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Test–retest repeatability of the apparent diffusion coefficient in sacroiliac joint MRI in patients with axial spondyloarthritis and healthy individuals

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Abstract

Background: The apparent diffusion coefficient (ADC) may be used as a biomarker to diagnose axial spondyloarthritis (axSpA) and monitor therapeutic response.

Purpose: To measure the repeatability of the ADC in healthy individuals and in patients with axSpA with and without active sacroiliitis in a test–retest set-up, and to correlate ADC to conventional magnetic resonance imaging (MRI) bone marrow edema (BME) scores and clinical findings.

Material and Methods: A total of 25 patients with axSpA and 24 sex- and age-matched healthy individuals were prospectively examined with MRI twice within 10 days. Short tau inversion recovery (STIR), T1-weighted and diffusion-weighted imaging sequences were performed. Mono-exponential ADC maps were based on four b-values: 0; 50; 500; and 800. Inter-study repeatability and intra-reader reproducibility were investigated in subgroups, as were associations with conventional MRI and clinical findings.

Results: The inter-study repeatability for the median ADC was moderate for all individuals (intraclass correlation coefficient [ICC] 0.66); it was good in patients with axSpA (ICC 0.79) and poor in healthy individuals (ICC 0.27). Significant differences in ADC were found between women and men ($P = 0.03$), and between patients with versus without BME on STIR ($P = 0.01$). ADC was associated with an MRI BME score and with age in women.

Conclusion: ADC seems to be a repeatable parameter in patients with axSpA but not in healthy individuals. ADC is correlated with MRI sacroiliac joint BME score and with age in women.

Keywords

Skeletal–axial, magnetic resonance diffusion/perfusion, arthritides, inflammation, spondyloarthritis, apparent diffusion coefficient mapping

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Introduction

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease, which generally starts in early adulthood. The non-radiographic form affects men and women equally and is present in up to 1%–2% of the population, whereas the more severe form ankylosing spondylitis is prevalent and more frequent in men than women (ratio of 2:1). Untreated axSpA causes severe pain, fatigue, and reduced physical function and may lead

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to structural bone damage and ankylosis. Thus, early diagnosis and treatment is needed (1).

Bone marrow edema (BME) localized in the sacroiliac joints (SIJ) as assessed by short tau inversion recovery (STIR) or T2-weighted (T2W) fat-saturated (FS) sequences is a cornerstone in the classification criteria for axSpA (2). Because diffusion-weighted imaging (DWI) can quantify water diffusion by measuring the apparent diffusion coefficient (ADC), it may be used as an alternative or supplementary imaging method to STIR or T2W FS sequences (3). Several studies have investigated the utility of ADC to diagnose/detect active sacroiliitis (4–7). The studies have shown that significantly higher ADC values can distinguish patients with active early sacroiliitis from patients with mechanical low back pain (4), healthy individuals (5,6), or patients with chronic sacroilitis (6,7). The ADC can also be used to monitor the response to therapy and to detect changes in disease activity in patients with ankylosing spondylitis during tumor necrosis factor (TNF) inhibitor therapy, but not in patients being treated with intravenously administered corticosteroids and non-steroid anti-inflammatory drugs (NSAIDs) (8). However, to be implemented in clinical practice, it is important that the ADC method is reproducible and reliable, and that the normal variation of ADC is below the observed differences between patients and healthy individuals and changes during treatment.

The primary objective of this study was to investigate the repeatability of ADC measured in the SIJs of healthy individuals and in patients with axSpA. The secondary objective was to correlate ADC with conventional magnetic resonance imaging (MRI) scores and the clinical characteristics of patients.

Material and Methods

Participants

The study was approved by the Ethical Committee of the Capital Region of Denmark (approval number: H-3-2012-085) and all participants gave their written informed consent. Patients with inflammatory back pain and axSpA according to the Assessment of Spondyloarthritis International Society criteria for axSpA (9), as judged by an SpA expert rheumatologist were included. Patients were not allowed to have taken intravenous, intra-articular, or intramuscular glucocorticoids in the three months before study inclusion, or started or changed dose of oral glucocorticoids or tumor necrosis factor (TNF) inhibitor. Moreover, changes in NSAIDs were not permitted within the two weeks before the first MRI examination or during the study. Healthy individuals were excluded if they had had arthritis or pain in the peripheral joints or the spine during the preceding three months. In addition, healthy individuals with first- and second-degree relatives with peripheral or axial SpA, psoriatic arthritis, or rheumatoid arthritis were disqualified as participants in the study. Finally, women were excluded if they were lactating, pregnant, or had an imminent wish to become pregnant.

