The Development of Metaphyseal Cortex—Implications for Distal Radius Fractures During Growth

FRANK RAUCH,1 CHRISTINA NEU,1,2 FRIEDRICH MANZ,2 and ECKHARD SCHOENAU1

ABSTRACT

Fractures of the distal radial metaphysis are very common in otherwise healthy children. The reasons for this high fracture incidence are not entirely clear. To address this problem, we undertook a detailed analysis of distal radius development using peripheral quantitative computed tomography (pQCT) at a site 4% proximal to the radial articular surface. The study population comprised 337 healthy children and adolescents (aged 6–18 years; 171 girls) and 107 adults (aged 29–40 years; 88 women). Total volumetric bone mineral density (vBMD) remained stable at about 70% of the adult value between the ages of 6–7 years and 14–15 years in both genders. Cortical thickness increased little between 6–7 years and 12–13 years in girls and 14–15 years in boys. Strength-Strain Index (SSI; a parameter combining geometry and density) was still at only 20% of the adult value in girls aged 10–11 years and at 21% of the adult level in boys aged 12–13 years. At these ages, factors that contribute to the mechanical challenge to the distal radius in case of a fall (forearm length and body weight) had already reached 49% and 36% of the adult value in girls and boys, respectively. The shaping of the distal radius cortex (metaphyseal inwaisting) was assessed by analyzing the decrease in cross-sectional bone size between adjacent bone slices in a separate population of 44 children (aged 8–19 years; 26 girls). The rates of periosteal resorption and endocortical apposition were estimated to average 8 μm/day and 10 μm/day, respectively, during the growth period. In conclusion, during growth the increase in distal radius strength lags behind the increase in mechanical challenges caused by a fall, because metaphyseal cortical thickness does not increase sufficiently. The endocortical apposition rate is already very high at that site and apparently cannot be further increased to levels that would be necessary to keep bone strength adapted to the mechanical requirements. (J Bone Miner Res 2001;16:1547–1555)

Key words: children, cortex, fractures, metaphysis, radius

INTRODUCTION

The distal radius is the most frequent site of fractures during childhood and adolescence.1–8 Population-based studies from Europe,1,4,8,9 Asia,2,6 and North America5 universally found that the incidence of distal radius fractures depends on gender and age. Peak fracture incidence occurs at 10–12 years of age in girls and at 12–14 years in boys and is similar to that observed in postmenopausal women.1,5

The reasons for the high incidence of distal radius fractures in children and adolescents are not entirely clear. Most of these fractures occur after light trauma, typically after a fall during physical activity.3,8 The marked gender difference in fracture rates that was noted in the older studies may have been caused by the fact that boys traditionally were more engaged in sports activities than girls.4,8 As the activity patterns of boys and girls have become more similar, gender differences in fracture rates also have decreased.4,8 However, the marked variation with age cannot

1Childrens’ Hospital, University of Cologne, Cologne, Germany.
2Research Institute of Child Nutrition, Dortmund, Germany.
be explained simply by the frequency of accidents or risk-prone behavior.\(^{5,10}\) Consequently, bone fragility is commonly assumed to underlie distal radius fractures in children and adolescents.\(^{5,10}\)

The peak incidence of fractures at the distal radius occurs at or slightly before the time when peak height velocity is reached during the pubertal growth spurt.\(^{5,8,11}\) This observation has been related to the fact that peak height velocity occurs earlier than peak bone mass accrual.\(^{11-13}\) This dissociation between the growth curves for bone length and bone mass generally is thought to cause transient bone weakness.\(^{5,10-13}\)

However, there is little evidence from densitometric studies that the distal radius actually gets weaker during the pubertal growth spurt. Bone mineral content (BMC) and areal bone mineral density (BMD)—two parameters that are commonly thought to reflect bone strength—do not decrease at any time during childhood and adolescence.\(^{5,14-16}\) It has been noted that the ratio between metaphyseal and diaphyseal areal BMD reaches a nadir at the time when distal radius fracture rates are highest.\(^{16}\) Yet, this is not caused by a decrease in areal BMD at the metaphyseal site, but rather a more rapid increase at the diaphysis. Higher diaphyseal than metaphyseal areal BMD does not in itself explain high fracture rates at the distal radius.

