

Bone Quality Assessment by Quantitative Ultrasound of Proximal Phalanges of the Hand in Healthy Subjects Aged 3–21 Years

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ABSTRACT

Bone quality by quantitative ultrasound was assessed in 1083 (587 males) healthy white subjects aged 3–21 y. Amplitude-dependent speed of sound (AD-SoS) through the distal end of the first phalanx diaphysis of the last four fingers of the hand was measured by an ultrasound device (DBM Sonic 1200, IGEA, Carpi, Italy). Mean AD-SoS values increased progressively from 3 to 21 y (males, 1845.9–2119.1 m/s, $p < 0.0001$; females, 1842.3–2098.8 m/s, $p < 0.0001$). They did not differ ($p = \text{NS}$) between sexes up to age 11, but females showed higher ($p < 0.05 - p < 0.0001$) AD-SoS values than males in age groups 12, 13, and 14 y. There was no difference ($p = \text{NS}$) of AD-SoS values between sexes in pubertal stages 1, 2, and 5, but females had higher mean AD-SoS values than males in stages 3 ($p < 0.01$) and 4 ($p < 0.001$). Independent predictors of AD-SoS were weight, body mass index, pubertal stage, and mean width of fingers in males, and age, pubertal stage, and mean width of fingers in females ($p < 0.01 - p < 0.0001$). However, 7.8% in

males and 3.6% in females of the increment of AD-SoS values can be related to the finger anatomy alone. AD-SoS values probably reflect the architectural organization of growing bone or changes in bone elasticity. Increased bone density and size may be additional factors influencing AD-SoS. Measurement of AD-SoS at the hand phalanges may be a simple, noninvasive, and radiation-free technique to assess bone quality in children. (*Pediatr Res* 49: 713–718, 2001)

Abbreviations:

AD-SoS, amplitude-dependent speed of sound
BMI, body mass index
BMD, bone mineral density
CV, coefficient of variation
sCV, standardized coefficient of variation
QUS, quantitative ultrasound
ROI, region of interest

Prospective studies have shown that the incidence of osteoporotic fractures is inversely related to bone mass (1). Peak bone mass is considered a main determinant of BMD in adulthood; thus, maximizing peak bone mass is important for preventing osteoporosis (1). It has been generally accepted that most of peak bone mass at any skeletal site is attained during the mid thirties in both sexes (2, 3), but in lumbar spine and in femoral neck, bone mass accumulation is virtually completed in late adolescence to young adulthood (2–4). Thus, failure to gain sufficient bone mass during skeletal growth and the period of bone consolidation may predispose to the development of senile osteoporosis (5). Some years ago Dent (6) and more recently Kreipe (7) suggested that “senile osteoporosis is a pediatric disease.” Therefore, the assessment of bone mineral status during childhood and adolescence may be a useful tool

in identifying subjects with reduced bone mass who could be exposed to an increased risk of osteoporosis in adulthood.

For preventive studies in large population of children and adolescents, it would be necessary to assess BMD with a technique that is relatively cost-effective and free of ionizing radiation. QUS is a new and noninvasive method of estimating BMD and bone elasticity (8–13). This technique is safe, easy to use, and radiation-free; the equipment can be transported, and it is relatively cheap in comparison with more expensive densitometric techniques such as dual-energy x-ray absorptiometry and quantitative computed tomography (13, 14). Clinical studies showed that QUS was able to discriminate between osteoporotic and healthy women (11, 14, 15), and it may predict fracture independent of BMD (11). Moreover, QUS seems to be a useful method to recognize osteopenic children (16, 17).

In this study we assessed ultrasound velocity at proximal phalanges of the hand in healthy children and adolescents to obtain normative values for the 3- to 21-y-old population.

