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ORIGINAL ARTICLE

Reference values for digital X-ray radiogrammetry parameters in children and adolescents in comparison to estimates in patients with distal radius fractures

Diane M. Renz · Ansgar Malich · Andreas Ulrich · Alexander Pfeil · Hans-Joachim Mentzel · Florian Streitparth · Martin H. Maurer · Ulf K. Teichgräber · Joachim Böttcher

Abstract The first objective of this study was to determine normative digital X-ray radiogrammetry (DXR) values, based on original digital images, in a pediatric population (aged 6–18 years). The second aim was to compare these reference data with patients suffering from distal radius fractures, whereas both cohorts originated from the same geographical region and were evaluated using the same technical parameters as well as inclusion and exclusion criteria. DXR-BMD and DXR-MCI of the metacarpal bones II–IV were assessed on standardized digital hand radiographs, without printing or scanning procedures. DXR parameters were estimated separately by gender and among six age groups; values in the fracture group were compared to age- and gender-matched normative data using Student's t tests and Z scores. In the reference cohort (150 boys, 138 girls), gender differences were found in bone mineral density (DXR-BMD), with higher values for girls from 11 to 14 years and for boys from 15 to 18 years ($p < 0.05$). Girls had higher normative metacarpal index (DXR-MCI) values than boys, with significant differences at 11–14 years ($p < 0.05$). In the case–control investigation, the fracture group (95 boys, 69 girls) presented lower DXR-BMD at 15–18 years in boys and 13–16 years in girls vs. the reference cohort ($p < 0.05$); DXR-MCI was lower at 11–18 years in boys and 11–16 years in girls ($p < 0.05$). Mean Z scores in the fracture group for DXR-BMD were −0.42 (boys) and −0.46 (girls), and for DXR-MCI were −0.51 (boys) and −0.53 (girls). These findings indicate that the fully digital DXR technique can be accurately applied in pediatric populations ≥ 6 years of age. The lower DXR-BMD and DXR-MCI values in the fracture group suggest promising early identification of individuals with increased fracture risk, without the need for additional radiation exposure, enabling the initiation of prevention strategies to possibly reduce the incidence of osteoporosis later in life.

D. M. Renz (✉) · F. Streitparth · M. H. Maurer
Department of Radiology, Charité University Medicine Berlin, Campus Virchow Clinic, Augustenburger Platz 1, 13353 Berlin, Germany
e-mail: diane.renz@charite.de

A. Malich · A. Ulrich
Institute of Diagnostic Radiology, Suedharz Clinic Nordhausen, Dr. Robert-Koch-Str. 39, 99734 Nordhausen, Germany

A. Pfeil
Department of Internal Medicine III, Jena University Hospital, Friedrich-Schiller-University, Erlanger Allee 101, 07740 Jena, Germany

H.-J. Mentzel · U. K. Teichgräber
Institute of Diagnostic and Interventional Radiology, Jena University Hospital, Friedrich-Schiller-University, Erlanger Allee 101, 07740 Jena, Germany

J. Böttcher
Institute of Diagnostic and Interventional Radiology, SRH Clinic Gera, Str. des Friedens 122, 07548 Gera, Germany

Introduction

The incidence of fractures is characterized by two age peaks, one due to bone loss later in life and the other in early adolescence [1–4]. The most common fractures in childhood and adolescence occur at the distal forearm, particularly at the distal radius, accounting for approximately 25 % of all pediatric fractures, with increasing incidence over the past decades [1, 4–6]. In addition to acute consequences such as immobilization, pediatric

distal radius fractures can result in long-term implications, including lasting functional limitations, diminished working capacity, and substantial health care costs [4–6]. Osteoporosis was once considered as solely a disease of the elderly; recently, it is more and more agreed that osteoporosis can have a pediatric origin [7–9]. Individuals who fail to achieve optimal peak bone mass during growth and maturation are predisposed to develop osteoporosis later in their lives [10, 11].

In order to provide effective prevention strategies against the development of osteoporosis, it is important to identify individuals with increased risk as early as possible [9–11]. However, routine measurements of bone mass and bone mineral density (BMD) in children and adolescents are complicated, as their higher sensitivity to ionizing radiation requires strict indications for techniques using radiation exposure [12–14]. Dual-energy X-ray absorptiometry (DXA), the gold standard for diagnosis of osteoporosis in adults, has also become the most widely used osteodensitometric technique in children and adolescents, due to its high safety, good accuracy, relatively low cost, and widespread availability [15–18]. However, in addition to increased radiation exposure, DXA presents further challenges in pediatric populations, as measurement of DXA can be impaired if pediatric bones are too small or too large compared to the calendar age of the children and in the case of obesity [13, 14, 19]. This influence of soft tissue fat becomes more relevant in childhood populations due to their rising incidence of obesity, and high body mass index (BMI) has been proven to increase fracture risk in children [6, 17]. Quantitative ultrasound (QUS) is a promising, radiation-free, possibly portable osteodensitometric technique in pediatric populations; however, as current limitations varying interobserver reproducibility and the possible influence of environment factors during the measurement are discussed [13, 20–23].

