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MUSKOLOSKELETAL IMAGING

ORIGINAL ARTICLE

Detection of synovial inflammation in the sacroiliac joint space through intravoxel incoherent motion imaging: an alternative to contrast agents

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PURPOSE

We investigated the diagnostic accuracy of simplified intravoxel incoherent motion (IVIM) imaging for detecting synovial inflammation in the sacroiliac joint (SIJ) in a population with active sacroiliitis.

METHODS

In accordance with the Assessment of Spondyloarthritis International Society criteria, 86 SIJs of 46 patients with active sacroiliitis were included in this retrospective study conducted between November 2020 and January 2022. Based on T1-weighted post-gadolinium images, the SIJs were divided into two groups: synovial inflammation positive (SIP) (n = 28) and synovial inflammation negative (SIN) (n = 58). Synovial areas in the SIJ space were independently and blindly reviewed for the presence of inflammation by two radiologists with differing levels of expertise in radiology. Using four *b* values, apparent diffusion coefficient (ADC)= ADC (0, 800) and the simplified 3T IVIM method parameters true diffusion coefficient (D_1)= ADC (50, 800), D= ADC (400, 800), f_1= f (0, 50, 800), f_2= f (0, 400, 800), pseudodiffusion coefficient (D*)= D* (0, 50, 400, 800), ADC_{low} = ADC (0, 50), and ADC_{diff}= ADC_{low} – D were generated voxel by voxel for each patient. The IVIM and ADC parameters at the SIN and SIP joints were compared.

RESULTS

The D parameter was significantly increased in SIP areas ($1.23 \pm 0.34 \times 10^{-3}$ mm^2/s) compared with SIN areas ($1.02 \pm 0.16 \times 10^{-3}$ mm^2/s) ($P = 0.004$). Conversely, the D* parameter was significantly decreased in SIP areas ($21.78 \pm 3.77 \times 10^{-3}$ mm^2/s) compared with SIN areas ($16.19 \pm 4.58 \times 10^{-3}$ mm^2/s) ($P < 0.001$). When the optimal cut-off value of 1.11×10^{-3} mm^2/s was selected, the sensitivity for the D value was 71% and the specificity was 72% [area under the curve (AUC): 0.716)]. When the optimal cut-off value of 21.06×10^{-3} mm^2/s was selected, the sensitivity for the D* value was 78.6%, and the specificity was 79.3% (AUC: 0.829). The interclass correlation coefficient was excellent for f_1, f_2 D*, D, and ADC_{diff}, good for ADC_{low} and D_1, but reasonable for ADC.

CONCLUSION

The presence of synovial inflammation in the SIJ can be evaluated with high sensitivity and specificity using only four b values through the simplified IVIM method without the need for a contrast agent.

CLINICAL SIGNIFICANCE

IVIM imaging is a technique that allows us to gain insights into tissue perfusion without the administration of contrast agents, utilizing diffusion-weighted images. In this study, for the first time, we demonstrated the potential of detecting synovial inflammation in the SIJ using IVIM, specifically through the pseudodiffusion (D*) parameter, without the need for contrast agents.

KEYWORDS

Diffusion magnetic resonance imaging, intravoxel incoherent motion, perfusion fraction, pseudodiffusion, sacroilitiis, synovial inflammation

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Synovial inflammation in the sacroiliac joint (SIJ) space can be evaluated using T1-weighted (T1w) post-gadolinium (Gd) images through magnetic resonance imaging (MRI). An assessment of the SIJ is commonly performed in cases of spondyloarthritis (SpA), which is a chronic inflammatory arthritis that can affect both axial and peripheral joints.[1] The most common clinical finding in patients affected by axial SpA (axSpA) is inflammatory low back pain (ILBP), and the frequency of radiological sacroiliitis is increasing.[2] In this context, the clinical value of MRI of the SIJ has increased since the presence of sacroiliitis in MRI was accepted as a diagnostic criterion by the Assessment of Spondyloarthritis International Society (ASAS).[3]