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METHODS

Subjects. We examined 1083 (587 males and 496 females) healthy white subjects, aged 3–21 y, randomly enrolled in nursery, primary, or secondary schools, and in medical school of our university. The subjects were subdivided in 1-y age groups and by sex (Table 1). All subjects were examined by one of us (G.B., S.B.). An extensive clinical history was obtained by interview with the children's parents or the subject as appropriate. All subjects had normal weight and length at birth, and did not take drugs known to affect bone or mineral metabolism. There was no history of any chronic or bone disease. None suffered from bone fractures or diseases at the site of ultrasound velocity assessment. In all subjects, height, weight, and BMI were in the normal age distribution, and their pubertal stage was appropriate for chronologic age.

Consent. Informed written consent to perform the study was obtained from the parents of each subject when the chronologic age of the child was <18 y and directly from each subject whose chronologic age was >18 y. The study was approved by the ethics committee for human investigation of our department. The headmaster and the school teachers committees of the enrolled schools approved the study.

Assessment of anthropometric findings. Standing height and weight were measured with portable stadiometer and balance, respectively, by one of us (G.B., S.B.). BMI was calculated using the formula weight (in kilograms) divided by height (in square meters). Pubertal stage was assessed according to Tanner and Whitehouse (18).

Ultrasound velocity measurement. The device used (DBM Sonic 1200, IGEA, Carpi, Italy) is based on the transmission of ultrasound through the distal end of the first phalanx diaphysis in proximity of the condyles (ROI) of the last four fingers of the hand. The condyles at the distal diaphysis provide a convenient point for placing the probes, which is an essential feature for reproducibility of measurements (10, 15). The distal end of the diaphysis of the proximal phalanxes contains both

cortical and trabecular bone, as well as a small medullary canal (13, 19); the anatomic ROI is mostly cortical bone (approximately 60%) (19, 20).

Two 12-mm-diameter transducers on a high-precision (± 0.02 mm) caliper, which measures the distance between the two probes, are positioned on the lateral and medial surface of each finger. The emitter probe generates an ultrasound signal with a frequency of 1.25 MHz, and the receiver probe receives the ultrasounds that have crossed the phalanx (21). The medial and lateral surface of the phalanx at the ROI is approximately parallel, hence reducing ultrasound scattering (10). The coupling of the probes with the skin is mediated by standard ultrasound gel. The device calculates the speed of sound (SoS, in meters per second) through the phalanx by measuring the width of the finger (including soft tissues) divided by the time of flight, defined as the time from emitted pulse to received signal, considering the signal that reaches a predetermined minimum amplitude value (2 mV) for the first time; thus, the assessed ultrasound velocity is AD-SoS (21). The probes are gently rotated until the best signal (defined in terms of number of peaks and the amplitude of the peaks) is recorded on the screen. The final result is the average AD-SoS over four fingers. At each measuring session, the reference speed of the subject's soft tissue is measured by applying the probes to the soft tissue area of the first interdigital space. The value is then automatically used by the device when measuring AD-SoS in the phalanx to take account of soft tissue interference.

In all subjects, AD-SoS was measured in the nondominant hand by the same operator (G.F.). In addition, the difference between AD-SoS values in dominant and nondominant hands was assessed in 25 (12 males and 13 females) healthy white children and adolescents, aged 7–18 y, by the same operator (G.B.). All the osteosonogrammetry data were stored on a portable personal computer connected to the device.

Precision. Short-time precision was assessed *in vivo* by measuring AD-SoS in four healthy white children (two males