Digital X-ray radiogrammetry (DXR) provides automatic radiogeometric bone analysis, and the value of this relatively novel computer-assisted diagnosis (CAD) technique in the assessment of different primary and secondary forms of osteoporosis has been reported in detail for adults, but also for children and adolescents [24–34]. Several investigations have demonstrated that DXR parameters show a close correlation with BMD measurements of the reference standard DXA; DXR allows identification of women at risk for osteoporotic fractures, although DXR calculates BMD at peripheral and not axial skeletal sites [24, 28, 29]. As DXR-BMD can be assessed using hand radiographs, which are commonly acquired in pediatric populations—e.g., for ruling out fractures or for assessing skeletal age—additional ionizing radiation is not necessary [30–34]. Reference values for DXR parameters have been generated in both adult populations and in children and adolescents, whereas hand radiographs had been printed out and subsequently scanned for osteodensitometric CAD analysis [30, 33, 35, 36].

Thus, the first aim of this investigation was to determine reference values for bone mineral density (DXR-BMD) and metacarpal index (DXR-MCI) in a pediatric population aged 6–18 years based on original digital hand radiographs, without circuitous printing and scanning processes. The second objective was to compare these reference data with age- and gender-matched patients suffering from distal radius fractures, whereas both cohorts originated from the same geographical region and were evaluated using the same technical parameters as well as inclusion and exclusion criteria. Early identification of children and adolescents at increased risk of experiencing fractures and developing osteoporosis can provide specific prevention strategies, such as dietary consumption and physical activity.

Materials and methods

Subjects

This retrospective analysis of a consecutive enrollment of children and adolescents included Caucasian German subjects aged 6 to 18 years. For analysis of the cortical bone partition, digital hand radiographs were used in anteroposterior projection, performed under standardized technical parameters at the same radiological department. In both, the reference cohort (without any fracture) and the group with distal radius fractures, the clinical indication of the hand radiographs was trauma during daily living or sports activities; some patients received further radiographs—e.g., of the wrist—depending on their clinical symptoms. Each trauma was categorized by orthopedic surgeons as adequate to cause a distal radius fracture. The X-ray examinations of the affected hand were obtained within three days after the trauma, before necessary therapeutic strategies were initiated (e.g., immobilization). All subjects originated from the same geographical region.

The following exclusion criteria were defined:

- Visible metallic material or splints after osteosynthesis;
- Previous fractures of the upper extremities;
- Pathological abnormalities of the hand skeleton;
- Superposition of the metacarpal bones on X-ray examination;
- Bone-affecting diseases, early and late puberty;
- Use of medication with an influence on bone metabolism, e.g., steroids;
- Incomplete analysis by the DXR system;

- In the fracture cohort, distal radius fractures involving the epiphyseal growth plate were excluded, as this injury is typically characterized by fragility of the cartilage tissue.

Two experienced radiologists evaluated all radiographs and confirmed or excluded distal radius fractures. All hand radiographs were analyzed as original fully digital images using Sectra Osteoporosis Package (Sectra Medical Systems, Linköping, Sweden) as part of the picture archiving and communication system (PACS) of the hospital, without the influence of printing and/or scanning procedures. All X-ray examinations were performed in the course of routine patient care; no radiographs were obtained solely for study purposes. The study was designed in accordance with local ethics committee guidelines and the Declaration of Helsinki. All patients and their parents gave their consent for the scientific use of their clinical and radiological data.

In the present study, 452 subjects fulfilled the inclusion and exclusion criteria and could be enrolled: 164 patients (95 boys, 69 girls) experienced a distal radius fracture, and 288 children and adolescents (150 boys, 138 girls) had no fracture after adequate trauma, and therefore functioned as the reference cohort. The trauma severity was not significantly different between the fracture and reference cohorts (similar trauma severity associated with fracture graded according to the method described by Landin [4]). All subjects were assigned to one of six subgroups based on their calendar age, and all data were analyzed separately by gender:

- Group 1: 6–8 years
- Group 2: 9–10 years
- Group 3: 11–12 years
- Group 4: 13–14 years
- Group 5: 15–16 years
- Group 6: 17– 18 years

Additionally, skeletal age was evaluated by both radiologists in all subjects according to the method described by Thiemann-Nitz [37]. In all included children and adolescents, skeletal age groups were in concordance with the calendar age groups (+/− one year).

