



Whole body magnetic resonance imaging in healthy children and adolescents. Bone marrow appearances of the axial skeleton

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ABSTRACT

Objective: To describe the findings of focal high signal on T2 weighted (T2W) images of the bone marrow in the axial skeleton as assessed by whole-body MRI in healthy and asymptomatic children and adolescents.

Material and methods: We assessed the bone marrow of the mandible, shoulder girdle, thorax, spine, and pelvis on water-only Dixon T2W sequences as part of a whole-body MRI protocol in 196 healthy and asymptomatic children aged 5–19 years. Intensity (0–2 scale) and extension (1–4 scale) of focal high signal areas in the bone marrow were scored and divided into minor or major findings, based on intensity and extension to identify the potentially conspicuous lesions in a clinical setting.

Results: We registered 415 areas of increased signal in the axial skeleton whereof 75 (38.3%) were major findings. Fifty-eight (29.6%) individuals had at least one major finding, mainly located in the pelvis (54, 72%). We found no differences according to gender. The number of minor findings increased with age ($p = 0.020$), but there were no significant differences in the number of major findings. The most conspicuous findings were in the pelvis, spine and sternum.

Conclusion: Non-specific bone marrow T2W hyperintensities in the axial skeleton are frequently detected on whole-body MRI in healthy, asymptomatic children. Awareness of this is important as some findings may resemble clinically silent lesions in children with suspected multifocal skeletal disease.

1. Introduction

Whole-body MRI allows for full assessment of the whole skeleton in a single examination and has emerged as an important tool in the management of multifocal bone disease in children [1]. To date, no unifying protocol for whole body MRI exists, but a fat suppressed T2 weighted (T2W) sequence is most often included. A fat suppressed T2W sequence is sometimes even used as the only sequence for detection of bone marrow pathology [1,2,3].

On T2W fat suppressed images bone marrow pathology typically

presents as hyperintense signal, however, this signal is non-specific and simply reflects areas of higher water density compared to surrounding tissue [4]. It can be found in a variety of disorders ranging from infection and inflammation to trauma and tumor and has also been reported in the hands and feet in healthy children [5–7]. In the axial skeleton, findings of T2W hyperintensities may have both diagnostic and therapeutic implications, even when clinical symptoms are lacking. This is especially true for inflammatory disorders, e.g., in chronic non-bacterial osteomyelitis (CNO) or juvenile spondylarthritis (JSpA) [8–10]. Currently, there is a paucity of evidence on normal findings in the bone marrow on

Abbreviations: T2W, T2-weighted; T1W, T1-weighted; DWI, Diffusion weighted imaging; CNO, Chronic non-bacterial osteomyelitis; JSpA, Juvenile Spondylarthritis.

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whole-body MRI [1]. We therefore set out to describe the appearance of bone marrow on fat suppressed T2W sequences, as assessed on whole-body MRI in healthy asymptomatic children and adolescents. The aim of our study is to increase the awareness of incidental bone marrow T2W hyperintensities that may mimic disease.

Our hypothesis is that focal T2W hyperintensities in the bone marrow on whole-body MRI may also be seen in healthy children and adolescents. Here we describe bone marrow signals in the mandible, shoulder girdle, thorax, spine, and pelvis. The results from the appendicular skeleton will be presented in a separate paper.

2. Methods

2.1. Study design and subjects

In a prospective multi-center cross-sectional study, healthy individuals aged 5–19 years residing respectively in southern and northern Norway were invited to undergo a whole-body MRI for research purposes only. The study was performed at the Department of Radiology, Oslo University Hospital and University Hospital Northern-Norway. The inclusion period was November 2018 to February 2020. The study was approved by the Regional Ethics Committee (REK; no 2016/1696) and written informed consent was obtained from all the participating individuals and/or their caregivers.

Exclusion criteria were contraindications for MRI, history of cancer, current infection, chronic or systemic diseases, musculoskeletal disorders, or a recent symptomatic trauma (within the last 4 weeks). We also excluded individuals with musculoskeletal complaints impairing everyday activity and/or necessitating a consultation by a physician within the last 6 months. Self-reported sport-activities and hours of physical exercise per week were registered, as well as height and weight.

All participants were contacted within 18 months after the initial MRI-scan to confirm that no musculoskeletal symptoms had occurred. The children with the most conspicuous nonspecific bone marrow hyperintensities were invited to undergo a follow-up MRI. Standard ethical practice for research in healthy individuals was followed and incidental findings were managed according to proposed guidelines [11,12].

2.2. Imaging protocol

MRI examinations were performed on 1,5 Tesla MRI-scanners from two different vendors (Philips medical systems, Best the Netherlands, Intera model release 2.3. or Magnetom Siemens Aera, software e11c). The T2 Dixon images were obtained as part of a whole-body MRI-protocol consisting of coronal scans from skull-base to toes in 3–5 steps with the following sequences: Dixon T2W, T1W, and diffusion-weighted (DWI) sequences (b50 and b1000). Total scan time was approximately 30–45 min. The children watched a movie or listened to music during the examination. All examinations were performed during free breathing with no use of sedation. The imaging protocol is available online (Supplement 1).

2.3. Image analysis

Prior to this study, we devised and validated a child-specific scoring system for bone marrow on whole-body MRI. Signal-intensity and -extension proved to be the most reliable features with kappa values of moderate to good for both inter- and intra-observer variability and were used in the analysis of the images [13]. We scored focal high signal intensity areas in the bone marrow seen on the water-only Dixon T2W sequences in five anatomical regions: mandible, shoulder girdle, thorax, spine, and pelvis. Fat-only Dixon T2W, T1W and DWI sequences were only used to tailor further management of findings when necessary. One radiologist (EvB) reviewed all images and in case of uncertainty, images were scored in consensus with a second radiologist (LSOM), both readers

with 15 years of experience in pediatric radiology.

Signal intensity was graded at a 0–2 scale, where 0 = absent, 1 = mildly increased, and 2 = moderate increased up to fluid-like signal as compared to the fatty marrow. Extension was graded at a 1–4 scale, where 1 = very subtle lesion (<5%), 2 = involvement of 1/3 of bone segment, 3 = involvement of 2/3 of bone segment, 4 = involvement of whole bone segment. Focal high signal intensity areas were divided into “major”- or “minor” findings based on intensity and extension, where “major findings” reflect signal changes more likely to be confused with pathology in a clinical setting (Table 1). Periosteal reaction/high signal in adjacent soft tissue was registered if present.

2.4. Statistical analysis

Numbers with percentages and means with standard deviations or medians with inter quartile range (IQR) were reported by means of descriptive statistics, when appropriate. Differences in the number of findings between genders were examined using Mann-Whitney-*U* test and differences according to age groups (5–9 years, 10–12 years, 13–15 years, 16–19 years), sport activity (none, 1–2 h, 3–6 h or 7–15 h per week) and localization were examined using Kruskal-Wallis test. Pearson Chi-Square test was used to explore differences in the location of major and minor findings. All statistical analyses were performed using Predictive Analytics Software (SPSS) version 27 (IBM, Armonk, NY), and a *p*-value < 0.05 was considered statistically significant.

3. Results

Whole-body MRI was obtained in 196 individuals (101 females, 51.5%), mean age 12 years (SD 3,6) (Table 2) with 47–52 individuals per age group (Table 3).

Overall, we identified 415 focal high signal intensity areas, whereof 75 (18.1%) were classified as major findings (Fig. 1).

Ninety-five of 415 findings (22.9%) were symmetrically distributed, whereof 18 (18.9%) were major findings. The distribution of major and minor findings according to age group is listed in Table 3.