These studies were limited to the analysis of parameters reflecting bone mass. However, bone cross-sectional strength is not only determined by mass but also by geometry.\(^{17,18}\) A given amount of material will increase the strength of a structure more if it is located farther from the center of the structure.\(^{18}\) Both aspects of bone strength can be measured by peripheral quantitative computed tomography (pQCT) and can be conveniently combined into a single number, the so-called Strength-Strain Index (SSI).\(^{19}\) The SSI has been shown to provide a good estimate of the mechanical strength of the human radius.\(^{20,21}\)

Whether a bone will break in a given situation does not only depend on bone strength, but also on the mechanical forces that are applied to the bone.\(^{22}\) The force applied to the distal radius in a fall is proportional to body weight. In addition, the strain in the bone tissue depends on bone length. Following the beam theory, a given force causes greater deformation when a structure is longer, and whole bone strength is inversely related to bone length.\(^{23}\) Thus, whether a fall on the outstretched arm results in a fracture or not depends on the balance between bone strength on one side and the product of body weight and forearm length on the other.

To understand the developmental changes in distal radius strength, the situation of metaphyseal bone during longitudinal growth has to be considered. As long as bone length increases, new bone is added continuously at the junction between growth plate and metaphysis.\(^{24}\) At the opposite end of the metaphysis all trabeculae are removed and the cortex is integrated into the diaphysis. As the growth plate proceeds in a distal direction, a section of newly created metaphyseal bone continues to decrease its diameter by periosteal resorption until it has reached the cross-sectional size of the diaphysis (metaphyseal inwaisting). This inwaisting process can be assessed by pQCT when two closely spaced sections of metaphyseal bone are analyzed.

In this study we examined the normal development of bone mass, geometry, and strength at the radial metaphysis using pQCT. In addition, we analyzed the relationship between distal radius bone strength and the mechanical challenges to which it is exposed in case of a fall. Finally, metaphyseal inwaisting was estimated to develop a quantitative model of distal radius development.

**MATERIALS AND METHODS**

**Subjects**

The healthy study population comprised 346 children and adolescents from 6 to 18 years of age as well as those of their parents who were below 40 years of age (\(n = 107\); aged 29–40 years; 88 women and 19 men). Five children had to be excluded from the present analysis because of motion artifacts during the measurement run. Results of four boys were excluded because a significant amount of trabeculated cortex interfered with the analysis of cortical bone at the proximal radius. Thus, 337 children and adolescents (171 girls and 166 boys) were included in the following evaluation. The children were participants in the Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study, an ongoing observational study investigating the interrelations of nutrition, growth, and metabolism in healthy children. pQCT was performed to establish reference data for this technique.\(^{25}\) Forearm length was measured at the nondominant side as the distance between the ulnar styloid process and the olecranon using a caliper. The stage of pubertal development was determined by physical examination using the grading system defined by Tanner for pubic hair.\(^{26}\) Examination for pubertal stage was refused by 24 boys and 24 girls.

Metaphyseal inwaisting could not be evaluated in the population described previously but was studied in a separate group of children and adolescents. This population comprised 44 ambulatory outpatients (26 girls and 18 boys) aged 8–19 years (mean ± SD, 14.7 ± 3.1 years) who were treated at the University Children’s Hospital of Cologne, Germany. pQCT analysis was performed to evaluate the possibility of a secondary bone disorder. The primary diagnoses were anorexia nervosa (\(n = 14\)), epileptic disorder necessitating anticonvulsant therapy but with an otherwise normal neurological status (\(n = 19\)), and phenylketonuria under dietetic therapy (\(n = 11\)). All of these patients had a height within 2 SD around the mean for age and gender. Thus, the longitudinal growth process was not disturbed in these subjects and therefore metaphyseal inwaisting was considered to be close to normal.