Clinical assessment

Patients with AxSpA and healthy individuals were assessed by one clinical axSpA expert using the Bath Ankylosing Spondylitis (AS) Metrology Index (BASMI) (10), the Bath AS Disease Activity Index (BASDAI) (11), and the Bath AS Functional Index (BASFI) (12). Before the first MRI examination, individuals were assessed using the global visual analog scale (VAS-global) (13) and the pain visual analog scale (VAS-pain). In patients with axSpA, the serum concentration of C-reactive protein (CRP) was assessed. BASDAI, BASFI, VAS-global, and VAS-pain reassessments were performed before the second MRI examination. In addition, the patients with axSpA were asked if their disease was much worse, worse, unchanged, better, or much better compared to the first visit.

MRI technique

The patients and healthy individuals had two MRI scans performed with an interval of seven days (±2 days) between the scans. All examinations were performed using the same system (1.5-T Achieva, Philips, Best, the Netherlands) with a combination of a dedicated five-channel spine coil and a two-channel flexible coil. The technical parameters of the coronal oblique sequences are listed in Table 1.

Image analysis

All MRI scans were anonymized. Examinations from time point 1 (tp1) (n = 49) were anonymized using one series of random numbers, and the examinations from time point 2 (tp2) (n = 49) were anonymized using a different series of random numbers to make it possible to measure the variation over one week (i.e. inter-study repeatability). Moreover, all examinations from tp2 (n = 49) were re-anonymized and read again by the same reader to assess intra-reader reproducibility. These image series were used for assessment of ADC and for evaluation of SPARCC SIJ Inflammation Index and SIJ Structural Scores.

Mono-exponential gray-scale ADC maps were calculated on basis of all four b-values in dedicated software (Intellispace release 6.01. Philips, Best, the

Table 1. Parameters for the coronal oblique sequences.

Sequence	TR (ms)	TE (ms)	TI (ms)	b (s/mm^2)	FOV (mm)	Matrix	ST (mm)	Gap (mm)	Time (min:s)
STIR	2550	60	160	–	300 × 235	240 × 150	4	0.8	3:27
T1W	550	14	–	–	330 × 270	370 × 170	4	0	2:55
DWI	2000	75	–	0; 50; 500; 800	330 × 186	157 × 89	5	1.4	5:26

DWI, diffusion-weighted multishot spin echo planar imaging; FOV, field of view; ST, slice thickness; STIR, short tau inversion recovery; T1W, T1-weighted turbo spin echo; TE, echo time; TI, inversion time; TR, repetition time.

Netherlands). Using four consecutive slices, each SIJ was divided into four quadrants defined by a horizontal line that divided each joint into an upper and lower half of equal length. The first slice was defined as the most anterior slice where >1 cm of a SIJ was visible. The region of interest (ROI) was a free hand-drawn anatomic band-shaped ROI covering the length of the SIJ quadrant in a 5-mm depth from the joint cavity. ADC values were measured at a total of 32 ROIs for each individual (i.e. one ROI per quadrant per slice). The assessments were performed by a single assessor with >10 years of experience in axSpA and body ADC imaging.

All MRIs of the SIJs were evaluated for BME according to the Spondyloarthritis Research Consortium of Canada (SPARCC) SIJ Inflammation Index (14), and for fat, erosion, backfill, and ankylosis according to the SPARCC SIJ Structural Scores (15). This was done by one assessor with >10 years of experience in scoring MRIs from patients with axSpA.

Statistical analysis

Participants were characterized by descriptive statistics. Clinical test results variations between axSpA patients and healthy individuals were assessed by Mann–Whitney U test. Changes between tp1 and tp2 in patients with axSpA were assessed using Wilcoxon's signed rank test. Changes in VAS-global, VAS-pain, and BASDAI in patients with axSpA were stratified according to self-reported axSpA disease activity and compared using the Kruskal–Wallis test.

Inter-study repeatability and intra-reader reproducibility were investigated using Bland–Altman plots and using a single measure two-way mixed intra-class correlation coefficient (ICC). The ICC results were defined as: poor <0.5; moderate = 0.51–0.75; good = 0.76–0.90; and excellent >0.91 (16). These assessments were performed for two different ADCs measures (i.e. the median [ADC_{med}] and 95th percentile [ADC_{95}]). The standard error of measurement (SEM) and smallest detectable change (SDC) were calculated to estimate the absolute measurement error. The SDC was also calculated as a percentage of the mean from tp1 and tp2. Variations of both ADC measures among the different subgroups were assessed using independent *t*-tests. Correlations with age, clinical tests, SPARRC MRI SIJ Inflammation and SIJ Structural Scores (SSS scores) were assessed using Spearman's Rho. All data were analyzed using SPSS software (ver. 22.0, IBM Corp., Armonk, NY, USA) and *P* values <0.05 were considered statistically significant.