There were no differences in the total number of high signal areas according to gender (*p* = 0.41), hence the results were pooled. We did not find any differences in the overall number of major findings between age groups, but there was a statistically significant association between major findings and age in the ischiopubic region where children aged 5–9 years predominated (*p* = 0.010) (Fig. 1). In the sternum, only adolescents aged 16–19 years were involved. For minor findings, there was a significantly higher number in the age-group 16–19 years (median = 2.0, IQR = 2.0) compared to the age-group 5–9 years (median = 1.0, IQR = 3.0), *p* = 0.02.

There was a statistically significant difference in minor findings for the four self-reported training groups (*p* = 0.006). Post-hoc pairwise comparisons (with Bonferroni correction for multiple tests) indicated that the median score for those training 7–15 h per week was significantly higher than for the no-training group (*p* = 0.025), for those training 1–2 h per week (*p* = 0.001) and for those training 3–6 h per week (*p* = 0.04). For major findings, differences between the groups were small. No linear association was found but pairwise comparisons (with Bonferroni correction for multiple tests) indicated significantly

Table 1

Subclassification of MRI-findings into minor or major on water-only Dixon T2W images, based on signal intensity on a 0–2 scale and signal extension on a 0–4 scale.

	Signal intensity on a 0–2 scale / extension on a 0–4 scale
Major MRI findings	Signal intensity 1 and extension 3–4 or Signal intensity 2 and extension 2–4
Minor MRI findings	Signal intensity 1 and extension < 3, or Signal intensity 2 and extension < 2

Table 2
Demographic details on the healthy pediatric cohort compared to the general population.

Variables	Study subjects, n = 196	Data from Statistics Norway *
Oslo University Hospital / University Hospital North Norway, n (%)	78 (39.8%) / 118 (60.2%)	-
Female, n (%)	101 (51.5%)	374,152 (48.8%) **
Age, years (range)	12.0 (6.0 – 18.9)	(6.0–15.0)
Median BMI, kg/m2 (range)	18 (13–30)	18 (-)
Sports-activity at least once a week, n (%)	167 (85%)	(84% – 89%)

*Statistics Norway, Helseforhold, levekårsundersøkelsen. Statistisk Sentralbyrå, statistikkbanken.

<https://www.ssb.no/statbank/table/06658>. Accessed 24. May 2021.

**<https://www.ssb.no/a/barnogunge/2020/tabeller/befolkning/bef0000.html>. Age 6–17. Accessed 01. May 2022.

Table 3
High signal areas on water-only Dixon T2W images in the axial skeleton in 196 healthy children and adolescents by age group.

	5–9 years (n = 47)	10–12 years (n = 52)	13–15 years (n = 47)	16–19 years (n = 50)	Total (n = 196)
Major findings	17	17	18	23	75
Minor findings	58	85	89	108	340

higher median score for those training 7–15 h as compared to those training 1–2 h ($p = 0.003$) and 3–6 h ($p = 0.027$), but not as compared to the no-training group ($p = 0.148$).

Fifty-eight individuals (29.6%) had at least one major finding in the axial skeleton (median 1.0, IQR = 0). 137 individuals (69.9%) had at least one minor finding (median 1.0, IQR = 3). Forty-seven examinations (24.0%) revealed no focal bone marrow hyperintensities whereof 20 (42.6%) had one or more anatomical areas missing or hampered by artifacts and were thus not available for scoring. In total, 47 examinations (24.0%) had some images disturbed by artifacts or were incomplete (5 examinations). The artifacts mainly involved mandible, shoulder-girdle, and thorax (legend Fig. 1). Movement artifacts were noted in 35 of the 47 examinations (74.5%), in 4 (8.5%) the mandibles were not available for scoring due to metallic artifacts from braces, and

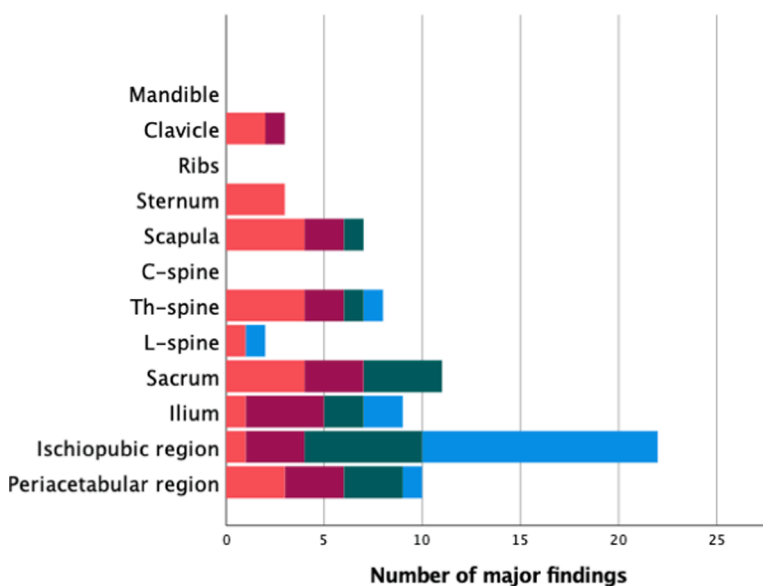


Fig. 1. Number and distribution of the 75 major findings (based on T2-w Dixon water only images) by anatomical location in 196 healthy individuals aged 5–19 years. Number of anatomical locations excluded from the analysis due to imaging artifacts or missing data: Mandible 35(17.9%), Clavicle 29(14.8%), Scapula 27(13.8%), Sternum 28(14.3%), Ribs 26 (13.3%), C-spine 23(11.7%), Th-spine 10(5.1%), L-spine 10(5.1%), Sacrum 4(2.0%), Ilium 4(2.0%), Ischiopubic region 3(1.5%), Periacetabular region 3 (1.5%).

in three (6.4%), one or more areas were not accessible due to low signal. No swap- or distortion artifacts were registered.

The majority of focal bone marrow hyperintensities were located in the pelvis, with a total of 276 findings, whereof 52 were classified as major findings. In 17 (32.7%), the major findings were symmetrical according to side. Sixty-six of the 224 minor findings (29.5%) were symmetrical. Twenty-two major findings (42.3%) were located in the ischiopubic region (Fig. 2 a-c), adjacent to the ischiopubic synchondrosis in 15 individuals, all in the prepubertal age group between 6 and 11 years (5 females, mean 8.5 years (Fig. 2a) and bilaterally in two individuals. In 8 individuals the major findings were located at the sacroiliac joint, either on the sacral (3) or the iliac (8) side (Fig. 3a, b). Three were symmetrical, all on the iliac side. Four individuals aged 13–17 years (mean 15.6 years), had major findings adjacent to an unfused lateral sacral apophysis (Fig. 3c). Sixty-eight examinations (35.4%) revealed no focal hyperintensities in the pelvis.

In the spine, we registered major findings in 10 individuals, mainly located in the thoracic part (Fig. 4a-f). Two individuals had a major finding in the lumbar spine, located in pars interarticularis of the vertebral body in both cases (Fig. 4g).

We registered high signal intensity areas in the sternum in 19/168 individuals (11.3%). In nine (6 females), these were located at the manubriosternal joint (Fig. 5a-d) and defined as major findings in three. All nine were adolescents between 15 and 18 years.

No high signal intensity areas were seen in the the ribs.

Periosteal reaction was only registered in three individuals and were in each case associated with major findings at the ischiopubic synchondrosis.

