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Original Article

Hylonome

# Peripheral quantitative computed tomography of the proximal radius in young subjects – New reference data and interpretation of results

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**Abstract**

The aim of this contribution is to provide reference data for peripheral quantitative computed tomography (Stratec XCT2000®) performed at the proximal radius (the so-called '65% site') of young subjects and to discuss the interpretation of such analyses. Data from a previous reference data study on 469 subjects between 6 and 40 years were re-analyzed and smooth curves were fitted. The corresponding equations allow for calculation of age-, height- and sex-specific z-scores of total cross-sectional area, cortical cross-sectional area, bone mineral content, cortical bone mineral density, total bone mineral density, Strength-Strain Index, muscle cross-sectional area and the ratio between bone mineral content and muscle cross-sectional area. These data should facilitate the clinical use of peripheral quantitative computed tomography in young subjects.

**Keywords:** Bone Geometry, Bone Mineral Density, Bone Size, Children, Peripheral Quantitative Computed Tomography

Peripheral quantitative computed tomography (pQCT) is gaining popularity in the field of pediatric bone disorders. This technique analyzes cross-sectional images of long bones, which allows for evaluation of bone size, shape and mineral density. To use pQCT for the diagnosis and follow-up of pediatric bone disorders it is essential to have detailed reference data for the site of measurement.

We have previously published results of pQCT analyses at the proximal radius in healthy children, adolescents and young adults[1-5]. Results were given as mean and standard deviations of two-year age groups. Although this is a simple way of displaying such data, this method of presentation is not ideal for clinical use, because the mean and standard deviations may change considerably between successive age groups. When a patient's test results are compared to such reference data, the interpretation of the result as 'normal' or 'low' can differ markedly, depending on whether the patient is slightly younger or slightly older than the cut-off age between two age groups. It is preferable to present reference data in a way that avoids discontinuities. We have recently presented such improved reference data for pQCT measurements at the distal radius[6]. In the present contribution, we update the reference material concerning the proximal radius.

Whatever method of bone densitometry is used, it is important to interpret results in light of bone physiology. The present contribution therefore has a twofold aim. First, to present new and easily usable reference material for pQCT at the proximal radius of young subjects, and second, to provide a framework for the interpretation of results.

## Subjects and methods

### Subjects

As described previously in detail, the study population comprised 469 healthy children, adolescents and young adults[2]. The children and adolescent group (defined as an age below 21 years) included 166 males and 184 females. The young adult group (21.0 to 39.9 years of age) was comprised of 30 men and 89 women. All subjects of the present analysis were either participants of the DONALD (Dortmund Nutritional and Anthropometric Longitudinally Designed) Study or parents of participants. The DONALD Study is an

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| | Periosteal Apposition | Intracortical Remodeling | Endocortical Apposition | Endocortical Resorption |
|---|---|---|---|---|
| Total CSA | ↑ | ↔ | ↔ | ↔ |
| Cortical CSA | ↑ | ↔ | ↔ | ↓ |
| BMC | ↑ | ↓ | ↑ | ↓ |
| Total vBMD | ↑ | ↓ | ↑ | ↓ |
| Cortical vBMD | ↔ | ↓ | ↔ | ↔ |
| Strength-Strain Index | ↑ | ↓ | ↑ | ↓ |

CSA: cross-sectional area; BMC: bone mineral content; vBMD: volumetric bone mineral density

**Table 1.** Relationship between pQCT parameters at the 65% site of the radius and metabolic processes in bone tissue.

ongoing observational study investigating the interrelations of nutrition, growth and metabolism in healthy children. This study is performed at the Research Institute for Child Nutrition in Dortmund, Germany. The cohort was initially recruited for an anthropometric study in a representative sample of school children of Dortmund and later through personal recommendation of parents whose children were already participating. Overall, the study population mostly comprised middle class families and all participants were of Caucasian origin. On an annual basis, all participants undergo a full medical history and examination starting in infancy.

Height was determined to the next succeeding 1 mm using a Harpenden stadiometer. Age at testing was calculated to two decimals. Forearm length was measured at the non-dominant forearm as the distance between the ulnar styloid process and the olecranon using a caliper. Informed consent was obtained from the children's parents or from the subjects aged 18 years or older. In addition, written assent was also obtained from subjects between 14 and 17 years of age.

## Peripheral quantitative computed tomography

Peripheral QCT was performed at the proximal forearm using the Stratec XCT2000® equipment (Stratec Inc., Pforzheim, Germany). Measurements were performed at the non-dominant forearm. The scanner was positioned on the proximal forearm at a site whose distance to the ulnar styloid process corresponded to 65% of forearm length ('65% site'). A single tomographic slice of 2.0 mm thickness was taken at a voxel size of 0.4 x 0.4 x 2 mm. The speed of the translational scan movement was set at 15 mm/s. Image acquisition, processing and the calculation of numerical values were performed using the manufacturer's software package (XCT 5.40). The cortex of the radial diaphysis was analyzed at a threshold of 710 mg/cm$^3$ using the software's CORTBD routine. For the determination of the Strength-Strain Index a threshold value of 480 mg/cm$^3$ was used. Voxels peripheral of the bones' outer edges with an absorptiometric density between 20 and 60 mg/cm$^3$ were interpreted as representing muscle.

