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Bone Mineral and Soft Tissue Measurements by Dual-Energy X-Ray Absorptiometry During Growth

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There have been several previous compilations of reference ranges of total body bone mineral measured by dual-energy X-ray absorptiometry (DXA) in children and young adults during growth, but little attempt to compare the results or to consider differences arising from the use of instruments from different manufacturers. We measured bone mineral and soft tissue in 216 girls, aged 11–17 years, using a Hologic scanner. Our results were compared with those from four other studies, all performed on white subjects, but in different countries, and including measurements performed with Hologic, Lunar, and Norland scanners. The general pattern of bone growth with age was very similar in all the studies. Quantitative differences could largely be accounted for by known differences of calibration of DXA scanners from the different manufacturers. When bone mass was plotted against lean or total mass instead of age there were also close similarities. An apparent difference between boys and girls in one study was shown to be due to differences in soft tissue composition, rather than different patterns of bone growth. Conclusions from this apparent difference concerning the effect of estrogen at puberty were shown to be unwarranted. (Bone 31:492–496; 2002)

Key Words: Dual-energy X-ray absorptiometry (DXA); Bone mineral; Body composition; Children and adolescents.

Introduction

There is interest in studying the accumulation of bone mineral during the growth of children, due in part to the recognition that the risk of osteoporosis in later life is influenced by peak bone mass in early adulthood, and also because some drugs, such as corticosteroids and anticonvulsants, may have a deleterious effect. The most convenient and precise technique used to measure bone mineral is dual-energy X-ray absorptiometry (DXA), which delivers only a very low radiation dose, permitting its use in the pediatric population and allowing for repeated measurements. Although measurement of spine and hip bone mineral dominates in the investigation of osteoporosis in adults, total body measurements are more appropriate during growth. DXA also has the advantage that measurements of soft tissue fat and lean masses can be determined at the same time, allowing bone mass to be related to these variables, as well as to age and weight.

There have been several compilations of reference ranges for subjects <20 years of age, which are necessary for the evaluation of the effects of disease or treatment on bone.[2,3,5–7,11] However, little attempt has been made to compare the published results with one another. One factor that has been ignored completely is that the accuracy of DXA is not absolute. In X-ray attenuation terms there are three main components, bone mineral, fat, and lean soft tissue. As only two X-ray energies are used, complete solution of the equations is not possible and it is necessary to make assumptions about fat distribution. Manufacturers do not reveal what assumptions they make or acknowledge any lack of accuracy, but it is well established (even if not well recognized) that results from different manufacturers and different software give different results for bone mineral, fat, and lean soft tissue.[9,10]

In the various publications, bone mineral mass (usually referred to as bone mineral content [BMC]) has been plotted against age. The inclusion of measurements of soft tissue composition enables relationships between BMC and weight or lean body mass to be considered. Schiessl et al. used this facility to reanalyze the data from Zanchetta et al.[11] to examine differences between boys and girls at puberty to deduce the effects of estrogen on bone strength and mass.[8] They postulated that estrogen lowers the remodeling threshold, so that, at puberty in girls, bone mass should begin to increase faster than previously and more than in boys with similar muscle strengths, as indicated by lean mass. They cited the apparent increase in slope of total body bone mineral content (TBBMC) plotted against total lean mass in the data from Zanchetta et al. as support for this argument. We compiled our own reference ranges of bone and soft tissue masses in teenage girls (data presently unpublished). In some respects our results differed from those of Zanchetta et al. and did not support the deductions of Schiessl et al. We therefore present our own data, compare the results with other publications, consider the differences between results from DXA scanners from the different manufacturers, and reexamine the deductions concerning hormone effects.

Subjects and Methods

Our measurements were made on 216 healthy white female volunteers, aged 11–17 years, recruited from two state-funded secondary schools in Edinburgh, between them embracing a representative range of socioeconomic classes. Informed consent was given and the study was approved by the hospital ethics committee. Total body and regional measurements of bone, fat,

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Table 1. Bone and soft tissue masses in Edinburgh teenage girls (mean ± SD)