In four cases the major findings had a specific appearance: one simple bone cyst in the left scapula and three hemangiomas in the thoracic spine. The specific diagnosis was suggested on the initial whole-body MRI scan and confirmed on follow-up imaging.

4. Discussion

We have shown that focal areas of high signal on T2W images that may be interpreted as pathology is a common finding in the axial skeleton of healthy asymptomatic children and adolescents. From a clinical point of view, the most interesting findings were in the pelvis, spine, and sternum. Comparison with data from Statistics Norway with respect to BMI-curves and reported hours of training per week, indicate that our cohort is representative of the general Norwegian pediatric population

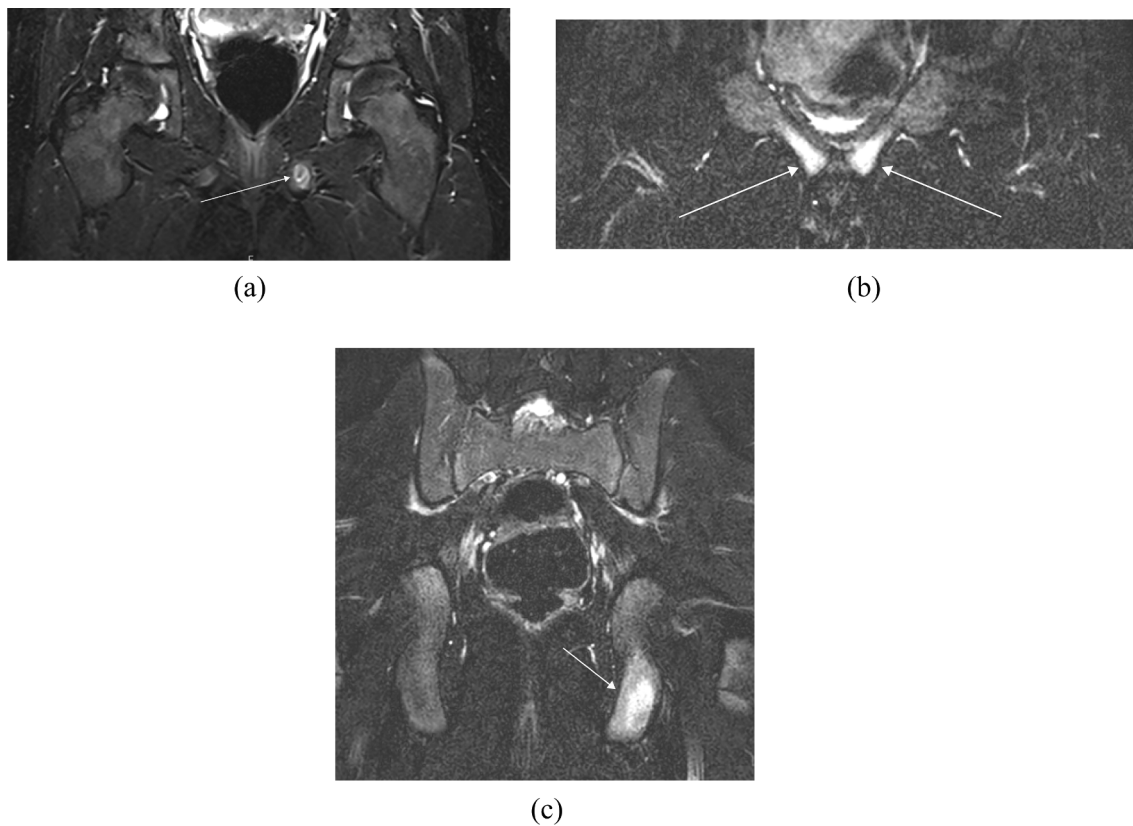


Fig. 2. a-c T2-W Dixon water-only coronal image of the pelvis shows a major finding (a) adjacent to the left ischiopubic synchondrosis in a 6-year-old boy, (b) at the symphysis bilaterally in an 8-year-old girl and (c) in the left ischial tuberosity in a 14-year-old boy.

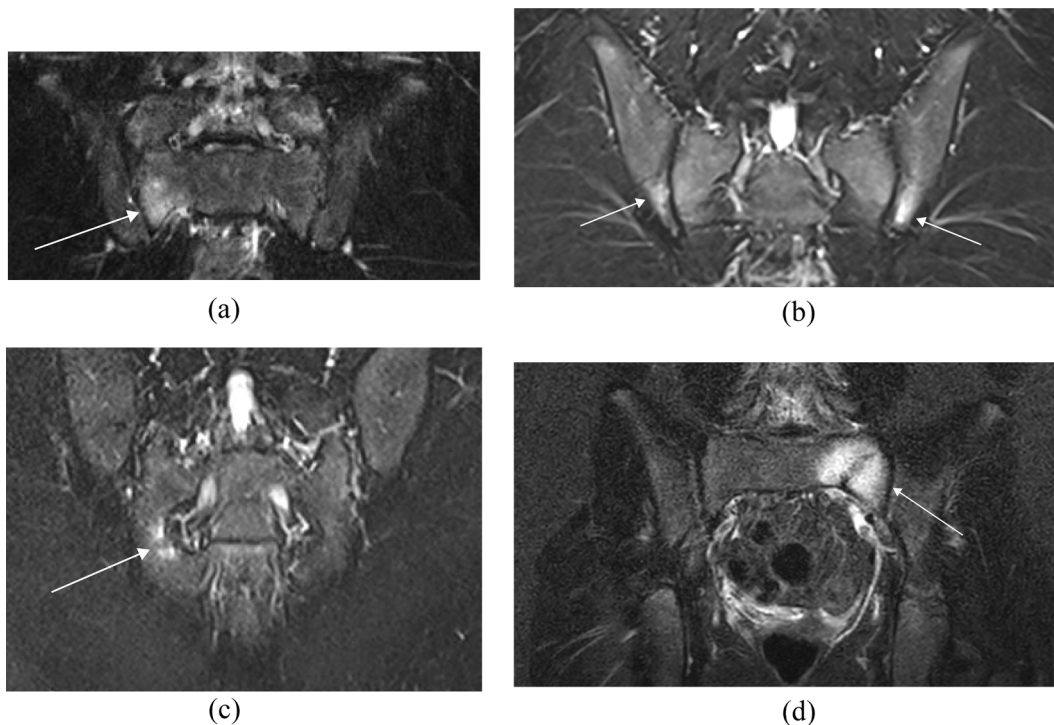


Fig. 3. a-d T2-W Dixon water-only coronal image of the pelvis shows a major finding (a) in the right sacrum adjacent to the SI-joint in a 11-year-old boy, (b) in the ilium adjacent to the SI-joint bilaterally in a 10-year-old boy, (c) in the lateral segmental apophysis of the left sacrum, possibly related to closure of the physis, in a 15-year-old boy and (d) resembling a fatigue fracture in the left sacrum of a 12-year-old girl.

