Acta Pædiatrica, 2005; 94: 1030–1037

Growth tracking of femoral and humeral strength from infancy through late adolescence

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Abstract

Aim: To determine to what degree femoral and humeral strengths "track", or remain at the same ranked position relative to other individuals during the entire growth period. *Methods:* Radiographs of 20 individuals, equally divided by sex, were measured at 6-mo or annual intervals from 6 mo to 17 y of age. The section modulus, a measure of bending/torsional strength, was derived from cortical and subperiosteal breadths taken at the femoral midshaft and at 40% of the bone length from the distal end of the humerus. Body size was also assessed as the product of body weight and bone length. Growth tracking was evaluated in two ways: as Spearman rank-order correlations between strengths at each age point and strengths at 17 y of age, and as the number of individual changes in rank over specified age intervals. All analyses were carried out within sex. *Results:* The degree of growth tracking varied by sex, skeletal location, and age. Correlations were higher for the humerus ($r = 0.56$–0.83) than for the femur ($r = 0.10$–0.63). Males showed particularly poor tracking for the femur, most likely due to late and variable adolescent growth spurts in body size. Standardizing for body size improved tracking for the male femur, but not for the humerus. Over the entire growth period, individuals averaged 5–8 out of a possible 9 changes in rank. Early childhood (<6 y) was the least stable period.

Conclusion: Previously documented growth tracking of skeletal parameters over relatively short (1–6-y) time periods can not necessarily be extrapolated to longer time intervals, nor can results from one skeletal region or time period be applied to another region or time period. Variation in timing of growth events, and body size for weight-bearing elements, may have important influences on growth tracking.

Key Words: *Adolescents, body size, bone strength, children, growth tracking*

Introduction

The degree to which skeletal parameters "track", or maintain their ranked position relative to other individuals during growth [1], has important implications for both early detection and future prediction of increased fracture risk. The peak bone mass (PBM) obtained by late adolescence or early adulthood is widely acknowledged to be a critical factor in determining fracture likelihood in older adults [2–4]. If PBM strongly correlates with bone mass earlier in development, then it might be possible to implement strategies to enhance PBM prior to the initiation or completion of rapid adolescent growth [5–8]. Similarly, an increased risk for childhood fractures may be detectable sufficiently early to employ appropriate interventions [9–12]. More generally, the degree of skeletal tracking during growth may give insights into the genetic control of bone structural parameters and the extent to which relative bone mass or strength is modifiable by environmental factors [1,13,14].

Several longitudinal growth studies have indicated an apparently high level of tracking of bone mineral content (BMC), width (BW), area, and/or density in children measured over periods ranging from 7 mo to 6 y [1,13,14]. However, all of these studies were limited to either adolescence or pre-adolescence, and none were of sufficient duration to track skeletal parameters through the majority of the growth period. Thus, individual tracking of skeletal parameters from early childhood through later adolescence, when PBM should be close to attained [15,16], has not yet been evaluated. In addition, skeletal structural parameters that are more directly related to bone strength *per se*, i.e., bone section moduli [10,17–19], have not to date been included in growth-tracking studies.

The present investigation assesses growth tracking in femoral and humeral diaphyseal strength in a sample

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(Received 14 October 2003; revised 8 July 2004 and 21 October 2004; accepted 27 October 2004)

ISSN 0803-5253 print/ISSN 1651-2227 online
DOI: 10.1080/08035250510026535

of children measured radiographically at intervals of 6 mo or 1 y from near birth through 17 y of age. The effects on growth tracking of standardizing femoral and humeral strengths by body size are also assessed.