In studies conducted with patients with ankylosing spondylitis (AS), synovial inflammation has been demonstrated to predict disease activity and is associated with the degree of pain.[4] In 2019, the ASAS-MRI working group stated that increased contrast enhancement in the cartilaginous component of the SIJ reflects inflammation at the osteochondral interface, consistent with the early histopathological features of AS. Synovial inflammation may be associated with microenvironmental permeability changes in the joint space before bone marrow edema (BME) becomes apparent.[5] In recent years, concerns have emerged regarding the accumulation of Gd in the brain and the risk of nephrogenic systemic fibrosis associated with its use.[6,7] In this context, we believe that the simplified intravoxel incoherent motion (IVIM) technique could be a useful and effective method for quantitatively monitoring early inflammatory progression in axSpA cases without the need for Gd administration. The concept of IVIM, as defined by LeBihan, allows the separation of molecular diffusion and capillary perfusion using a biexponential model and helps calculate tissue perfusion without contrast agent administration.[8] The biexponential model calculates the true diffusion coefficient (D), pseudodiffusion coefficient (D*), and perfusion fraction (f). Notably, D* refers to blood velocity and the length of microvessel segments, whereas f signifies the microvascular blood flow.[8] The simplified IVIM model, developed recently using fewer b values, yielded more consistent and accurate results compared with the biexponential IVIM model.[9,10]

Main points

- Intravoxel incoherent motion (IVIM) imaging may serve as an alternative method to contrast agents for the detection of synovial inflammation in the sacroiliac joint.
- The most valuable parameter in the detection of synovial inflammation with simplified IVIM is pseudodiffusion coefficient.
- Using simplified IVIM with only four b values can shorten sequence time and yield results with high specificity and sensitivity.

The detection of synovial inflammation, which emerges in the early stages of axSpA, using quantitative methods such as IVIM, is likely to contribute to early diagnosis and treatment monitoring. In our literature review, we found that IVIM studies related to sacroiliac (SI) MRI have focused primarily on BME.[11-13] An IVIM study evaluating synovial inflammation in the SIJ is not yet available in the literature. The aim of this study is to detect the presence of synovial inflammation in SI MRI using the simplified IVIM model and compare its effectiveness with T1w post-Gd imaging in cases diagnosed with axSpA.

Methods

Study design and participants

The current study was designed retrospectively and approved by the Ondokuz Mayıs University Institutional Ethics Committee (decision no: 2021/206, decision date: 06.04.2021), along with a waiver for informed consent. This paper was drafted according to the guidelines laid down by the Standards for Reporting of Diagnostic Accuracy Studies.[14] Written consent was obtained from the patients to participate in the study.

Between November 2020 and January 2022, a total of 519 patients who underwent SIJ MRI examination on a 3Tesla (Philips, Ingenia, Best, the Netherlands) instead of 3T Philips Ingenia device with diffusion-weighted imaging at b values of 0, 50, 400, and 800 and T1w post-Gd images for ILBP were retrospectively screened. In total, 46 individuals aged between 18 and 45 years, without a history of malignancy, and with active sacroiliitis in accordance with the ASAS MRI criteria [the presence of BME larger than 1 cm in coronal oblique plane short tau inversion recovery (STIR) sequence], were included in the study (14 men and 32 women; mean age: 34.4 ± 7.9). Cases with chronic sacroiliitis were excluded, and all included patients had active sacroiliitis. The inclusion and exclusion criteria for this study are listed in Figure 1.