The reproducibility of primary and derived pQCT parameters was determined in a group of 9 healthy adult volunteers (all women; aged 34 to 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 standard deviations of the duplicate measurements, as proposed by Glüer et al[7]. Reproducibility was 1.41% for total cross-sectional area (CSA), 0.95% for cortical CSA, 1.15% for bone mineral content (BMC), 0.95% for total volumetric bone mineral density (vBMD), 0.68% for cortical vBMD, 3.23% for Strength-Strain Index, 1.93% for muscle CSA.

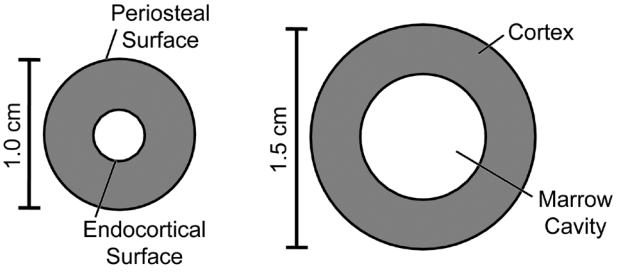
## Interpretation of individual pQCT parameters

**Total Cross-Sectional Area.** Total CSA is the area of the entire bone cross-section, thus comprising both cortical bone and the marrow cavity. This is a measure of the outer bone size. The same information can be gleaned from another pQCT parameter, 'periosteal perimeter', which is mathematically derived from total CSA by assuming the bone cross-section is circular. As total CSA is directly measured whereas periosteal perimeter is a calculated value, we find it more logical to use total CSA as a measure of outer bone size.

Outer bone size is a key determinant of diaphyseal bending strength, which makes total CSA one of the most important parameters of a pQCT analysis. Total CSA at the 65% site of the radius is influenced by only one physiological process, periosteal apposition, and therefore its interpretation is straightforward (Table 1).

**Cortical CSA.** Cortical CSA represents the surface area of the cortical bone cross-section. This is equivalent to total CSA minus the cross-sectional size of the marrow cavity. Cortical CSA is determined by the activities of the bone cells on its outer (periosteal) and its inner (endocortical) surface (Table 1).

**Volumetric Cortical Bone Mineral Density.** Cortical vBMD represents the density of the solid cortex. It is sometimes erroneously presumed that cortical vBMD is equivalent to material density, i.e., the degree of mineralization of




| | | |
|---|---|---|
| Cortical vBMD | 100% | 100% |
| Cortical Thickness | 100% | 100% |
| Total Diameter | 100% | 150% |
| Total CSA | 100% | 225% |
| Cortical CSA | 100% | 153% |
| Bone Mineral Content | 100% | 153% |
| Section Modulus | 100% | 290% |
| Total vBMD | 100% | 68% |

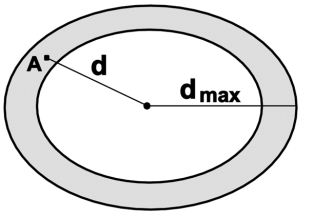
**Figure 1.** Schematic cross-sectional view of two long bone diaphyses. The two bones have the same cortical thickness and cortical volumetric bone mineral density (vBMD), but the diameter of the right bone is 50% larger. Consequently, the total cross-sectional area (CSA) of the right bone (i.e., the area encircled by the periosteal surface) is more than twice as large as in the left bone. Cortical CSA (i.e., the area between the periosteal and endocortical surfaces) and bone mineral content are about 50% higher in the right bone. Section modulus (a parameter reflecting resistance to bending forces) is almost three times higher in the right bone, even though the total vBMD is lower by almost a third. This example highlights the fact that total vBMD of a long bone diaphysis is a biomechanically irrelevant measure.

the bone matrix. However, cortical vBMD not only reflects material density but also cortical porosity[8,9].

Conceptually, cortical vBMD is a very attractive parameter. In the absence of a mineralization defect (osteomalacia), cortical vBMD should be mainly influenced by intracortical remodeling. Intracortical remodeling decreases cortical vBMD, because remodeling replaces old (and therefore higher density) material with new (lower density) bone material. In addition, more active intracortical remodeling activity leads to higher cortical porosity, which also lowers cortical vBMD.

Unfortunately, the utility of cortical vBMD is often limited by a technical issue, the partial volume effect[10]. Due to incompletely filled voxels at the periosteal and endocortical borders of the cortex, the 'real' cortical vBMD may be underestimated. The extent of the underestimation will be greater in thinner cortices, because these have a higher surface to volume ratio than thicker cortices. As a result of this technical problem, pQCT results for cortical vBMD increase with cortical thickness, even if the mass of mineral per unit volume of the cortical compartment remains identical. Consequently, the age-dependent reference values for cortical vBMD are only useful if cortical thickness is normal for age. Possibly, the utility of cortical vBMD measures could be increased by using an algorithm that is meant to eliminate the influence of the partial volume effect, but this has not yet been tested in children[11].