Materials and methods

Radiographs and anthropometric data were obtained from the archives of the Denver Child Research Study [20]. This was a long-term longitudinal growth study of normal children living within the Denver, Colorado, area. Individuals included in the present study were examined between 1941 and 1967. All subjects were of European ancestry and of middle- to upper middle-class socio-economic status. A total of 20 individuals, 10 boys and 10 girls, with the most complete radiographic records were selected for study. Data were obtained at 6-mo intervals from 6 mo through 14 y of age, and annually thereafter to 17 y of age, for a total of 31 age points per individual. Missing data (7% of femoral data and 14% of humeral data) were estimated through linear interpolation from adjacent examinations [21]. Data were not smoothed prior to analysis, as had been done in a previous growth velocity study of the same sample [22]. Data smoothing is useful for the examination of very small changes per unit of time, i.e., growth velocities over short time intervals, but is not necessary for longer-term growth-tracking analyses.

Anteroposterior radiographs of the humerus and femur taken in the original study [23] were measured as described in detail elsewhere [21,22]. Briefly, subperiosteal and cortical breadths perpendicular to the longitudinal axis of the diaphysis were measured to the nearest 0.01 mm using sharp-tipped digital calipers at 50% of femoral length and at 40% of humeral length from their distal ends (bone lengths as described in the above references). Appropriate adjustments were made for missing (undeveloped) epiphyses. Measurements were corrected for radiographic magnification, which averaged 2.5 to 4%. Films showing evidence of significant departures from a standardized subject-positioning protocol were not included. Bone breadths were then used to calculate the polar section modulus (Z_p), a measure of bone bending and torsional strength [17,18], using the following formula: $Z_p = [\pi/32 \cdot (T^4 - M^4)]/(T/2)$, where T is the total subperiosteal breadth and M is the medullary cavity breadth [24]. This calculation assumes a circular or cylindrical cross section, which is not strictly true for any long-bone diaphysis. However, violation of this assumption is not too severe at the locations measured [21,22]. Measurement error based on repeated measurements averaged about 3% for the derived section modulus in both the femur and humerus.

Changes in bone structural parameters during growth have been shown to be strongly correlated with changes in body size [17,18,22]. The most appropriate body "size" parameter for evaluating bending/torsional strength of a long-bone diaphysis is the product of body weight and a moment arm, which can be taken as proportional to that bone's length [10,25]. Thus, body size here was evaluated as body weight · femoral length for the femoral section modulus, and body weight · humeral length for the humeral section modulus. Body weights were obtained from the archived records for the Denver Growth Study sample (Siervogel, pers. comm.). Bone lengths used in these indices were the maximum lengths of the femur and humerus, measured directly from radiographs. In individuals with incomplete epiphyses, maximum lengths were estimated from diaphyseal lengths using previously described methods [22].

Growth tracking of bone strengths was assessed in two ways. First, Spearman (ranked-order) correlations were calculated between individual section moduli at each age point, through 16 y of age, and the corresponding values for those individuals at 17 y of age. While long-bone cortices continue to grow throughout late adolescence and adulthood [26–28], by 17 y values close to PBM are attained [15,16]; also, at this age most individuals should have reached Tanner stage 5 in maturity [14]. Thus, relative rankings at 17 y can be taken as an appropriate predicted "endpoint" with which to compare rankings earlier in development. Correlations are presented both graphically for each age point, and as means over two age ranges: the full sample range of 0.5–16 y, and only 6–16 y. The latter age range was chosen for additional analysis because it represents the approximate limit of school-aged children and eliminates young children, where growth tracking may be of less interest. As shown below, young children also display poorer tracking than older children and adolescents. Comparisons of mean correlation coefficients between the sexes were carried out using two-sample *t*-tests. Paired *t*-tests were used to compare correlations for raw and body size-standardized properties, and femoral and humeral properties.