To detect inflammation in the joint space

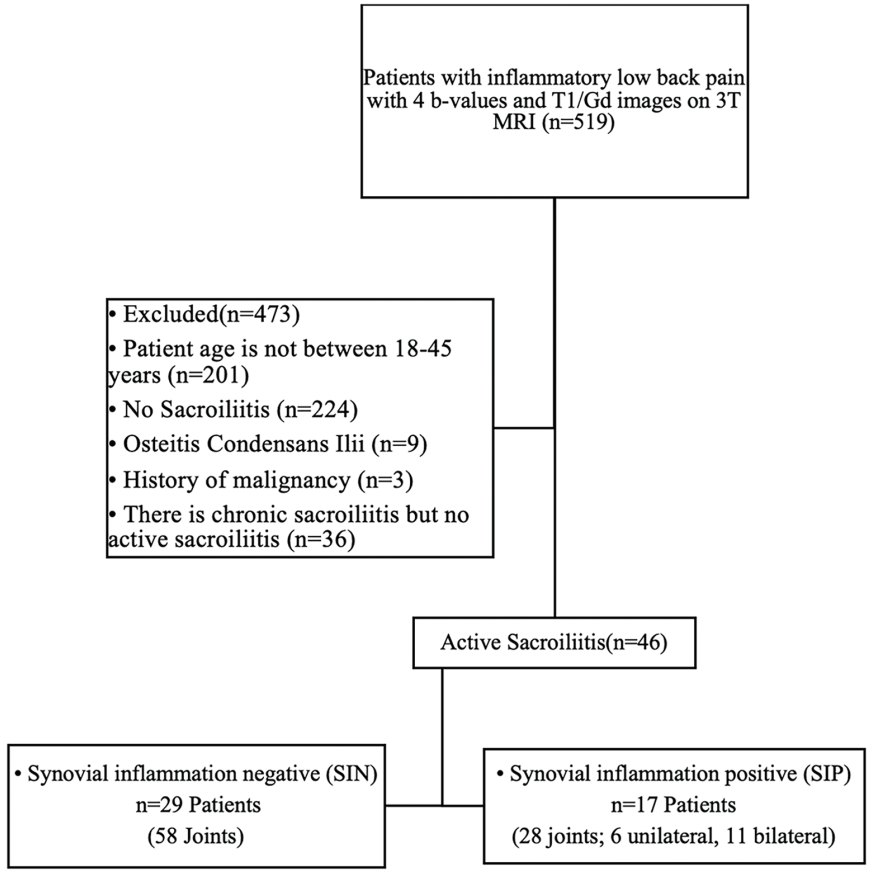

Figure 1. Study flowchart. Gd, gadolinium; MRI, magnetic resonance imaging.

of the selected patients, T1w post-Gd images were used as the gold standard test. The synovial areas in the lower third of the SIJ space were reviewed for the presence of contrast enhancement by two radiologists with 2 (M.A.) and 13 (A.B.Ö.) years of experience in musculoskeletal radiology following their radiology residency. Joints with contrast enhancement in the synovium were categorized as synovial inflammation positive (SIP), whereas those without contrast enhancement were categorized as synovial inflammation negative (SIN). Subsequently, a consensus was reached regarding the patients where a common opinion was not achieved to reach a final decision. Among the 17 patients with synovial enhancement, 11 displayed bilateral synovial involvement and 6 showed unilateral synovial involvement. The SIN group comprised 58 SIJs belonging to 29 patients for whom contrast enhancement in the joint space could not be detected, and 28 joints belonging to 17 patients exhibiting synovial enhancement formed the SIP group (Figure 1). Both radiologists were blinded to all clinical patient data and each other's findings. The clinical and laboratory parameters [sedimentation and C-reactive protein (CRP)] of the patients were obtained from the hospital information system 1 month before and after the MRI examination date. We confirmed from the hospital system that all patients included in the study received anti-inflammatory treatment. However, we were unable to standardize or compare their treatment protocols and follow-ups.

Magnetic resonance imaging technique

All examinations were performed on a 3.0 T Philips Ingenia MR (Philips, Netherlands) using a torso coil. The standard sequences included coronal oblique T1w, coronal oblique T2-weighted (T2w), coronal oblique T2w-fat suppressed (FS), coronal oblique STIR, axial oblique T2w-FS, axial oblique precontrast T1w-FS, coronal T1w-FS with IV contrast, and axial T1w-FS with IV contrast. The details of the MRI protocol are provided in Table 1. The diffusion MRI protocol is shown in Table 2.

Image analyses

Postprocessing image analysis

In the simplified IVIM method, IVIM parameters are calculated using the following equation, as stated in previous research:[8,9,15]

$$Apparent\ Diffusion\ Coefficient(ADC)(i,j) = \frac{\ln(S(b_i)) - \ln(S(b_j))}{j-i}$$

Using this equation, various ADC values were obtained from b_0= 0, b_1= 50, b_2= 400, and b_3= 800 s/mm^2, such as D_1= ADC (50, 800), D_2= D = ADC (400, 800), ADC_{low}= ADC (0, 50), and ADC= ADC (0, 800). Using these ADC values, f_1 and f_2 values were obtained:

$$f_1 = f(0,50,800) = 1 - \frac{S(b_1)}{S(0)} \cdot exp^{D_1 \cdot b_1}$$
$$f_2 = f(0,400,800) = 1 - \frac{S(b_2)}{S(0)} \cdot exp^{D_2 \cdot b_2}$$

Furthermore, D* was obtained based on the above parameters using the following equation:

$$D^* = -\frac{1}{b_1} \cdot \ln\left(\frac{1}{f_2} \cdot \left(\frac{S(b_1)}{S(0)} - (1-f_2) \cdot exp^{D_2 \cdot b_1}\right)\right)$$

Subsequently, the perfusion-sensitive diffusion parameter corresponding to the difference between D_2 and ADC_{low} was calculated.

$$ADC_{diff} = ADC_{low} - D_2$$

All images were generated in a Bash environment on macOS using a script developed in our radiology department. The Functional Magnetic Resonance Imaging of the Brain Software Library was employed as the image processing algorithm, and dcm2niix was used for DICOM-to-NIfTI conversion.[16,17] Furthermore, all voxels with a perfusion fraction below 0% and above 100% were removed from the image to avoid miscalculations.