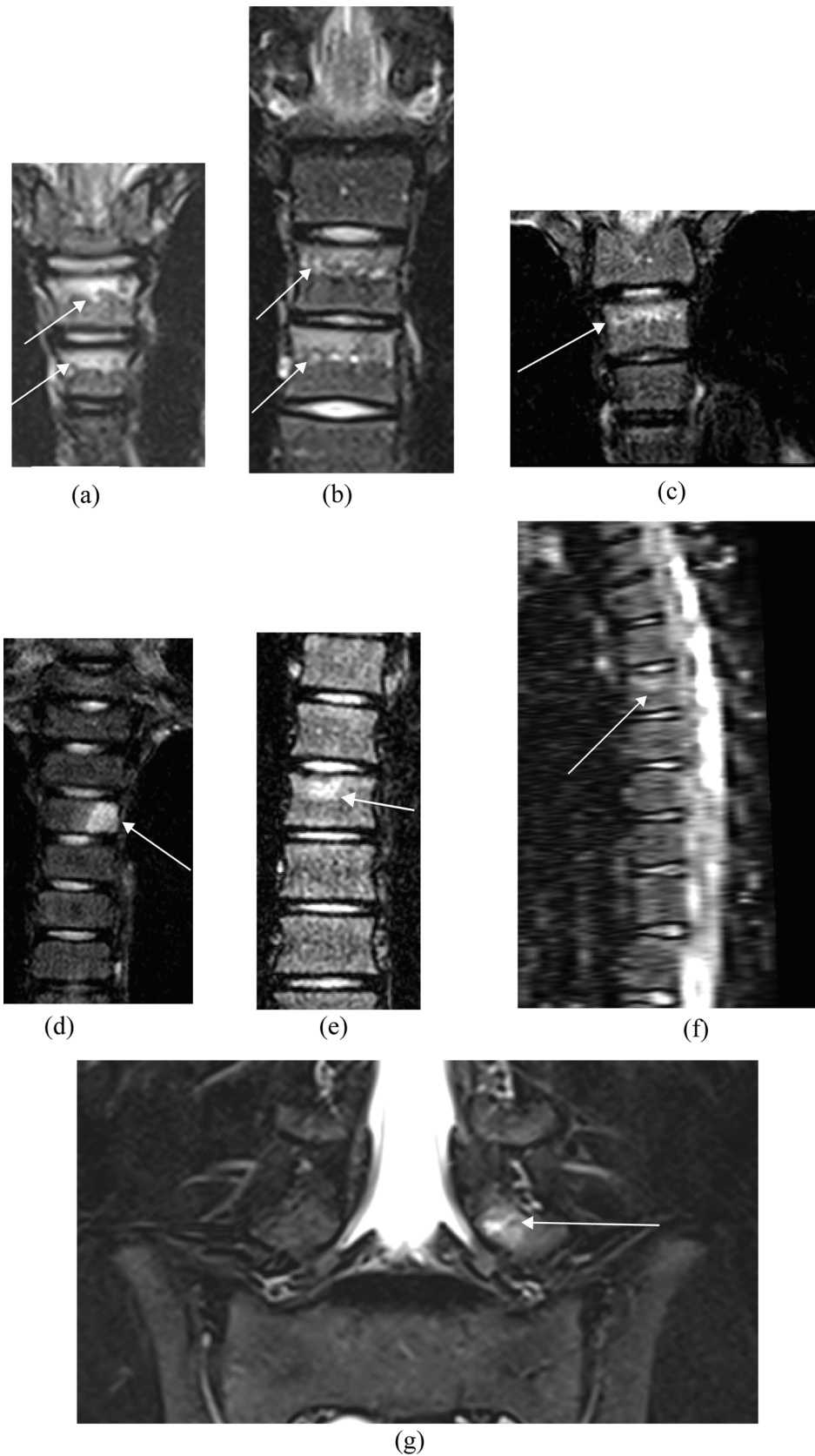


Fig. 4. a-g T2-W Dixon water-only coronal image of the thoracic spine (a-e) with sagittal reconstruction in f and coronal image of the lumbar spine in g. The images in a-c show major findings involving the entire upper part of one or two thoracic vertebrae in (a) a 7-year-old boy, (b) a 17-year-old boy and in (c) a 15-year-old boy. In d the major finding involves the left part of a thoracic vertebra in a 13-year-old boy and in e-f it surrounds an irregularity in the upper endplate of a thoracic vertebra in a 12-year-old girl. In g the major finding is located in the lumbar spine, resembling a spondylolysis in the left 5th vertebra of a 9-year-old girl.

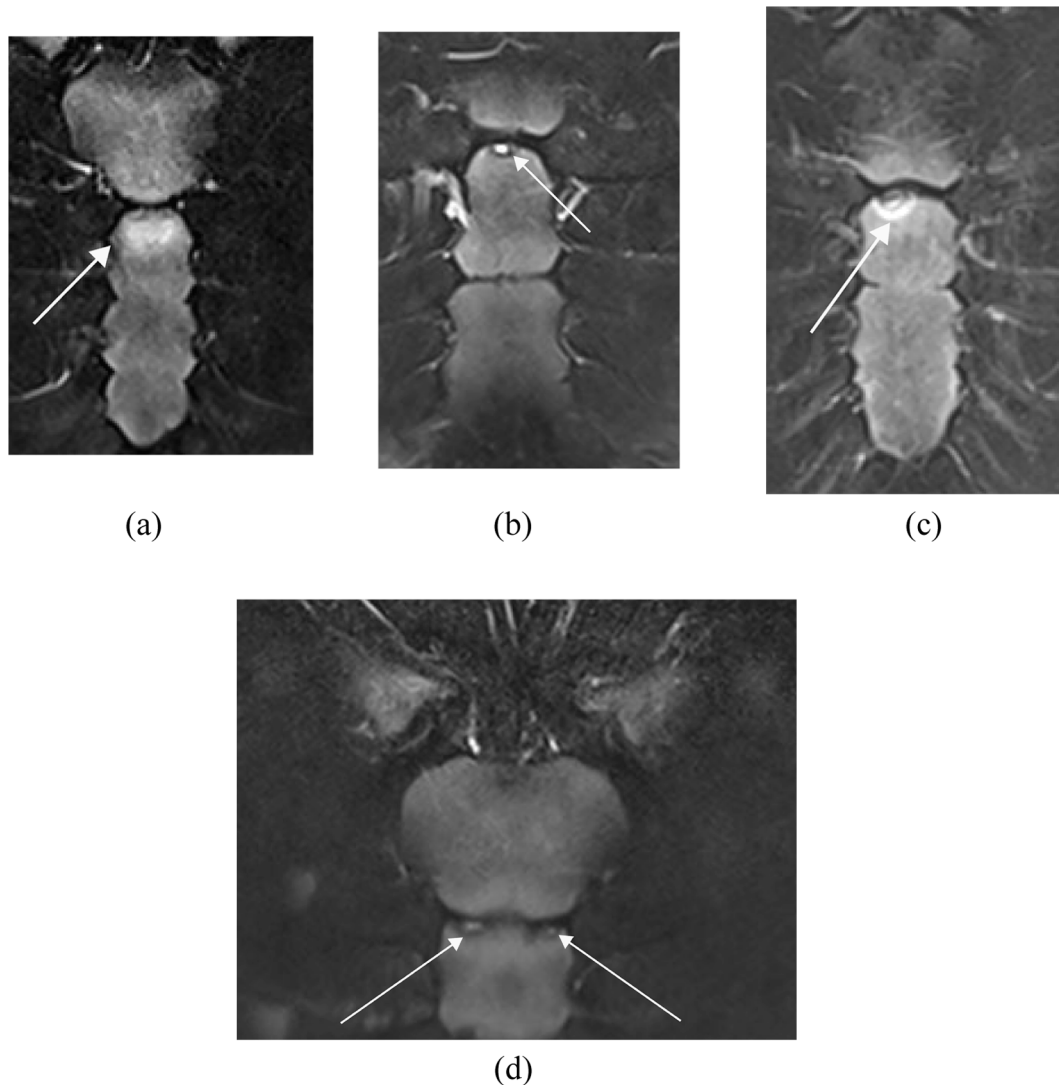


Fig. 5. a-d T2-W Dixon water-only coronal images of the thorax shows major (a and c) and minor (b and d) findings at the manubriosternal joint in (a) a 17-year-old girl, (b) a 15-year-old girl, (c) an 18-year-old girl and (d) an 18-year-old boy.

