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ORIGINAL ARTICLE RADIOLOGY

Efficacy of diffusion weighted imaging in sacroiliac joint MRI in children

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ABSTRACT

OBJECTIVE: Because of the immature bone marrow signal in children, assessment of the sacroiliac joint is more difficult than in adults. Aim of this study is to evaluate the efficacy of diffusion-weighted imaging (DWI) in sacroiliac joint magnetic resonance imaging (MRI).

METHODS: Sacroiliac joint MRI, including DWI sequences, were evaluated by two pediatric radiologists in 54 patients with sacroiliitis and 85 completely normal controls. In MRI evaluation, subchondral bone marrow edema and contrast enhancement in the sacroiliac joints were considered as active sacroiliitis. Apparent diffusion coefficient (ADC) measurements were made in six areas from each sacroiliac joint. A total of 1668 fields were evaluated retrospectively without their diagnosis being known.

RESULTS: When the postcontrast T1W series were referenced, the sensitivity, specificity, positive predictive value, and negative predictive value of short time inversion recovery (STIR) images in the diagnosis of sacroiliitis were 88%, 92%, 83% and 94% respectively, compared to contrast-enhanced images. False positive results in STIR images were observed secondary to the flaring signal in the immature bone marrow. ADC measurements obtained from diffusion-weighted images were recorded in all patients and healthy groups. The ADC values were $1.35x10^{-3}$ mm^2/s (SD: 0.21) in the areas of sacroiliitis, $0.44x10^{-3}$ mm^2/s (SD: 0.71) in the normal bone marrow and $0.72x10^{-3}$ mm^2/s (SD: 0.76) in the immature bone marrow areas.

CONCLUSION: Although STIR studies are an effective sequence in the diagnosis of sacroiliitis, they cause false positive results in immature bone marrow in children in inexperienced hands. DWI is an objective method that prevents errors in the assessment of sacroiliitis by means of ADC measurements in the immature skeleton. In addition, it is a short and effective MRI series that makes important contributions to the diagnosis without the need for contrast-enhanced examinations in children.

Keywords: ADC; DWI; immature bone; MRI; sacroiliac joint; sacroiliitis.

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Sacroiliitis occurs in about 1/3 of children with the enthesitis related arthritis. Spinal mobility decreases over time in patients who develop sacroiliitis, which may result in permanent damage in the long term [1]. Inflammatory back pain often develops relatively late in pediatric patients with active sacroiliitis. Therefore, early diagnosis and treatment is important due to the benefits of early biological agent therapy in patients with axial skeletal involvement [2, 3].

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Magnetic resonance imaging (MRI) is the first modality for the evaluation of the sacroiliac joint (SIJ) without exposing the young pelvis to ionizing radiation. It can help detect bone marrow edema, which cannot be seen on radiography or computed tomography (CT). This allows for the identification of acute sacroiliac joint inflammation earlier than other modalities [4, 5].

The Assessment in SpondyloArthritis International Society (ASAS) classification system, first published in 2009 and revised in 2016, utilizes the imaging features of SIJ on MRI to evaluate the presence of sacroiliitis [6, 7]. In children, it is difficult to evaluate SIJ due to its complex structure and the skeleton being immature. The sacral apophysis ossifies during childhood and typically fuses between the ages of 16–20 years. SIJ can sometimes remain immature until late adolescence [4]. In the immature SIJ, the hyperintensity observed in the non-ossifying apophysis on STIR images may be misinterpreted as inflammation [8].

Contrast agent use is not favorable in children with long life expectancy since they can result in the need for invasive procedures, such as vascular access and pose risks of contrast accumulation in tissues. Diffusion-weighted imaging (DWI), which can support the diagnosis without prolonging the examination time, can provide more accurate results in a less invasive manner.

DWI is a MRI sequence based on the measurement of the random Brownian motion of water molecules within a voxel of tissue. The DWI signal can be quantified by apparent diffusion coefficient (ADC) maps [9, 10]. Musculoskeletal system abnormalities have also been examined with DWI, which has been shown to successfully detect bone marrow changes and metastasis [11–13].