Volume of interest definition

The entire synovium located in the lower third of the SIJ was segmented using ITK-SNAP (http://www.itksnap.org) with diffusion-weighted b = 0 images in the SIN group.[8] In the SIP group, subtracted images were created from the T1w-FS post-Gd and precontrast T1w-FS images. In these subtracted images, the entire contrast-enhanced synovial component was revealed. Subsequently, the subtracted images were fused with the diffusion-weighted b = 0 images on ITK-SNAP, and all areas exhibiting contrast enhancement in the synovial area were segmented. The segmented images in both groups were then extracted as mask images (Figure 2). Finally, the mean value of the intensities in the ADC, f_1, f_2, D, D_1, D*, ADC_{low}, and ADC_{diff} mask images was automatically calculated using the fslstats command.[16]

Statistical analysis

Statistical analyses were performed using SPSS software version 22.0. The variables were investigated by conducting a Shapiro–Wilk test to determine whether they exhibited a normal distribution. Descriptive analyses were performed using the means and standard deviations for the normally distributed variables. Additionally, the Student's t-test was employed to compare the normally distributed variables, and the Mann–Whitney U test was used to compare the non-normally distributed variables. Non-parametric variables were presented with standard deviation and median (min–max) or interquartile range (IQR) values. Furthermore, Pearson's χ^2 test was implemented to compare the genders of the two groups. The intraclass correlation coefficient (ICC) statistic was used to assess intraobserver agreement for the IVIM parameters. The diagnostic performance of

Table 1. Magnetic resonance imaging protocol

	T1W	T2W	T2W-FS	STIR	T2W-FS	T1W-FS (precontrast)	T1W-FS (post iv contrast)	T1W-FS (post iv contrast)
Plane	Coronal oblique	Coronal oblique	Coronal oblique	Coronal oblique	Axial oblique	Axial oblique	Coronal	Axial
Repetition time (ms)	500	4000	4000	shortest	4000	500	500	500
Echo time (ms)	8	80	80	80	80	8	8	8
FOV (RL × AP)	210 × 210	210 × 210	210 × 210	250 × 250	240 × 240	240 × 240	210 × 210	240 × 240
Number of excitations	1	1	1	1	1	1	1	1
Matrix size	264 × 279	212 × 199	212 × 199	256 × 204	268 × 264	344 × 294	264 × 279	344 × 294
Slice thickness (mm)	3	3	3	3	3.5	4	3	4
Gap (mm)	0.3	0.3	0.3	0.6	0.35	0.8	0.3	0.8

T1W, T1-weighted; T2W, T2-weighted; FS, fat-suppressed; STIR; short tau inversion recovery; iv, intravenous; FOV, field of view; RL, right-left; AP, anterior-posterior.

the IVIM parameters to detect synovial inflammation in the SIJ was calculated by conducting a receiver operating characteristic (ROC) curve analysis. The Youden index was used to determine the cut-off value in the ROC analysis.

Results

Patient and clinical characteristics

The results of the analyses revealed no significant difference between the age distributions of the two groups ($P = 0.11$). Notably, the number of women was significantly higher in the SIP group (22% vs. 78%) ($P = 0.007$). Although no statistically significant difference was observed between the CRP values of the groups, the sedimentation rate was significantly higher in the SIP group (SIN median: 13, IQR: 17; SIP median: 23, IQR: 20; $P = 0.027$). The clinical and demographic data of the patients are summarized in Table 3.