Imaging acquisition and analysis

All hand radiographs were obtained in anteroposterior projection using the Philips BuckyDiagnost TH system (Philips Healthcare; Best, The Netherlands), with the following standardized, age-adapted technical parameters: maximum tube voltage 56 kV, maximum exposure level 8 mAs, exposure time 4 ms, film focus distance 100 cm, and filter with 1.0 mm aluminum plus 0.1–0.2 mm copper. The Sectra Osteoporosis Package was used to determine cortical DXR-BMD and DXR-MCI on metacarpal bones II–IV of the original digital hand radiographs. As the DXR technique has been described in detail [24–27], the calculation of DXR-BMD and DXR-MCI is only summarized here. The CAD estimates of cortical bone parameters were performed automatically, without user interaction. DXR-BMD (in g/cm^2) was computed considering the total cortical volume per area (VPA), with correction for porosity and relation to DXA measurements of the mid-distal forearm [24–27]. DXR-MCI is a dimensionless parameter, calculated as the ratio of cortical thickness to outer metacarpal width: 2 × cortical thickness/outer metacarpal width [26, 38].

Statistical evaluation

The statistical analysis of this investigation was performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). In order to establish digital reference values for DXR-BMD and DXR-MCI in healthy children, the calculations of the means, including standard deviations (SDs), were conducted separately for the six age groups and the genders. As the values of DXR-BMD and DXR-MCI were normally distributed, Student's t tests for independent samples were performed to indicate possibly significant differences between males and females of the same age groups. The findings of the DXR parameters in boys and girls with distal radius fractures were compared to the normative data, also by using Student's t tests for independent samples, separately for each age group. Additionally, the DXR-BMD and DXR-MCI of each patient with a distal radius fracture were associated with age- and gender-matched reference values using Z scores. These Z scores were computed as follows:

$$Z\ \text{score}_{\text{individual}} = \frac{\left(\text{DXR-parameter}_{\text{individual}} - \text{mean DXR-parameter}_{\text{age- and gender-matched reference group}}\right)}{\text{SD}_{\text{age- and gender-matched reference group}}}$$

As the Z scores were also normally distributed, means were calculated for the male and female fracture cohorts and compared. The Z scores for DXR-BMD and DXR-MCI were further categorized as reduced (Z scores between -1 and -2 SD, as well as ≤ -2 SD), regular (Z scores ± 1 SD), or increased values (Z scores between 1 and 2 SD, as well as ≥ 2 SD). For correlation analyses, Pearson's correlation coefficients were performed. In all statistical analyses, p values less than 0.05 (two-sided) were considered to indicate significance.

Results

Normative DXR values of healthy children and adolescents

The reference values for the 288 healthy children and adolescents are presented in Table 1 (for the 150 boys) and Table 2 (for the 138 girls). Between the age groups 6–8 and 17–18 years for boys, the mean DXR-BMD increased from 0.383 to 0.617 g/cm^2 and the mean DXR-MCI from 0.319 to 0.466 (Table 1). Boys showed the highest average

elevation of normative DXR-BMD ($+26.4$ %) and DXR-MCI ($+26.3$ %) in the age group of 15–16 years compared to 13–14 years (Table 1). In the female reference cohort, the mean DXR-BMD was 0.369 g/cm^2 and the mean DXR-MCI 0.325 at 6–8 years, compared to 0.565 g/cm^2 and 0.473 at 17–18 years (Table 2). Normative DXR-BMD increased mostly accentuated in girls from 11 to 14 years; the highest average elevation of normative DXR-MCI was 17.2 % in the age group 13–14 years compared to 11–12 years (Table 2). Strong positive correlations between DXR-BMD/DXR-MCI and age were found for both genders: Pearson's correlation coefficients $r = 0.86$ (DXR-BMD) and $r = 0.73$ (DXR-MCI) for boys, and $r = 0.81$ (DXR-BMD) and $r = 0.71$ (DXR-MCI) for girls, whereas all correlations were highly significant ($p < 0.01$). The correlations between DXR-BMD and DXR-MCI were $r = 0.88$ (boys; $p < 0.01$) and $r = 0.84$ (girls; $p < 0.01$).