The aim of this study was to reveal pathological signal changes in the bone marrow in children with sacroiliitis using short time inversion recovery (STIR) supported by DWI sequences and determine whether this could eliminate the need for contrast-enhanced examinations. We also performed ADC measurements to provide a better understanding of signal changes that can be easily misinterpreted in the immature skeleton.

Highlight key points

- In pediatric patients, T2W signal in immature bone may be mistaken for bone marrow edema, which may lead to misconceptions.
- In less experienced hands, the diagnosis and treatment phase can be troublesome with false positive results.
- It is possible to objectively evaluate mature - immature normal bone marrow signal and bone marrow edema in sacroiliitis with ADC maps by making use of different diffusion properties, without using contrast agent in a short-term examination.

MATERIALS AND METHODS

Between January 2017 and December 2019, a total of 380 pediatric patients aged 0–17 years who underwent the MRI of SIJ were retrospectively evaluated by two pediatric radiologists. Of these patients, 85 patients (50 male,35 female, mean age 12 years) had completely normal findings and 54 patients (33 male, 21 female, mean age 13 years) had radiologically active sacroiliitis. Patients without sacroiliitis but with chronic changes and patients without DWI or postcontrast T1W sequences were excluded from the study. All patients included in the study had pre and post-contrast T1W, STIR and diffusion sequences. All sequences were evaluated at different times and their contribution to the diagnosis was compared.

The protocol of MRI

All the MRI scans were performed with a 1.5 Tesla system (Magnetom Avanto; Siemens Healthineers, Erlangen, Germany) using the standard departmental protocol. Imaging was performed in the supline position with body flexed array coil. The main sequences are as follows:

A) STIR sequence (matrix, 256 × 256; slice thickness, 3 mm; field of view: 250 mm, repetition time (TR), 3.000 ms; and echo time (TE), 38 ms, invertion time (TI), 150 ms)

B) T1-weighted spin echo non-fat-saturated and fat saturated sequences (matrix, 320 × 320; slice thickness, 3 mm, TR, 445 ms; and TE, 21 ms),

C) T1-weighted spin echo fat-saturated post-contrast sequences (matrix, 320 × 320; slice thickness, 3 mm; TR, 490 ms; and TE, 12 ms)

D) Diffusion-weighted sequences at the b-values of 0, 400 and 800 (matrix, 192 × 192; slice thickness, 3 mm; TR, 5200 ms; and TE, 58 ms). ADC maps were created by the scanner.

All the sequences except DWI were obtained in the oblique coronal (parallel to the long axis of SIJ) and axial planes using a four-channel surface coil. DWI sequences were obtained in the axial plane. The fat-saturated contrast-enhanced T1-weighted images were obtained after the administration of 0.1 mmol/kg of body weight of gadopentetate dimeglumine.

Definitions of MRI

The MRI evaluated in the group with the diagnosis of sacroiliitis belonged to the period when the patient had active complaints.

The SIJ space and surrounding bone marrow were evaluated on each imaging sequence separately. MRI images of the patients and control groups were evaluated retrospectively and without knowing their diagnosis. Based on the ASAS criteria, it was defined as subchondral bone marrow edema/osteitis on a T2-weighted sequence such as STIR or T2 FS, or sacroiliitis in the presence of increased bone marrow contrast on a T1-weighted sequence. The presence of other inflammatory lesions, such as synovitis, enthesitis or capsulitis, alone without concomitant bone marrow edema, was not considered active sacroiliitis on MRI [11, 12].

ADC measurements were taken from each sacroiliac joint (superior, middle, and inferior portions of the sacral and iliac bones) in all of the patients and performed in 1668 areas. A circular region of interest (ROI) with an area of 25–80 mm^2 was placed on the subarticular surface of SIJ.

Subchondral sclerosis (low signal on T1- and T2-weighted sequences), cortical bone erosions, and joint space narrowing were defined as chronic changes.

Two radiologists with 12 and 13 years of experience in pediatric radiology evaluated all the images blinded to the patients' identity information by using codes rather than names. The STIR and postcontrast T1-weighted sequences of all the patients were evaluated separately by the two radiologists at different times. The first radiologist assessed the STIR sequences, while the second radiologist evaluated the contrast-enhanced T1-weighted sequences of the same patient. Both radiologists assessed the images in a random order.