**Bone Mineral Content.** BMC in the setting of pQCT analyses represents the mass of mineral per unit of axial bone




$$\text{Polar moment of inertia} = \Sigma(d^2 \times A) \quad [mm^4]$$

$$\text{Section modulus} = \frac{\Sigma(d^2 \times A)}{d_{max}} \quad [mm^3]$$

$$\text{SSI} = \frac{\Sigma(d^2 \times A \times vBMDvox/vBMDmax)}{d_{max}} \quad [mm^3]$$

**Figure 2.** Definitions of polar moment of inertia, section modulus and Strength Strain Index (SSI). A schematic view of a bone's cross-section is shown. The polar moment of inertia is the sum of the bone-filled voxel areas multiplied by the square of this distance for each voxel. The section modulus is the ratio between the polar moment of inertia and the maximal distance of a bone-filled voxel from the center. A=cross-sectional area of a voxel; d=distance of the voxel from the center of gravity; vBMDvox=volumetric density bone mineral density in the voxel (mg/cm$^3$); dmax=maximum distance of any of the voxels of the cortical cross-section from the center of gravity; vBMDmax=maximum mineral density under physiological conditions (1200 mg/cm$^3$)[25].

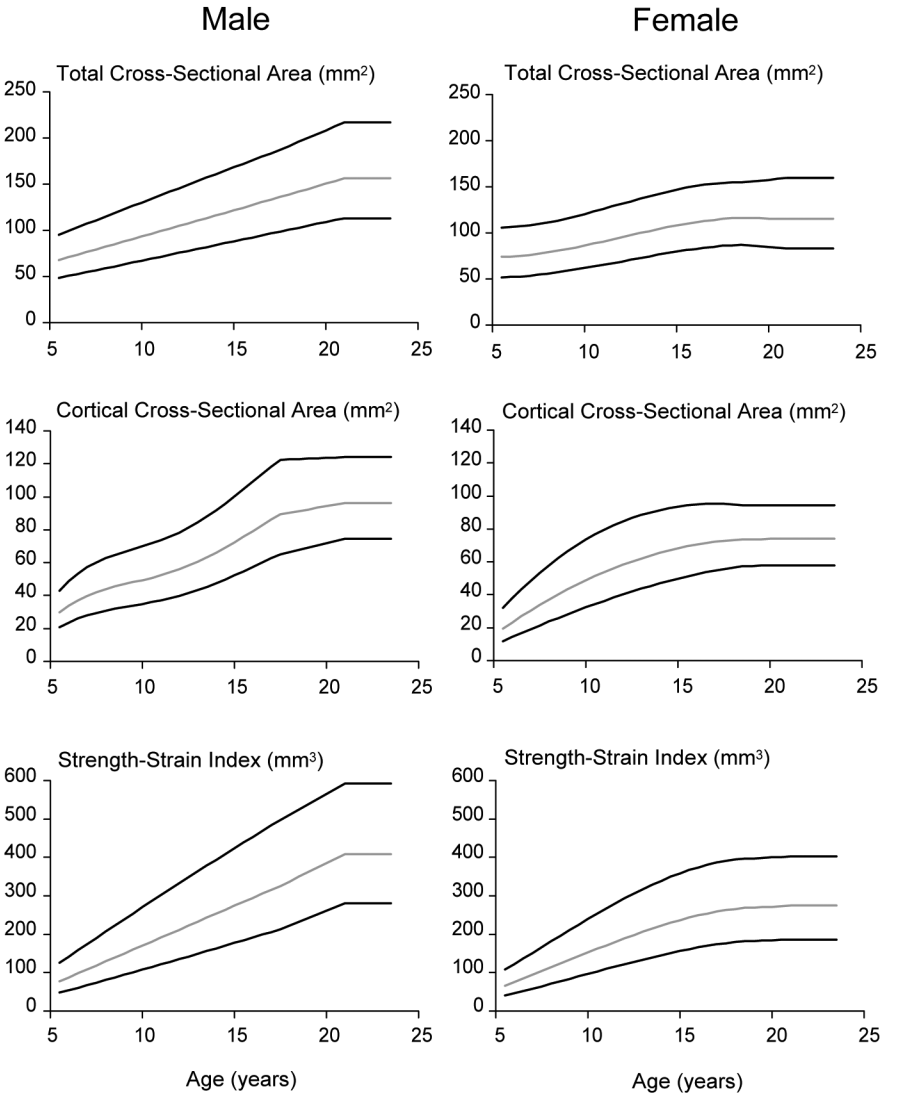



**Figure 3.** Age-dependent reference ranges for pQCT results of proximal radius (65% site) structure. Shown are the mean (gray middle line) and the range of 2 standard deviations around the mean (black lines).

length. It is therefore given in units such as mg/mm. Thus, a BMC result of 80 mg/mm means that a bone slice of 1 mm thickness contains 80 mg of mineral. It should be noted that this definition of BMC is different from that used in dual-energy X-ray absorptiometry, where BMC usually refers to the amount of mineral in the entire bone regions studied and thus is in addition influenced by bone length or the size of the region of interest. BMC at the 65% site of the radius is influenced by processes on all three cortical surfaces (Table 1).