N	Age	Weight (kg)	TBBMC (g)	Fat (kg)	Lean (kg)
16	11.8 ± 0.22	43.8 ± 8.1	1352 ± 64	10.92 ± 3.78	30.35 ± 4.71
109	12.5 ± 0.24	46.8 ± 8.7	1490 ± 267	11.44 ± 4.55	32.65 ± 4.99
38	13.5 ± 0.29	51.4 ± 8.9	1716 ± 261	12.93 ± 5.78	35.82 ± 3.71
23	14.3 ± 0.23	58.5 ± 10.4	2070 ± 296	14.64 ± 5.85	40.79 ± 4.93
21	15.4 ± 0.23	57.2 ± 8.2	2009 ± 286	14.63 ± 4.13	39.76 ± 4.54
9	16.8 ± 0.69	57.4 ± 6.1	2133 ± 365	14.91 ± 2.99	40.35 ± 4.31

KEY: TBBMC, total body bone mineral content.

and lean soft tissue were made using a Hologic QDR 1000W DXA scanner with v5.51 software in the "enhanced" mode.

The published studies included in the comparisons were limited to those investigating white subjects <20 years of age, with DXA measurements of total body bone mineral and lean and fat soft tissue, but with no restriction on geography, diet, or DXA instrument. It was necessary to compile the data in a common format.

Zanchetta et al. measured 433 females and 345 males ranging in age from 2 to 20 years in Buenos Aires, Argentina, from different socioeconomic classes.[11] Subjects with a history of chronic disease, undergoing treatment with drugs known to affect bone metabolism, or weight or height outside the 3rd–97th percentile for age were excluded. They used a Norland XR-26 high-speed (HS) instrument, but did not indicate what software was used. They presented tables of mean values in 1 year age bands for BMC, bone mineral areal density (BMD), and body composition, and plotted total body BMC against age. Their tables allowed other relationships to be plotted. They also presented results of lumbar spine and femoral neck BMD.

Faulkner et al. published two studies, the second,[2] considered here, updated an earlier one,[3] increasing the number of subjects to 506 females and 471 males, age range 8–17 years, from two schools in middle-class neighborhoods of Saskatoon, Sasketchewan, Canada. They used a Hologic QDR 2000 fan-beam instrument in the array mode, with v4.56A software. TBBMC, BMD, and fat and lean measurements were tabulated in 1 year age intervals and results of spine and hip scanning were included. Plots of TBBMC and TBBMD vs. age were included.

Ogle et al. used a Lunar DPX with v3.4 software in Sydney, Australia, to measure 128 female and 137 male subjects in the age range of 4–26 years.[7] The subjects investigated included siblings of hospital outpatients, children of staff, friends, or medical students. They were healthy and without known medical disease and within the 1st–99th percentile of the median height and weight. No tables of results were presented, but graphs of TBBMC, fat, and lean soft tissue were provided, including data points, and curves fitted using segmental polynomial models. We digitized their published graphs and determined the coordinates of the points to calculate means in brackets of 2.5 years, with an upper age limit of 20 years.

Mølgaard et al. presented their bone and soft tissue measurements in separate articles.[5,6] They measured 201 female and 142 male subjects, aged 5–19 years, from five schools in Copenhagen, Denmark, using a Hologic QDR 1000W (the same model as ours) with v5.61 software. Subjects with chronic disease or taking medication that might affect bone mineralization were excluded. Smoothed values of mean TBBMC and bone area (BA) were tabulated,[5] from which BMD could be calculated. Fat and lean measurements were presented as plots of mean values.[5] We digitized their graphs to tabulate the soft tissue results.

Results

The results from Edinburgh are summarized in **Table 1** as means and standard deviations (SDs) at 1 year age intervals, except at the top bracket, where 2 years were combined, owing to small numbers.

Each of the original studies compared directly the plots of BMC vs. age for females and males. In each case, the increase in BMC with age was almost identical in the two genders up to the age of about 15 years, when the graph for females reached a plateau. BMC in males rose further to reach a higher plateau about 2 years later.

We were more concerned with examining the differences between centers and instruments, so all the plots of BMC against age for females are combined in **Figure 1**a and for males in Figure 1b. It can be seen that the general patterns were very similar. The curves from Zanchetta et al., using a Norland scanner, and Ogle et al., using a Lunar scanner, were very close,