Results

Study population

Study participants were recruited from the rheumatology outpatient clinics at Rigshospitalet–Glostrup and at Herlev–Gentofte Hospitals, Denmark. Age and sex-matched healthy individuals were recruited from staff members at Department of Radiology at Herlev–Gentofte Hospital, Denmark. MRI of SIJs were performed twice within a mean of 6.8 days (SD = 0.93; range = 4–10 days). A total of 25 patients with axSpA and 24 healthy individuals were included in the study. There were no statistically significant demographic differences between the patients and the healthy individuals (Table 2). However, patients with axSpA had significantly higher VAS-pain, VAS-global, BASDAI, and BASFI scores than the healthy individuals. No statistically significant differences were observed between men and women in clinical tests. In patients with axSpA, VAS-pain, VAS-global, and BASDAI differed significantly between tp1 and tp2 (Table 2). The other clinical tests and SPARCC scores did not reveal any significant differences between tp1 and tp2. At tp2, a total of 1, 5, 14, and 2 patients with SpA claimed to be much better, better, unchanged, and worse (SpA-activity), respectively. Three patients with axSpA did not answer this question. No statistically significant differences in VAS-pain, VAS-global, BASDAI, and SPARCC Inflammation scores were observed among the four groups who provided answers to the change in axSpA-activity question.

Inter-study repeatability

Table 3 provides the results of the reliability assessments. When all participants were pooled into one group, the inter-study repeatability assessed using the

Table 2. Characteristics of patients and healthy individuals.

	Healthy individuals (n = 24)	Patients (n = 25)		*P* value for comparison of healthy individuals vs. patients tp1	*P* value for comparison of patients tp1 and tp2
		Tp1	Tp2		
Female (age)	11 (42.55 ± 13.32)	12 (36.1 ± 9.86)	–	0.20	–
Male (age)	13 (44.38 ± 7.59)	13 (41.85 ± 10.32)	–	0.48	–
Symptom duration (years)	–	12.84 ± 8.50	–	–	–
Disease duration (years)	–	6.68 ± 6.41	–	–	–
NSAIDs	0	17	–	–	–
DMARDs	0	2	–	–	–
TNF inhibitor	0	7	–	–	–
Glucocorticoids	0	0	–	–	–
Pain	0 (0–0.5)	50 (24–67)	30 (17–59)	<0.01	<0.01
VAS global	0 (0–0)	60 (23–71)	32 (19–63)	<0.01	0.01
BASDAI	1 (0–3)	47 (24–66)	45 (19–57)	<0.01	0.03
BASFI	0 (0–0)	34 (25–53)	34 (14–54)	<0.01	0.17
BASMI	0 (0–0)	38.2 (32.7–45.4)	–	<0.01	–
C-reactive protein (mg/L)	–	10.20 ± 4.86	–	–	–
SPARCC MRI SIJ BME	0.13 ± 0.45	6.36 ± 11.17	6.48 ± 11.47	<0.01	0.84
SPARCC MRI SIJ fat	0.13 ± 0.61	7.20 ± 10.29	7.68 ± 10.49	<0.01	0.80
SPARCC MRI SIJ erosion	0.00	0.48 ± 1.76	1.08 ± 2.43	0.19	0.12
SPARCC MRI SIJ backfill	0.00	0.84 ± 3.04	0.88 ± 0.00	0.01	0.83
SPARCC MRI SIJ ankylosis	0.00	4.52 ± 6.77	4.88 ± 7.54	<0.01	0.92

Values are given as mean ± SD or median (IQR).

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; DMARDs, disease-modifying anti-rheumatic drugs; IQR, interquartile range; NSAIDs, non-steroid anti-inflammatory drugs; SPARCC, Spondyloarthritis Research Consortium of Canada; TNF, tumor necrosis factor; VAS, visual analog scale.

ADC_{med} and ADC_{95} value was moderate. The inter-study repeatability of patients with axSpA was good for ADC values assessed using both the ADC_{med} and the ADC_{95}, whereas for healthy individuals, it was poor for both ADC values. For all female participants, the ADC_{med} and ADC_{95} repeatability were poor, and for male participants the ADC_{med} and ADC_{95} repeatability were moderate. For patients with active inflammation (STIR positives) the ADC_{med} and ADC_{95} repeatability were good (Fig. 1) whereas for individuals without active inflammation (STIR negatives) the ADC_{med} and the ADC_{95} were poor (Fig. 2, Table 3).

The intra-reader reproducibility in all individuals and all subgroups was good to excellent for the ADC_{med} assessment method and moderate to good for ADC_{95} (Table 3). Bland–Altman plots (Fig. 3) revealed a small systematic difference in both ADC_{med} and ADC_{95} and a larger random error. Large differences in the variance between individuals in the subgroups were found, while smaller differences in residuals within individuals. The SDC for the ADC_{med} varied from 22% in patients with SpA to 48% in healthy individuals, and for the ADC_{95} the SDC varied from 28% in STIR-positive individuals to 65% in healthy participants (Table 3). Statistically significant differences in mean of the ADC_{med} and ADC_{95} values were observed for men and women, and for STIR-positive and STIR-negative participants; however, no significant differences were found between patients with SpA and healthy individuals (Fig. 4).