Intravoxel incoherent motion analyses of the sacroiliac joints in the study groups

The ADC, D_1, D, f_1, f_2, D*, ADC_{low}, and ADC_{diff} values of the joint spaces in the SIN and SIP groups are summarized in Table 4. Notably, although the means of ADC and D_1 were higher in the SIP areas than in the SIN areas, the differences were not statistically significant ($P = 0.057$, $P = 0.053$). However, D was significantly higher in the SIP group ($P = 0.004$). Furthermore, although f_1, ADC_{low}, and ADC_{diff} were higher in the SIP areas, the differences were not statistically significant ($P = 0.143$, $P = 0.131$, $P = 0.153$). In the SIP areas, D* was observed to be significantly decreased ($P < 0.001$).

The diagnostic performance of D* and D in detecting synovial enhancement in patients with active sacroiliitis is shown in Figure 3. The best D cut-off value for diagnosing synovial enhancement in patients with active sacroiliitis was 1.11×10^{-3} mm²/s, for which the sensitivity of D was 71% and specificity was 72% [area under the curve (AUC): 0.716, 95% confidence interval (CI): 0.574–0.857, $P = 0.001$]. Moreover, the best D* cut-off value for the diagnosis of synovial enhancement in patients with active sacroiliitis was 21.06×10^{-3} mm²/s, with the sensitivity of D* being 78.6% and specificity being 79.3% (AUC: 0.829, 95% CI: 0.723–0.936, $P < 0.001$).

Interobserver agreement assessment

The interobserver agreement for f_1, f_2, D*, D, and ADC_{diff} were excellent, with the ICC being 0.793 for f_1, 0.802 for f_2, 0.978 for D*, 0.772 for D, and 0.774 for ADC_{diff} ($P < 0.001$). Furthermore, interobserver agreement for ADC_{low} and D_1 was good, with the ICC being 0.727 for ADC_{low} and 0.625 for D_1 ($P < 0.001$). Interobserver agreement for ADC was reliable, with an ICC of 0.535 ($P < 0.001$).

Table 2. Diffusion magnetic resonance imaging protocol details

Name	Value
FOV (RL × AP)	250 × 250 mm
Slice thickness	4 mm
Spacing between slices	5
Slice number	39
Echo time	0.08 s
Repetition time	1.5 s
Diffusion gradients	3 orthogonal directions
b values	0, 50, 400, 800 (NEX: 4)
Acquisition time	4:30 min

NEX, number of excitation.

Discussion

In this study, simplified IVIM parameters were examined to quantitatively determine synovial inflammation in patients with axSpA

