Int J Clin Exp Med 2015;8(4):5904-5910
www.ijcem.com /ISSN:1940-5901/IJCEM0006016

Original Article

The relationship between histopathological and imaging features of sacroiliitis

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Received January 16, 2015; Accepted March 31, 2015; Epub April 15, 2015; Published April 30, 2015

Abstract: This study aimed to investigate the histopathological feature of sacroiliitis and to examine its relationship with imaging features using various imaging techniques. Computed-tomography (CT)-guided needle biopsy of the sacroiliac (SI) joints was performed in 36 patients with spondyloarthritis. Histopathological examination was performed on the samples and subjects were divided as with or without sacroiliitis according histopathology. Magnetic resonance imaging (MRI), Single-photon emission CT (SPECT), CT scans and plain X-rays of the SI joints were conducted. Histopathological changes indicative of sacroiliitis were found in 29 (81%) of the 36 patients, with changes in cartilage (72.4%) and subchondral bone (72.4%) being the most common features. Histopathological sacroiliitis was not found in seven (19.4%) patients. Using MRI, sacroiliitis was found in 29 (80.5%) patients. Increased SI index (> 1.34) by SPECT scans indicative of sacroiliitis was found in 29 (80.5%) patients. Sacroiliitis was detected by CT and plain X-rays in 23 (63.8%) and 19 (52.7%) patients, respectively. Using the histopathological sacroiliitis as the gold standard, sensitivity for SPECT, MRI, CT and plain X-rays was 92.8%, 96.4%, 73.3%, respectively, and 64.2% and the corresponding specificity was 62.5%, 75%, 87.5% and 87.5%, respectively. Needle biopsy is an important method for the diagnosis of sacroiliitis. MRI and SPECT have comparable diagnostic value as CT and plain X-rays and can quantify the inflammatory activity. A combination of these two techniques could increase the sensitivity and specificity and serve as a valuable tool for the diagnosis, assessment and monitoring of sacroiliitis.

Keywords: Sacroiliitis, histopathology, imaging

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease characterized by sacroiliitis, spondylitis and enthesitis. It affects primarily young adult males and severe involvement in the axial joints leads to disability, compromised skeletal growth and poor quality of life. Sacroiliitis is one of the early manifestations of AS and it is crucial for the early establishment of diagnosis [1]. The common widely used techniques to define sacroiliitis, including plain X-rays and computed tomography (CT), rely on the macrostructural changes of the bone and hence, diagnosis is often delayed for up to six years even using the more sensitive CT. Single-photon emission CT (SPECT) can reveal changes in vascularity and metabolism at the joint. Magnetic resonance imaging (MRI) can detect cartilage invasion and bone marrow edema, which are indicative of sacroiliitis. These two imaging techniques have the potential to improve the early diagnosis of sacroiliitis. Histopathological examination by needle biopsy of the sacroiliac (SI) joints reveals features of sacroiliitis, including histopathological changes in the cartilage, synovium and bone marrow that can precede macrostructural changes of the bone, providing definite and reliable diagnosis. The main objective of this study was to determine the major histopathological features of sacroiliitis and to investigate their relationship with those obtained by plain X-rays, CT, MRI and SPECT. CT-guided needle biopsy of the SI joints, along with plain X-rays, CT, MRI and SPECT scans were performed on 36 patients with spondyloarthritis and the results are presented here.

Patients and methods

Patients

Thirty-six patients with axial spondyloarthritis diagnosed according to the 2009 Assessment of SponsyloArthritis international Society (ASAS) criteria were recruited from the rheumatology outpatient clinic and inpatient ward of the Guangdong Provincial People's Hospital between January 2007 and December 2013. Twenty-eight patients were AS, six were undifferentiated spondyloarthritis and two were psoriatic arthritis. All patients underwent X-rays, CT, MRI and SPECT/CT scans of the SI joints one week prior to the needle biopsy. Patients were divided into two groups: with and without sacroiliitis, according to the histopathological examination.