To further evaluate tracking without specific reference to any particular time point (i.e., 17 y), the variation in rankings within individuals over different age ranges was also assessed. First, individual changes in rank over 0.5–17 y and 6–17 y, corresponding to the two age periods used in correlation analyses, were assessed. Due to marked non-normality in some data distributions, non-parametric Mann-Whitney tests were used to compare males and females. In addition, average changes in rank within three successive age periods, 0.5–5.5 y, 6–10.5 y, and 11–17 y, were compared. These were chosen to represent approximately the pre- (elementary) school, school-age but

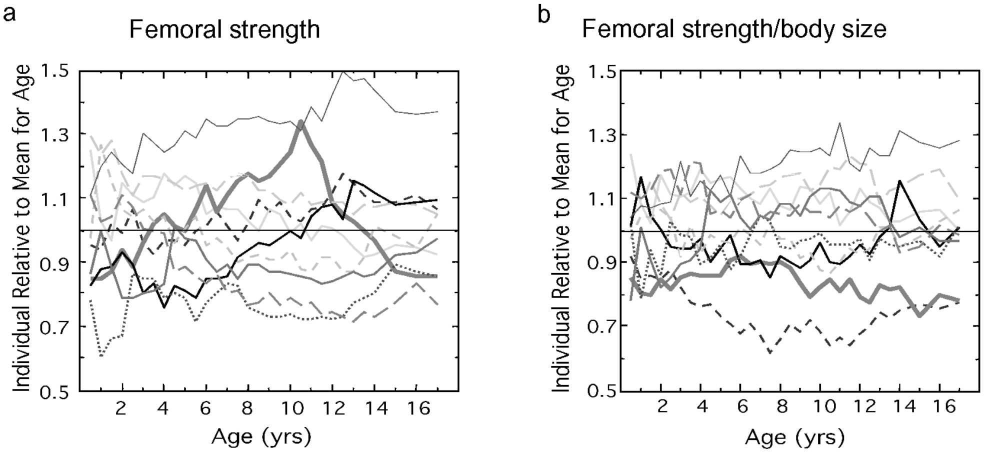

Figure 1. Individual values for femoral strength, divided by the mean value at each age, in 10 girls. (a) Raw strength (section modulus); (b) strength/(body weight·femoral length). Matching line patterns = same individual in (a) and (b).

pre-adolescent, and adolescent time periods, respectively. It is realized that girls enter adolescence earlier than boys; however, the above cut-off ages preserve a similar number of age points within each age group and sex (11, 10, and 10 age points, respectively; note that data were available at 6-mo intervals through age 14 y, and annually thereafter), which facilitates interpretations of sex and age group differences in the number of rank changes. In addition, 10.5 y is well prior to the age of peak adolescent growth velocity for bone strength in almost all of the girls as well as boys in this sample [22]. Non-parametric Wilcoxon paired sample tests were used to compare the three age periods.

All analyses were carried out within sex, using both raw bone strengths and bone strengths divided by the body size variable. All statistics and graphics were generated using SYSTAT [29].

Results

To illustrate graphically the degree of individual variability in growth tracking observed in the sample, Figure 1 plots individual age curves for a) raw femoral strength and b) femoral strength standardized over body size in each of the 10 girls in the study. To better visualize changes in relative position through time, individual values are expressed relative to the mean value at each age. Figure 1a shows that while some individuals maintain a similar relative position through time, others exhibit considerable changes in relative position. Standardizing by body size generally reduces positional variation (Figure 1b), especially for individuals showing large variability in raw strength (compare curves for individual represented by heavy line in Figures 1a and 1b). Overall positional variability (i.e., line crossing) in both plots appears somewhat greater in early childhood, an impression confirmed by later analyses (see below).

Rank-order correlations between individual values at each age and their corresponding values at 17 y are shown in Figure 2, by sex, for raw and body size-standardized femoral and humeral strengths. The level at which correlations reach statistical significance ($r = 0.648$; $p < 0.05$) is included on the plots for reference. Mean rank-order correlations over the two broader age ranges (0.5–16 and 6–16 y) are given in Table I.