Correlation between ADC and conventional MRI scores and clinical findings

ADC_{med} and ADC_{95} values were correlated with SPARCC BME scores in patients with axSpA and STIR-positive patients and the ADC_{95} values were correlated with SPARCC BME scores in men (Fig. 5). The ADC_{med} value was correlated with age in women ($\rho = -0.43$, $P = 0.02$) and in patients with axSpA ($\rho = -0.46$, $P = 0.02$). No significant correlations were found between ADC values and VAS-pain, VAS-global, BASDAI, BASFI, or BASMI scores or CRP levels. No significant correlations in ADC values and SSS scores were observed.

Discussion

Repeatability measures the stability of an MRI system and is one of several factors used to assess reliability. ADC repeatability studies have been performed on different other organs but not bone marrow. MRI was

Table 3. SPARCC BME scores, inter-study and intra-reader inter-class correlation coefficients, ADC measurements, SEM, and SDC.

	SPARCC BME	Inter-study ICC	Intra-reader ICC	MR1 ($\mu mm^2/s$)	MR2 ($\mu mm^2/s$)	Mean difference ADC* ($\mu mm^2/s$)	Mean square between subjects	Residual mean square within subjects	SEM ($\mu mm^2/s$)	SDC ($\mu mm^2/s$)	SDC (%)
ADC_{med}											
All participants (n = 49)	3.37 ± 8.73	0.66 (0.46–0.80)	0.92 (0.86–0.95)	640 ± 143	645 ± 147	−12 ± 119	348,788	7110	69.4	192	30
SpA (n = 25)	6.48 ± 11.47	0.79 (0.58–0.79)	0.92 (0.82–0.96)	644 ± 164	649 ± 186	−5 ± 113	55,265	6418	51.8	144	22
Healthy (n = 24)	0.13 ± 0.45	0.27 (−0.18–0.61)	0.95 (0.88–0.98)	635 ± 120	641 ± 96	−20 ± 128	14,012	8146	109.4	303	48
Women (n = 23)	3.52 ± 8.13	0.42 (0.10–0.71)	0.87 (0.72–0.94)	708 ± 112	702 ± 126	−6 ± 128	20,249	8218	97.5	270	38
Men (n = 26)	3.23 ± 9.38	0.72 (0.45–0.87)	0.93 (0.86–0.97)	578 ± 142	598 ± 148	−28 ± 111	36,874	6118	58.7	163	28
STIR pos. (n = 7)	17.86 ± 16.91	0.78 (0.16–0.96)	0.92 (0.59–0.99)	760 ± 187	801 ± 266	−41 ± 153	93,793	11,777	71.8	199	26
STIR neg. (n = 42)	0.95 ± 2.35	0.48 (0.20–0.69)	0.89 (0.81–0.94)	618 ± 125	619 ± 99	−7 ± 114	18,546	6471	79.0	219	36
ADC_{95}											
All participants (n = 49)		0.57 (0.33–0.77)	0.74 (0.58–0.85)	1094 ± 299	1133 ± 293	−50.4 ± 276	137,609	38,199	208.4	578	52
SpA (n = 25)		0.79 (0.58–0.79)	0.73 (0.47–0.87)	1126 ± 353	1210 ± 363	−83 ± 284	216,191	40,422	158.1	438	38
Healthy (n = 24)		0.27 (0.17–0.61)	0.68 (0.39–0.85)	1059 ± 230	1056 ± 177	−14 ± 269	46,665	36,280	250.9	695	65
Women (n = 23)		0.45 (0.04–0.73)	0.59 (0.24–0.81)	1224 ± 303	1207 ± 267	17 ± 301	118,146	45,290	223.2	619	51
Men (n = 26)		0.63 (0.31–0.82)	0.88 (0.75–0.94)	975 ± 245	1071 ± 305	−112 ± 242	127,641	29,195	147.2	408	40
STIR pos. (n = 7)		0.75 (0.08–0.95)	0.64 (-0.12–0.93)	1407 ± 402	1488 ± 426	−80 ± 295	299,296	43,579	147.5	409	28
STIR neg. (n = 42)		0.29 (-0.03–0.55)	0.69 (0.48–0.82)	1038 ± 243	1072 ± 219	44 ± 277	68,847	38,291	233.4	647	61

Values are given as mean ± SD or ICC (95% CI).

*Mean difference ADC of MR2-MR1 (bias) and corresponding SD (precision).