CT-guided needle biopsy and histopathological examination

CT scans of the SI joints were obtained by 4 multi-detectors spiral GERT CT system (GE Inc.). Written informed consents were obtained from all patients before the biopsy. Coagulation test and platelet count were performed prior to the biopsy to ensure that the patients were fit for the procedure. With the patient in a prone position, transverse CT slices were obtained proximally, starting from the lower limit of the SI joints, with a section thickness of 3 mm and a section interval of 3 mm. Biopsies were performed under CT image control. Survey images were obtained to localize the needle position for optimal access to the synovium in the medial portion of the SI joints. After local anaesthesia, a posterior approach to the SI joints was chosen with the FANSEEN lung biopsy needle being headed to the iliac side of the joint to obtain tissue samples. Biopsy samples were then processed and examined under the light microscope.

Histopathological features for diagnosis of sacroiliitis included osteomyelitis, and/or pannus formation, and/or inflammatory cell infiltration, and pathological changes of the cartilage and/or subchondral bone, including cartilage degeneration, destruction, fibrosis and ossification, and/or subchondral bone plate disruption, erosion, necrosis and sclerosis, and/or synovitis, and/or enthesitis [2, 3].

MRI scans of the SI joints

The MRI of the SI joints was obtained with a Power Track 6000 MRI system (Philips). The following sequences were used: T1-weighted spin-echo pulse sequence, T2-weighted turbo spin-echo pulse sequence, fast field-echo sequence, fat-saturated T2-weighted sequence (spectral presaturation with inversion recovery [SPIR] sequence or Short tau inversion recovery [STIR] sequence).

The following features were recorded: 1) the integrity of the SI joints structure depicting the smooth articular cartilage surrounded by low-signal-intensity iliac and sacral cortical borders; 2) abnormality in the cartilage line, including blurring, irregularity, disruption and disappearance; 3) abnormality in the subchondral bone, including blurring, irregularity, disruption and disappearance; 4) abnormality in the juxta-articular structure, including bone marrow edema (low-signal-intensity on T1-weighted sequence and high-signal-intensity on T2-weighted or SPIR or STIR sequence), sclerosis (low-signal-intensity on any sequence) and fat deposition (low-signal-intensity on SPIR or STIR sequence but high-signal-intensity on other sequences). According to the definitions proposed by Bollow et al, sacroiliitis was defined as any of abnormality in the integrity of the SI joint structure, and/or cartilage line, and/or subchondral bone, and/or abnormality in the juxta-articular structure [4]. In addition, for diagnosis of active sacroiliitis, if there was only one change of signal (signal for bone marrow edema or osteitis was recommended) on a single MRI slice, the signal must be present on at least two consecutive slices [5]. If there was more than one changes of signal on single slice, one slice may be sufficient for diagnosis.

SPECT scans of the SI joints

Skeletal SPECT scans were conducted by Precedence 6 multi-detectors SPECT/CT system (Philips). Anteroposterior and posteroanterior skeletal scintigraphy was performed three hours after intravenous injection of 99 mTc-methylene diphosphonate (99 mTc-MDP). Images of the SI joints were obtained to define sacroiliitis. A region of interest (ROI) with a shape of square was automatically created by the system and placed on the SI joints. Another identical ROI was placed on the sacrum on the posterior pelvis. The SI index was then calculated as the ratio between the total number of counts in the ROI of the SI joint and that of the sacrum. An SI index > 1.34 indicated sacroiliitis [6].

Table 1. Rate of success of acquiring biopsy samples

Samples	Number of cases	Percentage (%)
Cartilage	33	91
Subchondral bone	30	83
Synovium	27	75
Bone marrow	26	72
Entheses	9	22

Table 2. Histopathological features of sacroiliitis

Abnormality in samples	Sacroiliitis (n = 29)	Normal (n = 7)
Cartilage	26 (89.6%)	5 (71.4%)
Subchondral bone	21 (72.4%)	5 (71.4%)
Synovium	18 (62%)	3 (42.8%)
Bone marrow	13 (44.8%)	4 (57.1%)
Entheses	9 (31%)	0

Statistical analyses

Statistical analyses were performed by the Statistical Package for Social Science 21.0. Continuous date were expressed as mean ± SD and were compared using Student's t-test. Categorical date were compared using Chi-square test with correction using Fisher's exact test. A *p*-value < 0.05 was considered statistical significance.