In children between 6 and 10 years of age, no significant differences in DXR-BMD were observed between boys and girls. DXR-BMD reference values were significantly higher for girls at ages 11–12 and 13–14 years compared to the corresponding male groups, and boys presented

Table 1 Normative digital values for the DXR parameters BMD and MCI in 150 healthy boys

Calendar age group (years)	n	DXR-BMD (g/cm^2)	Percentage difference of DXR-BMD in comparison to next youngest age group	DXR-MCI	Percentage difference of DXR-MCI in comparison to next youngest age group
6–8	16	0.383 ± 0.031	–	0.319 ± 0.032	–
9–10	19	0.406 ± 0.027	+6.0	0.336 ± 0.024	+5.3
11–12	23	0.428 ± 0.041*	+5.4	0.349 ± 0.045*	+3.9
13–14	24	0.469 ± 0.063**	+9.6	0.358 ± 0.057**	+2.6
15–16	29	0.593 ± 0.051**	+26.4	0.452 ± 0.061	+26.3
17–18	39	0.617 ± 0.050**	+4.0	0.466 ± 0.058	+3.1

DXR values are presented as mean ± SD

DXR digital X-ray radiogrammetry, *DXR-BMD* bone mineral density, *DXR-MCI metacarpal index*, *SD* standard deviation

Student's t tests: significant differences between boys and girls (* $p < 0.05$, ** $p < 0.01$)

Table 2 Normative digital values for the DXR parameters BMD and MCI in 138 healthy girls

Calendar age group (years)	n	DXR-BMD (g/cm^2)	Percentage difference of DXR-BMD in comparison to next youngest age group	DXR-MCI	Percentage difference of DXR-MCI in comparison to next youngest age group
6–8	17	0.369 ± 0.051	–	0.325 ± 0.040	–
9–10	18	0.403 ± 0.033	+9.2	0.358 ± 0.047	+10.2
11–12	20	0.458 ± 0.054*	+13.6	0.379 ± 0.045*	+5.9
13–14	24	0.522 ± 0.044**	+14.0	0.444 ± 0.056**	+17.2
15–16	31	0.546 ± 0.047**	+4.6	0.461 ± 0.050	+3.8
17–18	28	0.565 ± 0.065**	+3.5	0.473 ± 0.064	+2.6

DXR values are presented as mean ± SD

DXR digital X-ray radiogrammetry, *DXR-BMD* bone mineral density, *DXR-MCI* metacarpal index, *SD* standard deviation

Student's t tests: significant differences between boys and girls (* $p < 0.05$, ** $p < 0.01$)

Table 3 Values for the DXR parameters BMD and MCI in 95 boys with distal radius fractures after adequate trauma

Calendar age group (years)	n	DXR-BMD (g/cm²)	Significance of difference compared to normative values (Student's t tests)	DXR-MCI	Significance of difference compared to normative values (Student's t tests)
6-8	12	0.380 ± 0.054	ns	0.312 ± 0.026	ns
9–10	15	0.400 ± 0.046	ns	0.321 ± 0.042	ns
11–12	19	0.422 ± 0.031	ns	0.324 ± 0.035	$p < 0.05$
13–14	18	0.455 ± 0.056	ns	0.330 ± 0.031	$p < 0.05$
15–16	21	0.545 ± 0.071	$p < 0.01$	0.410 ± 0.061	$p < 0.05$
17–18	10	0.572 ± 0.063	$p < 0.05$	0.425 ± 0.054	$p < 0.05$

DXR values are presented as mean $\pm$ SD

DXR digital X-ray radiogrammetry, *DXR-BMD* bone mineral density, *DXR-MCI* metacarpal index, *ns* not significant, *SD* standard deviation

Table 4 Values for the DXR parameters BMD and MCI in 69 girls with distal radius fractures after adequate trauma

Calendar age group (years)	n	DXR-BMD (g/cm²)	Significance of difference compared to normative values (Student's t tests)	DXR-MCI	Significance of difference compared to normative values (Student's t tests)
6–8	11	0.365 ± 0.016	ns	0.318 ± 0.013	ns
9–10	12	0.397 ± 0.016	ns	0.333 ± 0.035	ns
11–12	14	0.443 ± 0.054	ns	0.345 ± 0.050	$p < 0.05$
13–14	12	0.478 ± 0.057	$p < 0.05$	0.409 ± 0.041	$p < 0.05$
15–16	10	0.502 ± 0.062	$p < 0.05$	0.423 ± 0.044	$p < 0.05$
17–18	10	0.529 ± 0.098	ns	0.450 ± 0.067	ns

DXR values are presented as mean $\pm$ SD

DXR digital X-ray radiogrammetry, *DXR-BMD* bone mineral density, *DXR-MCI* metacarpal index, *ns* not significant, *SD* standard deviation

significantly higher DXR-BMD from 15 to 18 years of age (Tables 1 and 2). With regard to DXR-MCI, all female age groups between 6 and 18 years had higher reference values compared to the equivalent male cohorts; these differences reached significance for the age groups 11–12 and 13–14 years (Tables 1 and 2).