Raw femoral strength exhibits higher correlations in girls than in boys (Table I), although even in girls correlations begin to decline prior to 14 y of age and are not statistically significant prior to 12 y of age (Figure 2a). Correlations for femoral strength in boys drop steeply immediately preceding 17 y and are non-significant prior to 16 y. Standardizing femoral strength by body size significantly improves correlations, except in older girls (Table I). The improvement is especially marked in older boys (Figure 2b), resulting in non-significantly different correlations in the two sexes beyond 6 y of age (Table I).

Raw humeral strength shows higher correlations with 17-y values than raw femoral strength in both sexes from 6 y of age onward (all humeral correlations statistically significant except in 7.5-y-old boys), and in boys throughout development (Table I, Figure 2c). In contrast to the femur, standardizing by body size does not improve humeral strength correlations in either sex (Figure 2d) and in fact results in a significant *decline* in average humeral correlations in most comparisons (Table I).

Table II shows the median, minimum, and maximum changes in rankings within individuals over the 0.5–17 and 6–17-y age ranges. Results are generally consistent with those obtained in the correlational

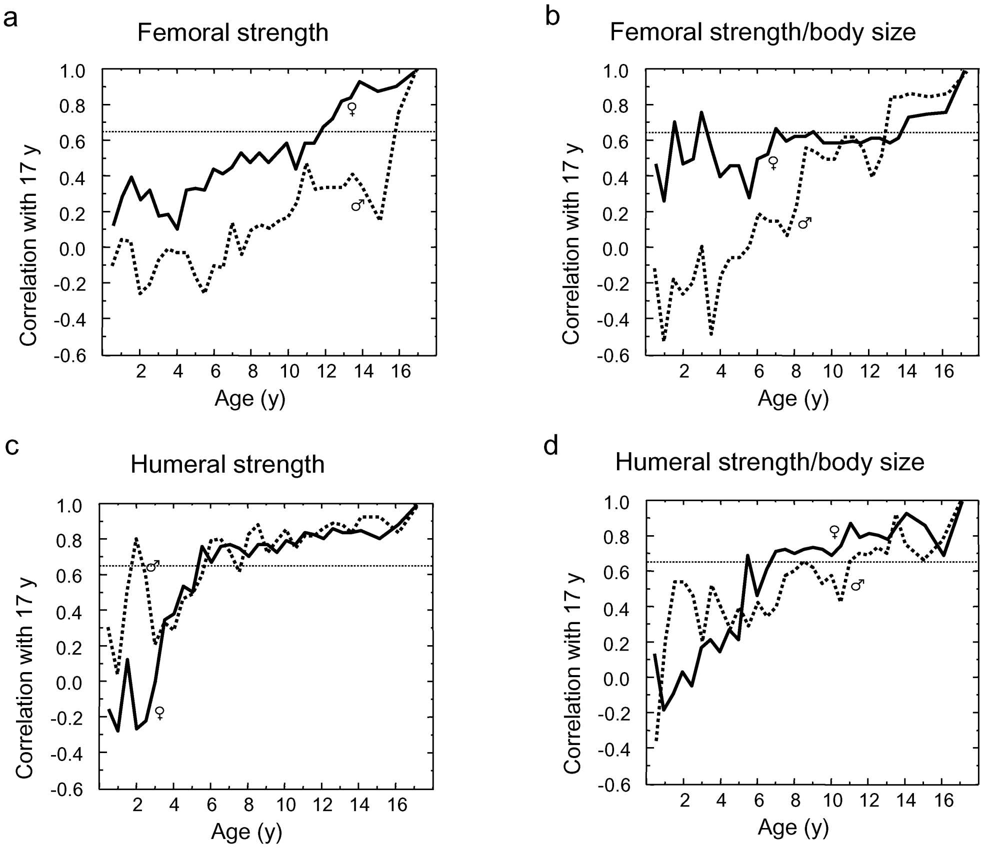

Figure 2. Spearman rank-order correlations at each age point with value at 17 y. Solid lines: girls; heavy dotted lines: boys. Thin dotted line indicates statistical significance at $p < 0.05$.