BME, bone marrow edema; CI, confidence interval; ICC, intra-class correlation coefficient; SDC, smallest detectable change (1.96 × SEM × sqrt2), SDC percentage of mean of MR1 and MR2; SEM, standard error of measurement (= SD × sqrt1 − ICC); SPARCC, Spondyloarthritis Research Consortium of Canada.

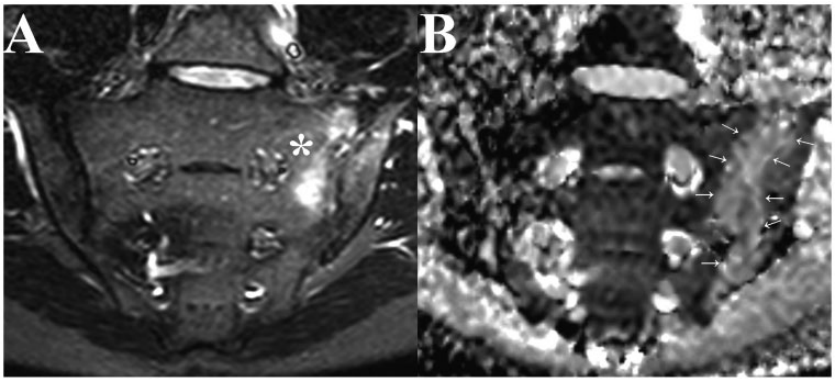

Fig. 1. A 33-year-old man with axial spondyloarthritis for five years. (a) On STIR, bone marrow edema (BME) is evident in two areas of the left sacral part of the sacroiliac joint (SIJ) (asterisk). (b) On the ADC map, a bright area covering the whole SIJ (arrows) is evident suggesting the inflammation to be more widespread than the BME visualized on STIR.

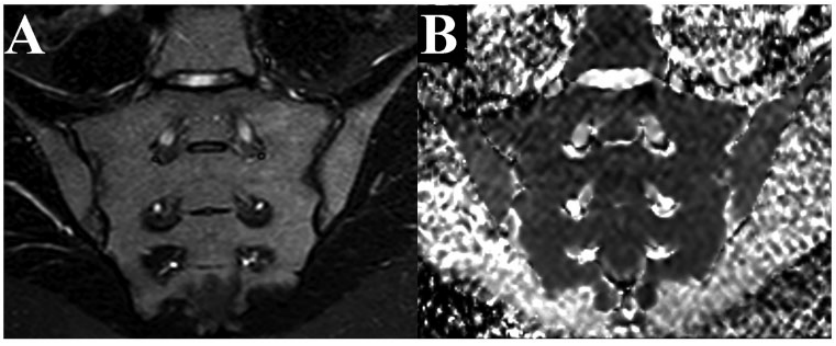

Fig. 2. A 19-year-old man with newly diagnosed axial spondyloarthritis. Both on STIR (a) and the ADC map (b), a low homogeneous signal is present in both sacroiliac joints without areas of inflammation.

performed twice within eight days on 16 patients with squamous cell carcinomas in the head and neck. The ADC values for the primary tumors and the largest nodal metastasis were measured. The inter-study repeatability was excellent in both the primary tumors (ICC = 0.99) and the metastases (ICC = 0.86) (17). Highly repeatable median ADC values were observed in tumors in 15 pediatric oncology patients examined twice within 24 h (18). In addition, the ADC repeatability observed in 40 women with breast lesions examined twice within 11 days was almost perfect (ICC > 0.9) (19). Compared to the abovementioned studies, the overall inter-study repeatability in the present study was lower. This may be due to the large variations in inter-study repeatability observed among the subgroups (i.e. from good repeatability for the patients with axSpA to poor repeatability for the healthy individuals). The means of the median ADC values for the patients with axSpA and healthy individuals did not differ and the Bland–Altman plots did not reveal any systematic differences. The ICC was calculated as the proportion of the difference between the mean square variance between participants and the residual variance within subject and the sum of these variances. Therefore, when the variance between individuals is small and the residuals are proportionally high, the calculated ICC is low. The healthy control group was sex- and age-matched to ensure it was as similar as possible to the patients with axSpA. It should be noted that the controls were recruited from hospital staff and they may not necessarily be a representative control group.

The purpose of the Bland–Altman method is to quantify the width of the limits and then to provide a clinical interpretation of whether the variation is clinically acceptable or not.