Table 1. Anthropometric findings of the examined subjects

Age Group, y	Males				Females			
	n	Height (cm)	Weight (kg)	BMI	n	Height (cm)	Weight (kg)	BMI
3	11	103.9 ± 3.7	18.0 ± 2.0	16.7 ± 1.5	15	99.1 ± 4.6	15.8 ± 2.0	16.1 ± 1.6
4	24	108.0 ± 4.4	18.5 ± 2.4	15.9 ± 1.6	21	108.0 ± 3.9	17.8 ± 2.0	15.2 ± 1.3
5	18	116.5 ± 4.8	21.9 ± 2.4	16.2 ± 1.7	24	114.0 ± 3.6	20.5 ± 2.9	15.7 ± 1.7
6	23	121.3 ± 4.1	23.3 ± 3.5	15.8 ± 1.8	23	121.3 ± 4.9	24.2 ± 4.8	16.4 ± 2.2
7	21	128.2 ± 4.2	27.9 ± 4.4	16.9 ± 2.2	26	124.8 ± 3.7	25.0 ± 3.3	16.0 ± 1.8
8	22	133.1 ± 3.5	29.3 ± 3.4	16.5 ± 1.6	24	130.8 ± 5.5	29.5 ± 3.8	17.2 ± 1.4
9	18	137.4 ± 4.9	32.1 ± 4.5	16.9 ± 1.9	20	139.5 ± 4.7	34.8 ± 5.6	17.8 ± 2.1
10	28	142.8 ± 5.4	35.5 ± 4.6	17.4 ± 1.6	19	142.1 ± 4.5	33.4 ± 3.9	16.5 ± 1.3
11	30	147.8 ± 6.0	39.0 ± 6.6	17.8 ± 2.3	19	152.3 ± 5.9	43.4 ± 6.2	18.6 ± 1.9
12	25	154.3 ± 6.8	44.6 ± 9.0	18.6 ± 2.5	20	152.2 ± 5.3	44.0 ± 5.2	19.0 ± 1.9
13	21	162.0 ± 7.0	50.4 ± 7.1	19.1 ± 1.8	20	158.1 ± 5.2	48.3 ± 5.0	19.3 ± 1.5
14	44	168.6 ± 8.4	61.1 ± 8.2	21.5 ± 2.1	32	161.0 ± 6.2	53.4 ± 6.7	20.6 ± 2.4
15	65	172.7 ± 7.3	64.4 ± 8.9	21.5 ± 1.9	59	162.2 ± 5.5	55.8 ± 5.4	21.2 ± 1.9
16	63	174.3 ± 6.3	66.2 ± 7.8	21.7 ± 1.9	48	162.6 ± 6.3	56.8 ± 7.4	21.4 ± 1.7
17	58	175.2 ± 6.2	69.4 ± 7.9	22.6 ± 1.9	52	162.0 ± 5.3	56.8 ± 5.2	21.6 ± 1.6
18	55	175.8 ± 5.6	69.9 ± 7.0	22.6 ± 1.9	38	163.5 ± 6.4	57.9 ± 6.8	21.6 ± 1.8
19	28	177.3 ± 8.1	71.3 ± 8.4	22.7 ± 2.2	11	161.8 ± 4.7	57.6 ± 5.9	22.0 ± 1.3
20	22	178.2 ± 5.7	71.6 ± 8.2	22.5 ± 2.0	12	162.7 ± 4.8	55.3 ± 5.7	20.9 ± 2.4
21	11	173.8 ± 6.2	69.6 ± 5.0	23.1 ± 1.8	13	162.5 ± 5.5	55.5 ± 6.8	21.0 ± 2.1

and two females, aged 7–8 y) and four adolescents (two males and two females, aged 11–13 y) five times on one day by the same operator (G.B.) with repositioning. After 7–10 d, inter-operator precision was assessed measuring AD-SoS in the same eight subjects five times on one day by two operators (G.B., G.F.) with repositioning. Precision was expressed by the determination of the CV for each of the eight subjects using the formula: $CV\% = (SD/mean) \times 100$, where mean and SD are the mean and SD over five repeated measurements. Precision was defined as the mean value of the CV calculated on the eight subjects. An sCV was derived by normalizing the CV of each subject to the range over the mean according to the formula $sCV\% = CV\% / (\text{dynamic range}/\text{mean})$ (22). Dynamic range was derived from the difference between the highest AD-SoS value measured in the entire population of males or females and the lowest measurable AD-SoS value (1570 m/s) recorded in the device. Standardized precision was defined as the mean value of the sCV calculated on the eight subjects.