analyses. Boys show significantly more variability in raw femoral strength rankings than girls. Standardizing femoral strength by body size results in non-significant differences between the sexes among 6–17-y-olds. The median number of changes in rank for both raw and size-standardized properties varies between 5 and 8 for the complete age range, and between 3 and 6 for 6–17-y-olds, although within each period individuals range from 0 to 9 changes (the theoretical minimum and maximum number of changes possible in a sample of 10 individuals). Figure 3 compares changes in individual ranks in the 0.5–5.5, 6–10.5, and 11–17-y age groups, within sex. Significantly more changes in rank occur in the youngest age group than in the other two age groups in most comparisons. In girls the middle age period (6–10.5 y) shows more stability of ranks than

Table I. Mean rank-order correlations with 17-y-old values (0.5–16 and 6–16 y).

	Femoral strength		Humeral strength	
	Raw	Body size	Raw	Body size
0.5–16 y				
Females	0.501^{a}	$0.585^{a,b}$	0.558	0.537
Males	0.105^{a}	$0.285^{a,b}$	0.686^{c}	$0.516^{b,c}$
6–16 y				
Females	0.634^{a}	0.634	0.793^{c}	$0.756^{a,b,c}$
Males	0.222^{a}	0.539^{b}	0.832^{c}	$0.626^{a,b}$

[a] Significantly different between males and females ($p < 0.05$, two-sample *t*-tests).
[b] Significantly different from raw value ($p < 0.05$, paired *t*-tests).
[c] Significantly different from corresponding femoral value ($p < 0.05$, paired *t*-tests).

Table II. Changes in individual rank over 0.5–17 and 6–17 y (median, minimum–maximum).

	Femoral strength		Humeral strength	
	Raw	Body size	Raw	Body size
0.5–17 y				
Females	5.5 (2–8)^{a}	5 (2–8)^{a}	6.5 (3–9)	8 (5–9)
Males	8 (6–9)^{a}	7.5 (4–9)^{a}	6.5 (5–9)	7 (4–9)
6–17 y				
Females	3 (1–8)^{a}	4 (1–7)	4 (1–5)	4.5 (1–6)
Males	6 (0–8)^{a}	5 (1–8)	3 (1–7)	4.5 (0–8)

[a] Significantly different between males and females ($p < 0.05$, Mann-Whitney tests on individual ranks).