Informed consent was obtained from the children’s parents or from the subjects aged more than 17 years. The study protocol was approved by the Ethics Committee of the University of Cologne and by the Bundesamt für Strahlenschutz (Federal Agency for Protection from Radiation, Salzgitter, Germany).
pQCT

pQCT analysis in the healthy group was performed at the nondominant forearm using a technology (XCT 2000; Stratec, Inc., Pforzheim, Germany) described earlier.\(^{25}\) The scanner was positioned on the distal forearm and a scout view was carried out to position the scanner at the site on the radius in which distance to distal radial articular surface corresponded to 4% of forearm length. A single tomographic slice of 2.0-mm trans-sectional thickness was taken at a voxel size of 0.4 mm. Image processing and the calculation of numerical values was done using the manufacturer’s software package (version 5.40). Parameters determined at the distal radius were cross-sectional area, BMC, total volumetric BMD (vBMD), trabecular vBMD, and SSI. Cortical thickness was derived mathematically. The cross-sectional area of the radius was determined after detecting the outer bone contour at a threshold of 280 mg/cm\(^3\). BMC represents the mass of mineral per millimeter slice thickness. Total vBMD was defined as the mean mineral density of the total cross-section. Using the equipment’s default settings, trabecular vBMD was determined as the mean mineral density of the 45% central area of the bone’s cross-section. This geometric definition of trabecular bone includes some margin of safety to exclude admixture of cortical bone to the trabecular region of interest. The actual relative cross-sectional area of the trabecular compartment is considerably larger than 45%,\(^{27}\) but the resolution of the pQCT system is not sufficient to trace exactly the border between trabecular and cortical bone. The SSI is defined as the sum of the products of section modulus and vBMD of each voxel normalized to the maximal physiological vBMD of human bones (Fig. 1A).\(^{28}\) Voxels from the entire bone cross-section are integrated. Therefore, the SSI reflects the combined strength of trabecular and cortical bone.

**Determination of cortical vBMD at the proximal radius**

Cortical vBMD cannot be determined at the distal radius with the pQCT system used in this study because the spatial resolution is insufficient. Therefore, cortical vBMD was assessed at the radial diaphysis. The scanner was positioned at the site of the radius in which distance to the distal radial articular surface corresponded to 65% of forearm length. Cortical bone was identified at a threshold of 710 mg/cm\(^3\). Cortical vBMD was determined as the mean volumetric density of cortical bone. As a consequence of incomplete filling of voxels at the bone edges (partial volume effect), cortical vBMD is underestimated in cortices that are thinner than 2.5 mm.\(^{29}\) If cortical thickness is below this value, pQCT results for cortical vBMD increase with cortical thickness, even if the actual mineral density of the cortical compartment remains unchanged.\(^{30,32}\) Because cortical thickness at the proximal radius is below 2.5 mm in most children under 14 years of age and in many adults (C. M. Neu, F. Rauch, F. Manz, E. Schoenau, unpublished observations, 2000), adjustment for cortical thickness is necessary. This was done by statistical methods (see Statistical Analysis section).

**Cortical bone analysis at the distal radius**

The cortex at the distal radius is considerably thinner than at the proximal radius.\(^{27}\) For this reason, the partial volume effect not only affects the determination of cortical vBMD, but also of distal radius cortical thickness.\(^{30,32}\) To avoid this problem, an algorithm was developed that allows the calculation of cortical thickness at the distal radius from results that are less influenced by the partial volume effect. This algorithm is based on three simplifying assumptions. First, the analyzed section through the distal radius was postulated to be composed of two homogeneous compartments, trabecular and cortical bone (Fig. 1B). Second, the radial cross-section was assumed circular. Third, cortical vBMD was assumed identical at the distal and proximal sites.

