Quantitative Ultrasound of the Tibia: A Novel Approach for Assessment of Bone Status

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An ultrasound instrument has recently been developed for the diagnosis and monitoring of osteoporosis (SoundScan 2000, Myriad Ultrasound Systems Ltd., Israel). The instrument measures the speed of propagation of ultrasound waves (SOS, meters per second) along a fixed longitudinal distance of the cortical layer at the tibial shaft. Its in vivo precision is 0.25%. The performance of the SoundScan 2000 was studied in 307 Caucasian women (age range 24–87 years) who also had their bone mineral density (BMD) measured at the spine, femoral neck, and radial shaft by absorptiometric techniques. The SOS ranged from 3471–4226 m/sec (mean 3867). The standardized coefficient of variation (CV), an expression of the effective clinical precision corrected for the spread of measurements (CV/mean), was 1.6% for the tibial SOS, compared to 1.5%, 3.8%, and 4.4% for spinal, femoral, and radial BMD, respectively. Tibial SOS significantly correlated with age (r = -0.52), time since menopause (r = -0.43), height (r = 0.29), and weight (r = 0.16), as well as with BMD at the radius (r = 0.63), spine (r = 0.50), and femur (r = 0.47). After classification of bone measurements into tertiles, about 60% of the women with low tertile spinal BMD fell within the low tertile of either tibial SOS, femoral BMD, or radial BMD. The results show that measurement of tibial SOS is a precise method of assessing bone status without exposing the patient to sources of radiation. (Bone 17: 363-367; 1995)

Key Words: Ultrasound; Speed of sound; Tibia; Bone mineral density; Age; Weight.

Introduction

Commonly used methods of bone densitometry, such as dual-energy X-ray absorptiometry (DEXA) and quantitative computed tomography, measure the quantitative aspect of bone mineral density (BMD). However, qualitative factors, like elasticity, fatigue damage, and microarchitecture, have been implicated as additional factors contributing to bone strength.11 In this respect, ultrasonic measurement of bone has recently emerged as a promising noninvasive technology for assessment of bone strength and fracture risk. The technique is believed to reflect both qualitative and quantitative aspects of the bone, since the propagation of sound in bone is related to the elastic modulus and structure, as well as to the mass density.1,13,16,18,24 Current ultrasonic instruments measure speed of sound (SOS) or broadband ultrasound attenuation at the calcaneus or the patella and have been shown to correlate with axial BMD.21,23,28,32 However, the precision of these ultrasonic methods may be adversely affected by the surrounding soft tissue, as well as bone shape irregularity that interferes with correct probe positioning.

Recently, a new mobile ultrasonic bone instrument, which measures the SOS at the tibial shaft, has been introduced (SoundScan 2000, Myriad Ultrasound Systems Ltd., Rehovot, Israel). In contrast to current methods that measure the velocity of ultrasound waves transmitted across the bone, this new instrument is designed to measure SOS along a fixed longitudinal distance of the cortical layer parallel to the bone axis, overcoming soft tissue interference. This concept is likewise applied in industrial nondestructive testing and in geophysics for the evaluation of material structure and quality.15,19 The aims of the present study were to determine the accuracy and precision of the system; to compare the results obtained simultaneously in both tibiae; and to examine the relationship of tibial SOS with selected clinical variables and with BMD at the spine, proximal femur, and radial shaft.

Materials and Methods

The study group consisted of Caucasian women referred to the Jerusalem Osteoporosis Center for BMD measurement. Three hundred ten consecutive women who consented to have, in addition, an ultrasound measurement of the tibia, were enrolled into the study. Three women were excluded from the study because of extreme obesity or edema of the legs, that interfered with acoustic signal transmission. The age range of the remaining 307 women was 24–87 years (mean: 57 years; Table 1). Two hundred fifty-two of the women (82%) were postmenopausal: their mean age was 60, and the time since menopause 0–44 years (mean: 12 years). The study was approved by the institutional review board on research involving human subjects.

Bone Mineral Densitometry

BMD of the lumbar spine (L2–4) and the left femoral neck was measured by DEXA (Norland XR26, Norland Scientific Instruments, Fort Atkinson, WI). BMD of the left radial shaft, at the standard two thirds site of the forearm, was determined by single photon absorptiometry (Norland 2780).
Table 1. Data of study participants

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57 ± 10</td>
<td>24-87</td>
</tr>
<tr>
<td>Age at menopause (years)</td>
<td>48 ± 5</td>
<td>23-60</td>
</tr>
<tr>
<td>Time since menopause (years)</td>
<td>12 ± 10</td>
<td>0-44</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158 ± 7</td>
<td>133-175</td>
</tr>
<tr>
<td>Weight (cm)</td>
<td>64 ± 10</td>
<td>34-101</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26 ± 10</td>
<td>15-41</td>
</tr>
</tbody>
</table>

* n = 252.

