Determination of a standard site for the measurement of bone mineral density of the human calcaneus

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ABSTRACT

Ultrasound of the calcaneus may be used as a cheap, ionising radiation-free and easy to use indicator of skeletal status, and hence of osteoporotic fracture risk. At present ultrasound is not widely used as it suffers from high precision errors. As ultrasound parameters are determined in part by bone mineral density (BMD), an increase in the accuracy and precision of BMD measurements should reduce the precision error associated with ultrasound measurements. The aim of this study was to define an anatomical site on the calcaneus at which accurate and precise measurements of BMD can be made. Ten dry calcanei and 10 cadaveric feet were scanned using a DXA scanner; 9 anatomically defined regions (1 cm²) were selected in the posterior part of the calcaneus for analysis. The centre of region 1 was positioned halfway along the line joining the anterior border of the calcaneal tubercle and the peak of the posterior superior tubercle, and the remaining 8 regions were placed around this central area. The BMD in these 9 regions was compared with the whole bone BMD and the variability of BMD within each of the 9 regions was measured. The reproducibility of the technique was assessed by taking 10 repeated measurements of 2 bone and 2 cadaveric specimens, each specimen being removed and repositioned between measurements. Region 1 was found to be the most representative of total BMD in cadaveric feet. This region also showed the least variability of BMD and consistently gave the lowest coefficients of variation in the reproducibility study both in the bone and the cadaveric specimens. This region is hence the most suitable site on the calcaneus for measuring absolute values of and changes in BMD. The surface position of region 1 was found to be consistently along the line at 45° to the vertical, from the lateral malleolus to the heel. The identification of the surface location of region 1 relative to anatomical landmarks of the foot has enabled the same anatomical site to be measured in all subjects. This allows meaningful intersubject comparisons to be made. Preliminary data suggest that precision errors using ultrasound are also reduced when measurements are taken at this region of the calcaneus. The reduction in the precision error of ultrasound assessment of skeletal status may provide a cheap and safe way to identify individuals at risk from osteoporotic fracture.

Key words: Osteoporosis; ultrasonography.

INTRODUCTION

Osteoporosis is a multifactorial disease characterised by a reduction in bone mass and by abnormalities in the architecture of bones, that leaves the skeleton more prone to fracture (Nevitt, 1994). Measurements of bone mineral density (BMD) have been found to be the most accurate determinant of those at risk from osteoporosis (Cummings & Black, 1995; Slendema et al. 1990), following clinical risk factors such as early menopause and hysterectomy (Torgeson & Reid, 1993). With its large availability, ease of use and most importantly, low exposure to radiation, dual x-ray absorptiometry (DXA) has become the most widely used technique for measuring BMD (Genant et al. 1996; Miller et al. 1996). The associated large costs of DXA unfortunately render it impractical as a tool for use in a mass screening programme. Also the values of BMD obtained using DXA reflect predominantly the amount of mineral present in the bone and provide little information on the changes in microarchitecture which occur in osteoporosis.
Recently broadband ultrasound attenuation (BUA) has been put forward as a cheap, ionising radiation-free and easy to use indicator of skeletal status in the trabecular bone of the calcaneus (Langton et al. 1984). As attenuation of ultrasound waves by soft tissue and cortical bone is minimal (Kotski et al. 1994), BUA of the calcaneus is thought to be a measure of the absorption and scattering of ultrasound waves by the internal structure of the bone. The calcaneus has a complex and variable microarchitecture which shows a similar pattern of trabecular loss in osteoporosis to that seen in the spine (Blake et al. 1997). In vitro studies have confirmed that BUA values obtained from the calcaneus correlate with the histomorphometric appearance of the trabecular system. BUA thus reflects changes in both the mineralisation and structure of the underlying bone (Gluer et al. 1993).

BUA measurements are reported not only to distinguish between osteoporotic and healthy individuals as efficiently as DXA, but also to be capable of predicting osteoporotic fractures as accurately as DXA (Funke et al. 1995).