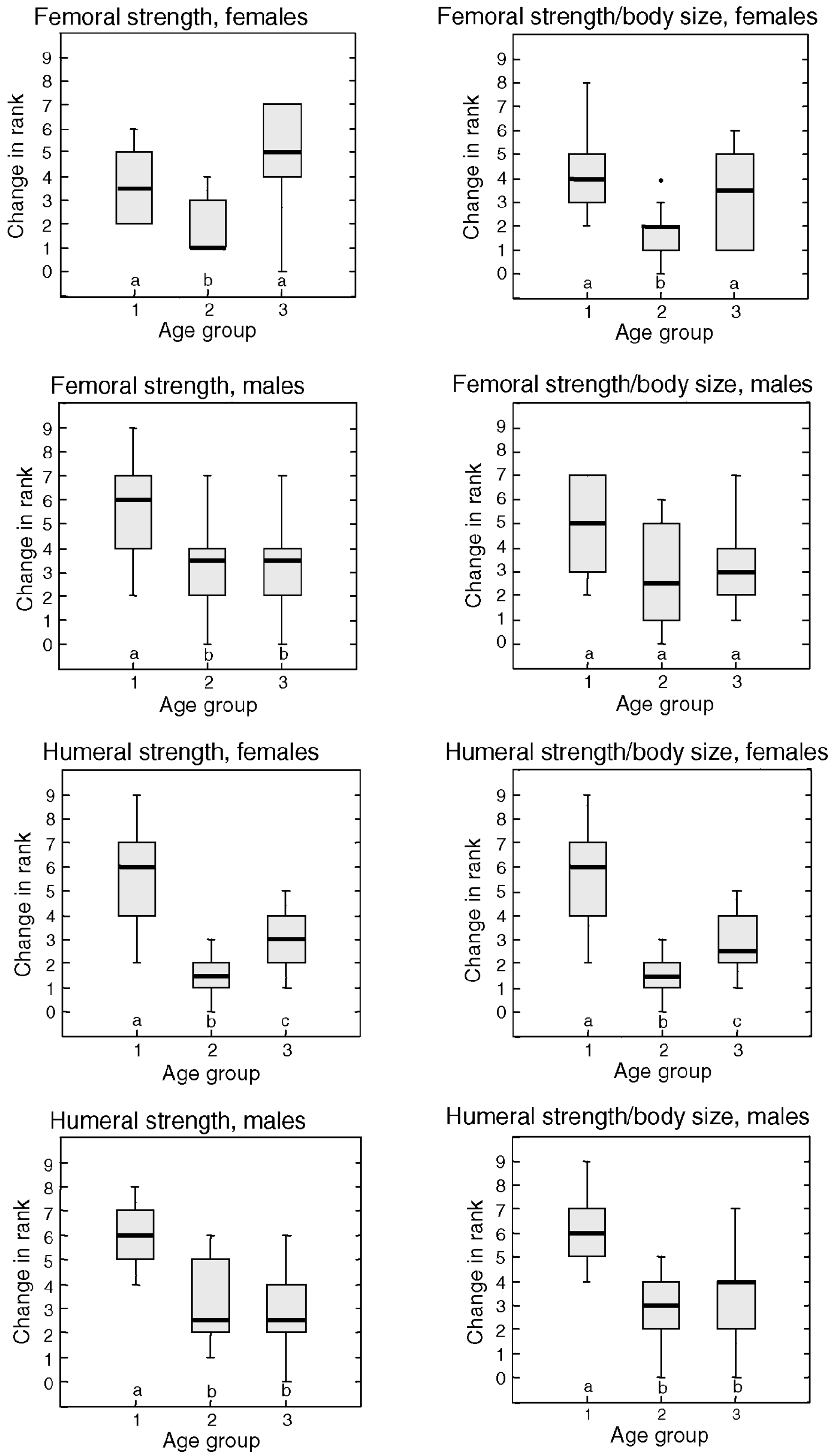

Figure 3. Number of individual changes in rank, within sex ($n = 10$), in three age groups: (1) 0.5–5.5 y, (2) 6–10.5 y, (3) 11–17 y. Letters indicate age group similarities/differences: same letter = non-significantly different, different letter = significantly different ($p < 0.05$, Wilcoxin paired-sample signed-ranks tests). Heavy line: median; shaded box: interquartile range; whiskers: values within 1.5 × interquartile range from edge of box; dots: outside values.

either of the other periods, while in boys the middle and latest age periods are equivalent. Standardizing femoral strength by body size reduces the difference in number of rank changes between the earliest and two later age periods in boys.

Discussion

Growth tracking of femoral and humeral diaphyseal strength in this sample varies depending on skeletal location, sex, and age period. As judged by correlations with values at 17 y of age, tracking of raw humeral strength is relatively good (statistically significant) from late childhood through late adolescence, while tracking of raw femoral strength is generally poorer, especially in males. Even in the humerus, however, among older children and adolescents tracking is not perfect: individuals vary by an average of 3 to 4 out of a possible 9 changes in rank between 6 and 17 y of age. The least stable period is early childhood (< 6 y), with medians of 5–6 changes in rank, except for femoral strength in girls (3.5–4 changes). Late childhood (6–10.5 y) is the most stable period in girls (medians of 1–2 changes in rank). Generally greater variability in rank in early childhood may be due to individual variability in adoption and refinement of bipedal gait (i.e., walking), which occurs between 0.5 and 3 y of age and has profound effects on both femoral and humeral strength [21,22]. Later childhood may be more stable (in girls) because it avoids both this earlier period and adolescence, when differences in timing of the adolescent growth spurt would be expected to contribute to more variation in rankings. It is not clear why boys do not show a similar decline in variability in late childhood (compared to adolescence).