Results

Rate of success of acquiring biopsy samples

Samples acquired from needle biopsy of the SI joints included cartilage, subchondral bone, synovium, bone marrow and entheses. **Table 1** shows the rate of success of acquiring biopsy samples. Cartilage was acquired in 33 patients (91%), followed by subchondral bone (30 patients, 83%), synovium (27 patients, 75%), bone marrow (26 patients, 72%) and entheses (8 patients, 22%).

Histopathological changes of sacroiliitis

Histopathological changes indicative of sacroiliitis were found in 29 (81%) of the 36 patients (**Table 2** and **Figure 1**). Involvement of the cartilage (26/29 patients, 89.6%) and subchondral bone (21/29 patients, 72.4%) was the most common changes, manifested as degeneration, destruction and fibrosis of the cartilage, disruption, erosion and ossification of the subchondral bone. Synovitis was found in 18/29 (62%) patients, manifested as hyperplasia of the lining cells and areolar connective tissue, infiltration of inflammatory cells and pannus formation. Osteomyelitis was found in 13/29 (44.8%) patients, manifested as hematopoietic cells replaced by lymphocytes and plasma cells, chronic changes such as fibrosis in necrotic bone and cancellous bone. Enthesitis was found in 9/29 (31%) patients, manifested as infiltration of inflammatory cells and fibrovascular tissue. In seven (19.4%) patients, there was no histopathological changes indicative of sacroiliitis.

Changes on MRI and SPECT scans

Twenty-nine (80.5%) of the 36 patients involving 56 SI joints showed changes on MRI indicative of sacroiliitis (**Table 3**). These changes included cartilage line and/or subchondral bone abnormality (24/29 patients, 82%), bone marrow edema (21/29 patients, 71%), fat deposition (17/29 patients, 59%) and sclerosis (22/29 patients, 76%). Sacroiliitis was not found on MRI in seven patients.

Increased SI index (> 1.34) by SPECT scans indicative of sacroiliitis was found in 29 (80.5%) of the 36 patients involving 52 SI joints. SI index was found normal (≤ 1.34) in seven patients.

Relationship between changes on histopathology and imaging

In the 28 cases with histopathological changes of sacroiliitis, sacroiliitis was detected by SPECT, MRI, CT and plain X-rays in 26, 27, 22, and 28 patients, respectively (**Table 4**), while in the 8 cases without histopathological changes of sacroiliitis, the corresponding figures were 4, 2, 1, and 1 patient, respectively.

Positive predictive values for SPECT, MRI, CT and plain X-rays were 89.6%, 93.1%, 95.6% and 94.7%, respectively (**Table 4**). The corresponding sensitivity was 92.8%, 96.4%, 73.3% and 64.2%, respectively and the corresponding specificity was 62.5%, 75%, 87.5% and 87.5%, respectively. **Figure 2** shows the receiver operating characteristic (ROC) curves for the four