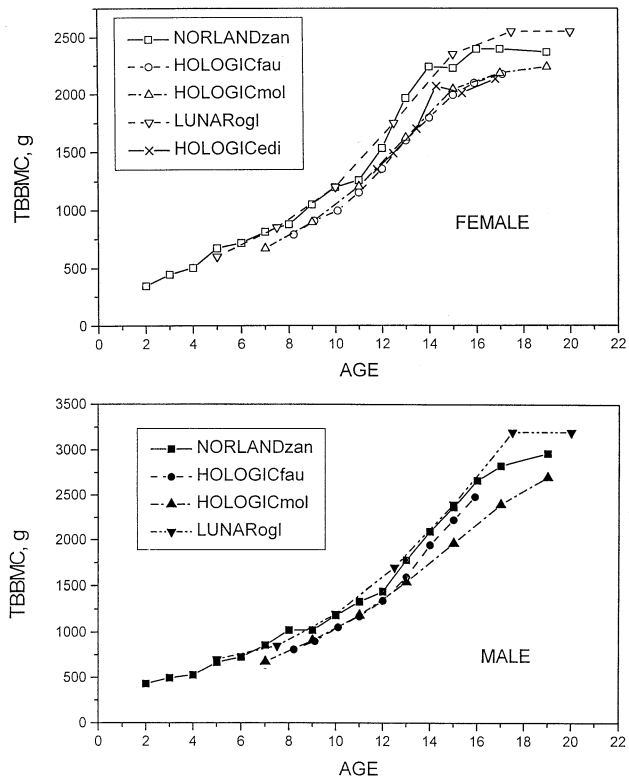

Figure 1. Total body bone mineral content plotted against age. In this and the other figures the plots are identified by the manufacturer of the instrument used and the first three letters of the name of the first investigator.

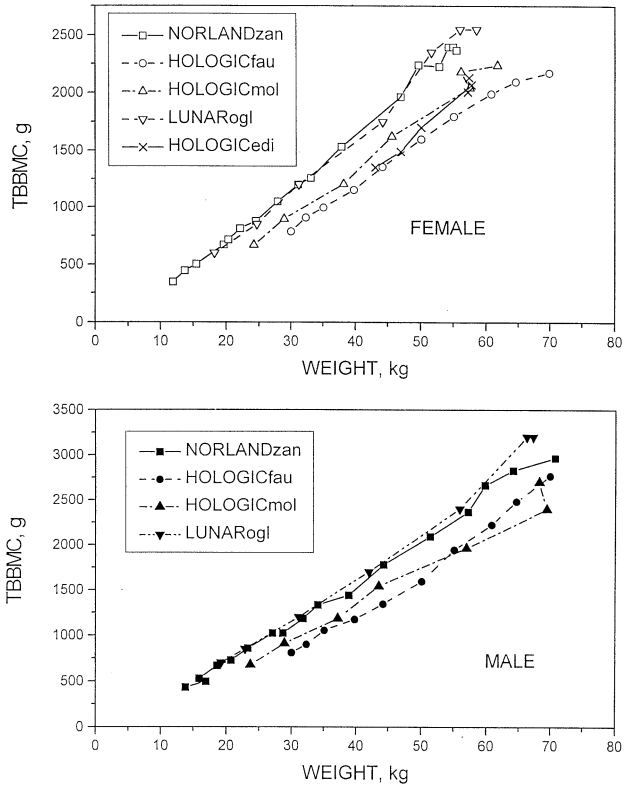

Figure 2. Total body bone mineral content plotted against weight.

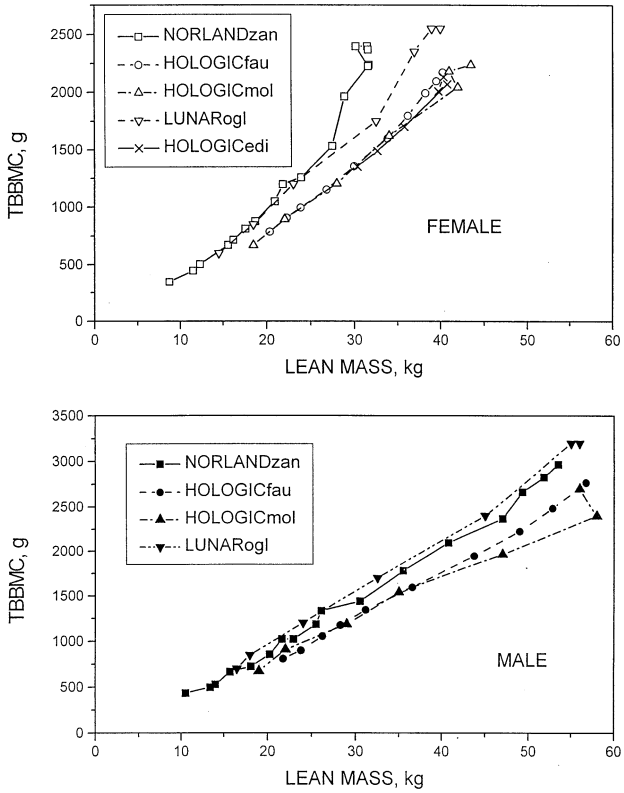

Figure 3. Total body bone mineral content plotted against lean body mass.

but BMC was higher at all ages when compared with the Faulkner, Mølgaard, and Edinburgh results, all obtained with Hologic instruments.

