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Unusually high calcaneal speed of sound measurements in children with small foot size

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Abstract

The purpose of this clinical note is to describe the performance of the Lunar Achilles Insight device in assessing bone quality at the calcaneus in 142 children between the ages of 5–11 years accessing healthcare in Johannesburg, South Africa. We observed an asymmetric bimodal distribution in speed of sound (SOS). The minor mode consisted of unusually high SOS values (1625 m/sec) which were primarily observed among children with foot size <19 cm and height <119 cm. Cortical regions of the bone may have been inadvertently included in the region of interest for smaller feet, causing unusually high SOS values. The unusually high SOS values indicate that the validity of SOS in this device as it is currently used for measuring bone quality in young children is questionable. Future studies using this device in young children should develop new methodology to account for smaller foot size.

Keywords

Ultrasound; bone quality; pediatrics; South Africa

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Introduction

Quantitative ultrasonography (QUS) assesses bone quality by measuring the attenuation and speed of ultrasound wave propagation through bone. Speed of sound (SOS), a measure of velocity, refers to the distance traveled by the ultrasound wave divided by its travel time, while BUA is the slope of the frequency-dependent attenuation associated with the transmitted ultrasound wave. In calcaneal QUS with the Lunar Achilles Insight device, SOS and BUA are combined to calculate a manufacturer-specific parameter known as stiffness index.

DXA is considered the gold standard for assessing bone health; however, QUS has some advantages over DXA. QUS does not require radiation exposure or high-level training, is portable, costs less than DXA to perform, and has a short scan time, making it potentially well-suited for assessing and tracking bone acquisition in resource-constrained settings.

Although the manufacturer does not recommend its use in subjects less than 20 years of age, data from the Lunar Achilles Insight device have been published on subjects as young as 2 years old (Herrmann et al. 2014, Sawyer et al. 2001). As part of a study to investigate the utility of QUS for assessing bone health in resource-constrained settings, we evaluated the performance of the Lunar Achilles Insight device in a group of children between the ages of 5–11 years in Johannesburg, South Africa. After observing a bimodal distribution in SOS values but not in BUA, we investigated what factors could account for this distribution.

Materials and Methods

Subjects

The Changes Bone Study is a longitudinal study of bone health in 440 children in Johannesburg, South Africa, including 220 HIV-infected children and 220 population-appropriate HIV-uninfected control children. The study examines DXA as a primary outcome (Arpadi et al. 2016), while calcaneal and distal radius QUS are included as secondary outcomes. A future paper will compare QUS to DXA as well as compare QUS measurements between HIV-infected and uninfected children. The purpose of the current report is to investigate reasons for the bimodal distribution of SOS we observed in calcaneal QUS data from 142 participant visits that occurred between December 2014 and December 2015. Parents or guardians provided written informed consent, and children provided assent if they were at least 7 years old and able to understand. The study was approved by the Institutional Review Boards of Columbia University (New York, NY, USA) and the University of the Witwatersrand (Johannesburg, South Africa).

Measurements

Measurements at the calcaneus of SOS in meters/second (m/sec) and BUA in decibels/megahertz (dB/MHz) were obtained by a Lunar Achilles Insight QUS device (GE Healthcare, Madison, WI, USA). The device's built-in quality assurance test was run prior to every use to ensure proper coupling, unit temperature, and water level. Standard operating procedures were followed as specified in the operator's manual provided by the

manufacturer. The size and location of the region of interest (ROI) as well as the proper positioning of the foot were determined by consulting the real-time QUS image produced by the device. The smallest ROI setting of approximately 18 mm was used. Shims were utilized for positioning participants' feet that were smaller than USA women's size 6 and UK women's size 4.5, as recommended by the manufacturer. In addition, calcaneus stiffness index (SI) was calculated by the device using the following equation adapted from Njeh et al. (1999): $SI = (0.67 \times BUA + 0.28 \times SOS) - 420$.

SOS exhibited an asymmetric bimodal distribution (See Figure 1). As the minor mode consisted of SOS values >1625 m/sec, we categorized these values as "high" SOS. The major mode of SOS <1625 m/sec was categorized as "low" SOS. In contrast, BUA had a slightly left-skewed distribution and did not appear to have any unusual measurements. Only one set of ultrasound measurements was taken for each child. However, we evaluated the agreement between ultrasound measurements in 8 children taken by the two operators and found intraclass correlation coefficients of 0.91 for BUA and 0.98 for SOS.