Ultrasonic Measurement

SOS (meters per second) was measured at the right tibia using a SoundScan 2000, versions 1.20 and 1.30 BETA (Myriad Ultrasound Systems) (Figure 1). To examine the effect of laterality, SOS values of both tibiae were determined in a subset of 83 women. The standard measurement site was defined as the midpoint between the apex of the medial malleolus and the distal patellar apex. The probe was moved manually across the midtibial plane, parallel to the long axis of the tibia, searching for the site with maximal SOS readings, around the tibial crest. Each measurement consisted of 150-200 readings, lasting about 5-10 min. The average of the five highest readings was considered as the representative result. The rationale for using the five highest samples lies in the process of the measurement that seeks for the highest possible readings.

Accuracy Testing

In vitro accuracy and reproducibility were determined on a calibrated phantom—a homogeneous block of Perspex with established velocity—using water as coupling medium, at a stable temperature of 20°C. Each of two operators performed 20 consecutive measurements, consisting of 35 readings each, for 2 consecutive days. The calculation was performed according to the formula recommended in the “Draft Guidance for Review of Bone Densitometer 510(k) Submission” by the FDA.

Precision Testing

In vivo precision was also performed and calculated according to the FDA recommendations. Ten healthy volunteers (6 women and 4 men, age range 22-48 years) were measured by two different operators. Each operator made three measurements on every subject; twice without repositioning the subject and using the same mark on the mid-tibia; and once on another day (with a maximal interval of 1 week). In addition to the coefficient of variation (CV), we also adopted the concept of standardized CV. This parameter compares the effective precision of different clinical measurements by taking into account the relative spread of the measured values in the study population, expressed as the mean/range ratio:

\[
\text{Standardized CV (\%)} = \left(\frac{\text{CV (\%)} \times 100}{\text{range/mean (\%)}}\right)
\]

For the purpose of standardized CV calculation, the range was defined as including all the values of the study population falling within 2 SD above or below the mean.

Statistical Methods

The significance of differences between the two tibiae were examined using the paired t-test. Pearson’s correlations were calculated and examined for statistical significance of the assessment of linear relationship between continuous variables. The relation between the various measurement methods was also examined after dividing the obtained values into tertiles. All p values denoted here are two tailed.

Results

Accuracy and Precision

The in vitro accuracy and reproducibility of the system were less than 0.1% for both intraoperator and interoperator measurements. The intra- and interoperator CV of tibial SOS measured without and with repositioning was around 0.25% (Table 2). The standardized CV of tibial SOS was 1.61% (Table 3). The respective values for the BMD measurements at the spine, femoral neck, and radial shaft were 1.46%, 3.78%, and 4.39%.

Side Comparison

SOS values obtained simultaneously on both tibiae showed a significantly high linear correlation (r = 0.86, p < 0.0001). The mean absolute difference between SOS values of the two tibiae was 1.4% (range 0-11%), and was less than 4% in all but three women (Table 4). Based on hand dominance, 72 of the women were right-sided, 9 were left-sided, and 2 were ambidextrous. The mean difference between tibial SOS at the dominant side and that measured at the nondominant side was only 0.3%, not statistically significant.

Correlation with Age, Menopausal State, and Body Habitus

Measurements at all sites inversely correlated with age (Table 5). The highest correlation was found for the SOS (r = -0.52) followed by the radial shaft BMD (r = -0.51), femoral neck BMD (r = -0.45), and lumbar spine BMD (r = -0.38), respectively. Similar inverse correlations were also found with

Table 2. Results of in vivo precision testing

<table>
<thead>
<tr>
<th></th>
<th>CV (%)</th>
<th>CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operator 1</td>
<td>0.26</td>
<td>0.28</td>
</tr>
<tr>
<td>Operator 2</td>
<td>0.22</td>
<td>0.23</td>
</tr>
<tr>
<td>Combined</td>
<td>0.26</td>
<td>0.24</td>
</tr>
</tbody>
</table>

*a Coefficient of variation obtained without repositioning the subject.

*b Coefficient of variation obtained with repositioning the subject.
menopausal age. The various measurements had similar correlation coefficients with height ($r = 0.29$–$0.36$). However, with respect to weight and body mass index, both tibial SOS and radial shaft BMD had lower correlation coefficients than lumbar spine BMD and femoral neck BMD. The correlations of the various measurements with age, height, weight, and body mass index among the postmenopausal women were similar to those found in the whole study population.

