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Original Article

Comparison of DXA Scans and Conventional X-rays for Spine Morphometry and Bone Age Determination in Children

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Abstract

Conventional lateral spine and hand radiographs are the standard tools to evaluate vertebral morphometry and bone age in children. Beside bone mineral density analyses, dual-energy X-ray absorptiometry (DXA) measurements with lower radiation exposure provide high-resolution scans which are not approved for diagnostic purposes. Data about the comparability of conventional radiographs and DXA in children are missing yet. The purpose of the trial was to evaluate whether conventional hand and spine radiographs can be replaced by DXA scans to diminish radiation exposure. Thirty-eight children with osteogenesis imperfecta or secondary osteoporosis or short stature (male, n = 20; age, 5.0–17.0 yr) were included and assessed once by additional DXA (GE iDXA) of the spine or the left hand. Intraclass correlation coefficients (ICCs) were used to express agreement between X-ray and iDXA assessment. Evaluation of the spine morphometry showed reasonable agreement between iDXA and radiography (ICC for fish-shape, 0.75; for wedge-shape, 0.65; and for compression fractures, 0.70). Bone age determination showed excellent agreement between iDXA and radiography (ICC, 0.97). IDXA-scans of the spine in a pediatric population should be used not only to assess bone mineral density but also to evaluate anatomic structures and vertebral morphometry. Therefore, iDXA can replace some radiographs in children with skeletal diseases.

Key Words: Bone age; children; DXA; osteogenesis imperfecta; spine morphometry.

Introduction

Conventional spine radiographs are the standard diagnostic tool to evaluate vertebrae, fractures, and morphometry in children suspicious of osteoporosis, osteogenesis imperfecta, or rare skeletal dysplasia. In addition, areal bone mineral density measurement (aBMD) using dual-energy X-ray absorption (DXA) is the state-of-the-art diagnostic instrument to diagnose osteoporosis *(1)*. With appropriate reference data, these methods can also be used in the pediatric context *(2–4)*. During the last few years, DXA scanners became available with a highly increased resolution. Therefore, it is tempting to use these scans for diagnostic imaging and particularly in follow-up examinations for specific indications, for example, osteogenesis imperfecta. Scans of the lateral spine can be done with a dramatically reduced amount of radiation compared to conventional radiographs.

To visualize the stability and anatomic structures of the skeleton, the conventional radiograph of the lateral spine is still the gold standard. In adults, vertebral fracture assessment is performed by the Genant score in adaption to the International Society of Clinical Densitometry (http://www.iscd.org/official-positions/2013-iscd-official-positions-adult/). In children, analyzation of the spine to assess vertebral fractures and pediatric osteoporosis differs and is performed according to the guidelines of the International Society of Clinical Densitometry for children *(5, 6)*. Additionally, different

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Table 1
Raw Data for Inter-rater Agreement of Spine Assessment

Vertebral Deformity	ICC	95% CI
X-ray fish-shape	0.71	0.60−0.80
X-ray wedge-shape	0.73	0.62−0.81
X-ray compression fracture	0.89	0.84−0.92
iDXA fish-shape	0.91	0.85−0.95
iDXA wedge-shape	0.88	0.80−0.92
iDXA compression fracture	0.96	0.93−0.97

Abbr: CI, confidence interval; ICC, intraclass correlation coefficient.

morphometric or semiquantitative methods are currently used to describe the vertebral shape *(7−9)*. Based on the fact that there are no approved drugs for children with osteogenesis imperfecta and juvenile osteoporosis yet, most children are treated with an "individual therapeutic off-label approach" *(10)*. Therefore, response and vertebral reshaping are followed critically every year by conventional spine morphometry *(8)*. An additional DXA scan is performed to follow aBMD.

Radiographs of the left hand are widely used in the field of pediatric endocrinology to investigate bone age and to calculate final height *(11, 12)*.