Weight to nearest 0.1 kilogram (kg) was measured by a digital scale and height to nearest 0.1 centimeter (cm) by a stadiometer. Foot size to the nearest 0.5 cm was measured from the tip of the longest toe to the back of the heel, using a measuring mat imprinted with a ruler.

Statistical Analysis

The characteristics of children with high SOS and low SOS were compared using *t*-tests or Wilcoxon tests for continuous variables and χ^2 tests or Fisher's exact tests for categorical variables. SOS was plotted against foot size, height, and age. Pearson correlation coefficients were calculated for foot size, age, and height. All analyses were conducted using SAS 9.4 (Cary, NC, USA).

Results

A total of 142 children (72 HIV-infected and 70 HIV-uninfected) were included in this analysis (See Table 1). Approximately half (47.9%) were female and the median age was 7.4 years. The mean weight was 23.8 kg and mean height was 120.3 cm.

SOS was bimodally distributed (See Figure 1). Of the 142 children, 26 (18%) had unusually high SOS (>1625 m/sec). Compared to children with low SOS, children with high SOS had a greater proportion of girls (65.4 vs 44.0%, $p=0.048$), a significantly lower median age (6.7 vs 7.8 years, $p<0.01$), lower mean weight (18.8 vs 25.0 kg, $p<0.01$), and lower mean height (112.1 vs 122.2 cm, $p<0.01$). Children with high SOS also had lower mean BUA (65.4 vs 93.9 m/sec, $p<0.01$) and higher mean stiffness index (98.0 vs 79.0, $p<0.01$) compared to children with low SOS. HIV status, however, did not differ between children with high SOS and low SOS ($p=0.0976$).

Figure 2A shows SOS plotted against foot size, grouped by age. The SOS data cluster into two groups corresponding to the two modes of the distribution of SOS—the low SOS group which includes a wide range of foot sizes and the high SOS group which includes predominantly smaller foot sizes, i.e. <19 cm. Of the 56 children with foot size <19 cm, 24

(42.9%) had high SOS. In contrast to SOS, BUA has an approximately linear relationship with foot size (See Figure 2B).

Because foot size was significantly correlated with both height ($R=0.91$, $p<0.01$) and age ($R=0.73$, $p<0.01$) and these variables are more commonly measured in clinical settings than foot size, we also assessed the relationships of height and age with SOS and BUA. When age and height are plotted against SOS, the SOS data again cluster into low and high SOS groups, with the majority of the high SOS group having shorter height (<119 cm) and younger age (<8 years) (Figures 2C and 2E). Of the 58 children with height <119 cm, 21 (36.2%) had high SOS, while 23 of the 90 (25.6%) children with age <8 years old had high SOS. Again, BUA has an approximately linear relationship with height and age (Figures 2D and 2F).

Discussion

In this study, we demonstrate the limited accuracy of SOS in the Lunar Achilles Insight QUS device when evaluating children with small foot sizes (<19 cm from longest toe to heel), despite using the standard shims supplied by the manufacturer in addition to selecting the smallest ROI available and positioning the ROI over the lowest echodensity area in the calcaneus. Among the children with small foot size, a large proportion have unusually high SOS results.

Alwis et al. (2010) reported a plot of SOS values versus age that appears similar to Figure 2E. Like us, they hypothesized that the outliers in their data were related to small foot size but did not specifically evaluate the relationship of foot size to high SOS values in their data.

There are several possible reasons for the apparent association of small foot size with high SOS values. The ROI of calcaneal QUS should consist primarily of trabecular bone. Several studies have described issues of heterogeneity and regional variation in the trabecular bone in the calcaneus, complicating ROI selection (Laugier et al. 1996, Lin et al. 1998). It is possible that higher density trabecular regions in the smaller feet are causing the elevations in SOS. However, it is more likely that some cortical regions at the back of the heel were inadvertently included in the ROI, causing unusually high SOS values. This would have occurred because the velocity of ultrasound in cortical bone is approximately twice that of ultrasound in trabecular bone (Kaufman and Siffert 2001). Thus, a small amount of cortical bone within the ROI would produce an early precursor signal that with earliest time of arrival processing would lead to a high value for SOS. In contrast, BUA is generally computed using the entire signal. Therefore, a presumed low amplitude early arrival precursor signal due to a cortical edge within the ROI would not be expected to cause significant alterations in BUA.