After completing the inter and intra-observer analyses, the presence of acute or active sacroiliitis was decided based on the consensus of the radiologists and a rheumatologist.

Statistical Methods

Statistical calculations were performed using the Statistical Package for the Social Sciences (SPSS) (version 23, Chicago, IL, USA). Descriptive statistical methods (mean, standard deviation, median, frequency, ratio) as well as Shapiro Wilk test and box plot graphics were used for the compliance of the variables with the normal distribution. Differences between the groups and ADC values were assessed using the Mann-Whitney U test. The Mann Whitney U test with Bonferroni correction was used in post hoc evaluations of the Kruskal Wallis test. The contrast-enhanced MRI sequences and STIR images were compared, and the consistency between their findings in detecting the disease was calculated with the chi-square analysis. Kappa fit analyzes were used an significance was evaluated at the $p<0.05$ level.

The specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) of the STIR images were calculated based on the reference standard for the presence of acute changes in contrast enhanced T1-weighted images.

The study protocol was approved by the Ethics Committee of Umraniye Training and Research Hospital on Mar 20, 2019 (B10.1.TKH.4.34.H.GP.0.01/56) and conducted in accordance with the principles of the Declaration of Helsinki.

Table 1. Clinical and laboratory findings of 54 patients diagnosed with sacroiliitis

	n	%
Gender		
Female	21	39
Male	33	61
Median age (range 6–17 years)	15	
High level of sedimentation	41	75
High level of CRP	32	60
HLA B27 (+)	18	33
CRMO	5	9
ERA	9	16
FMF	1	2
JIA	35	65
PsA	1	2
UC	3	6
Total	**54**	**100**

HLA: Human leukocyte antigen; CRP: C-reactive protein; CRMO: Chronic recurrent multifocal osteomyelitis; ERA: Enthesitis-related arthritis; FMF: Familial mediterranean fever; JIA: Juvenile idiopathic arthritis; PsA: Psoriatic arthritis; UC: Ulcerative colitis.

RESULTS

A total of 54 pediatric patients, 21 female (38.9%) and 23 male (61.1%) were evaluated. The mean age was 13 years, and the median age was 15 years (6–17 years). The patients' diagnosis was given in Table 1. Most of

Table 2. Chronic changes in the bones adjacent to the sacroiliac joint in patients with sacroiliitis

Chronic changes of SIJ	Sclerosis		Erosion	
	n	%	n	%
None	17	31.5	30	55.6
Right	4	7.4	5	9.3
Left	6	11.1	5	9.3
Bilateral	27	50.0	14	25.9

SIJ: Sacroiliac joint.

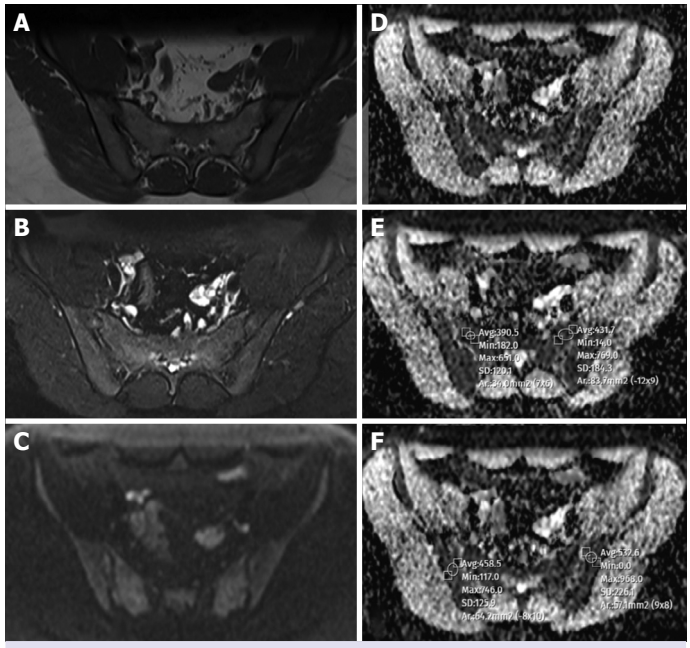

Figure 1. In control group, normal sacroiliac joint MRI. In the right column, axial T1W **(A)**, STIR **(B)** and diffusion **(C)** MR images are seen, respectively. There are ADC maps **(D–F)** in the left colon and ADC values measured in the subchondral bone marrow (mean: 0.44x10^{-3} mm^2/s).