DXR values of patients with distal radius fracture

In general, lower values of DXR-BMD and DXR-MCI were seen in children and adolescents with distal radius fractures compared to the reference data across all six age groups. For boys, significant differences between the fracture group and reference cohort were observed from 15 to 18 years for DXR-BMD and from 11 to 18 years for DXR-MCI (Table 3). In comparison, significant differences in DXR-BMD between the fracture group and reference cohort were detected at earlier ages, from 13 to 16 years, in female patients (Table 4). DXR-MCI was significantly lower in girls with distal radius fractures vs. the corresponding reference data between the ages of 11 and 16 years (Table 4).

Comparing DXR-BMD and DXR-MCI in children suffering from distal radius fractures with age- and gender-matched

normative data by Z scores, the Z scores were below 0 for both male and female fracture groups. For boys, the mean Z scores were -0.42 (range -3.65 to $+3.11$, SD 1.31) for DXR-BMD and -0.51 (range -3.08 to $+3.75$, SD 1.26) for DXR-MCI. The mean Z scores for girls with distal radius fractures compared to the male fracture group were slightly but not significantly lower: Z score $= -0.46$ (range -3.34 to $+2.02$, SD 1.04) for DXR-BMD and Z score $= -0.53$ (range -2.24 to 2.04, SD 0.85) for DXR-MCI.

Among the 95 boys with distal radius fractures, 26 boys had reduced Z scores for DXR-BMD ≤ -1 (between -1 and -2: $n = 16$, 16.8 %; ≤ -2: $n = 10$, 10.5 %; Fig. 1). In 57 male patients (60.0 %), the Z scores for DXR-BMD were within one reference range, and in 12 boys (12.6 %), Z scores for DXR-BMD were above 1. The female fracture cohort presented a similar distribution of Z scores for DXR-BMD compared to the male patients (Fig. 1). With respect to DXR-MCI, more than two-thirds of male and female patients with distal radius fractures showed Z scores within one reference range (Fig. 2). Z scores for DXR-MCI were below -1 in 23 of 95 males (between -1 and -2: $n = 15$, 15.8 %; ≤ -2: $n = 8$, 8.4 %) and in 18 of 69 girls (between -1 and -2: $n = 13$, 18.8 %; ≤ -2: $n = 5$,

Fig. 1 Distribution of Z scores for bone mineral density (DXR-BMD) in 95 boys and 69 girls aged 6–18 years experiencing distal radius fractures, with values presented as percentages
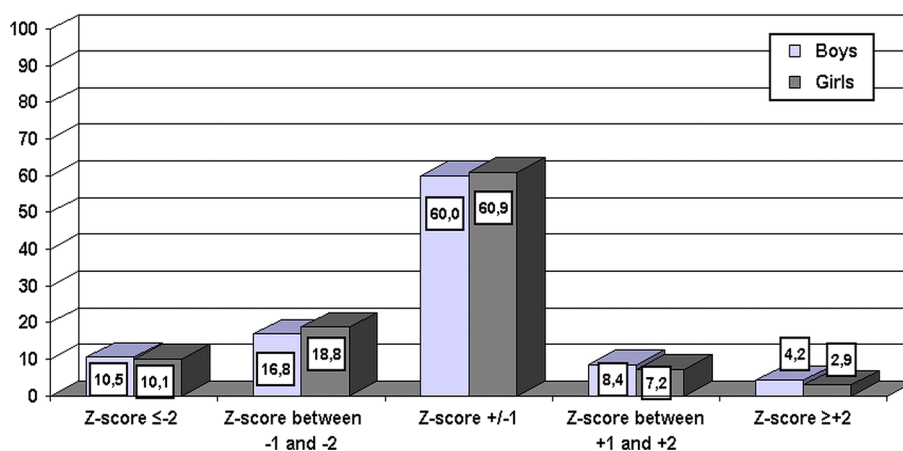
Fig. 2 Distribution of Z scores for metacarpal index (DXR-MCI) in 95 boys and 69 girls aged 6–18 years experiencing distal radius fractures, with values presented as percentages
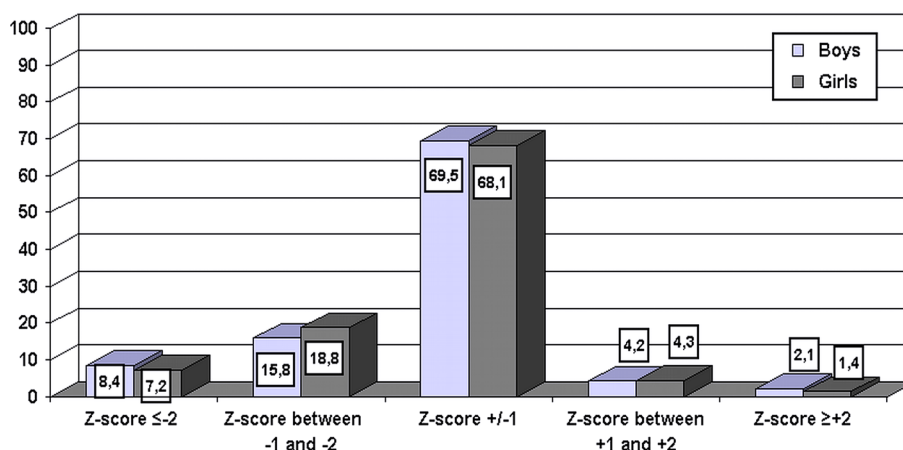
7.2 %). Increased Z scores for DXR-MCI ≥1 were found in six boys (between 1 and 2: $n = 4$, 4.2 %; ≥2: $n = 2$, 2.1 %) and in four girls (between 1 and 2: $n = 3$, 4.3 %; ≥2: $n = 1$, 1.4 %; Fig. 2).