At present ultrasound is not in widespread clinical use as it suffers from high precision errors (Graafmans et al. 1996). The calcaneus is a heterogeneous bone so that small changes in the position of the foot relative to the transducers can have large confounding effects on BUA measurements (Kolthoff et al. 1995). In recent studies the location of the transducers placed on the heel bear no relationship to the anatomy of the region (Laugier et al. 1996; Roux et al. 1996). In a population, variation in the size of the feet will undoubtedly result in the region of interest (ROI) being located at different anatomical regions of the calcaneus. A standard anatomically located ROI needs to be defined to enable the comparison between different subjects and repetitive measurements, allowing for precise, accurate recordings which should correlate well with osteoporotic fracture risk.

As BUA is influenced by BMD, variation in the BMD measured at slightly different anatomical sites of the calcaneus may contribute to the precision error. The high resolution scans of BMD that are made possible with DXA (Grampp et al. 1993) allow for an accurate assessment of the variation in BMD within the bone. This study therefore sets out to define a specific site on the human foot which can easily be located by the clinician and at which accurate and precise measurements of BMD can be made. This area should satisfy the following 3 criteria: (1) the measurements of BMD in this area should be representative of the whole bone BMD; (2) the area should have a low spatial variance in BMD, so that minor changes in the position of the measuring device have minimal effects on the measurement of BMD; (3) the measurements of BMD should be highly reproducible, hence reducing the precision error in the assessment of BMD over time and between subjects. An area that is able to fulfil all these criteria would be ideal as a site for the assessment of BMD using DXA. It is proposed that the precision error of BUA would be greatly reduced if measurements were taken at this site.

**Materials and Methods**

**Bone densitometry**

BMD measurements were made using a QDR-1000/W bone densitometer (Hologic, Waltham, MA), which was calibrated daily using the QDR-Anthropomorphic spine phantom and the subsequent long-term precision was found to be 0.35%.

A sample of 10 dry calcanei (5 left, 5 right) covering a broad spectrum of BMD values were chosen for the study. Bones which showed signs of damage or cortical thinning were excluded. In order to allow comparison with subsequent ultrasound measurements of the calcaneus, the DXA scans of the bones were all lateral projections. The bones were placed on bags of rice to simulate a soft tissue covering, the thickness of which was comparable to the thickness of soft tissue found around a human calcaneus.

As ultrasound recordings in the anterior part of the calcaneus are severely distorted by the ankle joint (Roux et al. 1996), this study attempted to define a ROI in the posterior part of the bone. Detailed BMD data of this region was obtained using the ultra high resolution protocol with a line spacing of 0.0254 cm and a point resolution of 0.0127 cm. After removal and repositioning of the dry bones, the posterior calcaneal BMD was measured a second and a third time, and the average of the 3 measurements were used in the analysis. A value for the whole bone BMD was obtained using the low resolution protocol, with a line spacing of 0.1168 cm and a point resolution of 0.1129 cm.

The same measurements of BMD were then carried out on 10 fixed cadaveric feet specimens obtained from 4 male and 6 female cadavers, ranging in age from 62 to 96 y. Each specimen was sealed in a plastic bag and aligned, lateral surface down, on the scanner table on top of a bag of rice.

All specimens, both dry bone and cadaveric were tested and the results analysed by the same operator using Hologic DXA software version 6.1.
Regions of interest

On the high resolution scans, 9 anatomically located subregions (1 cm²) were selected, an area comparable to that of focused ultrasound transducers. The centre of region 1 was positioned half way along a line joining the anterior border of the calcaneal tubercle and the peak of the posterior superior tubercle. The remaining 8 regions were placed surrounding this central region (Fig. 1).