**Total Volumetric Bone Mineral Density.** Total vBMD is defined as the ratio between BMC and the total cross-sectional area of a bone. In diaphyseal bone, bone mineral is present only in the cortex. Therefore, total vBMD represents the product of two factors, cortical vBMD and the ratio between cortical CSA and total CSA[8]. As this ratio varies more than cortical vBMD during normal bone development, it is the main determinant of total vBMD. The current metabolic bone literature is strongly focused on parameters that can be labeled as 'density', and therefore total vBMD is often seen as a somehow very important value. Whatever the merits of total vBMD may be, it should be noticed that it can not be expected to be a good indicator of bone strength (Figure 1).

**Strength-Strain Index.** The Strength-Strain Index is closely related to the polar moment of inertia and the section modulus. The definitions for all three parameters are shown in Figure 2. All three measures use the distance of bone-filled voxels from the center of the bone. The polar moment of inertia and section modulus are standard parameters in mechanics that describe the strength of elongated structures. In con-

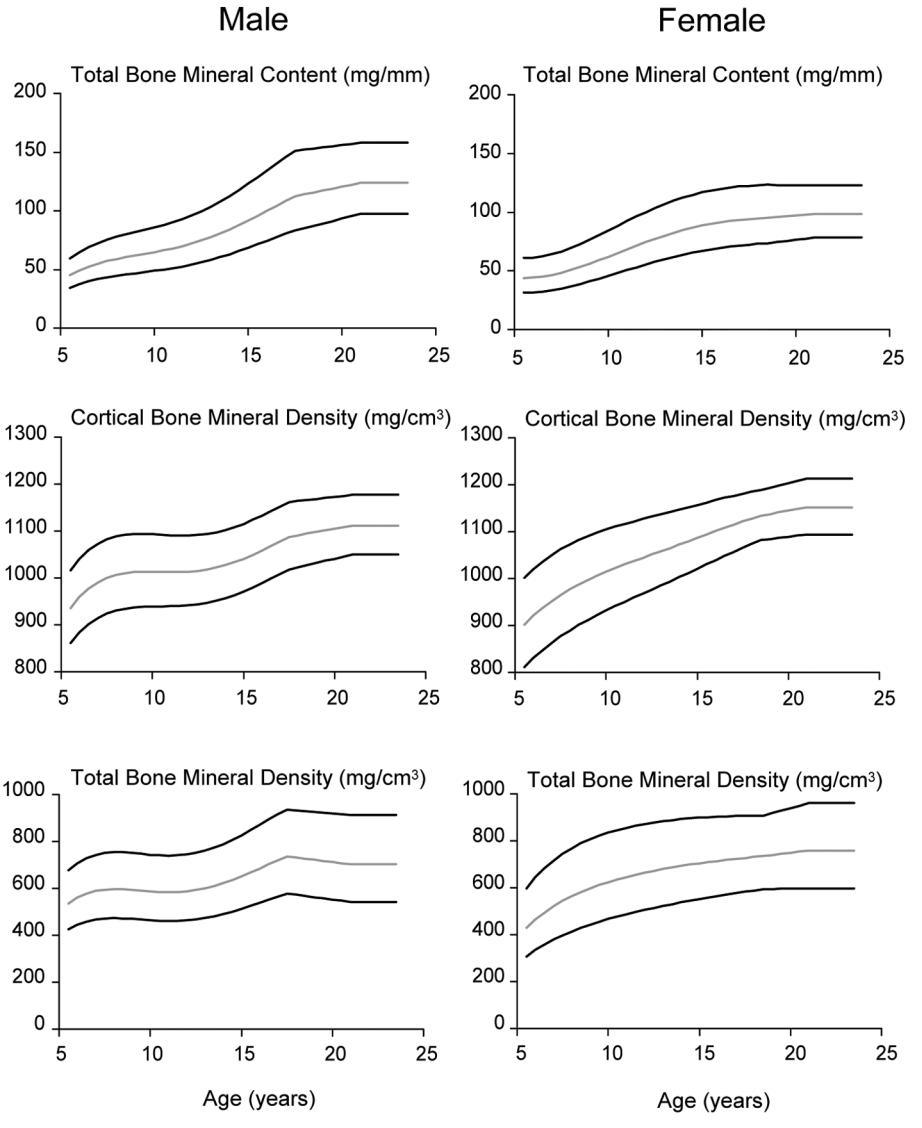



**Figure 4.** Age-dependent reference ranges for pQCT results of proximal radius (65% site) mass and densities. Shown are the mean (gray middle line) and the range of 2 standard deviations around the mean (black lines).

trast, the Strength-Strain Index has been specifically developed for the use of pQCT analysis and represents the section modulus weighed by the density of each voxel. The Strength-Strain Index thus combines a geometrical parameter of bone strength (section modulus) with a measure reflecting the properties of cortical bone tissue (cortical vBMD). It is therefore influenced by the same metabolic processes as the measures from which it is derived (Table 1). The use of Strength-Strain Index as a parameter of bone strength has been validated in both animal and human studies[12-14].