Discussion

Potential of DXR in pediatric populations

The clinical relevance of osteoporosis in childhood and adolescence is gaining increasing attention, among others due to effective prevention strategies and new medical treatments [7, 9, 39, 40]. Bone densitometry can be an effective monitoring tool in pediatric populations for children and adolescents with increased fracture risk, e.g., due to chronic bone-affecting diseases or other factors influencing bone metabolism [13, 31–34]. However, all osteodensitometric methods were initially developed for adults, and thus present drawbacks and challenges for children and adolescents [13, 14, 34]. Digital X-ray radiogrammetry is a user-independent osteodensitometric method with high precision and reproducibility [24, 41]. One major advantage of DXR in pediatric

populations is the use of hand radiographs, which are often routinely performed in children—e.g., for estimation of skeletal age—without the need for additional radiation exposure for prospective or retrospective osteodensitometric analysis [30–34]. Furthermore, in contrast to DXA measurements, assessments using DXR seem to be only minimally affected by surrounding fat tissue [13, 14, 42]. In published investigations, DXR parameters have extensively been assessed with hand radiographs that had been printed out and subsequently scanned into the DXR system [24–35]. One benefit of the present study was the sole use of original digital images for direct osteodensitometric analysis, thereby avoiding possible noise-related and smearing effects during the printing process, variations due to differences in print and scanner resolution, or slight alterations in positioning during the scanning process [27, 41]. To our knowledge, this is the first trial, which evaluated the clinical value of DXR in children and adolescents using original digital hand radiographs.

Original digital DXR reference data

The original digital normative values were obtained from healthy boys and girls without fractures after adequate

trauma. The DXR-BMD and DXR-MCI normative values were comparable to published reference data generated from printouts, with subsequent scanning to the DXR system, including healthy Caucasian males and females aged 6–18 years [30, 33]. The higher DXR-BMD values in healthy girls vs. boys from 11 to 14 years found in our study is caused by the fact that puberty occurs earlier in girls [30, 33, 35]. In the reference cohorts published by van Rijn et al. [33] and Malich et al. [30], higher DXR-BMD was also observed for girls aged 11 to 14 years, with significant differences only at 11–12 years. In our trial, the increase of normative DXR-BMD was mostly accentuated in girls between 11 and 14 years and in boys aged 15–16 years, i.e., maximum elevation around pubertal growth. At higher age levels, male age groups showed higher DXR-BMD values than corresponding female cohorts, which is in concordance with published reference data [30, 33, 35]. The earlier age of puberty might also be one reason that women reach their peak bone mass—as estimated by DXR—between 30 and 34 years of age, compared to men with peak bone mass at 45–49 years of age [35]. The strong correlation between DXR-BMD and age in our study was similar to corresponding coefficients found by Malich et al. [30]: $r = 0.83$ (males) and $r = 0.84$ (females). The excellent correlation between DXR-BMD and DXR-MCI was also similar to the results of Malich et al. [30]: $r = 0.85$ (males) and $r = 0.86$ (females). These highly significant associations indicate that the fully digital DXR technique can be applied with clinical confidence in pediatric populations aged ≥6 years.