For dry bone specimens, the whole calcaneus was included in the ROI of the whole bone low resolution scans. In the cadaveric specimens where surrounding bones interfered with the anterior calcaneal tubercle, the whole bone BMD value was determined from that part of the calcanei not overlapped by adjoining bones.

Protocols

Regional representation of whole bone BMD. The BMD of ultrasound regions were compared with whole bone BMD for both dry bone and cadaveric specimens. Linear regression analysis was used to show how representative the measurements of BMD for each region were of the whole bone BMD.

Variability study. The variability for each region was assessed by the number of shades of grey found in that particular area. The shades of grey on the scan are determined by the BMD of the bone, so the variability in the number of shades of grey represents the variability in the BMD of that region. The brightness and contrast controls of each scan were standardised before the assessment of variability.

Reproducibility study. The in vitro short term precision for each region was calculated over 10 repeated measurements of 2 bone and 2 cadaveric specimens. The specimens were chosen to be representative of high and low BMD. Each specimen was removed and repositioned between measurements.

Anatomically located region of interest

Once the region most suitable for DXA and ultrasound assessment of skeletal status had been determined from the BMD measurements, it needed to be located relative to a surface anatomical landmark. Radiographs of the cadaveric specimens were taken, with a grid of lead weights overlying the heel. From these, the centre of the selected region could be located on the specimens and this point was subsequently marked on both medial and lateral surfaces by single lead beads sutured onto the foot (Fig. 2). With the chosen ROI located on the surface of the feet, it could then be related physically to other surface landmarks.

BUA measurements at region 1

Preliminary BUA measurements were made at the selected region on the 10 cadaveric specimens, using a McCue CUBA clinical ultrasound scanner (McCue Ultrasonics, Winchester, UK). The long term precision of the scanner was found to be 0.4%.

After the feet were strapped into a foot clamp, the skin surfaces where the measurements were to be taken were cleaned with ethanol and then dried. For each of the specimens, the short term precision of BUA was calculated from 6 repeated measurements at the selected region, which then enabled the coefficient of variation for each specimen to be determined. The feet were removed and repositioned between each measurement.
RESULTS

Regional representation of whole bone BMD

$R^2$ values, a measure of how one variable depends on a second variable, were obtained from linear regression plots of regional BMD against whole bone BMD. Figure 3 shows examples of the dry bone linear regression analysis plots, with (1) the region with the best $R^2$ value, (2) a region with an intermediate $R^2$ value, and (3) the region with the lowest $R^2$ value. Figure 4 shows equivalent examples of the cadaveric feet linear regression analysis plots.

The $R^2$ values for the dry bone and cadaveric feet experiments, are presented in Table 1. For dry bone experiments, region 8 had the highest $R^2$ value (0.93), followed closely by region 1 (0.92), and region 7 (0.91). For cadaveric feet experiments, region 1 had the highest $R^2$ value (0.96), followed closely by region 7 (0.95), and region 9 (0.93). Regions 1 and 7 have $R^2$ values consistently above 0.90, and are therefore the regions which have BMD values most representative of the whole bone BMD.

Variability study

The spatial variability in BMD for each of the 9 regions was determined from the DXA scans and is shown in Figure 5. Both dry bone and cadaveric feet measurements of variability showed a similar regional profile, with greatest BMD variability in regions 3 and 9, and lowest BMD variability in regions 1 and 6. The
Table 1. \( R^2 \) values from linear regression analysis of the different region’s representation of whole bone BMD, for dry bone and cadaveric feet experiments

<table>
<thead>
<tr>
<th>Region No.</th>
<th>Dry bone ( R^2 ) value ((n = 10))</th>
<th>Cadaveric feet ( R^2 ) value ((n = 10))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.92</td>
<td>0.96</td>
</tr>
<tr>
<td>2</td>
<td>0.81</td>
<td>0.95</td>
</tr>
<tr>
<td>3</td>
<td>0.63</td>
<td>0.85</td>
</tr>
<tr>
<td>4</td>
<td>0.88</td>
<td>0.9</td>
</tr>
<tr>
<td>5</td>
<td>0.84</td>
<td>0.73</td>
</tr>
<tr>
<td>6</td>
<td>0.9</td>
<td>0.86</td>
</tr>
<tr>
<td>7</td>
<td>0.91</td>
<td>0.95</td>
</tr>
<tr>
<td>8</td>
<td>0.93</td>
<td>0.83</td>
</tr>
<tr>
<td>9</td>
<td>0.85</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Reproducibility study