As ADC measurements in axSpA is a research object and not in clinical use, it is complicated to state that a certain level is acceptable. The fact that previous studies (8,20) have found treatment-induced mean ADC changes of 217–301 $\mu mm^2/s$, and differences in mean ADC between active and inactive patients

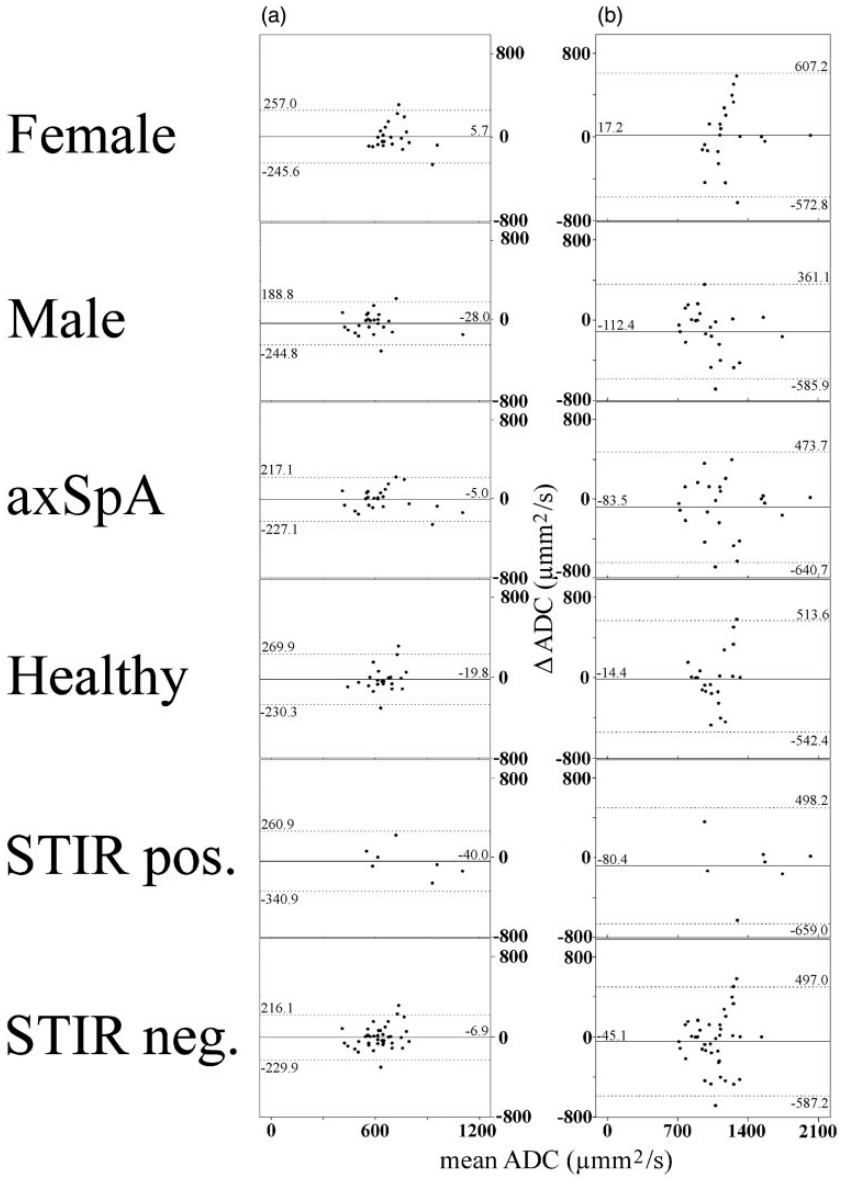

Fig. 3. Bland–Altman plots of median ADC (a) and 95th percentile ADC (b) in subgroups. Mean ADC (x-axis) and difference (Δ) ADC (y-axis) of the two time points. Mean of the difference (black line) and level of agreement (dotted lines) are provided.

with SpA and between axSpA and patients with lower back pain, which are clinically relevant groups to distinguish, have been reported to be in the range of 350–750 $\mu mm^2/s$ (4,7). This is above the 95% limits of agreement in our study (see Bland–Altman plot in Fig. 3), suggesting that the reproducibility of the mean ADC measurement method allows us to detect clinical meaningful changes. Therefore, the level of agreement for ADC_{med} seems clinically acceptable. The ADC_{95} has not been used by others, so the clinical importance of the level of agreement cannot be decided based on this study.

The ADC values correlated with the SPARCC inflammation scores in men, patients with axSpA, and STIR-positive individuals. Similar results for patients with axSpA have been presented by others (20,21); however, no similar subgroup analyses have been performed previously. The SPARCC inflammation score was based on BME visualized using a STIR sequence. BME is a radiological term for increased extracellular fluid. In axSpA, it is most likely produced by inflammatory cells (22). Because ADC reflects cellularity (23), a correlation between SPARCC scores and ADC values was expected.