In all of our evaluated age groups, normative DXR-MCI was higher for females; these differences were significant between the ages of 11 and 14 years. Van Rijn et al. [33] also detected significantly higher DXR-MCI values for healthy girls vs. age-matched boys from 11 to 15 years. Similarly, Böttcher et al. [35] observed a tendency for higher reference DXR-MCI values in healthy premenopausal women vs. men within comparable age groups. The metacarpal index—the ratio of cortical thickness to outer metacarpal width—functions as a relative measurement of cortical bone thickness normalized to outer bone diameter, and is frequently used as a reliable quantification of cortical bone mass [38, 43]. Premenopausal women, therefore, appear to have relatively smaller outer bone diameter of metacarpal bones compared to cortical thickness [38, 43, 44]. According to our findings and those of van Rijn et al. [33], differences in DXR-MCI between boys and girls were not significant between 15/16 and 18 years, presumably due to the accentuated increase of cortical thickness associated with puberty in male adolescents [44]. As DXR-MCI is a relative parameter, its correlation to age was lower than that of DXR-BMD; our correlations obtained from original digital images were slightly higher than corresponding coefficients published by Malich et al. ($r = 0.63$ [boys] and $r = 0.68$ [girls]) [30] and van Rijn et al. ($r = 0.68$ [boys] and $r = 0.69$ [girls]) [33].

DXR values in the fracture cohort

The reference collective and the cohort with distal radius fractures originated from the same geographical region and were evaluated using the same technical parameters as well as inclusion and exclusion criteria. Clark et al. [45] performed a meta-analysis of 10 investigations, in which children with fractures were compared with age-matched control subjects. Their meta-analysis found an association between fracture risk and low BMD, which was assessed by DXA in eight trials and by pQCT and QUS in one study each. Lower DXR-BMD values were observed in fracture vs. age-matched control subjects in all age groups in our trial, with significant differences from 15 to 18 years for boys and from 13 to 16 years for girls. Goulding et al. [15] compared BMD, estimated by DXA, in 100 girls with distal forearm fractures vs. 100 Caucasian control females and measured significantly lower BMD in girls with fractures in an overlapping age group of 11–15 years at the following sites: lumbar spine (L2–L4), femur trochanter, and ultradistal radius [15]. In a longitudinal study of 601 children, Jones et al. [46] found a peak age of fracture incidence at 11–12 years for girls and 13–14 years for boys, with the greatest number of fractures in both genders occurring at the wrist/forearm. Children in these age groups with elevated fracture risk may show reduced bone mineral accrual, resulting in lower BMD at later ages. As accentuated increase of normative DXR-BMD occurs earlier in girls (ages 11–14 years) than in boys (ages 15–16 vs. 13–14 years), a substantially lower increase of DXR-BMD can lead to an observed difference between the fracture group and reference cohort in the higher age groups; thus, our findings are feasible.

Comparing DXR parameters of the fracture group with age- and gender-matched reference data using Z scores, the mean Z score for DXR-BMD was below 0. Van Rijn et al. [33] used DXR to evaluate 19 boys and 26 girls with a history of forearm fractures and found a mean Z score of -0.1 for boys and -0.5 for girls; however, the interval considerably varied between onset of fractures and acquisition of hand radiographs, ranging from 0 to 12 years [33]. Ryan et al. [17] compared 76 African American children with forearm fractures to 74 age- and gender-matched control subjects by using DXA and noted a lower mean whole-body Z score for BMD in the fracture cohort; this difference approached but did not achieve statistical significance ($p = 0.05$). In our trial, more than one-fourth of the children with distal radius fractures showed Z scores for DXR-BMD ≤-1, which is in accordance with published DXA findings.

In the study of Goulding et al. [15], 25 % of girls with distal forearm fractures had *Z* scores for DXA-BMD below −1 at the ultradistal radius of the non-fractured arm within six weeks of cast removal of the fractured arm, while *Z* scores below −1 were defined by the authors as osteopenia [15]. With a similar study design, Goulding et al. [16] compared 100 boys with distal forearm fractures to 100 control males, and found that 28 % of boys in the fracture group had *Z* scores for DXA-BMD at the ultradistal radius of ≤−1. With respect to BMD measurements, a certain number of children, approximately one-third to one-fourth of a pediatric population, seem to be prone to fractures. Data from large observational studies have revealed that approximately one-third of patients suffer from recurrent fractures in their childhood and adolescence, most often resulting from slight or moderate trauma [39, 47]. The use of osteodensitometry for the early identification of children with low *Z* scores and therefore increased fracture risk would address an important public health issue, as strategies for reducing further fractures and the incidence of osteoporosis can be initiated. Prevention strategies are important with regard to the fact that the incidence of fractures, particularly at the site of the distal forearm, has been increased in pediatric populations over the past decades [1, 4–6].