TBBMC is plotted against weight in **Figure 2** . The relationships appear to be close to linear, which facilitates quantitative comparisons between centers and genders. The parameters of linear regressions are presented in **Table 2** . They were all highly significant, with $R > 0.99$ and $p < 0.0001$. There were no significant differences between the equations for males and females in the studies by Zanchetta, Mølgaard, and Ogle. The slope (regression coefficient) for females in the Faulkner study was less than that for males, due mainly to a departure from linearity above a weight of 50 kg.

The slopes and the TBBMC at 50 kg body weight were significantly greater for the Zanchetta/Norland and Ogle/Lunar combinations than for the Faulkner, Mølgaard, and Edinburgh/Hologic combinations. For example, when considering the two largest studies, the TBBMC at 50 kg for Zanchetta/Norland was, on average, 1.3 times that for Faulkner/Hologic.

Table 2. Parameters of linear regression equations of total body BMC (TBBMC) against weight: TBBMC (g) = $a + b *$ Weight (kg)

Study	DXA manufacturer	Gender	a	b	TBBMC at 50 kg
Zanchetta	Norland	F	−257	47.9	2138
		M	−250	46.4	2070
Faulkner	Hologic	F	−272	36.5	1553
		M	−483	43.2	1677
Molgaard	Hologic	F	−372	43.1	1783
		M	−294	41.0	1754
Ogle	Lunar	F	−382	51.0	2168
		M	−393	52.6	2237
Edinburgh	Hologic	F	150	30.1	1655

All regressions are highly significant, with $R > 0.99$ and $p < 0.0001$.

TBBMC is plotted against total lean mass, as measured by DXA, in **Figure 3** . The differences between Zanchetta and Ogle on the one hand and Faulkner, Mølgaard, and Edinburgh on the other were maintained. The most notable disparity is that the TBBMC/lean mass slope increased markedly from 27 kg upward in the Zanchetta-study females, but not in their male subjects or in the other studies. Further inspection suggests that this was due to a premature leveling-off of lean mass from the age of 14 years when compared with the other results and not to a real increase in TBBMC with age. This is clarified in **Figure 4**, where lean mass is plotted against age. The increase in weight in Zanchetta's subjects >14 years was due largely to increases in fat mass.

Discussion

The plots of TBBMC against age (Figure 1) show a very similar pattern. Where the same model of scanner and equivalent software were used, as with the Mølgaard and Edinburgh studies, the graphs were practically identical. This encouraged us to make use of the Mølgaard reference ranges in our work, as they covered a wider age range. There were quantitative differences between other studies, which can be associated with known differences of calibration of the DXA scanners used. We are not aware of any in vivo cross-calibration measurements for populations of the age ranges of interest, but limited data are available for adults. Tothill et al. compared total body bone mineral measurements between Hologic, Lunar, and Norland pencil-