[14].

The pelvis was the most common location for focal bone marrow hyperintensities. Bone marrow heterogeneity due to residual red marrow is a normal finding in the pelvis at all ages and is typically symmetrical [15–19]. Symmetry was not frequently registered in our study, but findings with a symmetrical appearance were mainly located in the pelvis. Thus, hematopoietic bone marrow could, at least in part, explain the high number of findings in this location.

Most major findings were related to a closing ischiopubic synchondrosis in prepubertal children (Fig. 2a), occasionally accompanied with mild periosteal reaction. This is a well-known MRI finding in healthy children at this age but may be misinterpreted as a neoplastic, traumatic, inflammatory or infectious process, especially when adjacent soft tissue is involved [20,21].

Major findings adjacent to the sacroiliac joint, mainly located on the iliac side and asymmetrical distributed in most cases, were equivalent with one of the ASAS (Assessment of Spondyloarthritis international Society) criteria for active sacroiliitis on MRI in adults [22]. To date, no such definition exists for children [23,24]. In a recent study, Herregods et al assessed the MRI appearance of the sacroiliac joints in a cohort of 251 individuals aged 6–18 years with or without low back pain [15]. The authors concluded that asymmetrical subchondral T2W signal, especially when more intense on the iliac side, “is unlikely to be normal

and should be considered suspicious for pathologic bone marrow edema”. Chauvin et al [25] described age-related MRI features of the sacroiliac joints in 70 healthy individuals aged 8–17 years but none of the individuals had findings suggestive of sacroiliitis. However, both Jaremko et al [23] and Weiss et al [8] detected areas of periarticular bone marrow edema in seven of 35 and one of 14 healthy control-subjects, respectively, in their studies on MRI of the sacroiliac joints in individuals with JSaA.

Occasionally we registered high signal intensity areas on both sides of an unfused segmental sacral apophysis. We believe that this signal may be physiological and related to closure of the physis, in the same way as proposed for the so-called “focal periphyseal edema” (FOPE) - zones in adolescent knees [26]. Fusion of the lateral sacral segments usually completes in the late adolescence [15,27–29]. This fits with the age of the four involved adolescents in our study. Herregods and Chauvin [15,25] both describe a rim of high T2W signal along the unfused segmental sacral physes as a common finding in healthy children, but they do not mention any focal periphyseal T2W hyperintensities.

One major finding in the sacrum of a 12-year-old girl had the appearance of a fatigue fracture (Fig.d). Fatigue fractures of the sacrum sometimes occur in young athletes due to repetitive stress loads [30] but are reported to be rare in children [31–33]. The condition is typically accompanied with low back-pain [31–33] and Hama et al [31] suggest a

possible association with spina bifida occulta. The girl in our study reported no regular weekly training activity and she had no clinical symptoms. A spina bifida occulta was not detected. On follow-up examination 10 weeks later, the signal had completely disappeared. A study by Broome et al [28] highlights the potential risk of confusing an asymmetric unfused physal plate with a fracture line. Hence, micro-traumatic changes at a closing sacral physis could be an alternative explanation for the major finding in this child.

Few focal T2W hyperintensities were seen in the spine. Similarly, spinal involvement is rare in most pediatric disease processes [34–37] but when present, e.g., in a patient with CNO or JSpA, it may have implications for management [10,38,39]. In three individuals, we found high signal involving the entire upper part of one or two adjacent vertebral bodies in the thoracic spine. One seven-year-old boy retrospectively, on direct questioning, remembered a fall on his back when skiing one week prior to the MRI examination. However, he insisted he never had any symptoms. On follow-up examinations 4–6 months later, the high signal had totally disappeared in all three children. This indicates that even minor and asymptomatic traumas may cause transient increased signal within the bone marrow in children, which is in accordance with previous observations [6].

Two individuals had high signal in pars interarticularis of the 5th lumbar vertebra with the appearance of spondylolysis, which is reported to be a fairly common finding in asymptomatic young individuals [40,41]. The condition is more likely to be found in athletes, especially in sports that involve extension and rotational forces to the lumbar spine [40,42] which is in accordance with our two study subjects, who were active in volleyball and gymnastic, respectively.

Nearly half of all high signal intensity areas in the sternum were located at the manubriosternal joint, equivalent to a previous study in adults by Jurik et al [43]. In a cohort of 75 healthy individuals and 122 spondylarthritis patients, bone marrow signal mimicking inflammatory changes at the manubriosternal joint was a frequent finding in the healthy cohort. Manubriosternal joint inflammation is reported to be common in adults with rheumatoid diseases [43–48], whereas data on children are lacking. However, in our own experience this site may occasionally be involved in children with CNO. We believe that both the minor and major findings in this location reflect the normal ossification process [44], or alternatively, early signs of manubriosternal fusion. The latter is mainly described in adults, with an increasing incidence with older age [49–51], but has also been observed in adolescents [49,51]. We only found high signal at this location in the oldest age-group.

We found a higher overall number of minor findings in the oldest age group, which possibly can be explained by a better delineation of focal hyperintense signal with increased amounts of fat in the surrounding marrow with age. We also registered significantly more minor findings in individuals with the highest level of self-reported sports activity. Most findings were in the pelvis, which is the area with the highest exposition to biomechanical forces. Mechanical stress has previously been proposed as a possible cause of high T2W signal in the bone marrow in healthy children [6,7]. For major findings, we found no linear association with reported hours of sports activity, but the relatively low number of major findings in this study does not allow any conclusions in this regard. Furthermore, objective measurement of physical activity is challenging, and self-reported sports activity is a poor marker for the true activity level in children [6].

Focal T2W bone marrow hyperintensities on whole-body MRI are non-specific, but in a clinical setting, they are commonly interpreted as pathology. Visualization of fatty marrow replacement on T1W and decreased ADC-values on DWI, e.g., in malignant bone marrow lesions, may contribute to increased diagnostic specificity [52,53]. However, we do not know in what way this additional information should be utilized to distinguish between early bone marrow pathology, especially inflammatory lesions, and normal bone marrow signal. Early inflammatory lesions may still contain fatty components, and the use of ADC cut-off values is limited by substantial variations in ADC values, particularly

related to age-dependent changes in bone marrow fat content and to movement artifacts [54–56]. Furthermore, there is a controversy in the literature regarding the additional value of applying DWI to the whole-body MRI [2,54,57–59] and published data on the use of whole-body DWI in non-oncological conditions, e.g., in inflammatory bone marrow disorders, is still limited [54,60]. Research addressing the added value of other sequences, particularly with regard to a better differentiation between pathological and normal bone marrow signal, will require a different study design also including diseased individuals, hence will be the scope for future studies.

4.1. Limitations and strengths

There are some limitations to our study. First, subjective assessment of intensity and extension is known to be hampered by inter- and intra-reader variability [61,62]. Signal intensity can be perceived differently depending on background intensity, window- and level settings and difficulties in standardizing the signal intensity scale on MRI [63,64]. To overcome this problem, we validated our scoring system [13], arranged several face-to-face calibration meetings, discussing findings and scales.

