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Nicoletta Zamberlan
Giorgio Radetti
Claudio Paganini
Davide Gatti
Maurizio Rossini
Vania Braga
Silvano Adami

Evaluation of cortical thickness and bone density by roentgen microdensitometry in growing males and females

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S. Adami (✉)
Cattedra di Reumatologia,
Ospedale di Valeggio,
I-37067 Valeggio (Verona), Italy
Fax: +39 +45 7950188

N. Zamberlan · D. Gatti · M. Rossini
V. Braga · S. Adami
Cattedra di Reumatologia,
Università degli Studi di Verona, Italy

G. Radetti · C. Paganini
Divisione di Pediatria,
Ospedale Civile di Bolzano, Italy

Abstract The bone mineral content (BMC) and the cortical thickness at the distal radius and at the II metacarpal were assessed in growing individuals (167 females and 158 males) by radiometric and quantitative roentgen microdensitometric methods. BMC adjusted for age and pubertal status was significantly higher in males than in females. However, the BMC corrected for bone volume (volumetric bone density, g/cm^3) and the metacarpal cortical index (cortical area/total area) were identical in males and females. BMC rose progressively with age, approaching a plateau by the end of puberty. Lower but still significant increases with age were also observed for volumetric bone density of the metacarpus and the metacarpal index. These increases were also most marked by the end of pubertal maturation and might be related to diminution of bone turnover.

Conclusion This study provides the normative data of bone mass in growing individuals by making use of a reasonably accurate and easily available technique. The results obtained indicate that most of the differences between males and females and the changes with age are related to changes in skeletal dimension rather than density.

Key words Bone mineral content · Children · Cortical thickness · Puberty · Roentgen microdensitometry

Abbreviations *BD* bone density · *BMC* bone mineral content · *BMCr* bone mineral content of ultradistal radius · *CV* coefficient of variation · *DEXA* dual-energy X-ray absorptiometry · *MI* metacarpal index · *QCT* quantitative computed tomography · *vBD* volumetric bone density

Introduction

Osteoporotic fractures are related to bone mass and density (BD), which depend on both the rate of bone loss with ageing and the bone mass present around the fourth decade of life. The latter basically coincides with the peak bone mass attained at maturity. Its variance is such that it may explain a large proportion of osteoporotic risk in postmenopausal women [12].

The variance in peak bone mass is explained not only by hereditary factors but also by intercurrent diseases, dietary habits, physical exercise and hormonal status, which are susceptible to some kind of intervention. This potential intervention is conceivable only if normative data on growing individuals are available.

The densitometric methods are precise but scarcely available. Another common problem in interpreting data from bone mass measurements arises in children with growing skeletal size, since densitometric methods evaluate the bone mineral content (BMC) but not the volumetric density. This can be measured accurately only by quantitative computed tomography (QCT), which cannot be used extensively in children for its cost and for the excessive X-ray exposure.

We have studied in a large number of growing children the bone status by radiometric methods and quantitative roentgen microdensitometry of metacarpus and ultra-distal radius with a method based on X-ray pictures which are routinely obtained for the assessment of skeletal age. In this study we assess the accuracy and the precision of the method and generated normative values for growing individuals.

Patients and methods

The X-ray of the non-dominant wrist of 167 females and 158 males aged 3–21 years were studied. The subjects were recruited from the local department of radiology among the healthy children undergoing skeletal age evaluation during a routine health survey of a scholar population. The protocol was approved by the Ethical Committee of the Bolzano Hospital.

Informed consent was obtained from the children's parents or from the subjects aged more than 18 years. All subjects were healthy and they had physical activity appropriate for age. The mean daily calcium intake was assessed by a dietary questionnaire and was more than 800 mg in all participants. Furthermore, none were taking drugs known to interfere with calcium metabolism. Clinical characteristics of the subjects are reported in Table 1. All subjects were within two standard deviations of the means for height and weight. They were subdivided according to a questionnaire answered by the parents and from a sexual inspection in two groups according to the appearance of menarche for girls (81 out of 167) and Tanner stage [19] > (66 out of 158) or ≤ 3 for boys. They were defined as prepubertal (stage 1), early pubertal (stage 2–3) and mid to late pubertal (stage 4–5). No child showed advanced or delayed sexual development according to chronological age. Bone age was evaluated according to the atlas of Greulich and Pyle [11]; none of the subjects below the age of 18 showed a difference of more than 1 year between chronological and bone age.