Another explanation might be the presence of fast and slow waves (Breban et al. 2010). Although such waves have not been detected in the medial-lateral direction in adult calcanei, it is possible that in children the trabecular architecture is distinct from that of adults. Although this could be further investigated by looking at the non-linearity of the BUA data (Haia et al. 2008), we do not have access to either the raw (RF) signals or the spectral

information from which the BUA parameter (i.e., slope) is obtained. Future work should at least consider the possibility that pediatric calcaneal bone could give rise to fast and slow modes of ultrasound wave propagation.

Alternatively, the Achilles's assumption of a constant heel thickness of 4 cm may have played a role in producing the unusually high SOS values. Hausler et al. (1997) found that the fixed heel width caused the Achilles to overestimate SOS in adults, although it was not clinically significant. It is possible that the fixed heel width could lead to a significant overestimate of SOS in children with small feet. However, it seems unlikely that heel sizes, which are not likely to be bimodally distributed, would cause SOS to be bimodally distributed.

Based on our theory that the high SOS measurements included cortical bone, future analyses of our study data will exclude children with unusually high SOS measurements.

One limitation of this report is that we did not take multiple ultrasound measurements for each child at the same visit. However, as we stated earlier, we found good agreement between multiple ultrasound measurements in 8 children.

Our findings suggest that the Achilles may record unusually high SOS measurements in children with small foot size (<19 cm). Height <119 cm may be a reasonable and routinely measured surrogate for small foot size to identify those children for which Achilles QUS may be problematic, but age is less reliable. There are several potential modifications which may improve performance, all of which deserve further study: taking and averaging together multiple ultrasound measurements, discarding unusually high SOS measurements, and developing different shims and positioning for children with small foot size. Although we used the smallest ROI setting available on the device, it is possible that using a smaller ROI would catch less cortical bone (van den Bergh et al. 2001). Additionally, further research is warranted to determine whether BUA measurements in children with unusually high SOS are still valid. In conclusion, SOS values in young children with small foot size should be interpreted with caution.

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Figure 1.
The distribution of speed of sound (SOS) ultrasound measurements at the calcaneus in 142 South African children

Figure 2.

Speed of sound (SOS) and broadband ultrasound attenuation (BUA) measured by a Lunar Achilles Insight device at the calcaneus of 142 South African children. SOS and BUA plotted against foot size (length from longest toe to back of the heel) in (A) and (B). SOS and BUA plotted against height in (C) and (D). SOS and BUA plotted against age in (E) and (F). Most children with high SOS (> 1625 m/sec) had foot size < 19 cm, height < 119 cm, and age < 8 years.

Table 1

Characteristics of 142 HIV-infected and HIV-uninfected children with quantitative ultrasound measurements in Johannesburg, South Africa

	All (N=142)	High SOS (1625) (N=26)	Low SOS (<1625) (N=116)	p-value
HIV-infected, N (%)	72 (50.7)	17 (65.4)	55 (47.4)	0.0976
Female, N (%)	68 (47.9)	17 (65.4)	51 (44.0)	0.0482
Age, years, Median (IQR)	7.4 (6.7, 8.8)	6.7 (6.1, 7.2)	7.8 (6.8, 9.0)	<0.0001
Young Age, N (%) (<8 years)	90 (63.4)	23 (88.5)	67 (57.8)	0.0033
Weight, kg, Mean (SD)	23.8 (6.8)	19.1 (2.8)	24.9 (7.0)	<0.0001
Height, cm, Mean (SD)	120.3 (9.0)	112.7 (7.1)	122.1 (8.5)	<0.0001
Short Height, N (%) (<119 cm)	58 (41.1)	21 (80.8)	37 (32.2)	<0.0001
Small Feet, N (%) (Toe to Heel <19 cm)	56 (39.4)	24 (92.3)	32 (27.6)	<0.0001
SOS, m/sec, Median (IQR)	1568.6 (1552.9, 1588.1)	1690.7 (1674.6, 1701.4)	1564.8 (1548.1, 1575.2)	<0.0001
BUA, m/sec, Median (IQR)	88.4 (78.1, 100.5)	65.1 (53.6, 74.6)	94.0 (83.8, 103.1)	<0.0001
Stiffness Index, Median (IQR)	82.5 (73.0, 92.0)	97.0 (83.0, 104.0)	79.0 (71.5, 88.0)	<0.0001

IQR: Inter-quartile range; kg: kilograms; SD: standard deviation; cm: centimeters; m/sec: meters per second; SOS: speed of sound; BUA: broadband ultrasound attenuation