**Muscle Cross-Sectional Area.** In addition to these bone measures, pQCT allows for the determination of muscle CSA[3]. Measurements in 317 subjects from 6 to 40 years of age showed that the circumference at the 65% site averaged 99.5% of the maximum circumference of the forearm[3]. Therefore, the pQCT analysis at that location reflects the maximal CSA of the forearm musculature. The maximal CSA of a muscle is a surrogate marker of muscle force, which in turn provides the largest physiological loads on the skeleton. It thus becomes possible to evaluate the relationship between muscle and bone.

**Bone Mineral Content/Muscle CSA.** We have proposed this ratio as an indicator of the muscle-bone unit[15]. The underlying idea is that BMC in the cross-section is a surrogate measure of bone strength in uniaxial compression, whereas muscle CSA reflects muscle force. The ratio between the two should therefore indicate whether bone strength is adequately adapted to muscle force. One might

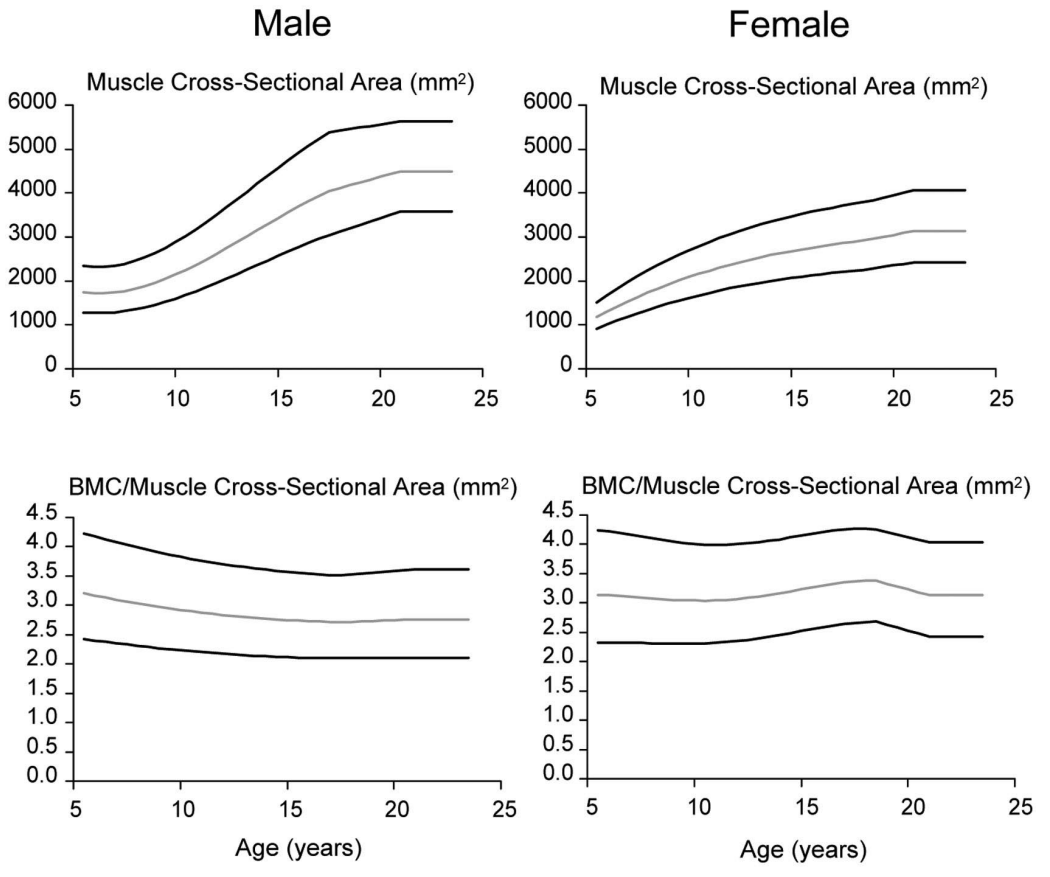



**Figure 5.** Age-dependent reference ranges for pQCT results of muscle size and muscle-bone relationship at the 65% site of the forearm. Shown are the mean (gray middle line) and the range of 2 standard deviations around the mean (black lines).

argue that it would be more logical to use the Strength-Strain Index rather than BMC as a measure of bone strength. However, the idea of proposing the BMC/Muscle CSA ratio was to develop a concept that was adaptable to other densitometric methods, such as DXA. From that perspective, BMC offered the advantage of being a very basic densitometric parameter that can be determined with a variety of techniques.

## Statistical analyses

Cole's LMS method was used to derive age- and sex-dependent reference data[16]. This method assumes that the data can be transformed to a normal distribution by a suitable power transformation (L). The distribution is then summarized by the median (M) and the coefficient of variation (S). The present data were skewed towards higher values, but were normally distributed after logarithmic transformation, which in the LMS system corresponds to a L of 016. Therefore, the value of L was fixed to 0 for all analyses, and only median and coefficient of variation need to be modeled to derive reference ranges.