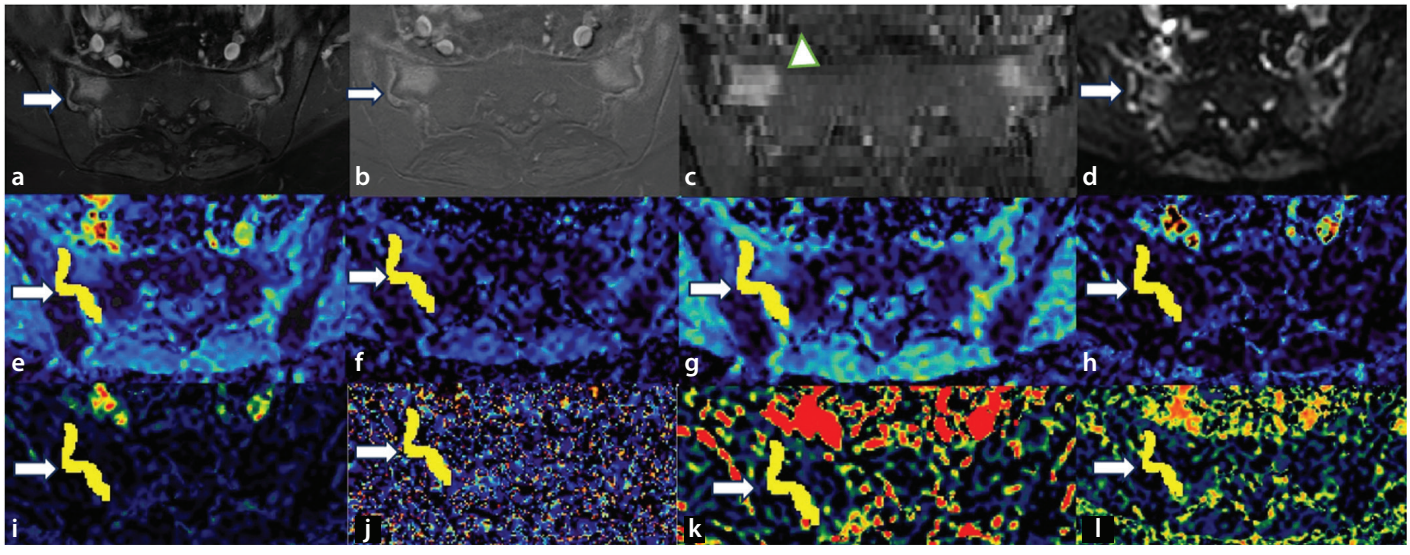

Figure 2. Sacroiliac magnetic resonance imaging (MRI) examination performed on a 40-year-old female patient diagnosed with axial spondyloarthritis reflecting active sacroiliitis in line with the Assessment of Spondyloarthritis International Society MRI criteria, with findings of bone marrow edema indicated by arrowheads on the short tau inversion recovery (STIR) series and synovial inflammation indicated by arrows on the fat-suppressed (FS) contrast-enhanced and diffusion-weighted imagining (DWI) series. **(a)** FS axial T1 postcontrast series and **(b)** subtracted images demonstrating enhancement in the joint space in the posteroinferior parts of both sacroiliac joints (SIJs). **(c)** Axial reformatted STIR images, **(d)** $b = 0$ DWI indicating fluid values in the joint space. **(e-l)** apparent diffusion coefficient (ADC), D, D_1, ADC_{low}, ADC_{diff}, D*, f_1, and f_2 maps with synovial enhanced areas marked with volume of interest in the right SIJ space indicated by arrows. At the marked volume, the following estimates were calculated: ADC = 1.9×10^{-3} mm²/s, D = 1.22×10^{-3} mm²/s, D_1 = 1.43×10^{-3} mm²/s, ADC_{low} = 1.76×10^{-3} mm²/s, ADC_{diff} = 16.02×10^{-3} mm²/s, D* = 16.58×10^{-3} mm²/s, f_1 = 7%, and f_2 = 20%.

Table 3. Demographic and clinical characteristics

Characteristic	SIP	SIN	*P* value
Female gender ratio (%)	78	22	0.007
Age (year) (mean ± SD)	30.88 ± 7.67	34.48 ± 8.10	0.85
CRP (mg/dL) (median, IQR)	3 (3)	3 (2)	0.659
ESR (mm/L) (median, IQR)	23 (20)	13 (17)	0.027

SIP, synovial inflammation positive; SIN, synovial inflammation negative; SD, standard deviation; CRP, C-reactive protein; IQR, interquartile range; ESR, erythrocyte sedimentation rate.

Table 4. Mean values of groups with and without synovial enhancement

Parameter	SIN (n = 58) Mean ± SD Median (min-max)	SIP (n = 28) Mean ± SD Median (min-max)	*P*
ADC ($\times10^{-3}$ mm^2/s)	1.39 ± 0.16 1.38 (0.99–1.90)	1.48 ± 0.21 1.52 (1.07–1.87)	0.057
D_1 ($\times10^{-3}$ mm^2/s)	1.25 ± 0.13 1.24 (0.92–1.71)	1.36 ± 0.26 1.38 (0.69–1.87)	0.053
D ($\times10^{-3}$ mm^2/s)	1.02 ± 0.16 1.01 (0.62–1.42)	1.23 ± 0.34 1.24 (0.46–1.87)	**0.004**
f_1%[a]	16.85 ± 4.04 15.88 (9.30–25.98)	18.81 ± 5.52 16.71 (11.42–31.53)	0.143
f_2%	31.23 ± 6,34 30.90 (17.88–49.39)	31.68 ± 6.12 32.15 (20.47–43.74)	0.752
D* ($\times10^{-3}$ mm^2/s)	21.78 ± 3.77 21.86 (14.77–32.33)	16.19 ± 4.58 15.11 (8.16–26.22)	**<0.001**
ADC_{low} ($\times10^{-3}$ mm^2/s)[a]	4.59 ± 1.16 4.47 (2.35–7.69)	5.21 ± 1.55 4.54 (2.94–9.25)	0.131
ADC_{diff} ($\times10^{-3}$ mm^2/s)[a]	4.09 ± 1.17 3.77 (2.09–6.91)	4.62 ± 0.16 4.13 (2.40–8.92)	0.153

Mann–Whitney U test was performed for parameters denoted with [a] due to non-normal distribution according to the Shapiro–Wilk test. The Student's t-test was performed for the other parameters.
Significant test results are noted in bold. SIN, synovial inflammation negative; SD, standard deviation; min, minimum; max, maximum; ADC, apparent diffusion coefficient; D, true diffusion coefficient; D*, pseudodiffusion coefficient.