In mathematical terms, the first of these assumptions can be translated into the following formula:

\[
\text{total vBMD} = \text{relative cortical area} \times \text{cortical vBMD} + (1 - \text{relative cortical area}) \times \text{trabecular vBMD} \quad (1)
\]
where relative cortical area is the fraction of the entire bone’s cross-section consisting of cortical bone (Fig. 1B). Eq. (1) can be reformulated to

relative cortical area
\[ = \frac{\text{total vBMD} - \text{trabecular vBMD}}{\text{cortical vBMD} - \text{trabecular vBMD}}. \tag{2} \]

Following the second assumption, outer and inner radii (Fig. 1B) correspond to

outer radius = \((\text{cross-sectional area} / \pi)^{1/2}\); \tag{3}

inner radius = \((\text{trabecular bone area} / \pi)^{1/2}\). \tag{4}

The area of the bone’s cross-section occupied by trabecular bone is

trabecular bone area = \((1 - \text{relative cortical area}) \times \text{cross-sectional area}\). \tag{5}

Substituting Eq. (4) for trabecular bone area, inner radius can be calculated as

inner radius = \([ (1 - \text{relative cortical area}) \times \text{cross-sectional area} / \pi ]^{1/2}\). \tag{6}

Cortical thickness is the difference between outer and inner radius. Substituting Eq. (2) for relative cortical area, cortical thickness can be calculated from Eqs. (3) and (6) as follows:

cortical thickness = \((\text{cross-sectional area} / \pi)^{1/2}\) - \([ (1 - \text{total vBMD} - \text{trabecular vBMD}) / (\text{cortical vBMD} - \text{trabecular vBMD}) ] \times \text{cross-sectional area} / \pi \]^{1/2}. \tag{7}

Cortical vBMD was assumed to be identical to the age- and gender-specific mean value of adjusted cortical vBMD at the proximal radius. For example, to calculate distal radius cortical thickness in an 11-year-old girl, the adjusted mean value of proximal radius cortical vBMD in the female 10- to 11-year age group was used.

The reproducibility of primary and derived pQCT parameters was determined in a group of 9 healthy adult volunteers (all women, aged 34–56 years) by performing the measurement twice, with repositioning of the forearm. Reproducibility was not tested in children because it was judged unethical to perform repeated analyses involving ionizing radiation in children solely for methodological purposes. The precision error was calculated as root-mean-square SDs of the duplicate measurements, as proposed by Glüer et al. Reproducibility was 1.40% for cross-sectional area, 0.91% for BMC, 1.49% for total vBMD, 0.82% for trabecular vBMD, 2.70% for cortical thickness, 5.39% for SSI, and 0.68% for cortical vBMD.

**Statistical analyses**

Results in children and adolescents were analyzed separately for both genders in age groups spanning 2 or 3 years (for the oldest group) and in pubertal stage groups. To allow for easy comparison of the developmental changes in all parameters, results were converted to percentages of the result in adults of the same gender. Paired or unpaired t-tests were used for comparisons between two groups, as appropriate. The significance of differences between more than two groups was calculated by analysis of variance (ANOVA). The differences of individual age and pubertal stage groups to the adult group were tested for significance using Bonferroni’s adjustment for multiple comparisons. Mean values for proximal radius cortical vBMD in all age groups were adjusted for proximal radius cortical thickness by multiple classification analysis after one-way ANOVA. This adjustment was performed separately for the two genders. Cortical thickness was entered first as a covariate; age or pubertal stage group was entered as main effect. To evaluate the age dependency of metaphyseal inwaisting, Pearson’s correlation coefficients were calculated. All calculations were performed using the SPSS software (version 6.0 for Windows; SPSS, Inc., Chicago, IL, USA).

**RESULTS**

Figure 2 shows the results of pQCT analyses as a percentage of the values obtained in adults. In all age groups of both genders, cross-sectional area was closer to the adult value than BMC \((p < 0.01\) in each age group; Fig. 2A). Consequently, total vBMD was lower in children and adolescents than in adults (Fig. 2B). Up to 14–15 years of age, total vBMD remained stable at about 70% of the adult value in both genders but increased rapidly thereafter. In contrast, trabecular vBMD did not vary with age in females \((p = \ldots\).
0.21) and increased only slightly after 15 years of age in males (Fig. 2B). This suggested that total vBMD was lower in children and adolescents than in adults mainly because they had relatively less cortical bone.