The radiographs were taken with a graduated aluminium reference standard calibrated versus a hydroxyapatite phantom positioned at the level of the styloid processes (Fig 1). The X-ray pictures were analysed by making use of a technical device (Radiometer, NIM, Verona, Italy) developed in our laboratory. With this technique the radiographic images are "captured" by a video camera and the grey levels of the digitalised image can be quantified against the reference standard. This allows a more accurate measurement of the cortical area based on an objective method (threshold grey gradient) and the evaluation of BD, which appear to be significantly related with dual energy X-ray absorptiometry (DEXA) measurements [1].

With this method we measured the outer diameter (D), the inner diameter (d), the length of the II metacarpus and the bone mineral content (BMCm) and the real bone density (BDm) of its middle region. The instrument allowed also the evaluation of the bone mineral content (BMCr) and the width (w) of the ultra-distal radius. The density measurements were not carried out when the distance between the aluminium phantom and the region of interest was above 3 cm.

Assuming a circular sectional area of both the metacarpus and the ultra-distal radius, the following parameters were calculated:

- Metacarpal Index (MI) [3] = $(D^2–d^2)/D^2$
- Medullary Area = $(d/2) \times (d/2) \times 3.14$
- Metacarpal Cortical Area = $(D/2) \times (D/2) \times 3.14$–MA
- Ultra-distal Radius Area = $(w/2) \times (w/2) \times 3.14$
- Bone Mineral Content correct for the cross-sectional area (volumetric BMC, volumetric BD (vBD) =
  - BMCm/MCA, for mid-metacarpus
  - BMCr/URA, for ultra-distal radius

Table 1 Weight and height in 167 (n = number) girls and 158 boys expressed as mean ± SD

Age	Girls			Boys		
	n	Weight (kg)	Height (cm)	n	Weight (kg)	Height (cm)
3– 5	22	16.7 ± 1.6	103 ± 4	17	16.4 ± 3.0	104 ± 8
6– 8	18	24.6 ± 9.5	122 ± 13	14	24.2 ± 9.4	120 ± 15
9–11	58	33.4 ± 8.3	137 ± 12	39	38.9 ± 9.0	142 ± 12
12–14	33	46.5 ± 9.3	154 ± 13	52	47.3 ± 8.0	152 ± 12
15–17	18	56.0 ± 9.1	156 ± 4	28	52.0 ± 5.6	167 ± 13
> 17	18	58.2 ± 7.4	160 ± 9	8	64.0 ± 6.0	173 ± 4

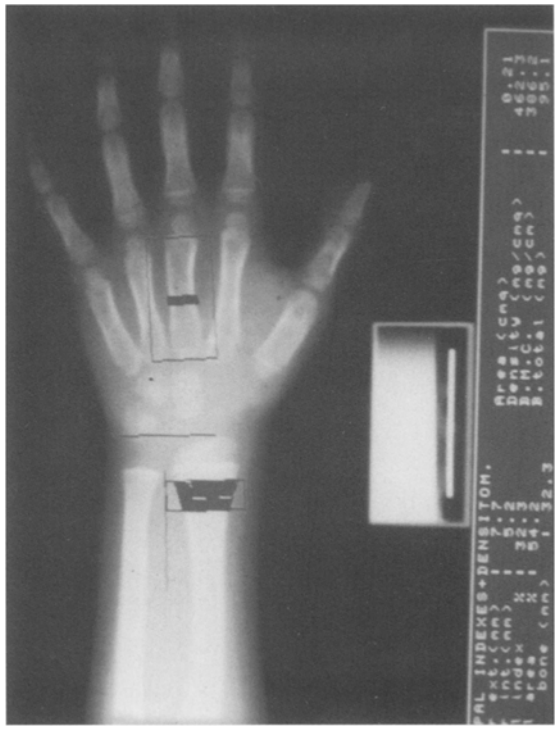

Fig. 1 Example of radiometric and microdensitometric analysis of hand digitalised X-ray