Given the fact that children have a greater risk of radiation-induced complications over lifetime than adults, we aimed to compare the morphometric assessment of conventional lateral spine radiographs with lateral DXA scans and conventional left hand radiographs with pictures of the left hand done by DXA within a clinical trial. Preliminary data for bone age determination with DXA have been reported based on Polish references and Greulich and Pyle *(13, 14, 16)*. We hypothesized that there is a high agreement between the DXA assessment and conventional radiographs regarding morphometric spine assessment and bone age determination.

Therefore, the purpose of our trial was to establish whether conventional hand and spine radiographs can be replaced by DXA measurements to diminish radiation exposure in children and adolescents.

Materials and Methods

Clinical Trial

The trial was performed as a monocenter prospective trial. A retrospective interpretation of prospective acquired data was done after the completion of the trial.

Thirty-eight patients (18 patients for lateral spine assessment and 20 patients for left hand assessment) were recruited between 2009 and 2010.

Female and male patients aged between 5 and 18 years could be included if a clinical indication for conventional radiography of the spine or left hand was given. All patients who presented in our clinic in the period of the trial were asked to participate. Patients participating in a clinical trial, not willing to follow trial procedures based on mental or other chronic disorders, and female patients while pregnant were excluded from the trial. Subjects involved in this trial were not included in other trials and publications simultaneously. The trial was approved by the local ethics committee (number: 06-175) and the German radiation board (certificate number: Z 5 − 22462/2 − 2008 − 081). Written informed consent was given by the patients and from their legal representatives before participation in the trial.

The primary objective was to evaluate the rate of agreement of morphologic assessment in conventional radiographs vs iDXA measurements of the spine or the left hand.

Radiographs and DXA measurements were performed on the same day. Radiographs were taken with Philips Optimus 65 BuckyDiagnost TH and VT (Philips Healthcare, the Netherlands). DXA measurements were performed using

Table 2
Inter-rater and Intrarater Agreement of Bone Age Determination

Vertebral Deformity	ICC	95% CI	Mean difference, investigator 1 − 2 (yr)	95% CI
Inter-rater agreement				
X-ray, cycle 1	0.95	0.86−0.98	0.32	−1.05 to 1.68
X-ray, cycle 2	0.96	0.90−0.98	0.03	−1.28 to 1.35
X-ray, cycle 3	0.95	0.88−0.98	−0.12	−1.56 to 1.31
iDXA, cycle 1	0.96	0.90−0.98	0.12	−1.11 to 1.36
iDXA, cycle 2	0.94	0.85−0.98	−0.17	−1.72 to 1.39
iDXA, cycle 3	0.98	0.95−0.99	−0.11	−0.95 to 0.72
			Mean difference intra-investigator (yr)	
Intrarater agreement				
X-ray	0.99	0.98−1.0	0.09	−0.65 to 0.84
iDXA	0.99	0.98−1.0	0.02	−0.39 to 0.43

Abbr: CI, confidence interval; ICC, intraclass correlation coefficient.

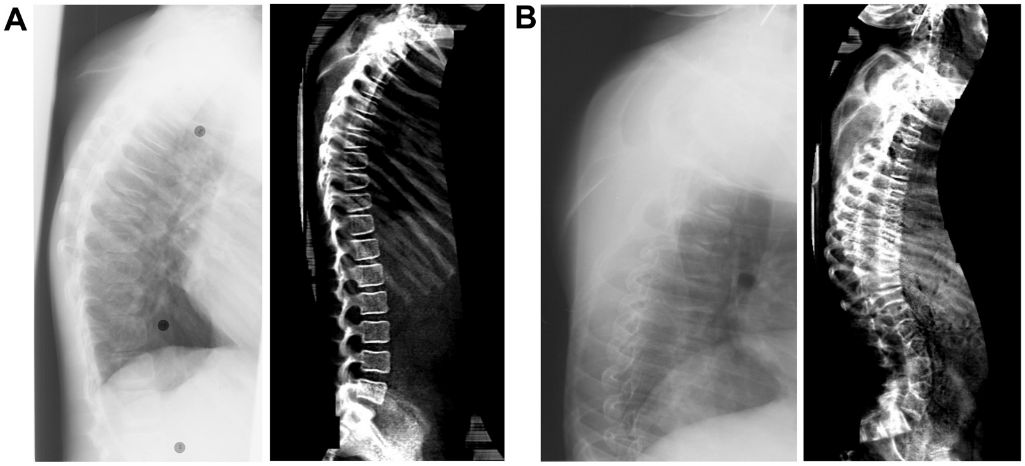


Fig. 1. Radiographs (left side) and iDXA pictures (right side) of the lateral spine of 2 individual patients. (**A**) A pair of images (radiograph and iDXA) which are eligible to perform the measurements. (**B**) An ineligible pair of images. In both patients, the quality of pictures seems to be comparable between the radiograph and the iDXA scan.