When ADC values were compared with clinical parameters, the ADC_{med} value correlated negatively with women and with the age of patients with axSpA. The ADC_{95} value correlated negatively in women and

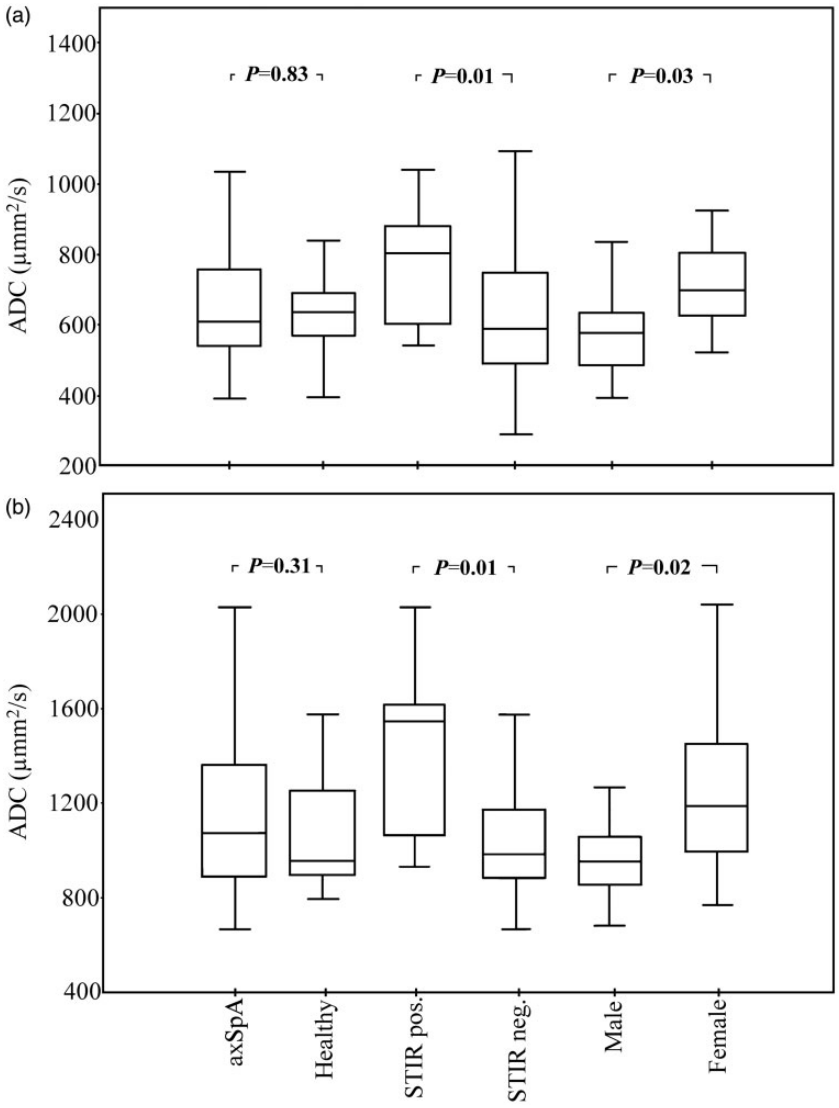

Fig. 4. Boxplot of median ADC (a) and 95th percentile ADC (b) in subgroups.

STIR-positive individuals with age. This result is consistent with the findings of a study that imaged the lumbar spines of 125 healthy individuals. The mean ADC value was significantly higher in women aged 20–40 years and 41–60 years than in those aged > 60 years. No similar difference was found in men. This observation may be due to the conversion of bone marrow from red hematopoietic marrow to yellow fat-containing marrow as the participants age (24). The mean ADC values of red bone marrow were also significantly higher than those of yellow bone marrow (25). Similarly, when red and yellow bone marrow were measured separately, a negative correlation between ADC values and age was observed in women (26). No correlation between ADC values and age was observed in other MRI studies of the lumbar spine. In one study, only men with a mean age of 55 years were enrolled (27) and in another study, only 9/30 healthy individuals were aged < 50 years (28). A correlation between ADC value and age may have been obscured in these studies due to the lack of young participants. A correlation between ADC values and age may be important in ADC studies that compare uneven age groups.

The sex difference in ADC values observed here is consistent with results from other studies of healthy volunteers (24,26). It may be due to the higher level of lipids in the red and yellow bone marrow of men, which reduces the level of free protons and restricts diffusion (26). This difference in sex should be taken into consideration when ADC study results are reported.

