CRP levels (Spearman correlation coefficients 0.51,  $p < 0.05$ ) and significantly higher in RA than that in OA ( $p < 0.05$  by Mann-Whitney U-test). In RA, the median total synovitis score was 4 with a range from 0 to 7, while the median total synovitis score was 3 with a range from 1 to 3 in OA (Table II). Thus, high total synovitis in histopathological analysis was associated with clinically active synovitis.

**Table III-A.** Relationship of the histopathological findings with US and MRI scores.

	Inflammatory cell infiltrates	Synovial lining layer thickness	Vascularity	Synovitis score
Gray scale, US	0.53*	0.04	0.45*	0.48*
Power Doppler, US	0.69**	0.50*	0.59**	0.84**
Synovitis, MRI	0.47*	0.20	0.28	0.48*

\*:  $p < 0.05$ . \*\*:  $p < 0.01$ .

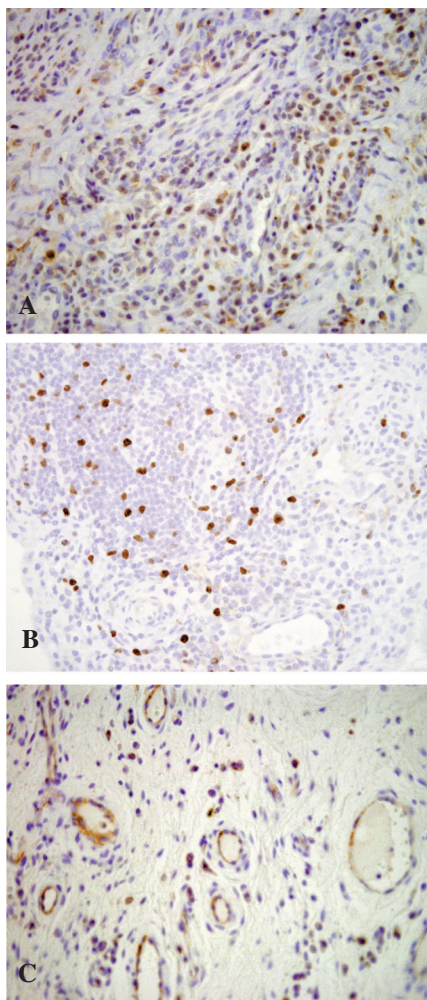
**Table III-B.** Relationship of the immunohistochemical findings with US and MRI scores.

	CD68	Ki-67	CD31
Gray scale, US	0.48*	0.48*	0.43
Power Doppler, US	0.71**	0.65**	0.70**
Synovitis, MRI	0.57**	0.45*	0.54*

\*:  $p < 0.05$ . \*\*:  $p < 0.01$ .

### Comparative analysis of the histopathological findings, US and MRI findings

Accumulating evidence has shown that active synovial inflammation is well illustrated by both PDUS and contrast-enhanced MRI and that the two modalities show high consistency in general (24). In the present study, PDUS was significantly correlated with con-



**Fig. 2.** Representative immunohistochemical stainings of synovial tissue from patients with rheumatoid arthritis (1:400). (A) CD68 (B) Ki-67 (C) CD31.

trast-enhanced MRI synovitis score (Spearman correlation coefficient 0.53,  $p < 0.05$ ). In Figure 1A, marked suprapatellar pouch enlargement with positive PD signal was observed, which was detected as synovitis with contrast enhancement effects in MRI. Positive PDUS (grade 2 or 3) and contrast-enhanced MRI findings (grade 2 or 3) were found in 9 and 17 of 20 arthritis patients, respectively, indicating that there was discrepancy between evaluation by the two modalities. MRI detectable synovitis did not always accompanied by high PDUS signal in the knee lesions as shown in Figure 1A.

We next compared imaging findings of preoperative US and MRI with histopathological findings of the operative specimens (Table II, Table III-A). We found that all of three imaging para-

**Table IV.** Sensitivity and specificity of US and MRI for histopathological changes.

Histopathology (HE)	Inflammatory cell infiltrates	Synovial lining layer thickness	Vascularity
Sensitivity US (Power Doppler)	67%	75%	100%
Specificity US (Power Doppler)	88%	75%	69%
Sensitivity MRI (Synovitis)	83%	75%	75%
Specificity MRI (Synovitis)	13%	8%	13%

Dichotomised scores: US, MRI; scores of 0/1 grouped as “(-)”, scores of 2/3 grouped as “(+)”. Inflammatory cell infiltrates; scores of 0/1 grouped as “(-)”, scores of 2/3 grouped as “(+)”. Synovial lining layer thickness; scores of 0/1 grouped as “(-)”, scores of 2/3 grouped as “(+)”. Vascularity; scores of 0/1 grouped as “(-)”, scores of 2/3 grouped as “(+)”.

eters, GSUS, PDUS, and contrast-enhanced MRI significantly correlated with pathological total synovitis score (Spearman correlation coefficients 0.48, 0.84 and 0.48,  $p < 0.05$ ,  $p < 0.01$  and  $p < 0.05$ , respectively). Of them, PDUS showed the highest correlation with the pathological changes. When pathological findings were separately analysed, significant correlation was found as follows; between inflammatory cell infiltrates and all of all of three imaging parameters, synovial lining thickness and PDUS, and in vascularity with GSUS and PDUS.

We further examined histopathology of the synovial tissues by quantitative parameters of immunohistochemical analysis. In brief, CD68, Ki-67, and CD31 were used as makers for macrophages, proliferative cells, and vascular endothelial cells, respectively and the staining areas were calculated by the digital image analyser (Fig. 2, Table III-B). The staining areas of CD68, Ki-67, and CD31 were correlated with scores of inflammatory cell infiltrations, synovial lining cell thickness, and vascularity (Spearman correlation coefficients 0.87, 0.45 and 0.76,  $p < 0.01$ ,  $p < 0.05$  and  $p < 0.01$ , respectively). In concordance with the findings in haematoxylin and eosin staining, PDUS and MRI synovitis showed high correlation with immunohistochemical parameters, but GSUS showed low correlation.