Statistical analysis. The results are expressed as mean \pm SD. Comparison of the data between males and females was determined using *t* test for unpaired samples. One-way ANOVA for repeated measurements corrected by the Bonferroni method was used to assess the age influence on AD-SoS values with sex. Linear regression analysis by Pearson's formula was performed to determine correlation coefficients between AD-SoS and anthropometric variables or mean width of fingers. Multiple regression analysis was performed to determine the significance of each independent variable (age, height, weight, BMI, pubertal stage, and mean width of fingers) correlated with AD-SoS after adjusting for the effect of the other independent variables. In addition, partial correlation analysis between AD-SoS and mean width of fingers controlling for age, height, weight, BMI, and pubertal stage was applied. All statistical analyses were performed using the SPSS for Windows software program (Statistical Package of Social Sciences, version 6.1, Chicago, IL, U.S.A.). A $p < 0.05$ was considered significant.

RESULTS

Variation of AD-SoS during childhood and adolescence. In both sexes, mean AD-SoS values increased progressively from 3 to 21 y (males, 1845.9–2119.1 m/s, increment 14.8%, $p < 0.0001$; females, 1842.3–2098.8 m/s, increment 13.9%, $p < 0.0001$). In male subjects, mean AD-SoS values showed a significant increase in the age groups 15 and 16 y in comparison with the 1-y younger age group; in female subjects, mean AD-SoS values did not show any change between 1-y age groups (Table 2). There was no difference of mean AD-SoS values between males and females up to age 11, as well as after 15, but females showed higher mean AD-SoS values than males in the age groups 12, 13, and 14 y (Table 2).

Mean width of fingers increased progressively from 3 to 21 y (males, 11.2–14.6 mm, increment 30.4%, $p < 0.0001$; females, 10.7–13.5 mm, increment 26.2%, $p < 0.0001$).

Variation of AD-SoS during pubertal stages. Mean AD-SoS values increased significantly from stage 3 to 4 and from stage 4 to 5 in males, and from stage 2 to 3 and from stage 3

Table 2. Mean AD-SoS values per 1-y class through the distal end of the first phalanx diaphysis of the last four fingers of the hand in healthy male and female subjects ages 3–21 y.

Age group, y	AD-SoS, males (m/s)	AD-SoS, females (m/s)
3	1845.9 \pm 25.5	1842.3 \pm 23.0
4	1853.7 \pm 21.5	1862.1 \pm 25.6
5	1880.0 \pm 35.2	1882.6 \pm 21.9
6	1883.5 \pm 35.5	1883.6 \pm 27.3
7	1891.5 \pm 37.4	1887.5 \pm 34.9
8	1924.2 \pm 29.4	1907.0 \pm 38.6
9	1925.9 \pm 38.7	1936.3 \pm 38.2
10	1928.4 \pm 42.3	1944.6 \pm 32.2
11	1949.6 \pm 40.6	1957.5 \pm 50.1
12	1949.5 \pm 45.5	2000.2 \pm 72.0‡
13	1967.8 \pm 42.4	2017.6 \pm 93.4§
14	1981.0 \pm 58.0	2034.9 \pm 45.3
15	2032.5 \pm 43.2*	2046.1 \pm 41.3
16	2067.7 \pm 47.9†	2059.1 \pm 39.5
17	2091.4 \pm 50.5	2079.2 \pm 50.9
18	2099.2 \pm 43.9	2083.3 \pm 39.5
19	2108.4 \pm 45.9	2088.6 \pm 28.1
20	2115.4 \pm 45.9	2094.5 \pm 34.4
21	2119.1 \pm 38.9	2099.8 \pm 46.1

Data are expressed as mean \pm SD.

* $p < 0.0001$ and † $p < 0.002$ in comparison with 1-y younger age group.