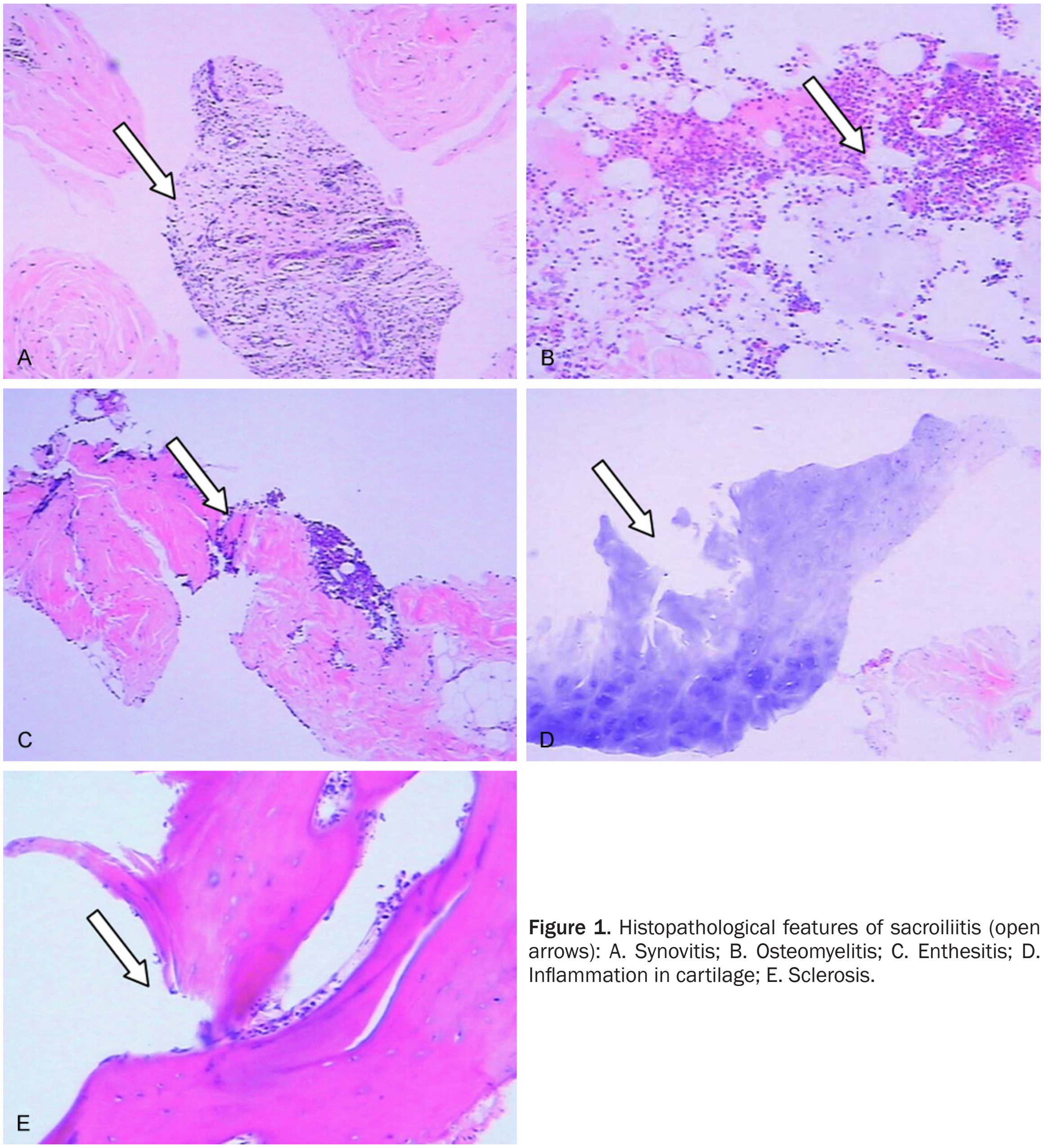

Figure 1. Histopathological features of sacroiliitis (open arrows): A. Synovitis; B. Osteomyelitis; C. Enthesitis; D. Inflammation in cartilage; E. Sclerosis.

Table 3. Imaging features of sacroiliitis on magnetic resonance imaging

Abnormality	Number of cases	Percentage (%)
Disruption of the structural integrity	29	80.5
Cartilage line abnormality	24	82
Subchondral bone abnormality	21	71
Bone marrow oedema	19	65
Fat deposition	17	59
Sclerosis	22	76

imaging techniques. The area under the ROC curves for SPECT, MRI, CT and X-rays was 0.79, 0.84, 0.83 and 0.76, respectively.

Discussion

Due to the complex structure of the SI joints, there are practical difficulties for histopathological studies and studies on relationship between histopathological and imaging features of SI joints are scanty. With the technique of CT-guided needle biopsy, obtaining samples

Table 4. Relationship between histopathological and imaging features of sacroiliitis

Techniques	Sacroiliitis on histopathology: Sacroiliitis on imaging (no. of cases)	Sacroiliitis on histopathology: Normal on imaging (no. of cases)	Normal on histopathology: Sacroiliitis on imaging (no. of cases)	Normal on histopathology: Normal on imaging (no. of cases)	Positive predictive value	Sensitivity	Specificity
SPECT	26	2	3	5	89.6%	92.8%	62.5%
MRI	27	1	2	6	93.1%	96.4%	75%
CT	22	6	1	7	95.6%	73.3%	87.5%
X-rays	18	10	1	7	94.7%	64.2%	87.5%

SPECT: Single-photon emission computed tomography; MRI: magnetic resonance imaging; CT: computed tomography.