Age-dependent regression curves for M and S were independently fitted for girls (from 6.0 to 18.5 years) and boys (from 6.0 to 17.5 years). The different age ranges for the sexes were due to the difference in availability of data. Height-dependent regression curves were established for heights ranging from 115 cm to 175 cm in girls and from 115 cm to 185 cm in boys. Linear, exponential, logarithmic and hyperbolic simple regression models, as well as polynomials of the second, third and fourth order were tested. The relationship with age was assumed to be linear, unless one of the other models yielded an adjusted coefficient of determination ($r^2$) which was higher by at least 0.03. In this case, the model with the maximum coefficient of determination was chosen. For the adult age range from 21 to 40 years, none of the pQCT parameters showed significant changes with age. Therefore, M and S were calculated as constant values. Very few data were available between 18.5 and 21 years in females (N=13) and between 17.5 and 21 years in males (N=11). For this age range, reference ranges were therefore obtained by linear interpolation between the endpoints of the regression curves (values at 18.5 years for females, at 17.5 years for males) and the 'adult' result.

| | S | M |
|---|---|---|
| **6.0 to 18.5 years** | | |
| Total CSA ($mm^2$) | 0.1951–0.002806 x age | 95.41-9.295 x age+1.161 x $age^2$-0.03233 x $age^3$ |
| Cortical CSA ($mm^2$) | 0.2991–0.009419 x age | -31.52+10.78 x age-0.2756 x $age^2$ |
| Strength-Strain Index ($mm^3$) | 0.2635–0.003721 x age | -6.876+7.305 x age+1.391 x $age^2$-0.05305 x $age^3$ |
| BMC (mg/mm) | 0.1825–0.002901 x age | 122.3-33.75 x age+4.707 x $age^2$-0.2327 x $age^3$+0.003924 x $age^4$ |
| Total vBMD ($mg/cm^3$) | 0.1918–0.004643 x age | 864.1-2399/age |
| Cortical vBMD ($mg/cm^3$) | 0.06491–0.002244 x age | 457.6+137.1 x age-13.48 x $age^2$+0.6514 x $age^3$-0.01170 x $age^4$ |
| Muscle CSA ($mm^2$) | 0.1254–0.0002685 x age | -605.5+402.7 x age-15.58 x $age^2$+0.2218 x $age^3$ |
| BMC/Muscle CSA | 0.1645–0.002651 x age | 2.144+0.4880 x age-0.08203 x $age^2$+0.005418 x $age^3$-0.0001197 x $age^4$ |
| **21 to 40 years** | | |
| Total CSA ($mm^2$) | 0.1631 | 115.2 |
| Cortical CSA ($mm^2$) | 0.1224 | 74.01 |
| Strength-Strain Index ($mm^3$) | 0.1922 | 274.1 |
| BMC (mg/mm) | 0.1133 | 98.10 |
| Total vBMD ($mg/cm^3$) | 0.1183 | 757.9 |
| Cortical vBMD ($mg/cm^3$) | 0.02595 | 1152 |
| Muscle CSA ($mm^2$) | 0.1287 | 3135 |
| BMC/Muscle CSA | 0.1265 | 3.129 |

Age represents chronological age in years; CSA: cross-sectional area; BMC: bone mineral content; vBMD: volumetric bone mineral density.

**Table 2.** Age-dependent reference data for pQCT analyses at the proximal radius (65% site) in females. Given are values for the age-dependent coefficients of variation (S) and mean values (M).

The use of z-scores implies that data are normally distributed, a condition which is often neglected when reference data for a method are presented. As the present data were normally distributed only after logarithmic transformation, it is necessary to calculate z-scores on the basis of the logarithmically transformed data. After back-transformation this results in asymmetrical reference ranges, as the lower end of the reference range (corresponding to a z-score of -2) is closer to the mean value than the upper end of the reference range (corresponding to a z-score of +2). This reflects the fact that the original data were skewed towards higher values. In this situation, the use of symmetrical reference ranges (based on mean ±2 SD of the untransformed data) would decrease the lower limit of the reference range, which would make the diagnostic procedure less sensitive for detecting low values.

## Results

Age- and sex-specific reference ranges for pQCT analyses at the proximal radius are shown graphically in Figures 3 to 5. Between 7.0 years and adulthood, total CSA increases by 51% in females, whereas in males the increase is 105% (Figure 3). In girls, the increase in total CSA, and thus periosteal apposition, reaches a maximum shortly after the age of 11 years but then slows down and almost comes to a standstill at approximately 15 years of age. In contrast, periosteal apposition continues in boys until the age of about 20 years. Consequently, total CSA is larger in males after the age of 14 years. The developmental changes in cortical CSA are similar to those of total CSA, even though gender differences are smaller. In girls, cortical CSA increases until the age of about 15 years and changes little thereafter. In boys, the rapid increase in cortical CSA continues until about 18 years of age. Strength-Strain Index shows a similar age-dependency as total CSA, with clearly higher values in males after age 15.

As to bone mass and density parameters, the maximum increase in BMC occurs between 10 and 11 years of age in girls, but almost six years later in boys (Figure 4). Due to this continuing increase, BMC is higher in males after the age of 15 years. In contrast, cortical BMD increases faster with age in girls than in boys, and consequently females have higher values after the age of 11 years. Total volumetric BMD continuously increases during development in girls and is higher in young adult females than in males.

Muscle CSA increases rapidly in boys, with a maximum rate of increase at about 14 years of age (Figure 5). In girls, the increase in muscle CSA is faster before the age of 10 years than after that age. The BMC/muscle CSA ratio slightly decreases with age in boys, but changes little in girls. Consequently, the BMC/muscle CSA ratio is significantly higher in girls than in boys after age 13.