GE Lunar iDXA (GE Medical; Solingen, Germany) and were analyzed using Encore software version 13.60. The effective radiation dose for the lateral spine was ∼325 μSv by X-ray and 12.1 μSv using iDXA and for the hand ∼1 μSv (X-ray) and 0.06 μSv (iDXA) as stated by the German radiation board for regular clinical use of the different machines.

Investigators and Assessment of Radiographs and DXA

Investigators

All scans (X-ray and DXA) were assessed by 2 independent investigators with a high expertise in evaluating bone radiographs in children and adolescents. Investigators were blinded to age and underlying disease of the individual patient except of the sex for hand radiograph assessment.

All spine scans were first rated for eligibility, meaning that it would be possible to measure the defined distances. After eligibility assessment, each scan was evaluated independently by both investigators to analyze inter-rater agreement. Bone age was assessed independently in 3 cycles to analyze interrater and intrarater agreement.

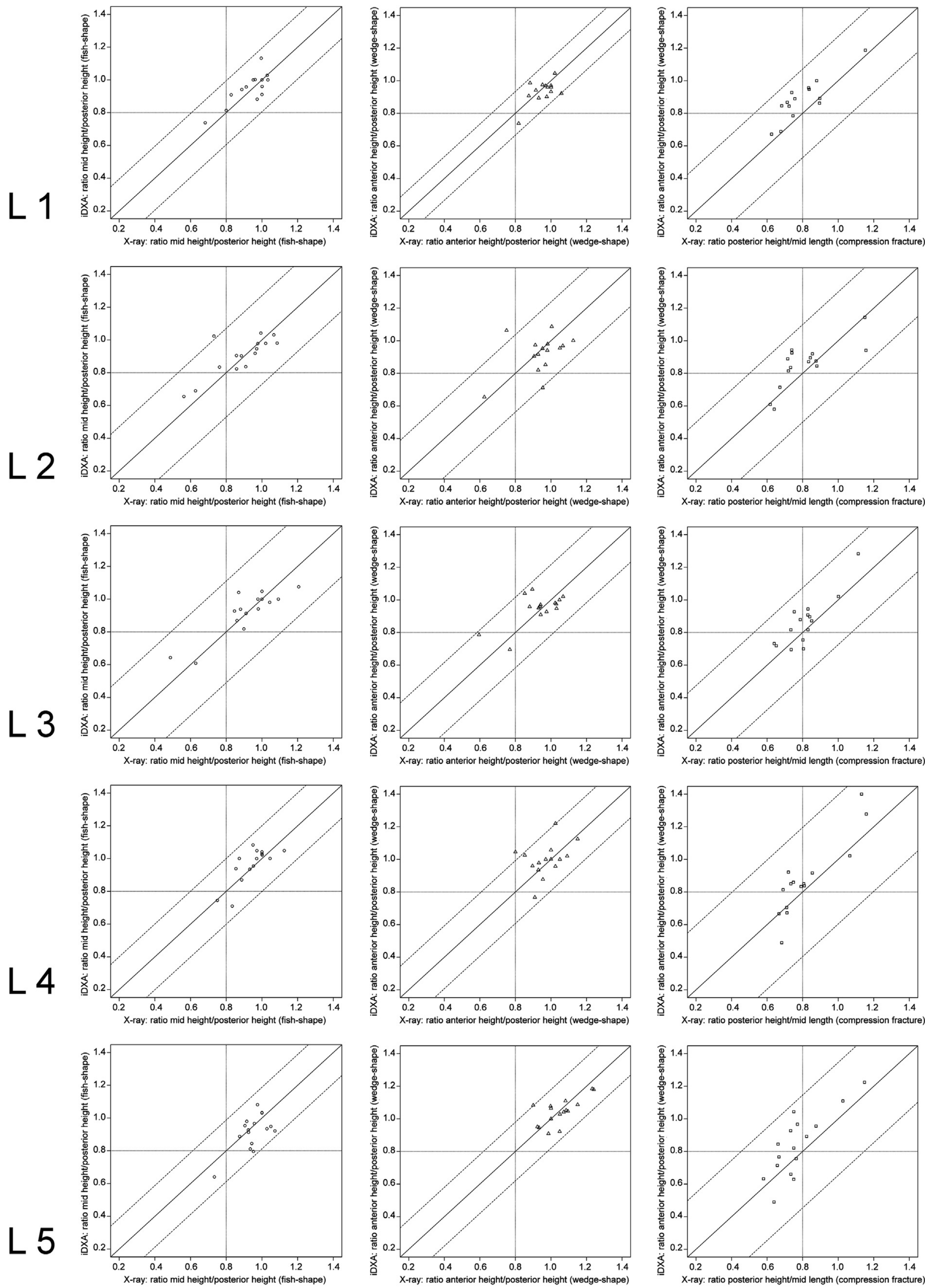
Assessment of the Lateral Spine

Lateral spine morphometry was analyzed using the method of Smith-Bindman *(15)*. It is frequently used to evaluate the vertebral morphometry in children with osteoporotic diseases *(8, 9)*. Four corners of each vertebra, the 2 midpoints of the end plates, and the 2 midpoints of the anterior and posterior lines were defined. Distances between these points were measured using a caliper with a precision of 1 mm on X-rays and by the ruler tool in the iDXA software. "Anterior height," "mid-height," "posterior height," and "mid-length" were recorded. Based on these measurements, the following spine indices for vertebral deformities were calculated: fish-shape (mid-height/posterior height); wedge-shape (anterior height/posterior height); compression fracture (posterior height/mid-length). Usually, a ratio of <0.8 is