Second, our definitions of minor and major findings do not necessarily reflect the clinical significance of all high signal intensity areas. Characteristics like shape and contour may also influence the interpretation. Lesions with similar appearance and equal size may be weighted differently depending on its location and interpretation of pathology versus normal variance will also inevitably depend on the reader's experience [65,66]. Importantly clinical findings and underlying diagnosis defines the pre-test likelihood for disease hence influence the positive predictive value of all findings [67].

STIR has until now been the most frequently used water-sensitive sequence in whole-body MRI-protocols [1] but has shown similar performance for T2W Dixon compared to STIR in the assessment of the bone marrow [68]. Any differences between sequences are more likely dependent on general technical parameters, hardware, software, and differences in patient handling.

Furthermore, the large field of view on whole-body MRI may be less sensitive to signal change and the bone marrow may appear differently when applying dedicated extremity coils, e.g., of the sacroiliac-joints, imaged directly in the oblique coronal plane [69]. However, in this study, we aimed to describe findings on the resultant images of a whole-body MRI.

Finally, we acknowledge that the number of findings may be underestimated

in areas hampered by artifacts, with fine structures, or in the periphery where dedicated protocols are better suited for the evaluation of bone marrow signal.

The main strength of our study is the large and representative study population of healthy and asymptomatic children and adolescents recruited for research purposes only from two geographical regions, and the close follow-up of all participants to ensure that there were no underreported or underlying disease. Further major strengths are the prospective study design that allows for a uniform imaging protocol and an equal distribution of gender and age, the validation of our scoring system and the thorough calibration preceding imaging analysis.

5. Conclusion

Bone marrow hyperintensities in the axial skeleton are frequently detected on whole-body MRI in healthy, asymptomatic children and adolescents. Awareness of this is important as some findings may resemble clinically silent lesions in individuals with suspected multifocal skeletal disease, particularly when located in the pelvis, spine, or sternum.

Keypoints:

- Whole body MRI of healthy children and adolescents frequently reveals focal areas of increased fluid-signal in the bone marrow that can resemble pathology.
- Certain patterns of increased bone marrow signal are more frequently seen than others in healthy individuals.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejrad.2022.110425>.