The coefficient of variation (CV%) was evaluated in 58 subjects in whom standard X-rays of the hands were taken in two different laboratories, 1–4 weeks apart from one an other, by adopting the formula for paired measurements proposed by Slosman et al. [18]. The CV within the same X-ray was 1.5%, 1.1% and 1.8% for the MI, metacarpal BD and radial BD respectively. The CV between the two X-ray pictures was 5%, 5.1%, 6.5% for metacarpal index, metacarpal volumetric BD and radial volumetric BD respectively [1]. In 19 subjects a lateral-oblique X-ray of the radius and of the second metacarpus were also taken. This allowed the calculation of the volumetric density by dividing the BMC by both bone width and depth. This data correlated linearly very well with the volumetric density calculated assuming a circular cross-sectional area of the two bone segments, with an intercept and a slope very close to zero and one respectively.

The differences between females and males were evaluated by analysis of covariance (age was the covariate). Simple and multiple regressions were carried out between age as independent vari-

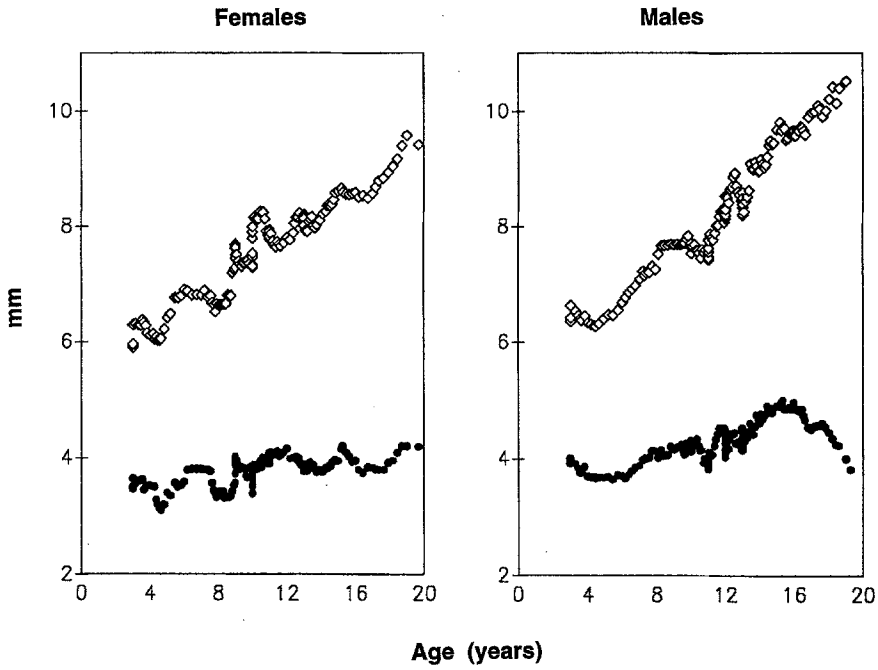

Fig. 2 Moving averages of inner (●) and outer (◇) diameter of mid-metacarpus in growing females and males. Each symbol represents the average of five values ordered according to increasing age (Computer program Stagraph, Inc. USA)

Table 2 Medullary area, cortical area and length of II metacarpus (left hand) in study subjects (median and 10–90 percentiles)