### Correlation Between Tibial SOS and BMD Measurements

There were significant linear correlations ($r = 0.47$–$0.63$; $p < 0.0001$), between tibial SOS and BMD measurements, the highest being with the radial shaft BMD (Table 6). The correlations among the various BMD measurements were of the same order of magnitude. Women whose spinal BMD values fell within the low tertile (<0.78 g/cm$^2$, corresponding to 3 SD below peak bone mass), were regarded as having significant spinal osteopenia. Sixty-one percent of these women also had their tibial SOS values within the low tertile (Figure 2). Similar results were observed with respect to femoral neck BMD and radial BMD values obtained in these women.

### Discussion

The mean tibial SOS value in our study (3867 m/sec) is similar to previously reported values in animal and human cortical bone, obtained by different techniques.$^{1,11,12,25}$ SOS in the cortical bone has been shown to be influenced by specific gravity, porosity, orientation (SOS is greater in the longitudinal direction, reflecting anisotropy of cortical bone), water content, and elasticity.$^{11,18}$ In addition to these material properties, when the thickness of bone is similar or less than the sound wavelength, any reduction in cortical thickness results in a decrease of SOS due to the dispersion effect. Thus, tibial SOS reflects both qualitative and quantitative properties of the bone.

Precision is of utmost importance in following subtle changes in bone. The present data indicate that tibial SOS has an excellent interoperator precision of $0.25\%$, comparable to reported values for calcaneal SOS, and superior to those of calcaneal ultrasound attenuation or patellar SOS.$^{13,25,31,32}$ Moreover, after correction for the spread of each measurement in the study population, the standardized CV of tibial SOS was $1.61\%$, similar to the value for lumbar spine BMD, and better than that of femoral BMD and radial BMD. For comparison, Miller et al.$^{25}$ found standardized CV for calcaneal ultrasound velocity to be as high as $12.7\%$, whereas that of the lumbar spine was $2.2\%$, a value that is close to ours.

Studies that compared femoral BMD measured bilaterally elicited large individual differences, mounting to $80\%$, which led some investigators to suggest that both sides need to be measured.$^{1,4,12,22}$ Nevertheless, for clinical purposes only one hip is usually measured. The differences between the SOS measured at the two tibiae appeared to be small, with only 3 of 83 cases exhibiting a difference larger than $4\%$, a value that corresponds to approximately 1 SD of the mean SOS value in the study population. Hand dominance could not predict which tibia had lower SOS values. Furthermore, when measured bilaterally, the correlations of tibial SOS with the BMD measurements were similar for both sides (data not shown). Therefore, either side could be measured, provided consistency is maintained.

The correlation coefficients of tibial SOS with clinical variables were generally comparable to the correlations of the BMD measurements with these variables. The only exceptions were the correlations with weight and body mass index that were lower with the appendicular than with the axial measurements. This may be rather surprising for a weight-bearing bone like the tibia, but is consistent with the findings of another study in which tibial BMD was not correlated with body weight.$^6$ These clinical associations, as well as the correlations between tibial shaft SOS and the BMD measurements, which were comparable to the correlations among various BMD measurements themselves, indicate that the results obtained by this new technique are biologically relevant.

That the correlations between tibial SOS and BMD measure-

### Table 3. Comparative data of speed of sound (SOS; meters per second) and bone mineral density (BMD; grams per square centimeter) measurements

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>Range</th>
<th>CV (%)</th>
<th>Standardized CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibial SOS</td>
<td>3867 ± 145</td>
<td>3471–4226</td>
<td>0.24</td>
<td>1.61</td>
</tr>
<tr>
<td>Lumbar spine BMD</td>
<td>0.860 ± 0.147</td>
<td>0.450–1.305</td>
<td>1.00$^a$</td>
<td>1.46</td>
</tr>
<tr>
<td>Femoral neck BMD</td>
<td>0.727 ± 0.120</td>
<td>0.424–1.075</td>
<td>2.50$^a$</td>
<td>3.78</td>
</tr>
<tr>
<td>Radial shaft BMD</td>
<td>0.646 ± 0.092</td>
<td>0.298–0.836</td>
<td>2.50$^a$</td>
<td>4.39</td>
</tr>
</tbody>
</table>

$^a$Manufacturer's data.

### Table 4. Difference between speed of sound (SOS; meters per second) values measured in both tibiae

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Mean ± SD (m/sec)</th>
<th>Range (m/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute value of difference (Dominant side SOS)</td>
<td>83</td>
<td>57 ± 66</td>
<td>2–417</td>
</tr>
<tr>
<td>(nondominant side SOS)</td>
<td>81$^b$</td>
<td>(−10) ± 87$^b$</td>
<td>(−417)–161</td>
</tr>
</tbody>
</table>

$^a$Two women were ambidextrous.