References

- [1] P. Zadig, E. von Brandis, R.K. Lein, K. Rosendahl, D. Avenarius, L.S. Ording Muller, Whole-body magnetic resonance imaging in children - how and why? A systematic review, *Pediatr. Radiol.*, 2020, 10.1007/s00247-020-04735-9:11.
- [2] L. Merlini, M. Carpentier, S. Ferrey, M. Anoshiravani, P.-A. Poletti, S. Hanquinet, Whole-body MRI in children: Would a 3D STIR sequence alone be sufficient for investigating common paediatric conditions? A comparative study, *Eur. J. Radiol.* 88 (2017) 155–162.
- [3] T.S. Sato, P.J. Ferguson, Whole-body MRI Imaging Is an Essential Tool in Diagnosing and Monitoring Patients With Sterile Osteomyelitis, *J. Rheumatol.* 48 (5) (2021) 635–637.
- [4] E. Jimenez-Boj, I. Nöbauer-Huhmann, B. Hanslik-Schnabel, R. Dorotka, A.-H. Wanivenhaus, F. Kainberger, S. Trattig, R. Axmann, W. Tsuji, S. Hermann, J. Smolen, G. Schett, Bone erosions and bone marrow edema as defined by magnetic resonance imaging reflect true bone marrow inflammation in rheumatoid arthritis, *Arthritis Rheum.* 56 (4) (2007) 1118–1124.
- [5] D.F.M. Avenarius, L.-S. Ording Müller, K. Rosendahl, Joint Fluid, Bone Marrow Edemalike Changes, and Ganglion Cysts in the Pediatric Wrist: Features That May Mimic Pathologic Abnormalities-Follow-Up of a Healthy Cohort, *AJR Am. J. Roentgenol.* 208 (6) (2017) 1352–1357.
- [6] L.-S. Müller, D. Avenarius, B. Damasio, O.P. Eldevik, C. Malattia, K. Lambot-Juhan, L. Tanturri, C.M. Owens, K. Rosendahl, The paediatric wrist revisited: redefining MR findings in healthy children, *Ann. Rheum. Dis.* 70 (4) (2011) 605–610.
- [7] N. Shabshin, M.E. Schweitzer, W.B. Morrison, J.A. Carrino, M.S. Keller, L. E. Grissom, High-signal T2 changes of the bone marrow of the foot and ankle in children: red marrow or traumatic changes? *Pediatr. Radiol.* 36 (7) (2006) 670–676.
- [8] P.F. Weiss, R. Xiao, D.M. Biko, N.A. Chauvin, Assessment of Sacroiliitis at Diagnosis of Juvenile Spondyloarthritis by Radiography, Magnetic Resonance Imaging, and Clinical Examination, *Arthritis Care Res. (Hoboken)* 68 (2) (2016) 187–194.
- [9] M.L. Stoll, R. Bhore, M. Dempsey-robertson, M. Punaro, Spondyloarthritis in a pediatric population: risk factors for sacroiliitis, *J. Rheumatol.* 37 (11) (2010) 2402–2408.
- [10] Y. Zhao, N.A. Chauvin, D. Jaramillo, J.M. Burnham, Aggressive Therapy Reduces Disease Activity without Skeletal Damage Progression in Chronic Nonbacterial Osteomyelitis, *J. Rheumatol.* 42 (7) (2015) 1245–1251.
- [11] T.C. Booth, A.D. Waldman, J.M. Wardlaw, S.A. Taylor, A. Jackson, Management of incidental findings during imaging research in “healthy” volunteers: current UK practice, *Br. J. Radiol.* 85 (1009) (2012) 11–21.
- [12] S.M. Wolf, F.P. Lawrenz, C.A. Nelson, J.P. Kahn, M.K. Cho, E.W. Clayton, J. G. Fletcher, M.K. Georgieff, D. Hammerschmidt, K. Hudson, J. Illes, V. Kapur, M. A. Keane, B.A. Koenig, B.S. LeRoy, E.G. McFarland, J. Paradise, L.S. Parker, S. F. Terry, B. Van Ness, B.S. Wilfond, Managing incidental findings in human subjects research: analysis and recommendations, *J. Law Med. Ethics* 36 (2) (2008) 219–248.
- [13] P. Zadig, E. von Brandis, P. d’Angelo, et al., Whole-body MRI in children aged 6–18 years. Reliability of identifying and grading high signal intensity changes within bone marrow. *Pediatr. Radiol.*, 2022, 10.1007/s00247-022-05312-y.
- [14] Statistics Norway, Helseforhold, levekårsundersøkelsen. Statistisk Sentralbyrå, statistikkbanken. Available via <https://www.ssb.no/statbank/table/06658>. Accessed 24. May 2021.
- [15] N. Herregods, L.B.O. Jans, M. Chen, J. Paschke, S.L. De Buyser, T. Renson, J. Dehoorne, R. Joos, R.G.W. Lambert, J.L. Jaremko, Normal subchondral high T2 signal on MRI mimicking sacroiliitis in children: frequency, age distribution, and relationship to skeletal maturity, *Eur. Radiol.* 31 (5) (2021) 3498–3507.
- [16] T. Laor, D. Jaramillo, MR Imaging Insights into Skeletal Maturation: What Is Normal? *Radiology* 250 (1) (2009) 28–38.
- [17] A. Taccone, M. Oddone, A. Dell’Acqua, M. Occhi, M.A. Ciccone, MRI “road-map” of normal age-related bone marrow.II.Thorax, pelvis and extremities, *Pediatr. Radiol.* 25 (8) (1995) 596–606.
- [18] K.L. Dawson, S.G. Moore, J.M. Rowland, Age-related marrow changes in the pelvis: MR and anatomic findings, *Radiology* 183 (1) (1992) 47–51.
- [19] K. Foster, S. Chapman, K. Johnson, MRI of the marrow in the paediatric skeleton, *Clin. Radiol.* 59 (8) (2004) 651–673.
- [20] A. Wait, T. Gaskill, Z. Sarwar, M. Busch, Van Neck Disease. Osteochondrosis of the Ischiopubic Synchrondrosis, *J. Pediatr. Orthop.* 31 (5) (2011) 520–524.
- [21] A.M. Herneth, S. Trattig, T.R. Bader, A. Ba-Ssalamah, W. Ponthold, K. Wandl-Vergesslich, L.S. Steinbach, MR imaging of the ischiopubic synchrondrosis, *Magn. Reson. Imag.* 18 (5) (2000) 519–524.
- [22] W.P. Maksymowycz, R.G.W. Lambert, M. Østergaard, S.J. Pedersen, P.M. Machado, U. Weber, A.N. Bennett, J. Braun, R. Burgos-Vargas, M. de Hooge, A.A. Deodhar, I. Eshed, A.G. Jurik, K.-G. Hermann, R.B.M. Landewé, H. Marzo-Ortega, V. Navarro-Compán, D. Poddubnyy, M. Rejniersse, M. Rudwaleit, J. Sieper, F.E. Van den Bosch, D. van der Heijde, I.E. van der Horst-Bruinsma, S. Wichuk, X. Baraliakos, MRI lesions in the sacroiliac joints of patients with spondyloarthritis: an update of definitions and validation by the ASAS MRI working group, *Ann. Rheum. Dis.* 78 (11) (2019) 1550–1558.
- [23] J.L. Jaremko, L. Liu, N.J. Winn, J.E. Ellsworth, R.G.W. Lambert, Diagnostic utility of magnetic resonance imaging and radiography in juvenile spondyloarthritis: evaluation of the sacroiliac joints in controls and affected subjects, *J. Rheumatol.* 41 (5) (2014) 963–970.
- [24] N. Herregods, J. Dehoorne, F. Van den Bosch, J.L. Jaremko, J. Van Vlaenderen, R. Joos, X. Baraliakos, G. Varkas, K. Verstraete, D. Elewaut, L. Jans, ASAS definition for sacroiliitis on MRI in SpA: applicable to children? *Pediatr. Rheumatol. Online J.* 15 (1) (2017) <https://doi.org/10.1186/s12969-017-0159-z>.
- [25] N.A. Chauvin, R. Xiao, T.G. Brandon, D.M. Biko, M. Francavilla, D. Khrichenko, P. F. Weiss, MRI of the Sacroiliac Joint in Healthy Children, *AJR Am. J. Roentgenol.* 212 (6) (2019) 1303–1309.
- [26] A.M. Zbojnicewicz, T. Laor, Focal Periphyseal Edema (FOPE) zone on MRI of the adolescent knee: a potentially painful manifestation of physiologic physal fusion? *AJR Am. J. Roentgenol.* 197 (4) (2011) 998–1004.
- [27] M. Bollow, J. Braun, J. Kannenberg, T. Biedermann, C. Schauer-Petrowskaja, S. Paris, S. Mutze, B. Hamm, Normal morphology of sacroiliac joints in children: magnetic resonance studies related to age and sex, *Skeletal Radiol.* 26 (12) (1997) 697–704.
- [28] D.R. Broome, L.A. Hayman, R.C. Herrick, R.M. Braverman, R.B. Glass, L.M. Fahr, Postnatal maturation of the sacrum and coccyx: MR imaging, helical CT, and conventional radiography, *AJR Am. J. Roentgenol.* 170 (4) (1998) 1061–1066.
- [29] A. Zeijden, A.G. Jurik, Anatomy of the sacroiliac joints in children and adolescents by computed tomography, *Pediatr. Rheumatol. Online J.* 15 (2017) 82.
- [30] A.W. Johnson, C.B. Weiss, K. Stento, D.L. Wheeler, Stress fractures of the sacrum. An atypical cause of low back pain in the female athlete, *Am. J. Sports Med.* 29 (4) (2001) 498–508.
- [31] S. Hama, Y. Takata, T. Sakai, K. Higashino, M. Abe, A. Nagamachi, K. Sairyō, Sacral fatigue fractures in children with sacral spina bifida occulta, *J. Pediatr. Orthop. B* 25 (3) (2016) 278–282.
- [32] K.S. Lam, A. Moulton, Stress fracture of the sacrum in a child, *Ann. Rheum. Dis.* 60 (2001) 87–88.
- [33] R.S.M. Portela, Fatigue Fractures of the Sacrum on Children: Case Report. *J. Orthopedics. Rheumatol.*, 2017, 4:3.
- [34] N. Principi, S. Esposito, Infectious Discitis and Spondylodiscitis in Children, *Int. J. Mol. Sci.* 17 (4) (2016) 539, <https://doi.org/10.3390/ijms17040539>.
- [35] V.M. Ravindra, I.M. Eli, M.H. Schmidt, D.L. Brockmeyer, Primary osseous tumors of the pediatric spinal column: review of pathology and surgical decision making, *Neurosurg Focus* 41 (2) (2016) E3, <https://doi.org/10.3171/2016.5.FOCUS16155>.
- [36] D. Saul, K. Dresing, Epidemiology of vertebral fractures in pediatric and adolescent patients, *Pediatr. Rep.* 10 (1) (2018) 7232, <https://doi.org/10.4081/pr.2018.7232>.
- [37] I. Sudol-Szopińska, I. Eshed, L. Jans, N. Herregods, J. Teh, J. Vojinovic, Classifications and imaging of juvenile spondyloarthritis, *J. Ultrason.* 18 (74) (2018) 224–233.
- [38] H. Gleeson, E. Wiltshire, J. Briody, et al., Childhood chronic recurrent multifocal osteomyelitis: pamidronate therapy decreases pain and improves vertebral shape, *J. Rheumatol.* 35 (2008) 707–712.
- [39] K. Vendhan, D. Sen, C. Fisher, Y. Ioannou, M.A. Hall-Craggs, Inflammatory changes of the lumbar spine in children and adolescents with enthesitis-related arthritis: magnetic resonance imaging findings, *Arthritis Care Res. (Hoboken)* 66 (1) (2014) 40–46.
- [40] T. Sakai, K. Sairyō, N. Suzue, H. Kosaka, N. Yasui, Incidence and etiology of lumbar spondylolysis: review of the literature, *J. Orthop. Sci.* 15 (3) (2010) 281–288.
- [41] T. Lemoine, J. Fournier, T. Odent, C. Sembély-Taveau, P. Merenda, D. Sirinelli, B. Morel, The prevalence of lumbar spondylolysis in young children: a retrospective analysis using CT, *Eur. Spine J.* 27 (5) (2018) 1067–1072.