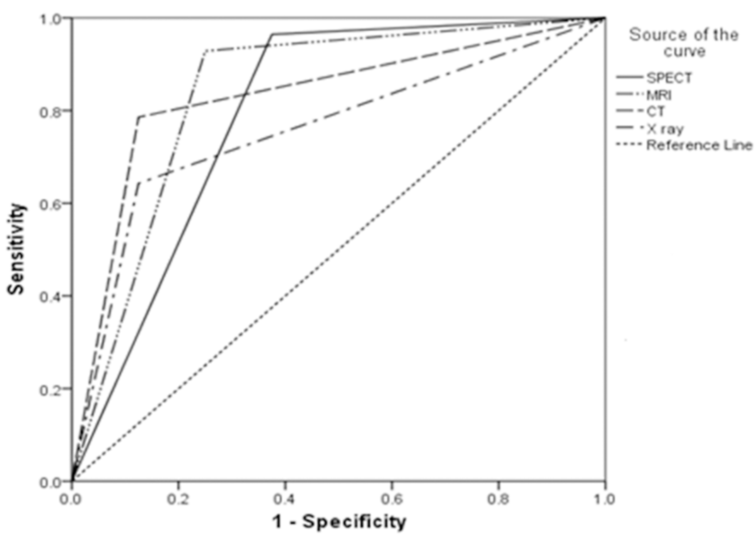

Figure 2. Receiver operating characteristic curves showing the sensitivity and specificity for the four imaging techniques in the diagnosis of sacroiliitis. SPECT: Single-photon emission computed tomography; MRI: magnetic resonance imaging; CT: computed tomography.

from the SI joints with accuracy and safety becomes possible. In this study, we used this procedure to study the histopathological features of sacroiliitis and its relationship with radiographic features on MRI, SPECT, CT and X-rays.

Our results showed that histopathological features of sacroiliitis included degeneration and destruction of cartilage, erosion, disruption, necrosis and sclerosis of subchondral bone, synovitis, pannus formation, enthesitis and osteomyelitis. Changes of cartilage and subchondral bone were the most common features followed by synovitis and osteomyelitis. Enthesitis was less common. The study by Francois et al showed that synovitis and subchondral bone pathology offer a more rational explanation for the widespread SI joint destruction than does enthesitis [3]. Our findings concurred with those by Francois et al that for sacroiliitis, changes in cartilage and subchondral bone, synovitis and bone marrow edema were more severe than enthesitis. The origin of sacroiliitis is still unknown. In our study, due to the small number of cases with negative findings on imaging, we could not determine the skeletal site responsible for the initiation of sacroiliitis. A larger sample will be required. However, histopathological sacroiliitis was present in patients without definite changes on various imaging techniques including SPECT, MRI and CT scans, suggesting that histopathological examinations by needle biopsy can reveal changes indicative of sacroiliitis before obvious changes in vascularity, metabolism and macrostructure. It can also reveal changes in synovium, bone marrow and cartilage, offering a more reliable diagnosis of sacroiliitis than do imaging techniques.