The lower correlations with 17-y-old values for the male femur may be due to interactions between bone strength and body size and the timing of adolescent growth spurts. Growth in femoral strength is closely related to growth in body size [22], which is not surprising given the role of the femur in support of body weight. The particularly low correlations for raw femoral strength among boys is probably a result of the relatively late age of peak adolescent growth velocity in body size (body weight·bone length) in boys, which averages 15.0 ± 0.8 (SD) y (maximum 17.0 y) in this sample [22].[1] (Note that this is later than the age of peak adolescent growth velocity in stature for this sample [22].) Thus, some, but not all boys were still rapidly growing in body size in the years immediately prior to the endpoint age of 17 y, which would affect their ranked position relative to other boys during this period. Girls in this sample have an earlier age of peak adolescent growth velocity in body size (12.5 ± 1.5 y, maximum 14.2 y) [22]; thus, in girls, tracking of femoral strength remains high for several years in late adolescence, declining only in earlier adolescence as the peak growth spurt in body size is approached. This explanation is supported by the results standardizing for body size: when differences in body size are accounted for, femoral strength tracking dramatically improves in boys and is equivalent to that in girls from late childhood through adolescence. In contrast, standardizing by body size does not improve humeral tracking. Again, this is not unexpected given the non-weight-bearing role of the upper limb and thus lower dependence of humeral strength on body size [22].

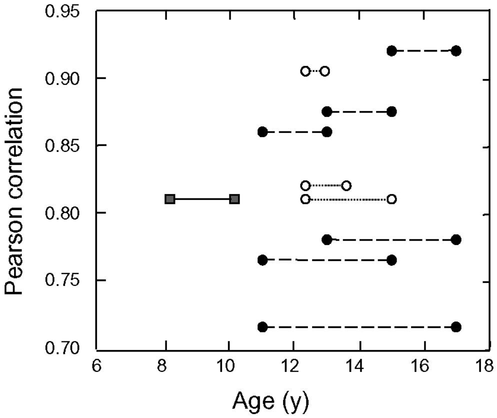

Figure 4. Mean Pearson correlations among girls in long-bone skeletal parameters measured over different age intervals in three previous studies. Gray filled squares and solid line: Ferrari et al., 1999 (femoral midshaft BMC and subperiosteal area); black filled circles and dashed lines: Magarey et al., 1999 (distal radial and ulnar shaft BMC and BW); open circles and dotted lines: Loro et al., 2000 (femoral midshaft subperiosteal and cortical areas).

The levels of growth tracking observed here, as assessed by correlation coefficients, are similar to those reported by previous investigators, when account is taken of the different time ranges included in these studies. Figure 4 shows the correlations obtained in three previous studies [1,13,14] between measurements of long-bone diaphyses taken 7 mo to 6 y apart in girls. Ferrari et al. [13] used dual-energy X-ray absorptiometry to measure 8–10-y-old girls and included a site at the midshaft femur. Magarey et al. [1] studied the distal radius and ulna in adolescent boys and girls (11–17 y) using single-energy photon absorptiometry. Although the precise location of their scan was not given, from the information provided it can be determined that it was located about 10% of the forearm length from the distal end, in a region composed of primarily compact bone, and thus is

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[1] The cited study [22] included ages beyond 17 y; thus, peak growth velocities could be determined through 17+ y. Seventeen years was chosen as the endpoint for the present study because it was the last age for which all individuals in the study sample had available data [21].

appropriately considered "diaphyseal". Loro et al. [14] used computed tomography in a sample of adolescent girls and boys (about 12–16 y) and included the midshaft femur. For each study, reported correlations for properties representative of bone geometric size—BMC, BW, subperiosteal, and cortical areas—were averaged (see Figure 4 legend). All authors reported Pearson rather than Spearman rank-order correlation coefficients. Rank-order coefficients are used in the present study because they better represent changes in the relative ordering of individuals during growth, and are also not affected by possible non-normal distributions within age groups. However, Pearson and Spearman correlations give similar results when applied to the present study sample, although Pearson correlations are slightly higher on average.