‡ $p < 0.01$, § $p < 0.05$, and || $p < 0.0001$ in comparison with males having the same chronologic age.

to 4 in females (Fig. 1). Mean AD-SoS values did not differ between males and females in stages 1, 2, and 5; but females had higher mean AD-SoS values in stages 3 and 4 in comparison with males (Fig. 1).

Correlation between AD-SoS and anthropometric variables or mean width of fingers. Correlation coefficients between AD-SoS and anthropometric variables or mean width of fingers are reported in Table 3. In both sexes, AD-SoS corre-

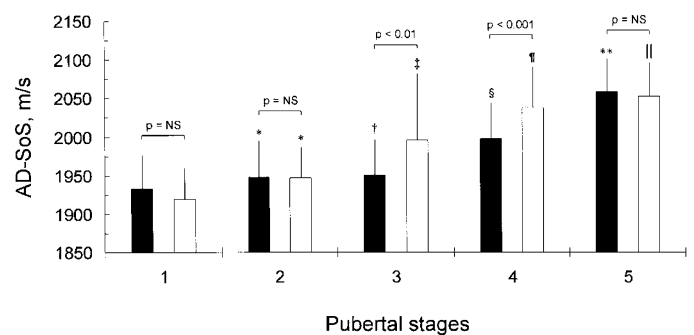


Fig. 1. AD-SoS (m/s) values through the distal end of the first phalanx diaphysis of the last four fingers of the hand in healthy male (filled columns) and female (open columns) subjects during pubertal stages. Stage 1: males, $n = 51$ (age 9–11 y); females, $n = 42$ (age 8–9 y); stage 2: males, $n = 49$ (age 10–13 y); females, $n = 39$ (age 9–12 y); stage 3: males, $n = 39$ (age 12–14 y); females, $n = 32$ (age 11–14 y); stage 4: males, $n = 39$ (age 14–16 y); females, $n = 41$ (age 13–15 y); stage 5: males, $n = 116$ (age 15–16 y); females, $n = 107$ (age 14–16 y). Data are expressed as mean plus SD. * $p = NS$ in comparison with stage 1; † $p = NS$ in comparison with stage 1 and 2; ‡ $p < 0.0001$ in comparison with stage 1, and $p < 0.001$ in comparison with stage 2; § $p < 0.0001$ in comparison with stages 1, 2, and 3; ¶ $p < 0.0001$ in comparison with stages 1 and 2, and $p < 0.002$ in comparison with stage 3; || $p < 0.0001$ in comparison with stages 1, 2, and 3, and $p = NS$ in comparison with stage 4; ** $p < 0.0001$ in comparison with stages 1, 2, 3, and 4.

Table 3. Correlation coefficients between AD-SoS and anthropometric variables or mean width of fingers in healthy male and female subjects ages 3–21 y.

	AD-SoS in males		AD-SoS in females	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
Age (y)	0.87	<0.0001	0.87	<0.0001
Height (cm)	0.81	<0.0001	0.84	<0.0001
Weight (kg)	0.77	<0.0001	0.82	<0.0001
BMI	0.59	<0.0001	0.64	<0.0001
Pubertal stage	0.74	<0.0001	0.73	<0.0001
Mean width of fingers (mm)	0.55	<0.0001	0.50	<0.0001

lated significantly with all the anthropometric variables and mean width of fingers. Moreover, age and mean width of fingers were significantly correlated (males, $r = 0.74$, $p < 0.0001$; females, $r = 0.65$, $p < 0.0001$). In both sexes, multiple regression analysis showed that the composite interaction of all the independent variables was predictive of AD-SoS (males, $r^2 = 0.63$, $p < 0.0001$; females, $r^2 = 0.60$, $p < 0.0001$). As independent predictors of AD-SoS, weight, BMI, pubertal stage, and mean width of fingers reached significance ($p < 0.01$, $p < 0.0001$, $p < 0.0001$, and $p < 0.001$, respectively) in males; whereas age, pubertal stage, and mean width of fingers reached significance ($p < 0.01$, $p < 0.0001$, and $p < 0.01$, respectively) in females. When partial correlation analysis was applied controlling for age, height, weight, BMI, and pubertal stage, AD-SoS remained significantly correlated with mean width of fingers, but there is a little effect on the strength of that correlation (Table 4).