The distribution of the measured coefficients of variation (CV) from the 4 specimens (2 bone, 2 cadaveric feet) is shown in Figure 6. The CVs were consistently less than 3% at all measured sites. Of the 4 specimens measured, the greatest CV value and the mean CV value for each region was recorded and results are presented in Table 2. Region 1 was found to be the most reproducible region with an average CV value of 0.92% and a greatest CV value of 1.26%, followed by region 4 with an average CV value of 0.99% and a greatest CV value of 1.58%. All averaged values were less than 2%. The 3 analysis studies clearly show region 1 to be the area which, (1) is the most representative of calcaneal BMD, (2) has the least variability in BMD measurements, and (3) has the most reproducible BMD measurements.

Surface anatomical location of region 1—medial surface of the foot

In the erect standing position the centre of region 1 was not consistently related to (1) the most posterior part of the heel, (2) the sole of the foot, or (3) the medial malleolus.

Surface anatomical location of region 1—lateral surface of the foot

Amongst the 10 specimens, the distance from the tip of the lateral malleolus to the centre of region 1 ranged from 36 to 50 mm. Despite this, there was found to be a consistent relationship relating the centre of region 1 to the point \( \frac{3}{4} \) of the way along a line, \( 45^\circ \) to the vertical, from the tip of the lateral malleolus to the most posterior part of the heel (Fig. 7). Region 1 can therefore be located as the 1 cm² area on the lateral surface of the foot, that surrounds the point \( \frac{3}{4} \) of the way along this line.

Reproducibility of BUA at region 1

The mean coefficient of variation value for repeated BUA measurements at region 1 was found to be 2.9% \((n = 10)\).
Fig. 7. Radiograph of an erect cadaveric foot, showing that the centre of region 1 can be located \( \frac{3}{4} \) of the way along the line at 45° to the vertical joining the lateral malleolus, to the heel (angle \( X = 45° \)).

**Discussion**

This study set out to define an anatomically located area on the human calcaneus which would give precision, low variability measurements of BMD and whose BMD measurement was representative of the whole calcaneus. Such an area would not only indicate an ideal site on the foot for DXA assessment of BMD but could also be used to reduce the precision errors associated with ultrasound measurements.

In assessing a representative region of the skeleton for early signs of osteoporosis the absolute values of BMD and hence the accuracy of any measurements are critical. Thus regional measurement of BMD must be representative of the whole calcaneal BMD, which in turn must correlate well with the skeletal response to osteoporosis. Our study has shown that BMD measurements in region 1 were the most representative of the whole bone BMD in both cadaveric and dry bone specimens.

The calcaneus, although not being a major site for osteoporotic fracture, is easily accessible, contains a large percentage of trabecular bone and is weight bearing. The loss of trabecular bone in the calcaneus following the menopause appears to be comparable with the response of the trabecular bone in the spine (Kotzki et al. 1993) and there is a strong correlation between calcaneal BMD and the incidence of osteoporotic fracture at other skeletal sites (Wasnich et al. 1987; Funke et al. 1995). The calcaneus is therefore a suitable model to study the osteoporotic changes that occur in the whole body (Lavelle-Jeantet et al. 1995).