Indeed, cortical thickness remained unchanged at about 0.5 mm from 6 to 13 years of age in girls and from 6 to 15 years in boys, amounting to roughly 40% of the adult value (Fig. 2C). A rapid increase in cortical thickness occurred after these ages. SSI was still at only 20% of the adult value in girls aged 10–11 years, and at 21% of the adult level in boys aged 12–13 years (Fig. 2C). In most age groups, adjusted cortical vBMD (measured at the proximal radius) was significantly lower in children than in adults, but the difference was small (Fig. 2C). The lowest results for adjusted cortical vBMD were obtained in girls at 6–7 years (89% of the adult value) and in boys in the age groups 6–7 years and 14–15 years (95% of the adult value each).

Analogous analyses were performed for the variation of these parameters with pubertal stage (Fig. 3). In both genders, total vBMD (Fig. 3B) and cortical thickness (Fig. 3C) did not change significantly until after pubertal stage 4. SSI showed no significant change between pubertal stage 1 and 3 in girls and between pubertal stage 1 and 4 in boys.

Forearm length appeared to increase linearly between 6 and 12 years in girls and from 6 to 14 years in boys (Fig. 4). The slopes of the corresponding regression lines indicated a similar “length velocity” in both genders (1.07 cm/year in girls and 1.06 cm/year in boys). The variation with age in the product of forearm length and body weight was shown in Fig. 5A as a percentage of the result in adults. Compared with the SSI at the distal radius, the product of forearm length and body weight was closer to the adult value throughout childhood and adolescence ($p < 0.05$ in each group). This shows that during this time of life bone strength at the distal radius lags behind the mechanical challenges caused by a fall.

To evaluate more precisely the adaptation of distal radius strength to the mechanical challenges in the event of a fall, we analyzed the ratio between SSI and the product of forearm length and body weight. For convenience, this ratio was named Strength/Weight Index. The Strength/Weight Index was significantly lower in children and adolescents from 6 to 15 years of age than in adults (Fig. 5B). Boys between the age of 10 and 15 years had a significantly lower Strength/Weight Index than boys who were younger or older. In girls, the decrease in Strength/Weight Index from 6–7 years to 10–11 years of age did not achieve statistical significance. Strength/Weight Index did not vary significantly between pubertal stages 1 and 4 when both genders were analyzed separately. Yet, the power to detect differences was limited by the small number of subjects in pubertal stages 2–4. When both genders were analyzed
together, the Strength/Weight Index was significantly lower in pubertal stage 3 than in pubertal stages 1 and 5. Two-way ANOVA of these data showed that gender differences were not significant either for age or pubertal stage groups (p > 0.2). The interaction term was highly significant between age group and gender (p < 0.001) but not between pubertal stage and gender. This suggested that the age variation in the Strength/Weight Index differed between girls and boys because of differences in the timing of pubertal development.

The study on metaphyseal inwaisting showed that the outer radius of the bone’s cross-section decreased by 0.34 ± 0.10 mm when moving 1 mm closer to the diaphysis. The degree of metaphyseal inwaisting was not associated with age (p = 0.33) and did not differ between genders (p = 0.20).

**DISCUSSION**

The development of metaphyseal cortex has received little attention until now. Most of the current knowledge on human cortical bone development derives from studies that examined diaphyseal bone.(34–36) Metaphyseal cortex is more difficult to study because it is thinner than diaphyseal cortex and its thickness changes markedly from the growth
plate to the diaphysis. Furthermore, metaphyseal cancellous bone interferes with the analysis of the cortex when methods are used that rely on two-dimensional projection images of a bone. However, even when cross-sectional images are analyzed with currently available pQCT systems, insufficient spatial resolution does not allow direct assessment of the thin metaphyseal cortex.

To circumvent this technical problem, we developed an algorithm to determine cortical thickness at the distal radius indirectly. To keep the calculations reasonably simple, it was assumed that the distal radius cross-section is circular in shape. This simplification obviously carries some error, because the cross-section of the distal radius is wider in the lateral direction than in the anteroposterior direction. To estimate the maximal magnitude of the error, cortical thickness was recalculated using the “extreme” alternative assumption that the radial cross-section is a rectangle with one side twice as long as the other. Thus calculated, the absolute values for cortical thickness were 18% lower than when the circular model was used, but the results relative to the adult value (as shown in Figs. 2C and 3C) differed by 0.2% at most (data not shown).