AD-SoS in dominant and nondominant hands. There was no significant difference ($p = \text{NS}$) of AD-SoS values between dominant and nondominant hands in both males (1992.5 ± 74.9 m/s and 1992.3 ± 73.8 m/s, respectively; mean difference between the hands, 4.8 ± 1.7 m/s) and females (1993.6 ± 69.9 m/s and 1994.0 ± 69.8 m/s, respectively; mean difference between the hands, 4.5 ± 1.8 m/s).

Precision. Intra- and interoperator CV *in vivo* was 0.55 and 0.91%, respectively. The highest measured AD-SoS value was 2193 and 2198 m/s, with a dynamic range of 623 and 628 m/s, in males and females, respectively. Thus, sCV was 1.75% in males and 1.74% in females.

DISCUSSION

In both sexes, mean AD-SoS values at the distal end of the proximal phalanx diaphysis progressively increased during childhood and adolescence. Similar results were found by

Table 4. Partial correlations between AD-SoS and mean width of fingers in healthy male and female subjects ages 3–21 y

	AD-SoS in males		AD-SoS in females	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
Mean width of fingers (mm)				
Controlling for age (y)	-0.28	<0.0001	-0.19	<0.0001
Controlling for height (cm)	-0.26	<0.0001	-0.28	<0.0001
Controlling for weight (kg)	-0.25	<0.0001	-0.29	<0.0001
Controlling for BMI	-0.19	<0.0001	0.09	<0.05
Controlling for pubertal stage	-0.34	<0.0001	-0.18	-0.01

Tormo *et al.* (23) in Spanish children aged 1–8 y, and by Halaba and Pluskiewicz (24) in Polish adolescents aged 9–15 y. Females had higher mean AD-SoS values than males at 12, 13, and 14 y, probably reflecting the earlier onset of pubertal development. During puberty, mean AD-SoS values increased earlier in females (between stages 2 and 3) than in males (between stages 3 and 4); females had higher mean AD-SoS values than males in stages 3 and 4, whereas no sex difference was found in the other stages of puberty.

Ultrasound velocity depends on the material properties of the medium through which the ultrasound wave travels, and there is general agreement that ultrasound velocity is influenced by bone density, architecture, and elasticity (8–14). This suggests that the increment of AD-SoS values we found during childhood and adolescence may reflect an increase of BMD or changes in structural characteristics of bone. Ash weight per unit volume of human skeletons (25, 26), as well as radial (27) and femoral (28) bone density assessed by quantitative computed tomography, does not change during life, suggesting that the increase of AD-SoS values with age could be related to the architectural organization of growing bone by changing cortical structure (number of lamellars and secondary osteons) (29–31) and trabecular orientation (changes in the arrangement of the trabecular struts reflecting the anisotropy of bone) (30, 31), number, or thickness. Indeed, studies by radiographic metacarpal morphometry (32–34) showed increased subperiosteal apposition in growing bone leading to increased cortical thickness and cortical area during childhood. A substantial gain in cortical bone on both subperiosteal and endosteal surfaces with a decline of medullary width was observed during adolescence (34). The influence of cortical thickness on AD-SoS is suggested by recent data *in vitro* (20, 21) showing that a reduction of cortical thickness was associated with a reduced AD-SoS. In addition, some studies in human vertebral (35, 36) and in bovine radial or femoral (10, 37) bone specimens showed that QUS reflected some structural characteristics of trabecular bone mainly related to trabecular orientation. Wuster *et al.* (13) showed similar results in human phalangeal bone. Furthermore, Hoffler *et al.* (38) showed that the mechanical properties of bone lamellae, obtained from the lateral portion of femoral neck of human cadavers, were independent of age and sex, suggesting that other factors such as bone mass and structure contributed to the mechanical properties of bone. On the other hand, it has been reported that QUS moderately correlated with BMD ($r = 0.40$ – 0.70) assessed by densitometric techniques (11, 12, 39). Therefore, we cannot exclude that the rise of AD-SoS values in phalanges during childhood and adolescence may reflect, at least in part, a small increase in cortical BMD as found at the second metacarpus by roentgen microdensitometry (40), or in trabecular BMD as showed at vertebral bodies in late puberty by quantitative computed tomography, reflecting an increase in trabecular number or thickness (28, 41). In this regard, a histomorphometric study on iliac bone specimens in growing children (1.5–22.9 y) demonstrated an age-dependent increase in both cortical width and trabecular bone volume, the latter being caused by an increase in trabecular thickness (42).