The equations for M and S that describe these age-dependent curves are given in Tables 2 and 3. In clinical pediatrics, reference data are mostly used to compare a patient's result to that of healthy children and adolescents of the same age. However, for measures that directly reflect

| | S | M |
|---|---|---|
| **6.0 to 17.5 years** | | |
| Total CSA ($mm^2$) | 0.1735–0.0007709 x age | 36.75+5.667 x age |
| Cortical CSA ($mm^2$) | 0.1929–0.001991 x age | -124.4+56.26 x age-7.086 x $age^2$+0.3981 x $age^3$-0.007830 x $age^4$ |
| Strength-Strain Index ($mm^3$) | 0.2552–0.002471 x age | -36.96+20.74 x age |
| BMC (mg/mm) | 0.1307+0.001054 x age | -110.4+57.52 x age-7.381 x $age^2$+0.4212 x $age^3$-0.008326 x $age^4$ |
| Total vBMD ($mg/cm^3$) | 0.1133+0.0004141 x age | -784.2+511.6 x age-68.05 x $age^2$+3.806 x $age^3$-0.07455 x $age^4$ |
| Cortical vBMD ($mg/cm^3$) | 0.04487–0.0006835 x age | 18.46+330.8 x age-40.09 x $age^2$+2.076 x $age^3$-0.03804 x $age^4$ |
| Muscle CSA ($mm^2$) | 0.1553–0.0007552 x age | 3481-627.0 x age+64.82 x $age^2$-1.551 x $age^3$ |
| BMC/Muscle CSA | 0.1645–0.002651 x age | 3.696-0.1053 x age+0.002812 x $age^2$ |
| **21 to 40 years** | | |
| Total CSA ($mm^2$) | 0.1629 | 156.5 |
| Cortical CSA ($mm^2$) | 0.1272 | 96.27 |
| Strength-Strain Index ($mm^3$) | 0.1862 | 408.3 |
| BMC (mg/mm) | 0.1211 | 123.9 |
| Cortical vBMD ($mg/cm^3$) | 0.02855 | 1111 |
| Total vBMD ($mg/cm^3$) | 0.1301 | 703.3 |
| Muscle CSA ($mm^2$) | 0.1132 | 4491 |
| BMC/Muscle CSA | 0.1361 | 2.758 |

Age represents chronological age in years; CSA: cross-sectional area; BMC: bone mineral content; vBMD: volumetric bone mineral density.

**Table 3.** Age-dependent reference data for pQCT analyses at the proximal radius (65% site) in males. Given are values for the age-dependent coefficients of variation (S) and mean values (M).

| | S | M |
|---|---|---|
| Total CSA ($mm^2$) | 0.2446–0.0006562 x ht | 530.7-8.057 x ht+0.03549 x $ht^2$+0.00003538 x $ht^3$-0.0000002970 x $ht^4$ |
| Cortical CSA ($mm^2$) | 0.4454–0.001738 x ht | -75.42+0.8602 x ht |
| Strength-Strain Index ($mm^3$) | 0.2405–0.0003540 x ht | -5221+147.4 x ht-1.547 x $ht^2$+0.007195 x $ht^3$-0.00001226 x $ht^4$ |
| BMC (mg/mm) | 0.1584–0.0001334 x ht | -9930+285.3 x ht-3.043 x $ht^2$+0.01432 x $ht^3$-0.00002500 x $ht^4$ |
| Total vBMD ($mg/cm^3$) | 0.3098–0.001130 x ht | -13610+382.9 x ht-3.933 x $ht^2$+0.01810 x $ht^3$-0.00003114 x $ht^4$ |
| Cortical vBMD ($mg/cm^3$) | 0.1282–0.0005743 x ht | -16693+491.4 x ht-5.140 x $ht^2$+0.02387 x $ht^3$-0.00004124 x $ht^4$ |
| Muscle CSA ($mm^2$) | 0.08759–0.0001993 x ht | 43292-1127 x ht-10.87 x $ht^2$-0.04468 x $ht^3$+0.00006744 x $ht^4$ |

ht represents height in cm; CSA: cross-sectional area; BMC: bone mineral content; vBMD: volumetric bone mineral density

**Table 4.** Height-dependent reference data for pQCT analyses at the proximal radius (65% site) in females. Given are values for the height-dependent coefficients of variation (S) and mean values (M). The data are valid for a height between 115 and 175 cm.