Age	Girls				Boys			
	n	Med area (mm^2)	Cort area (mm^2)	Length (mm)	*n*	Med area (mm^2)	Cort area (mm^2)	Length (mm)
3– 5	22	9.6 (5.7–12.5)	20.1 (15.0–25.6)	37.7 (33–84.1)	17	11.3 (7.1–13.8)	20.4 (18–25.5)	37.4 (33–41.3)
6– 8	18	10.4 (7.5–16.6)	24.6 (18.6–38)	45.6 (40–55.1)	14	11.6 (8.9–17.3)	27.8 (22–34.5)	45.6 (37–50.4)
9–11	58	11.9 (7–18.08)	33.8 (26.5–45)	54.05 (48.4–62)	39	13 (8.5–18.8)	32.5 (23.9–44)	54.5 (46–59.7)
12–14	33	12.2 (7.5–15.8)	38.6 (29–48.9)	58.2 (52–62.8)	52	15.8 (8–23.9)	39.8 (30.3–57)	59 (51–65.5)
15–17	18	12.2 (4.2–19.6)	43.5 (39–49.9)	60.4 (57–67.6)	28	17.3 (6–26.7)	56.5 (44.7–70)	66.3 (62–73.6)
> 17	18	11.5 (5.4–16.6)	54.4 (43–63.4)	62.8 (55–66.5)	8	15.9 (4.9–37.8)	67.5 (49.7–97)	69.2 (61.5–80)

able and all bone measurements as dependent variables. For all statistical tests, significance was defined as $P < 0.05$ (Statgraph, USA) after correction for the number of the tests.

Results

Sex differences in bone mass parameters

The outer diameter, inner diameter, length of the II metacarpus, calculated medullary and cortical area of the II metacarpus (Fig. 2, Table 2) were significantly higher in males than in females after adjustment for age ($P < 0.05$). However, when the subjects were divided according to their pubertal status (pre- and postpubertal status), the radiogrammetry indices were significantly higher in males after puberty only.

The MI (Fig. 3) was not significantly different in the two sexes. The BMC (mg/cm) could not be measured in 54 and 78 subjects due to inaccurate positioning of the aluminium phantom. The BMC was significantly higher in postpubertal males at mid-metacarpus ($P < 0.05$) and was higher in males both before and after puberty at the ultra-distal radius ($P < 0.05$).

BMC corrected for sectional area (vBD) (Tables 3, 4) was identical in both sexes both at the metacarpus and ultra-distal radius irrespective of puberty.

Changes in bone measurements with age

The outer diameter and the cortical area rose with age in both males and females both before and after puberty. The

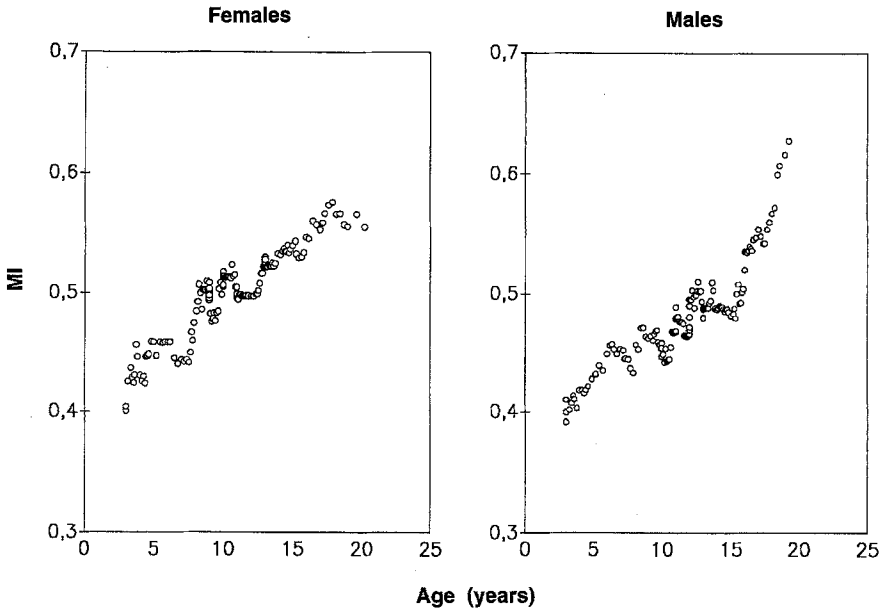

Fig. 3 Moving averages of the MI (D^2–d^2/D^2) in growing females and males. Each symbol represents the average of five values ordered according to increasing age (Computer program Stagraph, Inc. USA)

Table 3 BMC and vBD at the metacarpal site in study subjects (median and 10–90 percentiles)