the patients with sacroiliitis were in the JIA group. According to the affected side, there were 12 patients (22.2%) with right sacroiliitis, 13 patients (24.1%) with left sacroiliitis, and 29 patients (53.7%) with bilateral sacroiliitis. The rates of sclerotic changes and SIJ erosions are given in Table 2.

According to laboratory data, sedimentation in 41 (75.9%) patients and C-reactive protein (CRP) values in 32 (59.3%) patients were above the normal range, respectively. In addition, HLA B-27 positivity was found in 18 patients.

Table 3. Comparison of post-contrast T1-weighted sequences and STIR images in patients with sacroiliitis

	Postcontrast T1 weighted images		
STIR images	Sclerosis (+)	Sacroiliitis (-)	Diagnostic Screening Tests
Sclerosis (+)	50 (36.0)	10 (7.2)	Sensitivity: 92.59 Specificity: 88.24
Sacroiliitis (-)	4 (2.9)	75 (54.0)	PPV: 94.94; NPV: 89.93 Accuracy: 89.93
Total	**54 (38.8)**	**85 (61.2)**	

Kappa uyum: 0.792, p=0,001; STIR: Short time inversion recovery; PPV: Positive predictive value; NPV: Negative predictive value.

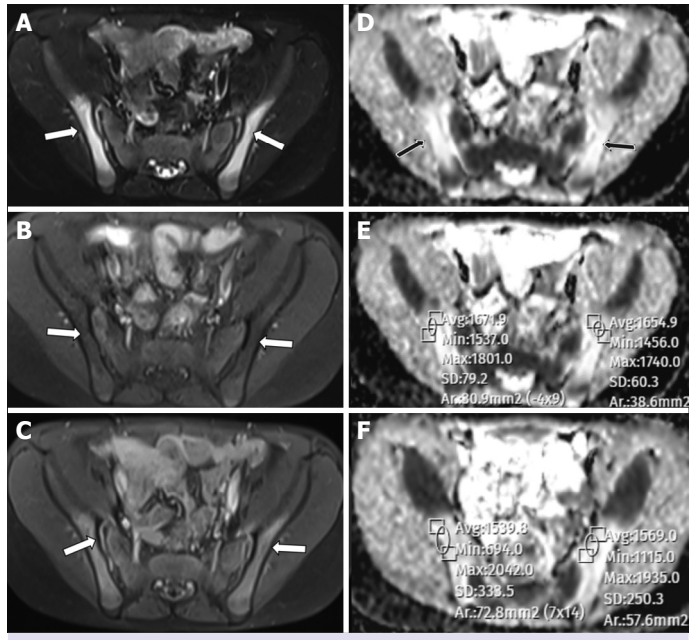

Figure 2. MRI images of a 15-year-old diagnosed with JIA. In the subchondral iliac bones adjacent to the SIJ, a hyperintense signal **(A)** in STIR images and hypointense signal **(B)** inT1W images consistent with bone marrow edema is observed. Diffuse enhancements are observed in the sacral bones adjacent to the sacroiliac joint in postcontrast images **(C)**. There are ADC maps in the left colon **(D–F)** and ADC values measured in the subchondral bone marrow in a patient with sacroiliitis (mean: 1.35x10^{-3} mm^2/s).

STIR and post-contrast T1-weighted sequences were compared. The sensitivity, specificity, positive predictive value and negative predictive value of the STIR images were calculated as 88%, 92%, 83%, and

TABLE 4. Evaluation of ADC measurements of normal and pathological bone marrow areas

	n	ADC (Value x10^{-3} mm^2/s)			
		Mean±SD	Min–Max	+p	Post-hoc
ADC 1	403	0.48±0.16	0.2–0.8		
ADC 2	245	1.35±0.21	1.05–1.82	**<0.001**	1<4
ADC 3	925	0.44±0.71	0.30–0.65		2>1,3,4
ADC 4	95	0.72±0.07	0.62–0.87		3<4

ADC: Apparent diffusion coefficient; SD: Standard deviation; Min: Minimum; Max: Maximum; ADC 1: ADC values of the normal areas in patients with sacroiliitis; ADC 2: ADC values of the pathological areas in patients with sacroiliitis; ADC 3: ADC values of the control group (normal); ADC 4: ADC values of the immature bone; +: Kruskal Wallis Test & Adjustment Bonferroni, Mann-Whitney U test.