No correlation between the levels of CRP and ADC values was found in the present study. Correlations

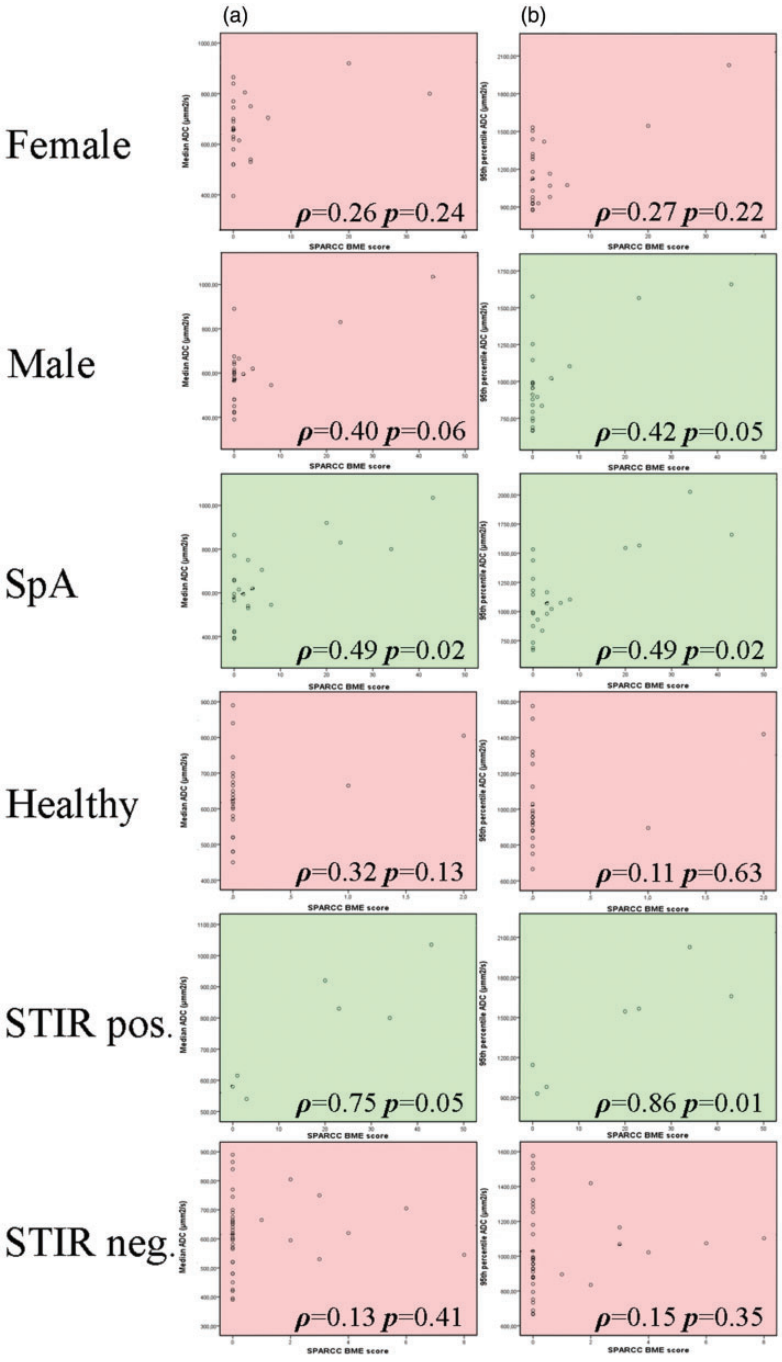

Fig. 5. Scatterplots of SPARCC BME and median ADC (a) and 95th percentile ADC (b). Spearman's ρ and *P* provided.

between ADC values and CRP levels in patients with axSpA have been observed in some studies (5,7) but not others (20,29). Possible explanations for the lack of an observed correlation in the current study include the low levels of CRP in the cohort and the small sample size. Another explanation may be that CRP is more responsive, i.e. can change over a few days depending on the ongoing inflammatory processes in the body, whereas BME in axSpA is less responsive, i.e. changes over weeks/months.

The strengths of this study include the test–retest set-up wherein all individuals were imaged twice within one week by the same technicians and using the same MRI scanner. In this way, the technical variation was minimized. However, for the same reason, generalizability was decreased because this was not a

daily practice set-up. Because only one assessor performed the evaluations, the inter-study repeatability may have been overestimated compared to a situation wherein two assessors evaluated the scans.

The axSpA population contained few patients with axSpA with active inflammation (STIR-positive patients), which may have limited the results for this group. The time interval between the two clinical assessments was short to minimize changes in axSpA disease activity. Nevertheless, lower BASDAI, VAS-pain, and VAS-global were scored statistically significantly lower at timepoint tp2 and these decreases were similar in all the self-reported SpA activity groups. Even though no change would be expected with only one week between tp1 and tp2, the individual patient may have experienced an improvement or worsening. By chance it turned out that more patients had improvement than worsening in this study. It cannot be ruled out that these differences may have influenced the ADC measurements.

In conclusion, ADC is a repeatable parameter when assessed in patients with axSpA but not in healthy individuals. ADC is correlated with conventional MRI BME score and, in women, with age, and this should be taken into consideration when interpreting DWI examinations.

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