| | S | M |
|---|---|---|
| Total CSA ($mm^2$) | 0.2708–0.0008019 x ht | -66.82+1.108 x ht |
| Cortical CSA ($mm^2$) | 0.2502–0.0006961 x ht | -3455+93.31 x ht-0.9288 x $ht^2$+0.004069 x $ht^3$-0.000006565 x $ht^4$ |
| Strength-Strain Index ($mm^3$) | 0.3144–0.0007995 x ht | -8687+241.9 x ht-2.487 x ht2+0.01126 x $ht^3$-0.00001869 x $ht^4$ |
| BMC (mg/mm) | 0.1148+0.00004315 x ht | -689.4+19.55 x ht-0.1918 x $ht^2$+0.0008110 x $ht^3$-0.000001180 x $ht^4$ |
| Total vBMD ($mg/cm^3$) | 0.1392–0.00009888 x ht | -79507+2110 x ht-20.66 x $ht^2$+0.08908 x $ht^3$-0.0001426 x $ht^4$ |
| Cortical vBMD ($mg/cm^3$) | 0.04618–0.00003109 x ht | -14650+411.2x ht-4.034 x $ht^2$+0.01748 x $ht^3$-0.00002817 x $ht^4$ |
| Muscle CSA ($mm^2$) | 0.07420–0.0004190 x ht | -144806+4036 x ht-41.39 x $ht^2$+0.1865 x $ht^3$-0.0003088 x $ht^4$ |

ht represents height in cm; CSA: cross-sectional area; BMC: bone mineral content; vBMD: volumetric bone mineral density

**Table 5.** Height-dependent reference data for pQCT analyses at the proximal radius (65% site) in males. Given are values for the height-dependent coefficients of variation (S) and mean values (M). The data are valid for a height between 115 and 185 cm.

some aspect of bone or muscle size (cross-sectional areas, BMC and Strength-Strain Index), it may often be more appropriate to relate results to height-dependent reference data. Age-dependent reference data may be more appropriate for vBMD results, as volumetric densities by definition are already adjusted for size. In any case, Tables 4 and 5 present height-dependent reference data to provide flexibility in the use of this material.

As indicated by Cole, a given test result can be converted into the age- and sex-specific z-score using the formula[16]: z-score = [Ln(patient's test result/M)]/S, where Ln is the natural logarithm, M corresponds to the age- (or height-) and sex-specific mean value as derived from the equations in Tables 2 to 5, and S is the age- (or height-) and sex-specific coefficient of variation as derived from the same Tables.

An example of how to use these data: Assume that a 12.4 year-old girl has a BMC of 60 mg/mm. As shown in Table 1, S can be calculated as 0.1825–0.002901x12.4 = 0.1465 and M is 122.3–33.75x12.4 + 4.707x12.42–0.2327x12.43 + 0.003924x12.$4^4$ = 76.65. The z-score of this girl therefore is [Ln(60/76.65)]/0.1465 = -1.67.

## Discussion

In this study, we derived smoothed reference ranges for pQCT results at the 65% site of the proximal radial diaphysis. Cole's LMS method was chosen to establish reference data because it is easy to implement and is widely used in the field of pediatric bone research[17,18].

We had previously presented results from the same study as mean and standard deviations in discrete age groups[1-5]. Although mathematically very simple, this approach is not practical for clinical use because of the discontinuities that arise when a patient crosses the cut-off age between two age intervals. The LMS method avoids discontinuities. Once the results presented in Tables 2 to 5 are entered into a spreadsheet program, z-scores can be calculated in an automated fashion.

Apart from the practical value of providing normative data, our results yield insight into the process of cortical bone growth at the 65% site of the radius. The bone expands in the cross-sectional plane by adding new material on the outer (periosteal) surface, a process that is called periosteal apposition[19]. The primary bone created by periosteal osteoblasts is then converted into secondary bone through intracortical remodeling. The inner delimitation of the cortex (the endocortical surface) either undergoes net formation (endocortical apposition) or net resorption (endocortical resorption). Endocortical apposition will make the marrow cavity smaller, whereas endocortical resorption enlarges the marrow cavity.

Our results show that total cross-sectional area at the radius 65% site is larger in males than in females at all stages of development. This is in accordance with results obtained by radiogrammetry at the 2nd metacarpal, and also at the proximal radial diaphysis[20,21]. Thus, periosteal apposition is more vigorous in boys than in girls. There are also gender-differences with regard to the endocortical surface at the site of measurement in this study, as there is endocortical resorption in boys but not in girls[2]. Consequently, gender-differences in cortical CSA are somewhat smaller than those in total CSA.

The Strength-Strain Index represents the section modulus weighed by cortical vBMD. As cortical vBMD changes relatively little during normal development, the age-dependent changes in Strength-Strain Index mostly reflect those of the section modulus, which in turn depends largely on bone size. It is therefore not surprising that the changes with age in Strength-Strain Index resemble those of total cross-sectional area.

The movements of the periosteal and endocortical surfaces are mirrored by changes in BMC. BMC keeps increasing longer in the male sex, which reflects the fact that rapid periosteal expansion continues longer in boys than in girls. In contrast, cortical vBMD is clearly higher in females after puberty than in males of the same age, suggesting that intracortical remodeling is lower in females.

The curves for muscle CSA reflect the fact that, on average, forearm muscles grow wider in boys than in girls. Apart from differences in average stature and forearm length, this gender difference is most probably caused by the rise in testosterone levels during male puberty[23]. The gender difference in BMC/muscle CSA ratio mirrors the observation that girls and boys have a similar muscle-bone relationship regarding external bone size, but girls have a relatively smaller marrow cavity[24].

In conclusion, this report presents reference data for pQCT analyses at the 65% site of the proximal radius and discusses the interpretation of results in children and adolescents. These data should facilitate the use of this technique in the pediatric setting.

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