94%, respectively in reference to the contrast-enhanced images (Table 3). False positive results in STIR images were observed secondary to the flaring signal in the immature bone marrow. The mean ADC values of the normal bone marrow was 0.44x10^{-3} mm^2/s (SD: 0.71) (Fig. 1), the mean ADC values were 1.35x10^{-3} mm^2/s (SD: 0.21) in the bone marrow areas in patients diagnosed with sacroiliitis (Fig. 2) and the mean ADC values of areas considered as immature bone marrow was 0.72x10^{-3} mm^2/s (SD: 0.76) (Fig. 3, 4; Table 4).

Ten patients had a suspicious "flaring" appearance on STIR images that could be mistaken for sacroiliitis. However, no significant enhancement was detected in post-contrast T1W images. These areas were evaluated as red bone marrow because of the involvement of the sacral faces, the lack of clinically supportive data, and the lack of significant contracture. Flaring in was evaluated as a red bone marrow signal due to immature bone. In this group, ADC measurements were made in a total of 120 areas compatible with immature bone marrow.

The ADC values ranged from 0.62 to 0.87x10^{-3} mm^2/s. Flaring was mostly seen in prepubertal female patients (Tables 4, Fig. 3).

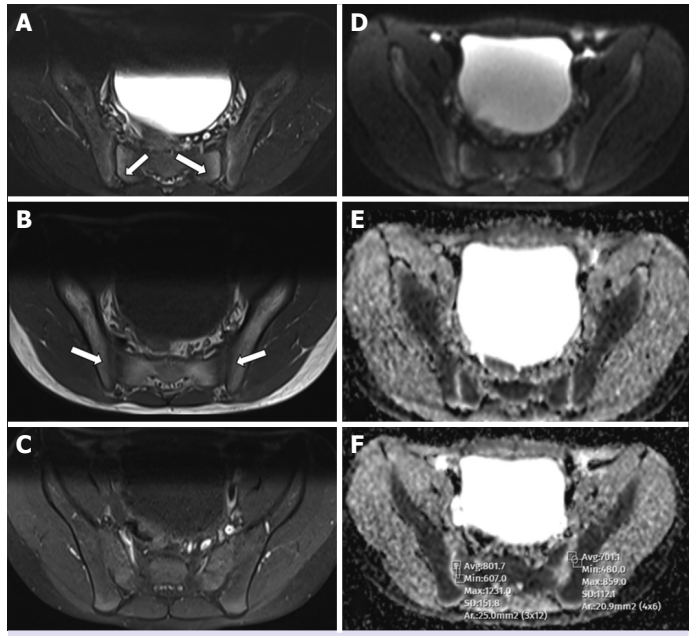

FIGURE 3. Images of the STIR **(A)**, T1W **(B)**, enhanced T1W **(C)**, diffusion **(D)** and ADC **(E, F)** sequences taken in the axial plane of a 13-year-old male patient are viewed, respectively. Flaring is observed in the subchondral bone marrow adjacent to the SIJ, more prominently on the sacral faces in STIR images. These areas were hypointense in T1W series and no significant enhancement was detected. It is slightly hyperintense on DWI, and ADC values were found to be 0.62–0.87x10^{-3} mm^2/s in these areas in ADC mapping.