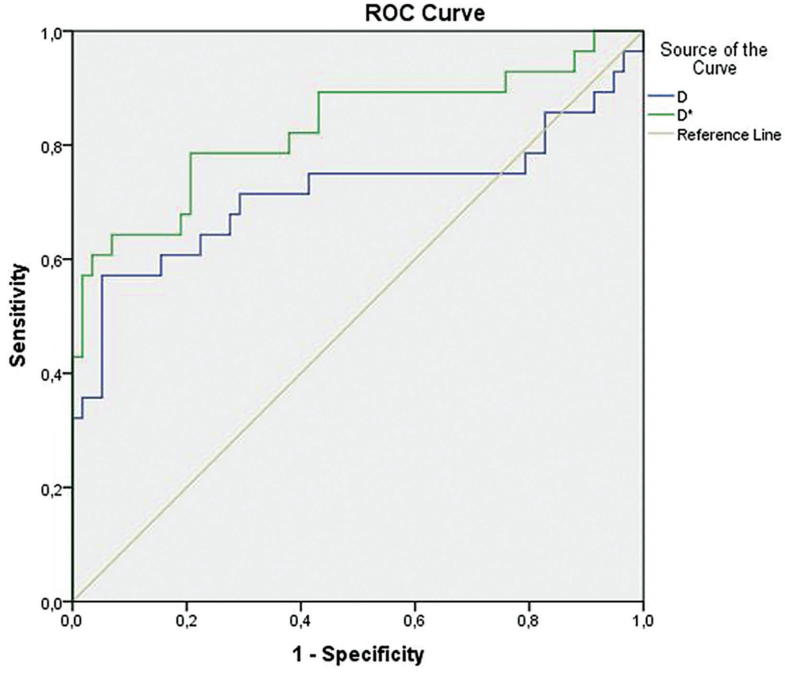

Figure 3. Receiver operating characteristic curve analysis of D* and D with regard to the diagnosis of synovial enhancement in active sacroiliitis cases. D, true diffusion coefficient; D*, pseudodiffusion coefficient.

accompanied by active sacroiliitis without using a contrast agent. The study results indicate that in areas where synovial contrast enhancement is detected in the SIJ and defined as SIP, the pseudodiffusion coefficient D* decreases, whereas the diffusion coefficient D, indicating pure diffusion in the extracellular space, increases. There was no significant difference between SIN and SIP areas in terms of ADC, f_1, f_2, D_1, ADC_{low}, or ADC_{diff}.

According to the study results, the decrease in the D* value in SIP areas indicates a reduction in intravascular blood flow and capillary network length. However, an increase in the D value suggests an increase in extracellular pure diffusion in SIP areas. Although f_1 and f_2 were affected by the amount of fluid in the extracellular space and intravascular compartment, ADC_{low}, D_1, ADC_{diff}, and ADC were impacted by both diffusion and perfusion. These findings indicate that, although an increase is observed in the amount of fluid in the extracellular space in areas of synovial inflammation, it is accompanied by a decrease in blood flow in the capillary bed in the SIP areas compared with the SIN areas. Furthermore, no significant change was observed in the value of f_1, which was affected by fluid areas in the extracellular space and the intravascular compartment. There was no significant difference in the ADC_{low}, D_1, and ADC values with regard to both diffusion and perfusion, or the ADC_{diff} value, which represents the diffusion parameter associated with perfusion. These findings highlight that an increase in the amount of fluid in the extracellular space in areas of synovial inflammation is accompanied by a decrease in blood flow in the capillary bed.

Zhao et al.[13], who compared the parameters of the IVIM method with those of dynamic contrast-enhanced (DCE) MRI in the SIJ, found D to be moderately correlated with relative enhancement and maximum enhancement (ME). In the same study, D* was observed to have a moderate negative correlation with ME. The current study identified a decrease in D* and an increase in D in areas characterized by Gd uptake. Notably, a decrease in the D* of the areas marked by contrast enhancement is consistent with the results of the current study. In a similar study, Guo et al.[1] investigated the correlation between DCE-MRI and IVIM DWI parameters in patients with axSpA, finding that D correlated with perfusion parameters derived from DCE-MRI. This finding is consistent with the observed increase in D in the areas of synovial inflammation in the present study. Liu et al.[18] found a higher true diffusion coefficient

(D_{slow}) in the IVIM DWI study examining BME areas in cases of active sacroiliitis; however, this difference was not statistically significant. Guo et al.[19] correlated IVIM MRI parameters with the clinical activity index for BME areas in axSpA cases, identifying a correlation between D and D* with the clinical activity index. Although our study addressed a different topic, two of the most valuable IVIM parameters were found to be consistent with our study.