A second assumption for the algorithm was that cortical vBMD at the distal radius is similar to that at the radial diaphysis. This assumption is unlikely to carry an error of more than a few percent, because direct studies of bone samples have found little variation in cortical vBMD between various skeletal sites. Possibly, cortical vBMD is slightly higher at the metaphyseal site than at the diaphyseal site during growth. The development of metaphyseal cortex is so fast that it probably consists mainly of primary (unremodeled) bone, in which density is about 10% higher than that of remodeled bone. If this is correct, our algorithm will slightly overestimate cortical thickness in children. In any case, our results for adults are in agreement with other studies using different methods.

This study shows that the development of bone mass and strength at the distal radius lags behind the increase in the mechanical factors that challenge bone stability in the event of a fall. This is not caused by lack of trabecular bone development, because trabecular vBMD hardly changes during childhood and adolescence. External bone size increases throughout childhood and adolescence, but this does not strengthen the bone sufficiently to keep pace with the increase in forearm length and body weight. The reason for sluggish bone development at the distal radius appears to lie in the fact that cortical thickness remains unchanged from 6 to 13 years in girls and from 6 to 15 years in boys. The consequence is a particularly vulnerable period around pubertal stage 3, corresponding to about 11 years of age in girls and 13 years in boys. Thus, the key question to understand the increased fragility of the distal radius at that age is, Why does the metaphyseal cortex not thicken during this time of rapid growth?

The results of this study allow some quantitative estimates of distal radius growth (Fig. 6). The site of pQCT analysis is located approximately 6–8 mm proximal to the growth plate, depending on forearm length. As estimated from our cross-sectional data, forearm length increases by about 1 cm/year during the growth period, which is in accordance with other studies. Because the distal growth plate contributes approximately 90% of this growth in length, the growth plate/metaphysis junction proceeds at a speed of roughly 9 mm/year. Consequently, the bone that was analyzed by pQCT was situated at the growth plate/metaphysis junction 8–11 months earlier. During this time cortical thickness must have increased from 0 to about 0.5 mm, corresponding to a rate of increase of 0.55–0.75 mm/year (1.5–2.0 μm/day).

The rate of periosteal resorption can be estimated based on the substudy on metaphyseal inwaisting. The radius of the bone’s cross-section at the 4% site decreased by 0.34

![FIG. 5.](image-url)
mm for each millimeter of increase in distance from the growth plate. Assuming a similar longitudinal growth rate as in the group of healthy children, this corresponds to a periosteal resorption rate of 0.34 mm/year × 9 mm/year = 3 mm/year or 8 μm/day. As noted before, endocortical apposition not only “compensates” this periosteal resorption but also increases cortical thickness at a rate of 1.5–2.0 μm/day. Thus, the endocortical apposition rate at the distal radius metaphysis should be about 9.5–10 μm/day. This rate of apposition on the inner surface of the metaphyseal cortex is extremely high compared with apposition rates at other sites of the growing skeleton. For example, the external size of long bone diaphyses increases by periosteal apposition, which typically is in the order of 0.5–0.8 μm/day.\(^{14}\) Thus, bone formation rate on the endocortical surface of the distal radial metaphysis is more than an order of magnitude higher than on the periosteal surfaces of long bone diaphyses.

In summary, bone strength at the distal radius lags behind the increase in mechanical challenges during growth because cortical thickness fails to increase. Rapid endocortical apposition is necessary just to keep metaphyseal cortical thickness constant. During phases of increased growth, endocortical apposition apparently cannot be increased further to levels that would be necessary to keep bone strength adapted to the mechanical challenges.

ACKNOWLEDGMENTS

We are indebted to the entire staff of the Research Institute for Child Nutrition for continuing support. The technical support of Stratec, Inc. is gratefully acknowledged.

REFERENCES


Address reprint requests to:
Frank Rauch, M.D.
Shriners Hospital for Children
1529 Cedar Avenue
Montreal, Quebec H3G 1A6, Canada

Received in original form September 8, 2000; in revised form December 30, 2000; accepted February 6, 2001.