defined as clinical relevant deformity analogous to the pediatric position article of the International Society for Clinical Densitometry *(5, 6)* Thoracic vertebrae 11 till lumbar vertebra 5 were chosen because these vertebrae are used in clinical routine to analyze spine deformities, and the projection on routine X-rays normally does not interfere with other structures.

Table 3
Results of Vertebral Morphometry Assessment and Agreement Between iDXA and Radiographs

Morphology	ICC	95% CI	Mean difference iDXA − X-ray	95% CI
Fish-shape	0.75	0.65−0.83	0.00	−0.17 to 0.17
Wedge-shape	0.65	0.53−0.75	−0.01	−0.19 to 0.17
Compression fracture	0.70	0.38−0.84	0.07	−0.13 to 0.26

Note: Presented are the ICCs between iDXA and radiograph assessment averaged for 2 investigators.
Abbr: CI, confidence interval; ICC, intraclass correlation coefficient.


L 1
L 2
L 3
L 4
L 5
iDXA: ratio mid height/posterior height (fish-shape)
X-ray: ratio mid height/posterior height (fish-shape)
iDXA: ratio anterior height/posterior height (wedge-shape)
X-ray: ratio anterior height/posterior height (wedge-shape)
X-ray: ratio posterior height/mid length (compression fracture)

Assessment of Bone Age

To compare the images of the hands, methods of clinical routine were used. Each scan was first judged to be eligible for determination of bone age and rating of anatomic variants such as additional epiphyses. Eligibility was defined when both investigators stated independently that they felt comfortable to assess bone age on this image. Bone age was determined using the method of Greulich and Pyle *(16)*, which is used in clinical routine and by the more detailed method of Tanner-Whitehouse *(17–19)*. It was decided to accept a difference of 1 year of bone age as the normal variant based on clinical routine.

Statistics

Continuous data were presented as means ± standard deviations and categorical data as frequencies and percentages.