Within an individual specimen, both dry bone and cadaveric, the discrepancy in bone densities found in the 9 regions was enormous. In some bones there was a 2-fold difference in BMD measurements between regions 1 and 2, or regions 1 and 9, demonstrating that small differences in the position of the region measured on the calcaneus, of the order of only a few millimetres, can result in large changes in the degree of bone mineral assessed. The variance in BMD within a region is therefore critical to the selected site. BMD measurements at a region which consistently has a low variability in BMD values, should minimise the precision error caused by small changes in the position of the measuring device.

**Assessment of fracture risk**

The effectiveness of any diagnostic procedure for assessing osteoporosis relies heavily on the precision of the BMD measurements to detect the degree of bone loss. Minor changes in BMD in particular, can only be deemed meaningful if the technique is precise.

To enhance the precision in the measurement of BMD, this study defined its ROIs relative to anatomical landmarks on the calcaneus. An anatomically located ROI permits far more meaningful comparison of BMD both between different subjects and in a single subject at different times. The precision error in repositioning the specimen is greatly reduced by the use of an anatomically located ROI, when compared with an ROI fixed relative to a foot plate (Brooke-Wavell et al. 1995). Uusi-Rasi et al. (1994) found that the coefficients of variation at most skeletal sites were some 0.5–2% larger when a fixed, rather than an anatomically locate ROI was used.

In this study, the reproducibility or precision of the regional BMD measurements (see Table 2) was generally better or comparable to those values reported in previous publications (e.g. 1.20%, Wasnich et al. 1987; 1.16%, Vogel et al. 1988; 1.28%, Kotzki et al. 1993; 0.70%, Sievanen et al. 1996), with...
Ultrasound as a screening tool

Controversy exists as to whether a screening programme based on BMD measurements to identify those at risk of osteoporotic fracture would be cost effective, with most studies recommending further evaluation of BMD measurements (Jergas & Genant, 1993; Riis, 1995). Recently BUA has been proposed as an alternative, cheap, ionising-radiation free and easy to use method of screening people for osteoporosis (Genant et al. 1996).

Ultrasound is not widely used in clinical practice at present, as it is subject to high precision errors (Graafmans et al. 1996). The reproducibility of BUA in vivo is reported to be between 3 and 7% (Kolthoff et al. 1995; Brooke-Wavell et al. 1995; Funke et al. 1995; Graafmans et al. 1996). This implies that a bone loss of the order of 2.5% per year in postmenopausal women would take at least 3 y to detect reliably (Laugier et al. 1994). This large variability may be the result of changes in the soft tissue surrounding the bone or, more likely, errors associated with repositioning the foot for subsequent measurements at the same anatomical site (Graafmans et al. 1996). In these earlier studies the transducers have been fixed relative to a foot clamp, with the assessment area bearing no relationship to the anatomy of the foot. With a large variation in the size of the subjects’ feet, it follows that by using a foot clamp, different anatomical locations on the foot will be assessed. Our preliminary data measuring BUA at region 1 shows that variability in measurements can be reduced to 2.9% by measuring at an anatomically defined area. This suggests that some of the errors associated with BUA are related to repositioning the transducers in a slightly different place. The ability to detect a clinically relevant bone loss within a year makes BUA measurement at region 1 a serious possibility for detecting early osteoporotic changes.

The centre of region 1 was found to lie consistently $\frac{1}{4}$ of the way along a line, 45° to the vertical, from the lateral malleolus to the most posterior part of the heel. The recognition of a surface region relative to anatomical landmarks where precise and accurate ultrasound recordings could be made is an exciting prospect. This could facilitate direct comparison of ultrasound assessment of skeletal status between different subjects.

In conclusion, we have identified an area on the calcaneus where accurate and precise measurements of BMD can be made which reflect the density of the whole bone. We have determined how this area can be identified reliably using surface landmarks on an individual and have provided preliminary data to suggest that by using this area the errors associated with BUA measurement can be reduced. The reduction in the precision error of ultrasound assessment of skeletal status may provide a cheap and safe method to identify individuals at risk from osteoporotic fractures.

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REFERENCES