Age	Girls			Boys		
	n	BMC (mg/cm)	vBD /mg/cm^3)	*n*	BMC (mg/cm)	vBD /mg/cm^3)
3– 5	11	130 (99–282)	655 (480–1398)	13	117 (96–166)	560 (517–694)
6– 8	15	182 (122–250)	678 (515– 783)	11	193 (156–241)	673 (587–776)
9–11	49	229 (182–290)	680 (554– 800)	35	233 (189–295)	657 (566–808)
12–14	28	276 (200–386)	744 (605– 899)	46	273 (233–391)	675 (578–770)
15–17	15	345 (272–420)	764 (613– 943)	22	372 (316–519)	717 (626–817)
> 17	18	416 (380–507)	819 (728–1045)	8	485 (378–594)	718 (609–790)

Table 4 BMC and vBD at the radial site in study subjects (median and 10–90 percentiles)

Age	Girls			Boys		
	n	BMC (mg/cm)	vBD /mg/cm^3)	*n*	BMC (mg/cm)	vBD /mg/cm^3)
3– 5	7	473 (285– 519)	183 (138–226)	3	554 (475– 736)	199 (187–249)
6– 8	15	548 (355– 731)	181 (136–326)	10	568 (402– 718)	194 (158–232)
9–11	45	695 (463– 959)	182 (136–225)	33	726 (543– 923)	176 (150–232)
12–14	28	852 (472–1141)	170 (139–266)	43	996 (678–1273)	185 (155–222)
15–17	12	994 (802–1170)	176 (140–205)	25	1280 (956–1704)	177 (151–216)
> 17	18	1221 (850–1550)	177 (160–213)	8	1446 (815–1767)	186 (140–209)

inner diameter and the medullary area rose significantly up to puberty, afterwards a decreasing trend was observed in both sexes which was statistically significant only in males ($r = 0.21$, $P < 0.05$).

In Table 5 the significant functions relating the bone measurements with age are shown. All indices of bone mass rose with age. The data were analysed by adopting several regression models. The best correlation coefficients were, as expected, exponential or multiplicative in all cases. The BD was significantly related with age only at the metacarpus, in both females and males, whereas the volumetric radial BD did not significantly change with age.

Discussion

Radiographic absorptiometry and radiogrammetry have been the only techniques for assessing bone status in the past, but they were completely neglected when photon and X-ray absorptiometry became available. More recently [1, 5, 15, 22], the development of computed analysis of digitalized X-ray pictures has increased the attention towards an easily available and inexpensive technique. With the apparatus developed in our laboratory a evaluation of cortical thickness and of bone density at several sites can be obtained. This is particularly advantageous in children where the X-ray of the hand also provides useful information regarding skeletal age.

Table 5 Correlation functions and percent variance explained (R) between age (= x) and bone measurements (= y)

MI		
Females	Log y = 0.01x – 0.40	R = 19.8
Males	Log y = 0.01x + 0.48	R = 18.5
All	Log y = 0.01x – 0.44	R = 18.2
Radial BMC		
Females	$y = 4.95x^{0.68}$	R = 52.6
Males	Log y = 0.08x + 5.7	R = 59.5
All	$y = 4.83x^{0.76}$	R = 51.6
Volumetric radial BD		
Females		ns
Males		ns
All		ns
Metacarpal BMC		
Females	Log y = 0.06x + 4.7	R = 67.1
Males	Log y = 0.08x + 4.5	R = 70.7
All	Log y = 0.07x + 4.69	R = 66.9
Volumetric metacarpal BD		
Females	$y = 5.93x^{0.25}$	R = 32.1
Males	$y = 6.1x^{0.14}$	R = 17.5
All	$y = 6x^{0.2}$	R = 24.7

The visual measurements of internal and external diameters for the evaluation of MI of long bones is tedious, time-consuming, observer-dependent and it has poor intra-observer reproducibility, ranging from 3.1% [7] up to 11% [16], which precludes its use for sequential evaluations. The availability of an automated computerised radiogrammetry of the metacarpus circumvents these drawbacks by decreasing the coefficient of variation to less than 2% [1], a value comparable to that observed with similar techniques by others [8].