For spine indices (i.e., fish-shaped, wedge-shaped, and compression fracture index) and bone age, intraclass correlation coefficients (ICCs) of type ICC (3.1; 2-way mixed model, single-measures, absolute agreement), mean differences, and corresponding 95% confidence intervals (CIs) were used to express the agreement between X-ray and iDXA assessment as well as between investigators (inter-rater agreement). For bone age, additionally, the agreement between cycles was analyzed (intrarater agreement). Scatterplots were used for graphical presentation.

Statistical analyses were performed with R version 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Clinical Characteristics of the Study Cohort

For spine evaluation, 18 children (9 male and 9 female) aged between 5 and 17 years (median, 10.3 years; prepubertal Tanner 1, n = 12) were included. The underlying diagnoses were osteogenesis imperfecta and juvenile idiopathic osteoporosis. For bone age evaluation, 20 children (11 male and 9 female) aged between 6 and 17 years (median 12.4 years; prepubertal Tanner 1, n = 10) were included. The underlying diagnoses were idiopathic short stature and constitutional delay of growth and puberty.

Reproducibility of Results by Investigators and Cycles

The spine was assessed once by each investigator. Data are presented averaged of 2 investigators. There was no reasonable difference between the different investigators (Table 1). Hand images were assessed 3 times by 2 investigators. No reasonable difference either in the 3 cycles or between the different investigators was detected (Table 2).

Results of Spine Assessment

Eligibility

In 18 patients, 7 vertebrae (th11–L5) were evaluated independently by 2 observers for eligibility (total number of vertebrae, n = 252 [18 × 7 × 2]). Of these 252 vertebrae, 216 were rated as eligible per conventional radiography vs 220 per iDXA. The measurability was evaluated concordant in 89.7% (205 rated as eligible; 21 rated as noneligible). Examples for good vs poor eligibility of vertebral evaluation are displayed for 2 individual patients in Fig. 1A and B.

Vertebral Morphometry

The level of agreement between the 2 different scan modalities is presented in Table 3. ICCs and 95% confidence intervals are presented for both scan techniques averaged of 2 investigators for fish-shaping, wedge-shaping, and compression fractures.

Additionally, the agreements between iDXA and X-ray ratios of fish-shape, wedge-shape, and compression deformities are presented in Fig. 2.

Results of the Assessment of Hands

Both investigators independently decided while assessing the bone age by the method of Tanner-Whitehouse that the resolution of iDXA hand scans is not high enough to assess all required anatomic details. Therefore, this precise assessment procedure was excluded from the analysis plan because of eligibility failure, and bone age was determined by the method of Greulich and Pyle as frequently used in clinical routine.

Examples for eligibility of hand evaluation are displayed for 2 individual patients in Fig. 3A and B.

The level of agreement between the scan modalities averaged of 2 investigators for 3 cycles is presented in Table 4 and Fig. 4. In Fig. 4, the X-ray and DXA values of the 3 replicate cycles were displayed. In case of perfect concordance, the points lie on the solid line. Except for 1 case, all points lay in the range of ±1 year. The mean differences between both methods were close to 0 with limits of corresponding confidence intervals close to ±1 year, indicating a good agreement. Therefore, the agreement between X-ray and DXA was high in all replicate assessments

Fig. 2. Agreement of morphometric assessment of the spine between iDXA and radiograph. Scatterplots presenting the results of spine morphometry ratios. Presented is the ratio of mid-height/posterior height (fish-shape; presented in circles) for each vertebra in the left column; the ratio of anterior height/posterior height (wedge-shape; presented in triangles) in the middle column, and the ratio of posterior height/mid-length (compression fracture; presented in rectangles) in the right column for the lumbar vertebrae 1–5 (L1–L5) which are used in clinical routine. Results are averaged of 2 investigators for iDXA and X-ray. Solid line = line of perfect concordance; dashed line = ±2 standard deviation; dotted line = cutoff value 0.8 which is clinically relevant.