Average correlations in the previous studies range between 0.72 and 0.92 (Figure 4), which are similar to those found here for raw femoral and humeral properties in girls measured over periods within 6 y of the age endpoint of 17 y (Figure 2). Two other trends are apparent in Figure 4. First, within studies, lower correlations are found between measurements taken over longer time periods. Second, in the only study that included sequential age ranges [1], correlations are lower for earlier versus later periods of adolescence. Both of these patterns also accord with those found in the present study, where correlations declined over longer time intervals and showed a more rapid decline (at least in the femur) during the mid-adolescent growth spurt. In the two previous studies that included boys [1,14], no marked difference in tracking between the sexes was reported, which is contrary to that observed for the femur in the present study. However, the longer-term study [1] was of the upper limb, where growth tracking was also similar between the sexes in the present study. The previous study that included the lower limb [14] extended for a maximum of only 3 y, and did not include late adolescence (Figure 4), when sex differences in femoral tracking appear to be most marked, for the reasons discussed above.

The major limitations of the present study are its reliance on radiography to estimate bone structural parameters, and the limited number of individuals examined. While the use of single-plane radiography inherently includes some assumptions about bone geometry, these assumptions, for the locations measured here, appear to be fairly well met [21,22]; furthermore, such assumptions are built into some other techniques that have been used for extracting structural information from image data, e.g., DXA [17,18]. The general advantages of radiography for long-term longitudinal studies, including the stability of measurements and precision in measuring geometric parameters, have been noted by others [30]. The relatively small number of individuals included in this study can be balanced against the very long and complete record of growth available for each individual, and over the same time interval in all individuals. The length of growth examined here is approximately three times longer than in any previous growth-tracking study, and represents the only opportunity to date to assess tracking from early childhood through late adolescence. The individuals included in this study were from a relatively homogeneous ethnic and environmental background [20]; thus, the opportunity for growth tracking should have been maximized. In terms of general growth patterns, they appear to be similar to other reported samples [22].

In conclusion, the results of this study, and those of other previous studies, argue for extreme caution in extrapolating from growth tracking documented over limited age ranges to assumed growth tracking over longer time periods. While skeletal parameters in early puberty may predict values a few years later at sexual maturity [14], this is less true for longer-term predictions from childhood through late adolescence. Thus, conclusions based on short-term studies such as "we are now in a position to identify those children who are genetically prone to attain low values for peak bone mass" [14, p. 3915], or that tracking in skeletal parameters "is likely to last during the entire period of bone growth" [13, p. 361] may be premature. In the present study sample, tracking of bone strength inevitably declines over time in both the femur and humerus; furthermore, it does so at varying rates that appear to be dependent on both the timing of growth events and the mechanical environment (weight bearing or non-weight bearing) of the bone. Because of these factors, extrapolation of tracking results from one skeletal region to another may also be problematic. For example, better tracking in the upper limb from late childhood through late adolescence does not imply an equal level of tracking in the lower limb. Conversely, lower-limb tracking can be improved by factoring in body size, but this procedure does not improve tracking in the non-weight-bearing upper limb. Further truly long-term studies of different skeletal regions are needed before the relative ranking of individuals in childhood is used as an index of future bone status or fracture risk.

Acknowledgments

I thank Dr Roger Siervogel for permission to study the Denver Child Research Study sample, and for assistance in obtaining archived data for the sample. This project was supported by the Wenner-Gren Foundation for Anthropological Research.

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