X-rays and CT scans are currently the common examinations for spondyloarthritis. Sacroiliitis was graded from 0 to 4 according to X-rays. Due to the poor resolution, although X-rays can provide reliable diagnosis of sacroiliitis of grade 3 or 4, it may underestimate the severity of grade 3 or misdiagnosis grade 1 and 2 sacroiliitis. Therefore, plain radiograph has limited value for the early diagnosis of sacroiliitis. CT scans have better resolution than plain radiographs and can detect subtle bony changes, such as subchondral bone sclerosis, cystic changes, erosion and joint space narrowing. However, CT scan relies on marcostructure changes of the joint structure and cannot reveal involvement of cartilage and bone marrow edema which are indicative of early sacroiliitis. Furthermore, active inflammatory changes cannot be seen or quantified by CT scan. MRI has been proposed as the most sensitive and specific imaging examination for sacroiliitis since 2003 [7]. In the 2009 ASAS classification criteria for axial spondyloarthritis, MRI is first integrated in the criteria as one of the key components. Using different sequence, MRI reveals the involvement of cartilage, bone marrow edema and fat deposition and thus, increases the sensitivity for early diagnosis of sacroiliitis. MRI can also differentiate both acute and chronic inflammatory lesions. In our study, sacroiliitis was detected by MRI in cases that showed negative findings on X-rays and CT scans. MRI increased the sensitivity from 64.2% (X-rays) and 73.3% (CT scans) to 96.4%. In a three-year study by Oostveen et al, using the X-rays as the gold standard, the sensitivity and specificity for MRI were 85% and 47%, respectively [8]. In our findings, using the histopathological sacroiliitis as the gold standard, the specificity for MRI was 75%. Our findings may further confirm the superiority of MRI in the early diagnosis of sacroiliitis. With good spatial resolution, CT scans can reveal definite bony changes of the SI joints, increasing the specificity (87.5%), positive predictive value (95.6%) while decreasing the false positive rate. However, CT scan cannot reveal features associated with early active inflammation such as cartilage involvement, bone marrow edema and fat deposition and hence, it has lower sensitivity (73.3%) than MRI.

Previous studies showed that for AS patients with mild or non-active sacroiliitis, MRI does not show superior sensitivity compared with other imaging techniques. In the past decades, SPECT scans by using the Tc-99m MDP to measure the local tracer uptake and accumulation assists the diagnosis of bone destruction, inflammation and tumor. SPECT scan reveals not only macrostructural changes of the bone and joints, but also the changes in vascularity and metabolism, which are indicative of early stage of diseases. Therefore, it has great potential to increase the sensitivity of early diagnosis [9]. Advances have been made on the utility of SPECT scans in active or arthritis. Bozkurt et al proposed that SPECT scans could be more sensitive for the staging of sacroiliitis in AS [10]. This conclusion was based on the observation that the primary histopathological inflammatory changes accompanying synovitis and involvement of cartilage and subchondral bone are infiltration of inflammatory cells, pannus invasion and increased eosinophils. The marked increase in metabolism due to these inflammatory changes leads to increased uptake of radionuclide and thus an increased SI index on SPECT scans. We used an advanced model of SPECT/CT system which provides improved radiation event localization information and, thus, higher spatial resolution images and lower false positive rate. With 6 multi-detectors, this system could also detect structural changes. In our study, using the histopathological sacroiliitis as the gold standard, the sensitivity (92.8% vs. 96.4%) and positive predictor value (89.6 vs. 93.1%) were comparable between SPECT and MRI scans. The limitations of SPECT scan, including inability for quantitative assessment for a specific location and limited information from the structural imaging, could contribute to its lower specificity. However, from the area under the ROC curve, the diagnostic value of MRI and SPECT scan was comparable. A combination use of both techniques can have the potential to increase the sensitivity and specificity for the diagnosis of sacroiliitis.

With the advances in imaging techniques, ultrasound has been used to examine the SI joints and methods for partial quantification of inflammatory activity have been proposed [11]. However, currently, due to the complexity of the axial joints, application of ultrasound has still been inconclusive.

One interesting finding from our study was that positive sacroiliitis on MRI and SPECT scans was found in the eight patients without histopathological evidence of sacroiliitis. This indicates that MRI and SPECT scans could yield false positive changes. Currently, histopathological examination remains as the primary measure for early diagnosis of sacroiliitis. But in view of the high sensitivity of MRI and SPECT scans and their ability to quantify inflammatory activity, these imaging technique are valuable for diagnosis and monitoring of sacroiliitis.

In our study, acquiring biopsy samples with good precision was hindered by the complex structure of the SI joints. We could not definitely rule out sacroiliitis in the eight cases with negative findings on histopathological examination. Therefore, the sensitivity and specificity for the various imaging techniques should be interpreted with caution. Selection of puncture location and angle of the biopsy path are crucial for successfully acquiring samples. CT-guided needle biopsy has the potential to be used in clinical setting for studies on spondyloarthritis.

Disclosure of conflict of interest

None.

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