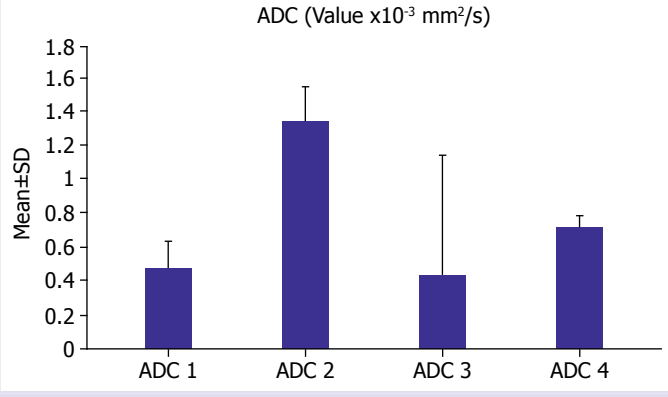

FIGURE 4. Graphical representation of ADC measurements from normal, immature bone and pathological bone marrow areas.

DISCUSSION

Sacroiliitis can be largely detected by STIR MRI sequences without the need for contrast material. However, the red bone marrow signal in immature bone causes misconceptions in children. With this study, we were able to make this distinction with objective measurements by adding diffusion sequences to the examination in children.

In children with JIA, the evaluation of inflammatory sacroiliitis with MRI has prominently increased in the

last few decades [14]. It is more difficult in children compared to adults due to the small field of view, red bone marrow and cartilage tissue density and the lack of cooperation. MRI is an important radiological imaging modality in the clinical diagnosis and treatment process, especially in detecting early sensitivity to inflammation. SIJ has a complex anatomy and normal variation in subchondral MRI signal in the immature skeleton [15]. As a result, false-positive results can be obtained by those with insufficient clinical experience, which can lead to unnecessary treatments due to the misinterpretation of MRI signal characteristics in the immature bone marrow [16]. DWI has recently been increasingly used in musculoskeletal imaging since it allows for the examination of microscopic structure in the tissue and shows diffusion and perfusion together when performed at low B values and true diffusion at high B values.

According to the ASAS classification criteria for the evaluation of sacroiliitis, the MRI protocol must contain T2-weighted sequences sensitive to free water (STIR or T2 FS) and T1-weighted fat-saturated post-contrast sequences for the detection of active inflammatory changes. Periarticular or subchondral bone marrow edema is essential for the diagnosis of active sacroiliitis in MRI, but the presence of synovitis, capsulitis or enthesitis are secondary supportive findings [11, 12, 17].

Previous studies have shown that contrast-enhanced T1-weighted images were more sensitive in the diagnosis of acute inflammatory lesions than the STIR and fat-saturated T2-weighted images [18–20]. In our study, when the contrast images were taken as reference, the specificity, sensitivity, PPV and NPV values of the STIR images were found to be 88%, 92%, 83%, and 94%, respectively. When we examined the inconsistencies between the STIR and post-contrast images, there were 10 patients aged 6 to 14 years in the false-positive group. It was observed that the ADC values were in the range of 0.62-0.87 in this group without significant enhancement in the post-contrast images, and the signal was evaluated as slightly hyperintense on the STIR images of these patients. When these cases were re-evaluated based on clinical and laboratory data, these areas were considered to result from the T2-weighted flaring of the immature bone marrow (Fig. 3).

Herregods et al. [21] described a rim of subchondral increased signal on the STIR images (flaring), which was frequently seen in children and usually symmetric. Earlier studies had suggested that these signal changes likely indicated ossifying epiphyseal cartilage consistent with immaturity, similar to other joints. Laor et al. [22] also noted that flaring was much more frequently observed in children at the sacral than the iliac side of SIJ. In our false-positive group (10 patients), we also observed this signal increase referred to as flaring, mostly on the sacral side.

In an MRI study conducted with healthy children, Chauvin et al. [23] reported that the SIJ findings varied according to age and gender. The authors emphasized that a high signal of bone marrow adjacent to SIJ could easily appear as inflammation to the untrained eye, and this signal was mostly bilateral in the prepubertal group.

On the other hand, in our study, 4 patients who had false-negative results on the STIR sequences with reference to the contrast-enhanced MRI, bone marrow signal changes were minimal and synovial enhancements were more evident. In the evaluation of these suspicious findings with DWI, we found high ADC values as in the patients with sacroiliitis. In both situations, we were able to achieve an accurate diagnosis in all the patients by adding DWI sequences to the MRI examinations in the presence of any conflicting finding in the STIR images.