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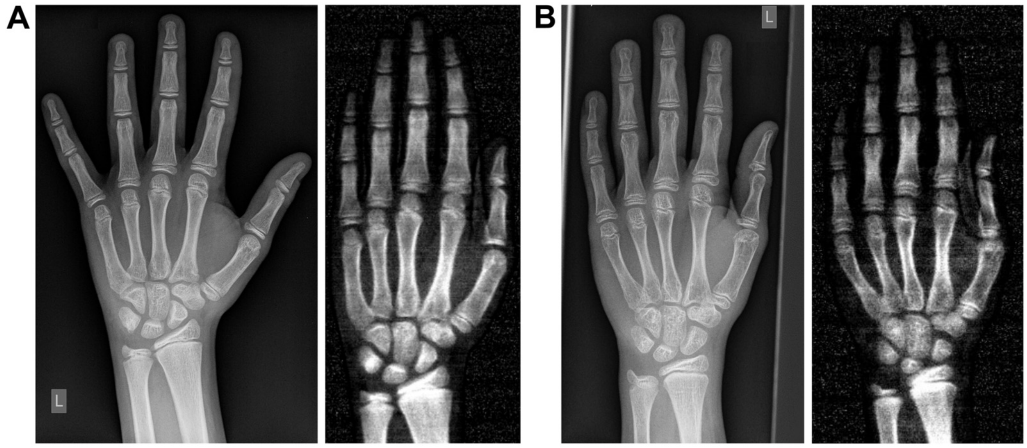

Fig. 3. Radiographs (left side) and iDXA pictures (right side) of the left hand of 2 individual trial patients. (**A**) An eligible pair of images on radiograph and iDXA. (**B**) A pair of images where the iDXA is not eligible in comparison to the radiograph.

(ICCs 0.97−0.99; see Table 2). The results are displayed in Table 4.

Discussion

The purpose of our trial was to establish whether conventional hand and spine radiographs can be replaced by DXA measurements to diminish radiation exposure in children and adolescents. This aim should be applied to examinations taken widely for diagnostic questions as well as for monitoring purposes in rare skeletal diseases.

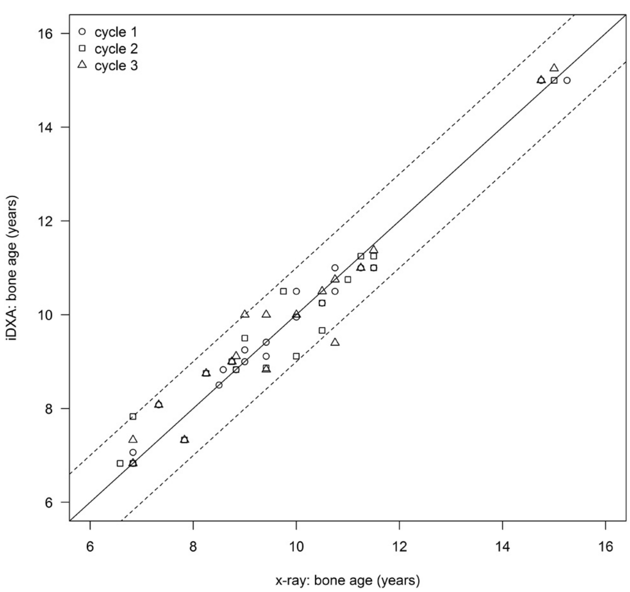

Fig. 4. Agreement of the bone age determination between iDXA and radiographs. Scatterplot presenting the difference of bone age determination by iDXA and radiography in years in 3 cycles averaged for 2 investigators (first cycle presented in circles; second cycle presented in rectangles; third cycle presented in triangles). Solid line = line of perfect concordance; dashed line = ±1 year.

Spine

Results of eligibility of vertebral evaluation presented good agreement between iDXA and conventional radiographic assessment. Vertebral morphometry assessment gives evidence that alteration of the vertebral configuration, for example, fish-shaped and wedge-shaped alterations can be detected and followed by iDXA measurement comparable to conventional spine radiographs. The high inter-rater agreement between iDXA and conventional radiography underlines that iDXA and conventional radiography are comparable regarding the assessed conditions also in children as it was shown in adults earlier *(20, 21)*.