Advantages of our case–control study compared to published investigations were the standardized acquisition of bone parameters directly after the trauma, which avoided possible impacts due to immobilization or increased physical activity of the non-fractured extremity, as well as the separate analysis of DXR-MCI, and the inclusion of *Z* scores. In order to minimize bone-influencing conditions, strict exclusion criteria were defined that included previous fractures of the upper extremities, as the inclusion of children and adolescents with recurrent fractures of the upper limbs would likely increase the number of *Z* scores for DXR-BMD ≤−1. In comparison to DXR-BMD, DXR-MCI measurements among the fracture groups generally revealed lower SDs. Therefore, despite modestly lower mean *Z* scores for DXR-MCI, slightly fewer patients had *Z* scores ≤−1 for DXR-MCI. One reason for the lower SDs might be the fact that DXR-MCI is a relative parameter. Significantly lower DXR-MCI values were found for the fracture group at the ages of 11–18 years for boys and 11–16 years for girls. These findings are in concordance with the results of Ma and Jones [3], who assessed metacarpal index using morphometry, and measured significantly lower values for children aged 9–16 years with wrist and forearm fractures compared to age- and gender-matched control subjects; however, differences in metacarpal index values were not significant for children with upper arm fractures (higher distance to measurement localization) [3]. In this context, the major limitation of the DXR technique in assessing the peripheral metacarpal

bone, and not axial sites associated with high osteoporotic fracture risk in adults, may be of minor relevance for pediatric populations, in whom most fractures occur at the distal forearm/wrist. The excellent correlation of our findings with results of the widely used DXA technique as well as the advantages of DXR in pediatric populations provide promising clinical benefit of DXR in children and adolescents for identifying individuals with increased fracture risk, thereby addressing both individual and public health issues.

Study limitations

There were certain limitations of this investigation. First, DXR provides estimates only of cortical bone mineralization, not trabecular bone architecture. However, isolated cortical bone fractures occur more frequently in children compared to adults [1, 4–6]. Another limitation of our study was that the number in each age subgroup of the normative and fracture cohorts was small, although 452 children and adolescents were in total enrolled; to obtain a minimum of 10 subjects in each subgroup, age intervals of 2–3 years were used. Despite the small number of subjects in the subgroups, however, the relatively low SDs suggest reliable findings. The reference cohort, which did not experience a distal radius fracture after trauma (trauma severity similar to the fracture group), may had higher DXR-BMD and DXR-MCI values compared to the general Caucasian population aged 6–18 years, which could be a study bias. However, the normative fully digital DXR values were comparable to published reference data obtained from printouts with subsequent scanning to the DXR system [30, 33]. The DXR technique was initially developed for adults, and a minimum metacarpal size is required to correctly identify the cortical edges of the diaphysis [30]. Therefore, the DXR method does not provide reliable results in subjects aged <6 years, which limits the application of DXR in young children [30–34]. Furthermore, a greater number of hand radiographs are not recognizable by the automatic DXR system in pediatric populations, even for children over 6 years of age, compared to adults [30–34]. In our study, 10 hand radiographs in the fracture group (5.7 %) and 12 images in the reference cohort (4.0 %) could not be correctly analyzed by the fully digital DXR system, and these patients had to been excluded. Van Rijn et al. [33] described a failure rate of 4.3 % in 535 healthy Caucasian children and adolescents. Thus, further technological improvements are needed for a more reliable use of the DXR system in younger children. The BoneXpert device is a beneficial, computer-assisted tool for the automatic evaluation of bone age in pediatric populations. Several bone parameters, including metacarpal index, thickness, width, and length, can be determined, only the assessment

of BMD is actually not possible with this CAD method [44, 48]. Optimal adaptation of osteodensitometric techniques to pediatric populations is important, particularly for these CAD methods, which can be easily integrated into routine clinical diagnosis, in order to obtain as much information as possible in children and adolescents from radiographs, which have been acquired for clinical purpose.

Conclusions

The estimation of bone mineral density and metacarpal index in children with distal radius fractures yielded significantly different results, with lower DXR-BMD and DXR-MCI values compared to age-matched control subjects, who experienced no fracture after trauma of similar severity. The early identification of children and adolescents with reduced bone mineralization and bone mass can aid in preventing recurrent fractures and in reducing the risk of osteoporosis later in life. With further technological improvement, DXR might be used for routine screening—e.g., in the case of chronic bone-affecting diseases—in order to identify children at high risk of fracture and to initiate early preventive strategies, including medication and dietary regimens as well as increased physical activity.

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