We also assessed the concordance of US and MRI findings with histopathological changes by using dichotomised scores (where grades 0–1 and 2–3 were grouped together for both imaging modalities). Compared to histopathological findings as the gold standard, for PDUS, the ranges for sensitivity and

specificity were 67–100% and 69–88%, and for contrast-enhanced MRI were 75–83% and 8–13% (Table IV). These results showed that PDUS was superior in specificity.

**Discussion**

The present study showed that both US and MRI well represented pathological components of active synovitis in the advanced inflammatory joint diseases which required surgical treatment. We found that PDUS visualised pathologically active synovitis more specifically than MRI, while contrast-enhanced MRI was more sensitive in patients with long-lasting arthritis. To our knowledge, this is the first study that simultaneously evaluates US and MRI with histopathological findings of the synovial tissue, though several studies have shown significant correlation between each imaging modality and pathological synovial inflammation (5, 6, 25, 26).

Both US and MRI are capable of directly visualising and objectively quantifying synovial inflammation and now are recognised as useful imaging modalities to assess disease activity and joint damage in inflammatory arthropathies, especially in RA. Abnormal MRI findings which corresponded to synovitis have been shown to correlate with clinical and laboratory measures of inflammation (27, 28), as represented by OMERACT-RAMRIS, which is designed to allow straightforward, reproducible scoring of these features. A number of studies have also shown usefulness of US for evaluation of synovitis (29-31). Because of the high sensitivity, both US and MRI contribute to early diagnosis of RA (32)

and detect subclinical synovitis, potentially leading to joint destruction even in remission (33). In this study, all RA patients except one showed substantial abnormalities (more than score 2) in either or both of US and MRI despite low to moderate clinical activity, as assessed by the disease activity score on 28 joints (DAS28). Consistently, the microscopic analysis revealed persistent histologically active synovitis, which might lead to further structural damages in future if operation was not conducted.

This study demonstrated that pathological synovitis score was more closely correlated with PDUS than GSUS and MRI synovitis score. In concordance with previous reports (34, 35), PDUS efficiently visualised neoangiogenesis in our hands. The findings were further supported by quantitative analysis using anti-CD31 staining in the tissues. PDUS also showed a good correlation with other pathological components such as inflammatory cell infiltrates, infiltration of macrophages which were quantified by CD68 staining cells, and synovial proliferation shown by accumulation of Ki-67 positive cells. Since angiogenesis and inflammation are closely integrated processes in RA and OA (36, 37), individual pathological components of synovitis are independent, but rather subsequent and dependent on each other. Consistently, previous studies have shown that positive PDUS is associated with not only local infiltration of Th17 cells, which promotes synthesis of VEGF and subsequent neoangiogenesis (7), but also future progression of joint destruction, which is directly mediated by CD68+ macrophage-derived osteoclasts in RA.

One of the factors to cause discrepancy between MRI findings and the pathological synovitis is regional heterogeneity of pathological changes in the inflamed knee joints. Previous study has showed a very close relationship between PDUS and those of dynamic Gd-enhanced MRI for assessing inflammatory activity in the metacarpophalangeal joints with RA (38). In this study, both imaging modalities assessed the findings all over the knee joint, while

the anatomical site of histopathological samples was chosen on the basis of abnormal findings in US, leading to bias potentially. More detail regional analysis using dynamic MRI may circumvent the issues. There are number of shortcoming to this study. Because of small sized number, we failed to find the effects of treatment in this study. US images were evaluated by a single experienced examiner. Although this might have had an influence in the interpretation of the pathological findings, we examined interobserver variability of US assessment before the start of the study. The interobserver agreement for the grading of GSUS and PDUS were moderate to good, with  $\kappa=0.44$  and  $\kappa=0.93$ , respectively.

On the other hand, the present study showed that MRI more sensitively detected synovitis than PDUS. Wakefield *et al.* have shown similar observation in tenosynovitis and referred that MRI should be considered when tenosynovitis was suspected even in negative US study (39). These findings indicate that MRI is superior to detecting mild changes in inflammatory arthropathy. In addition, MRI detects bone marrow oedema, which represents inflammatory cellular infiltrates within the subchondral bone and recognised as predictive of later CR progression in RA (40, 41). Although bone marrow oedema itself is not specific for RA, the finding is particularly useful for the diagnosis of early RA in combination with serological markers such as RF and anti-CCP antibody (42). This is another advantage of MRI over US, because US never illustrates pathological changes such as bone marrow oedema inside of bone cortex. In the present study no correlation was found between bone oedema and histopathological parameters of synovial inflammation (data not shown). Presumably, this is due to a limitation in the present study, because all samples were obtained from long-lasting joint lesions. Rather, MRI is useful for detecting early changes of joint diseases, but not changes of established arthropathy, with high sensitivity, though we have to be aware that the abnormal findings are often found even in normal individuals (43).

## Conclusion

In summary, this study evaluated the findings of US and MRI in comparison with those of histopathology of long-lasting synovitis, but we concluded that neither was superior to the other. Rather, both imaging techniques are useful for the visualisation of synovitis, though there are some differences between them. While contrast-enhanced MRI is more sensitive than PDUS in detecting synovitis, PDUS more faithfully illustrates the pathological features of synovitis. Thus, it is important to understand the advantages and disadvantages of individual modalities when the imaging techniques are applied to clinical assessment of chronic joint diseases.

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