- [42] M. Maurer, R.B. Soder, M. Baldisserotto, Spine abnormalities depicted by magnetic resonance imaging in adolescent rowers, *Am. J. Sports Med.* 39 (2) (2011) 392–397.
- [43] A.G. Jurik, A. Zejden, R.G.W. Lambert, K. Rufibach, J. Hodler, W. P. Maksymowych, S. Duewell, R.O. Kissling, U. Weber, Pitfalls in MR morphology of the sterno-costo-clavicular region using whole-body MRI, *Clin. Radiol.* 68 (8) (2013) 785–791.
- [44] J.I. Sebes, J.E. Salazar, The manubriosternal joint in rheumatoid disease, *AJR Am. J. Roentgenol.* 140 (1) (1983) 117–121.
- [45] A. Doube, A.K. Clarke, Symptomatic manubriosternal joint involvement in rheumatoid arthritis, *Ann. Rheum. Dis.* 48 (6) (1989) 516–517.
- [46] V. Ruiz-Esqueda, A.I. Garcia, J. Ramirez, N. Guanabens, Inflammatory arthropathy of the manubriosternal joint, *Rheumatology (Oxford)* 53 (10) (2014) 1731.
- [47] U. Weber, R.G.W. Lambert, K. Rufibach, W.P. Maksymowych, J. Hodler, A. Zejden, S. Duewell, R.O. Kissling, P.L. Filipow, A.G. Jurik, Anterior chest wall inflammation by whole-body magnetic resonance imaging in patients with spondyloarthritis: lack of association between clinical and imaging findings in a cross-sectional study, *Arthritis Res. Ther.* 14 (1) (2012) R3, <https://doi.org/10.1186/ar3551>.
- [48] V.S. Parker, C.M. Malhotra, G. Ho, S.R. Kaplan, Radiographic appearance of the sternomanubrial joint in arthritis and related conditions, *Radiology* 153 (2) (1984) 343–347.
- [49] J. Singh, R.K. Pathak, Sex and age related non-metric variation of the human sternum in a Northwest Indian postmortem sample: a pilot study, *Forensic Sci. Int.* 228 (1–3) (2013) 181.e1–181.e12.
- [50] E. Yekeler, M. Tunaci, A. Tunaci, M. Dursun, G. Acunas, Frequency of sternal variations and anomalies evaluated by MDCT, *AJR Am. J. Roentgenol.* 186 (4) (2006) 956–960.
- [51] G.T. Ashley, The morphological and pathological significance of synostosis at the manubrio-sternal joint, *Thorax* 9 (2) (1954) 159–166.
- [52] F.D. Grande, S.J. Farahani, J.A. Carrino, A. Chhabra, Bone marrow lesions: A systematic diagnostic approach, *Indian J. Radiol. Imag.* 24 (03) (2014) 279–287.
- [53] L.M. Fayad, M.A. Jacobs, X. Wang, J.A. Carrino, D.A. Bluemke, Musculoskeletal tumors: how to use anatomic, functional, and metabolic MR techniques, *Radiology* 265 (2) (2012) 340–356.
- [54] N. Leclair, G. Thörmer, I. Sorge, L. Ritter, V. Schuster, F.W. Hirsch, H. Zhang, Whole-body diffusion-weighted imaging in chronic recurrent multifocal osteomyelitis in children, *PLoS ONE* 11 (1) (2016) e0147523, <https://doi.org/10.1371/journal.pone.0147523>.
- [55] A. Colombo, L. Bombelli, P.E. Summers, G. Saia, F. Zugni, G. Marvaso, R. Grimm, B.A. Jereczek-Fossa, A.R. Padhani, G. Petralia, Effects of Sex and Age on Fat Fraction, Diffusion-Weighted Image Signal Intensity and Apparent Diffusion Coefficient in the Bone Marrow of Asymptomatic Individuals: A Cross-Sectional Whole-Body MRI Study, *Diagnostics (Basel)* 11 (5) (2021) 913, <https://doi.org/10.3390/diagnostics11050913>.
- [56] L.-S. Ording Müller, D. Avenarius, Ø.E. Olsen, High signal in bone marrow at diffusion-weighted imaging with body background suppression (DWIBS) in healthy children, *Pediatr. Radiol.* 41 (2) (2011) 221–226.
- [57] A. Latifoltojar, S. Punwani, A. Lopes, et al., Whole-body MRI for staging and interim response monitoring in paediatric and adolescent Hodgkin's lymphoma: a comparison with multi-modality reference standard including $¹⁸F-FDG-PET-CT$, *European (2018). Radiology*:1–11.
- [58] A.S. Littooj, T.C. Kwee, I. Barber, C. Granata, M.A. Vermoolen, G. Enríquez, J. Zsfros, S.Y. Soh, B. de Keizer, F.J.A. Beek, M.G. Hobbelink, M.B. Bierings, J. Stoker, R.A.J. Nievelstein, Whole-body MRI for initial staging of paediatric lymphoma: prospective comparison to an FDG-PET/CT-based reference standard, *Eur. Radiol.* 24 (5) (2014) 1153–1165.
- [59] S. Punwani, S.A. Taylor, Z.Z. Saad, A. Bainbridge, A. Groves, S. Daw, A. Shankar, S. Halligan, P.D. Humphries, Diffusion-weighted MRI of lymphoma: prognostic utility and implications for PET/MRI? *Eur. J. Nucl. Med. Mol. Imaging* 40 (3) (2013) 373–385.
- [60] V. Choida, A.-V. Madenidou, D. Sen, M.A. Hall-Craggs, C. Ciurtin, The role of whole-body MRI in musculoskeletal inflammation detection and treatment response evaluation in inflammatory arthritis across age: A systematic review, *Semin. Arthritis Rheum.* 52 (2022) 151953, <https://doi.org/10.1016/j.semarthrit.2022.151953>.
- [61] Y. Zhao, T.S. Sato, S.M. Nielsen, et al., Development of CROMRIS (ChRonic nonbacterial Osteomyelitis MRI Scoring) Tool and Evaluation of its Interrater Reliability, *J. Rheumatol.* 47 (2019) 739–747.
- [62] L. Tanturri de Horatio, M.B. Damasio, D. Barbuti, C. Bracaglia, K. Lambot-Juhan, P. Boavida, L.-S. Ording Müller, C. Malattia, L. Ravà, K. Rosendahl, P. Tomà, MRI assessment of bone marrow in children with juvenile idiopathic arthritis: intra- and inter-observer variability, *Pediatr. Radiol.* 42 (6) (2012) 714–720.
- [63] P. Sinha, S. Crucilla, T. Gandhi, D. Rose, A. Singh, S. Ganesh, U. Mathur, P. Bex, Mechanisms underlying simultaneous brightness contrast: Early and innate, *Vision Res.* 173 (2020) 41–49.
- [64] L.G. Nyul, J.K. Udupa, On standardizing the MR image intensity scale, *Magn. Reson. Med.* 42 (6) (1999) 1072–1081.
- [65] B.P. Wood, Whats the evidence? *Radiology* 213 (3) (1999) 635–637.
- [66] A.P. Brady, Error and discrepancy in radiology: inevitable or avoidable? *Insights Imag.* 8 (1) (2017) 171–182.
- [67] D.G. Altman, J.M. Bland, Diagnostic tests 2: Predictive values, *BMJ* 309 (1994) 102.
- [68] B. Heynen, C. Tamigneaux, V. Pasoglou, J. Malghem, B. Vande Berg, T. Kirchgessner, MRI detection of radiographically occult fractures of the hip and pelvis in the elderly: Comparison of T2-weighted Dixon sequence with T1-weighted and STIR sequences, *Diagn. Interv. Imaging* 100 (3) (2019) 169–175.
- [69] S. Wagle, J.T. Gu, J.L. Courtier, A.S. Phelps, C. Lin, J.D. MacKenzie, Value of dedicated small-field-of-view sacroiliac versus large-field-of-view pelvic magnetic resonance imaging for evaluating pediatric sacroiliitis, *Pediatr. Radiol.* 49 (7) (2019) 933–940.