In this study we have shown that bone mass measurements (cortical areas and BMCs) are significantly higher in males than in females at any age or pubertal phase. Similar results have been obtained by quantitative roentgen microdensitometry [21], single photon absortiometry [6] and by DEXA [4]. However, in all circumstances the so called BD values were obtained by dividing BMC for the projected area (areal BD, mg/cm^2) which is still dependent upon bone dimensions. In this study we have shown that females and males have superimposable values of both VBD (radial and metacarpal volumetric BD) and index of cortical thickness (MI), which are unrelated or corrected for bone dimensions. These findings indicate that the female disadvantage over males at completion of skeletal maturation, if any, might be related to inappropriate peak bone mass rather than peak bone density, which has been found also identical by QCT [10].

Our knowledge on the processes leading to accumulation of bone by healthy children and adolescents is almost exclusively based on densitometric techniques but little attention is usually paid to bone dimensions. We have shown that the metacarpal periosteal diameter continuously rises during growth. The medullary cavity widens up to the age of puberty. Afterwards it decreases and the MI achieves the value as found in young adults [1]. A similar series of changes in medullary cavity was also observed by Garn et al. [9]. This is accompanied by increases in medullary cavity by the age of puberty when the MI achieve the values found in young adults [1].

BMC and projected density at the level of both radius and metacarpus rose with skeletal maturation. Similar changes have been observed in densitometric studies of the lumbar spine in adolescents from 10 to 16 years of age [4, 20]. However, neither single nor dual-energy absortiometric techniques measure true BD or vBD (g/cm^3), since they usually adjust bone mineral to bone width or to bone area (g/cm or g/cm^2 respectively) but not to bone volume (area × bone depth). Because of that, larger bones will have higher measurements then smaller bones with equal density.

We have shown that estimated vBD of the radius remained constant from age 3 to age 21. These results emphasise the need, in evaluating the so called peak bone mass, to distinguish the changes in bone mass from the changes in the real BD.

The appendicular skeleton is largely made of compact bone but the ratio between cortical area and medullary cavity changes with skeletal maturation and there is a large interindividual variability. Thus, we have corrected the BMC of mid-metacarpus for the cortical area rather than the total cross-sectional area. By doing this we have been able to provide a reasonable measurement of the real cortical density despite the inevitable imprecision related to the assumption that the metacarpal is a cylinder.

We have shown that the real density of the cortical bone of the metacarpus (metacarpal vBD) rises with skeletal maturation. This increase is less apparent than that observed in bone mineral content and areal BD, but it is still significant. Similar results have been recently reported by Kröger et al. [14] who measured the vBD at the femoral neck in a longitudinal study in peri-adolescents subjects. This increase in cortical density might be derived from the changes in bone turnover occurring after puberty and associated with changes in remodelling space, osteoid tissue and low density bone [17]. In growing individuals bone turnover is high but it rapidly decreases to normal adult, premenopausal levels, a few years after puberty [13] with consequent increase in BD.

We have been unable to substantiate this hypothesis at the level of the radius, where we could not find significant changes in vBD with age. This is somewhat surprising since most of the bone of the ultra-distal radius is trabecular and much more sensitive to changes in turnover. Previous studies by QCT [10] and by DEXA [14] have shown that the density of trabecular spine bone increases by about 11% and 7% respectively at the time of puberty.

A possible explanation for our incapacity to reproduce these results at the ultra-distal radius level might be an inadequate precision of the microdensitometric method we have used. A further source of error derives from the theoretical assumption that the proportion of cortical over total bone is constant. This assumption might be imprecise, since trabecular bone is surrounded by a narrow border of cortical bone which makes up half of the total bone mass [2]. Thus, even small changes in the relative proportion of cortical bone substantially changes the averaged volumetric density.

In conclusion, the results of this study indicate that skeletal growth is mainly related to bone enlargement and relative diminution of medullary cavity in appendicular skeleton, whereas vBD is identical in males and females and it increases after puberty as a result of slowing bone turnover. The normative data provided in this study may be used for a reasonably accurate and convenient evaluation of the skeletal status in growing individuals.

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