The most common indication for lateral spine radiographs is the continuous monitoring of off-label therapies in patients with osteogenesis imperfecta or secondary osteoporosis. In those patients, X-rays of the lateral spine are taken at least yearly. At the first visit or at the start of an antiresorptive therapy, morphologic characterization of the spine and an

Table 4
Results of Bone Age Determination and Agreement Between iDXA and Radiographs

Cycle	ICC	95% CI	Mean difference iDXA − X-ray (yr)	95% CI
Cycle 1	0.99	0.98−1.0	0.03	−0.55 to 0.62
Cycle 2	0.98	0.94−0.99	−0.04	−1.01 to 0.93
Cycle 3	0.97	0.93−0.99	0.08	−0.94 to 1.10

Note: Presented are the ICCs between iDXA and radiograph assessment averaged for 2 investigators.

Abbr: CI, confidence interval; ICC, intraclass correlation coefficient.

assessment of the aBMD are mandatory. For clinical routine, we recommend to perform an initial X-ray at the first visit to clarify the indication for treatment. For children who will receive a medical treatment, we suggest an additional iDXA scan of the lateral spine. After the initial assessment, iDXA scans seem to be reasonable instead of yearly conventional radiographs to monitor efficacy of medical treatment and morphometric changes. With this regime, the total amount of radiation used in these children can be reduced.

Hand

The results of the 3 replicate assessments (3 times X-ray and 3 times DXA) showed a good agreement. Except for 1 case, all values lay in the range of ±1 year. This means, in general, the difference in bone age between both methods was clinically not important. However, results of the left hand assessments are not convincing to replace radiographs by iDXA in general. Based on the fact that the radiation exposure is clearly lower in hand X-rays compared to spine radiographs, the advantages are not as obvious as in spine radiographs. An analysis of bone age was possible in most cases and showed a strong agreement between iDXA and X-ray comparable to recent data *(13, 14)*. Nonetheless, it was difficult to assess small anatomic structures. Therefore, we would recommend continuing the assessment of the hand by X-rays if the question is the assessment of the anatomic structures (e.g., skeletal dysplasia differential diagnoses) such as extraepiphyses or "Madelung deformities," which appear to be better detectable on conventional radiographs. For bone age determination it seems reasonable to use iDXA.

Limitations

This study is limited by the small sample size (spine and hand assessment) and the specific indications for the spine investigations. Furthermore, our study is an exploratory study and further validation is needed. The sample size was initially calculated with 40 children in each group (hand and spine). Because of ethical reasons, we had to do an interim analysis to minimize radiation exposure even within the study. After ∼50% of the anticipated patients were included, we decided to stop recruiting because results seemed to be very congruent. Further validation is needed in a longitudinal trial with a higher sample size. Keeping this in mind, it was decided to stop recruiting because measuring 20 more children would probably not have had an additional effect on planning a validation trial.

No conclusions can be drawn on the replacement of lateral spine X-rays by iDXA scans in general. The comparison was made using GE iDXA and no conclusions about scans taken by other DXA scanners could be drawn. Additionally, data of alternative techniques to assess vertebral morphometry are lacking yet. Especially, methods without radiation (e.g., magnetic resonance imaging [MRI]) are not assessed for the morphometric assessment of the vertebrae in children. In general, MRI examination is difficult in the pediatric setting. A lot of children have to be sedated for MRI *(22)*. Finally, our results are limited by the fact that no subgroup analyses regarding sex, age, and pubertal status were done.

In conclusion, this study gives evidence that the use of iDXA scans should not be limited only to assessing bone mineral density in children. iDXA scans might be used to evaluate anatomic structures and vertebral morphometry and therefore can replace radiographs especially in children with chronic skeletal diseases who need continuous radiographs for follow-up investigations. The slightly reduced resolution of the iDXA scans seems to be balanced by the extremely reduced amount of radiation, at least regarding the examination of the spine. Further trials with a higher sample size and new standardized assessment tools of spine morphology are mandatory to approve DXA measurements for vertebral fracture assessment and morphometric spine analyses in children *(7, 23)*.

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