The dependence of AD-SoS on body size and mean width of fingers (bone plus soft tissues) suggests that skeletal mass *per se* may influence ultrasound velocity. Theoretically, ultrasound velocity should be independent of the dimensions of the sample, as found *in vitro* by using Perspex blocks having a width in the range of human adult fingers (11–17 mm) (20). However, this is true only when the sample thickness is very large compared with the wavelength of sound propagation (43). At a sample thickness close to the wavelength of ultrasound, a dispersion occurs and ultrasound velocity decreases with decreasing sample thickness (44). Indeed, as frequency (f) and wavelength (λ) are related to each other by the velocity of the sound wave (c) by the equation $c = \lambda f$ (8), if f is the frequency of the emitter probe of our device (1.25 MHz) and c is AD-SoS, in our subjects the value of λ would be approximately in the range of 1.5 mm (age group 3 y) to 1.7 mm (age group 21 y) by the equation $\lambda = c/f$. Therefore, as the frequency of the emitter probe is constant, the dependency of AD-SoS on the mean width of fingers could reflect an increase in wavelength related to changes of bone size or elasticity. According to the correlation between AD-SoS and mean width of fingers, at least 25% of the observed increase of AD-SoS can be explained by the finger anatomy alone. On the other hand, as age and finger width were closely correlated, at least 42% of the observed increase of finger width can be explained by the increase of age. However, partial correlation analysis between AD-SoS and finger width controlling for age suggested that only 7.8% in males and 3.6% in females of the observed increase of AD-SoS can be related to the finger anatomy alone. Furthermore, as bone is an anisotropic tissue, there is a directional dependency of ultrasound transmission velocity through bone; in any case, materials with a high elastic modulus, such as bone, can support both longitudinal and shear waves (8–10, 30). Thus, the mode of ultrasound transmission through bone, which depends on its structural characteristics, may also influence AD-SoS.

Thickness or the composition of soft tissue surrounding the finger at the ROI could be an additional factor influencing AD-SoS values. An *in vitro* study showed that the excision of the soft tissues from cadaver heels produced an increase in ultrasound velocity whereas the subsequent insertion of an artificial layer of fat into the ultrasound path lowered ultrasound velocity (45). It has been also demonstrated *in vivo* that ankle edema reduced the ultrasound velocity through the heel (46). However, we were unable to investigate the impact of soft tissues on AD-SoS.

We did not find any significant difference between dominant and nondominant hands, as previously reported in adults (13, 47), suggesting that it is sufficient to measure AD-SoS of one hand only.

In conclusion, our study shows that AD-SoS measured at the distal end of the proximal phalanx diaphysis of the hand increases during childhood and adolescence, probably reflecting the architectural organization of growing bone or changes of elasticity of bone tissue. In any case, a small increase in bone density or changes of bone size may also influence AD-SoS values. Measurement of AD-SoS at the hand phalanges may be a useful tool to assess bone quality in pediatric

age in view of the absence of radiation exposure, low cost, and portability of the equipment. However, further studies are needed to establish whether its primary role will be as a complementary measurement or as a replacement for dual-energy x-ray absorptiometry.

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