In correlation with some studies in the literature, we found that adding DWI sequences to the MRI examinations and performing ADC measurements in addition to conventional sequences increased the diagnostic performance of the radiologist in detecting the inflammatory changes of SIJ [24–28]. We consider that contrast material should not be used unless it is absolutely necessary, since it requires invasive interventions, prolongs the duration of the examination, and causes unnecessary anesthetic agent administration in patients requiring anesthesia. In addition, contrast agents should be used with caution, particularly given the concerns about intracranial gadolinium accumulation [29–31]. Compared to adults, the number of pathologies that can cause bone marrow edema is limited by the age of the child, and bone marrow edema observed in STIR images is more specific to sacroiliitis [32].

In our study, in the measurements made from a total of 648 areas in 54 patients with a diagnosis of sacroiliitis, the mean ADC value was $1.35x10^{-3}$ mm^2/s (SD: 0.21) in areas defined as sacroiliitis and $0.48x10^{-3}$ mm^2/s (SD: 0.16) in other normal areas of the same patients. In the control group, mean ADC values in immature bone marrow areas in a total of 95 high-signaled areas in 10 patients were found to be $0.72x10^{-3}$ mm^2/s (SD). Except for these areas,

the mean ADC value was 0.44 (SD) in the examinations made in 925 completely normal areas found (Table 4).

The mean ADC value of bone marrow edema around SIJ in the patients with sacroiliitis was significantly higher compared to the control group, which is consistent with the literature [19, 24, 25, 28, 32–34]. High ADC values in bone marrow edema appear to be due to the local increase in water movement, and thus diffusion. Hyperintense (flaring) signal changes observed on the STIR sequences of the immature bone marrow areas were also confusing in the diagnosis of sacroiliitis. The ADC values were measured as 0.62–0.87x10^{-3} mm^2/s in these areas, and although this was less than in the sacroiliitic areas, diffusion was only slightly increased compared to the normal bone marrow signal. However, since our results belong to a small patient group, it is not possible to generalize them to all patients with this condition.

Herregods et al. and Beltran et al. [21, 24] evaluated normal immature bone marrow signal changes in pediatric patients. However, neither study provided ADC data in the immature skeleton. To our knowledge, there is only one study in the literature including this evaluation. In that study, Bray et al. [35] reported that the mean ADC value was 0.52–0.67x10^{-3} mm^2/s in the fused group, 0.57–0.87x10^{-3} mm^2/s in the partial group, and 0.7–0.98x10^{-3} mm^2/s in the unfused group. In our study, the ADC values in the immature bone marrow were in the range of 0.62–0.87x10^{-3} mm^2/s in a limited number of patients, and the ADC values in sacroiliitis were measured to range from 1.05 to 1.82x10^{-3} mm^2/s. More extensive studies are needed to clarify these data.

There were some limitations to this study. First, it was a retrospective study and we did not have pathological confirmation of the disease. Also, DWI has limited spatial resolution compared to the other MRI sequences. Lastly, we did not evaluate minor criteria of sacroiliitis, such as synovitis, enthesitis and capsulitis because it is difficult to evaluate these findings due to the small field of view in children, and these findings would not be valuable for the diagnosis of sacroiliitis unless they are accompanied by bone marrow edema. In addition, the number of patients with confusion due to immature bone is not sufficient to generalize.

In conclusion, bone marrow edema, which is the most important parameter in the diagnosis of sacroiliitis in children, can often be detected as hyperintense signals in T2-weighted sequences. However, flaring in the immature bone marrow can be misinterpreted as inflammation by inexperienced clinicians and radiologists. DWI also offers quantifying diffusion coefficients of the lesions, which helps discriminate between normal, immature bone, and inflamed subchondral bone. Due to the advantages of providing useful findings in a short time without the need for contrast material use, DWI may be a feasible alternative to contrast-enhanced MRI. We anticipate that the DWI sequence will be adopted in the routine evaluation of SIJ for both the diagnosis and follow-up of sacroiliitis in the near future.

Ethics Committee Approval: The Umraniye Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 20.03.2019, number: B10.1.TKH.4.34.H.GP.0.01/56).

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