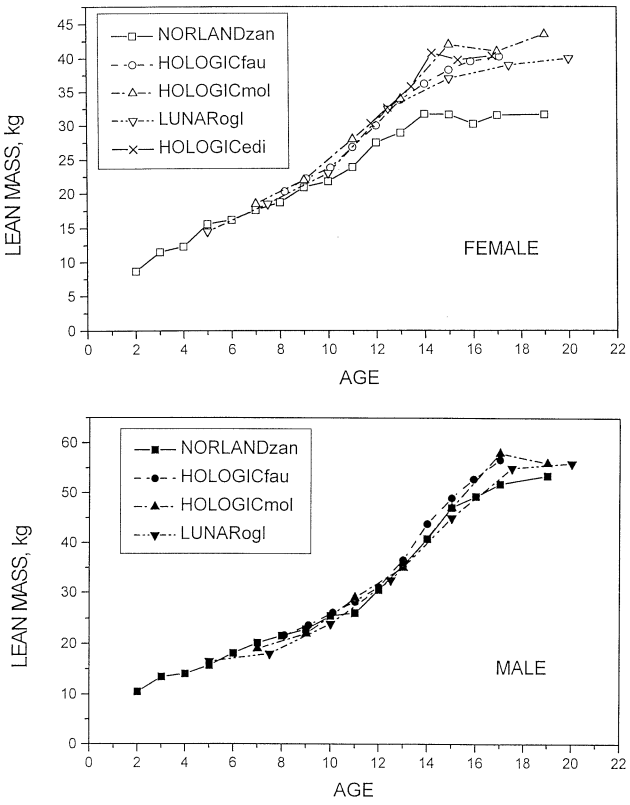

Figure 4. Total body lean mass plotted against age.

beam DXA scanners, both in vivo and in vitro.[9] Attention was paid to software versions, as all three manufacturers introduced new software during the course of the investigation, which altered the bone mineral results. We believe that the then "new" software corresponds to the current "enhanced" version, although a "standard whole body" option is also available. Similarly, Lunar offers both "extended" and "standard" options, so quotation of the software number alone is not sufficient. We found that the Norland XR-26 HS and Lunar DPX gave higher TBBMC values than the Hologic QDR 1000W, the linear regression equations being Lunar = 0.994·Hologic + 200 and Norland = 0.990·Hologic + 370, so that adult TBBMC was about 10% higher for Norland than Hologic, and Lunar 12% higher than Hologic. The numbers of subjects were small and it would be imprudent to extrapolate the corrections to young subjects, but the results suggest that the differences demonstrated in Figures 1 and 2 and Table 2 can largely be explained by the different scanners used. More in vivo cross calibrations would be desirable to produce accurate correction factors.

The equivalence of the fan-beam Hologic QDR 2000, used by Faulkner et al., to the pencil-beam Hologic QDR 1000W, used by Mølgaard and in Edinburgh, is not certain. We are not aware of any in vivo cross calibrations for total body bone mineral with these scanners. Comparisons of spine and hip BMD measurements with the two instruments were reassuring.[1,4] Differences were negligible. It must be recognized, however, that a dependence of BMC on the height of a bone above the couch in total body scanning with the fan-beam QDR 2000 is a possibility and this might affect comparison of the scanners for subjects with a wide range of sizes, such as in growth studies.

In considering the plots of TBBMC against lean mass in Figure 3, it is necessary to remember that DXA scanners differ in their calibration for fat and lean masses, as well as for bone. Again, no cross-calibrations are available for a pediatric population, but Tothill et al. found that in adults the mean fat recorded by the Norland XR-26 HS was 6.3% of body weight higher than by a Hologic QDR 1000W.[10] A Lunar DPX recorded a mean of 3.7% higher than the Hologic. A typical 65 kg young woman studied by Faulkner would have a lean mass measured by a Hologic scanner of 40 kg. Using the published regression equations, measurement with a Norland XR-26 HS would record 34.7 kg and with a Lunar DPX 36.0 kg. Such adjustments would reduce, but not eliminate, the differences between the Zanchetta and Ogle measurements and the others using Hologic instruments as portrayed in Figure 3. In fact, the differences would be more in line with the calibration differences referred to earlier.

The most important characteristic of Figure 3 is the apparent increase of the slope of the bone mass/lean mass plot above 27 kg in the females in the study by Zanchetta et al., but not in their males. Schiessl et al. used this disparity as evidence for an increase in estrogen secretion leading to an increase in bone formation, making the assumption that bone mass correlates better with lean mass than with total mass. This assumption was not validated. Our analysis of the data from Zanchetta et al. suggests that the increase in slope in Figure 3 is more likely due to a dependence of bone mass on total mass, coupled with a reduction in the proportion of lean mass in the total mass at around puberty in the girls. It is important to remember that all the studies were cross-sectional and were not following individuals over a period of years. It is also important to point out that the apparent steepening of the slope was unique to the study of Zanchetta et al. None of the other studies demonstrated such a marked disparity between boys and girls. We conclude that these DXA measurements of bone and soft tissue during growth do not provide evidence of the hormone effects postulated by Schiessl et al.

We also conclude that the results of bone measurements during growth from different centers are remarkably similar. The biggest disparities were attributable to differences between the calibrations adopted by different DXA manufacturers. If these are taken into account, it should be possible to use published reference ranges from other centers.

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