$^b$P = 0.31.

### Table 5. Pearson's correlation coefficients ($r$) between tibial speed of sound (SOS) or bone mineral density (BMD) measurements and clinical variables

<table>
<thead>
<tr>
<th></th>
<th>Tibial SOS (m/sec)</th>
<th>Lumbar spine BMD (g/cm$^2$)</th>
<th>Femoral neck BMD (g/cm$^2$)</th>
<th>Radial shaft BMD (g/cm$^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>$−0.52^b$</td>
<td>$−0.38^b$</td>
<td>$−0.45^b$</td>
<td>$−0.51^b$</td>
</tr>
<tr>
<td>Age at menopause (years)$^*$</td>
<td>0.00</td>
<td>0.10</td>
<td>0.06</td>
<td>0.06</td>
</tr>
<tr>
<td>Time since menopause (years)$^*$</td>
<td>$−0.43^b$</td>
<td>$−0.38^b$</td>
<td>$−0.44^b$</td>
<td>$−0.48^b$</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>0.29$^b$</td>
<td>0.30$^b$</td>
<td>0.33$^b$</td>
<td>0.36$^b$</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>0.16$^b$</td>
<td>0.31$^b$</td>
<td>0.38$^b$</td>
<td>0.21$^b$</td>
</tr>
<tr>
<td>Body mass index (kg/m$^2$)</td>
<td>0.00</td>
<td>0.15$^b$</td>
<td>0.21$^b$</td>
<td>0.01$^b$</td>
</tr>
</tbody>
</table>

$^a$n = 252 women; $^b$p < 0.0005; $^c$p < 0.01.
Table 6. Pearson's correlation coefficients (r) among tibial speed of sound (SOS; meters per second) and bone mineral density (BMD; grams per square centimeter) measurements*  

<table>
<thead>
<tr>
<th></th>
<th>Lumbar spine BMD</th>
<th>Femoral neck BMD</th>
<th>Radial shaft BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibial SOS</td>
<td>0.50</td>
<td>0.47</td>
<td>0.63</td>
</tr>
<tr>
<td>Lumbar spine BMD</td>
<td>0.68</td>
<td>0.55</td>
<td></td>
</tr>
<tr>
<td>Femoral neck BMD</td>
<td>0.55</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*All correlations are significant at the p < 0.0001 level.

ments were not higher than observed should not come as a surprise when the following points are considered. First, even when both ultrasound and BMD were measured on the same bone, for example, the calcaneus, the correlation did not exceed 0.7.10.29.32.33 This means that no more than 50% of the variability in the ultrasonic measurements of the bone could be accounted for by BMD, indicating that the two methods do not measure identical properties of the bone. Second, while population studies disclose significant correlations among bone mass measurements determined at different skeletal sites, marked regional variation in bone mass may be encountered at the individual level, reflecting different bone composition and/or mechanical strain. In a recently published study of 744 Japanese-American women whose BMD was determined at four skeletal sites, only 31% of the women had all BMD values within the same tertile, while 15% had marked heterogeneity with low tertile BMD in one site and high tertile BMD in another site.8 The moderate correlations between the different measurements applied in the present study explain why only about 60% of the subjects within the lowest spinal BMD tertile could be identified by tibial SOS or other BMD measurements. In a screening study of 1000 perimenopausal women, calcaneal ultrasound attenuation correctly identified only 44% of the women falling in the lowest quartile of spinal BMD.23 However, while the spine has been historically regarded as the preferred site for diagnosing osteoporosis, it is subject to the effect of age-related artifacts, that is, osteoarthrosis, sclerosis, or aortic calcification, which adversely affect the precision of spinal BMD measurement, and reduce its value as a measurement site in the elderly.20.26.27 This may explain why, in our study population, lumbar spine BMD had the lowest correlation with age. Proximal femur densitometry is also subject to accuracy errors due to hip geometry and positioning. These concerns are less of a problem at peripheral sites. Furthermore, appendicular BMD, including the radial shaft, which resembles in structure the tibial bone, has been shown to predict fracture risk.5.9.14 And, although the tibia has not been commonly used to assess bone status, its stiffness has been tested by vibration analysis,2 and a recent report demonstrated that measurement of BMD at the tibia provided useful clinical information regarding the diagnosis of metabolic bone diseases.5 In conclusion, the present study shows that ultrasound velocity measured along the tibial cortex is a precise, nonradiating technique for assessing bone status, which correlates significantly with BMD measured by DEXA or SPA. Additional studies are now in progress to evaluate the ability of tibial SOS to diagnose osteoporosis and to predict fracture risk for comparison with conventional BMD measurements.

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References


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