In our literature review, we identified two IVIM studies focusing on synovial inflammation that were also conducted on the knee joint. In the first study, an increase in f and D values was detected in inflamed synovial areas.[20] However, in the present study, although the f value registered an increase, it was not statistically significant. As noted by Andreou et al.[21], the decrease in D*, which was evident in the case of the patients participating in this study, may have prevented the f value from achieving a substantial increase. In their more recent pilot study, Huch et al.[22] compared the results obtained from the knee joint with detected synovitis in pediatric and young adult patients with data from healthy volunteers. This ongoing study has demonstrated that the D value is low and the f value is high based on data from eight patients.[22] Furthermore, the only study that compared the diffusion properties of inflamed and non-inflamed synovial fluid using contrast-enhanced MRI was conducted with a focus on the knee joints of children diagnosed with juvenile idiopathic arthritis, revealing that ADC values increase in the case of active disease.[23] In the present study, however, no significant change in ADC values was observed. Notably, the b values used to calculate the ADC in the aforementioned study were 50 and 600, as a result of which the tissue perfusion effect on the ADC was subtracted. This may be accepted as a parameter similar to the perfusion-free D value used in the present study. Therefore, in the present study, the D value exhibiting a minimal perfusion effect was significantly higher in the inflamed areas.

Notably, pathology studies have indicated that patients with AS experience extensive vascular congestion and obliteration, accompanied by an increase in lining cells, lymphocytes, and plasma cells in the SIJ.[24] Furthermore, histological studies have revealed increased mast cells, CD163 macrophages, and neutrophils in areas of synovial inflammation.[25] The mediators secreted from these cells can increase capillary permeability and the amount of extracellular fluid. This pathophysiological mechanism may explain the increase in D observed in this study, which reflects free diffusion in the extracellular space. In addition, vascular congestion and obliteration may have contributed to the decrease in D* values, which is associated with intravascular blood flow and overall decreased perfusion.

It should be noted that there is ongoing debate regarding the necessity of contrast application in SI MRI. According to the ASAS criteria, the administration of a contrast agent is primarily recommended to detect joint space enhancement rather than synovitis. Current guidelines suggest using the term "joint space enhancement" instead of synovitis.[26] In this context, this study is the first to investigate the performance of the simplified IVIM method in detecting synovial inflammation in SI MRI and its diagnostic superiority over using a contrast agent. In line with ASAS-EULAR recommendations, T1w post-Gd images are typically used to detect synovial inflammation.[27] However, the current study demonstrated the presence of synovial inflammation in patients with SpA with high specificity and sensitivity, without the need for T1w post-Gd images. Although previous IVIM studies on the SIJ have focused on BME areas detectable on STIR sequences, this pioneering study revealed synovial inflammation areas, traditionally requiring contrast agents, using the IVIM method. This approach not only demonstrated high specificity and sensitivity but also excellent interobserver agreement using only four *b* values.

Nonetheless, this study has several limitations. First, the patients' Bath Ankylosing Spondylitis Disease Activity Index scores and clinical follow-ups were not available for analysis; these data could enhance the reliability of results in future studies. Second, although pioneering, the study analyzed a relatively small number of patients. Third, although T1w post-Gd images were the gold standard for evaluating synovial inflammation, no evaluation based on histopathological data was conducted. Histopathological assessments were impractical because of the anatomical complexities of the SIJs and ethical considerations. Finally, as a cross-sectional study, it does not provide insights into longitudinal changes in the synovium over time. Future research should consider longitudinal studies to address these limitations comprehensively.

In conclusion, the results of this study indicate that in patients with axSpA and inflammation in the SIJ, there is an increase in fluid within the extracellular space accompanied by decreased blood flow. The simplified IVIM method, which involves a short sequence time and demonstrates high specificity and sensitivity using only four *b* values, allows for the detection of synovial inflammation without the need for any contrast material.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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