STUDY OF OSTEOPOROTIC FRACTURES (V5)
Quantitative Ultrasound of Bone

Introduction/overview of ultrasound measurements in SOF

Bone mass explains 30-90% of the variance in bone strength determined in vitro. However, bone mass is not the only determinant of bone strength: the geometry and quality of bone play vital roles Current methods of assessing bone health are inadequate. Parfitt postulated that bones are weakened by accumulation of fatigue damage, including microscopic fractures, as bone ages. In support of this hypothesis, Parfitt observed that women with vertebral fractures had greater bone age than women without fractures who had similar degrees of osteopenia.

The strength of trabecular bone also depends on the number and integrity of connections between trabecular rods and plates. Loss of these connections (decreased "connectivity") accounts for about 40% of the decrease in trabecular bone mass with aging in women. For the same bone mass, the strength of trabecular bone will vary inversely with its connectivity.

Ultrasound may be a useful measure of both the quality and quantity of bone. Two quantitative ultrasonic measurements in particular, sound velocity and broadband ultrasonic attenuation (BUA), may correlate with bone fragility. Ultrasonic transmission velocity, or speed of sound (SOS), is related to both the mass density and modulus of elasticity of a substance. The elastic modulus of a material depends upon a number of physical properties, and is believed to reflect fatigue damage and the size and spatial orientation of bone microstructure. BUA is thought to measure the attenuation of sound energy from scattering and absorption for a spectrum of frequencies (typically 0.2-0.6 MHz), but the exact correlates of BUA in bone remain unclear. Both SOS and BUA measurements correlate with bone strength in vitro, but in vivo the two measurements are not highly correlated with BMD at other sites, nor are they highly correlated to each other.

Clinical studies indicate these measures are lower in women who have osteoporotic fractures. Case-control and cross-sectional studies have found that women with hip, vertebral, and wrist fractures have lower calcaneus BUA results than normal controls. A single prospective study demonstrated that elderly women with lower BUA had a greater risk of hip fracture; whether ultrasound added information about the quality of bone in addition to measuring bone mass could not be determined as no measurements of bone mass were made. Heaney et.al. have reported that, compared to normal controls, speed of sound in the patella was significantly lower in women with vertebral fractures, and the difference was about as great as for bone density of the lumbar spine by antero-posterior (AP) dual photon absorptiometry of the spine. Unfortunately, this and other clinical studies of ultrasound were too small to determine whether ultrasound added to the prediction of fracture based on BMD alone, and no study has directly compared the predictive accuracy of ultrasound and BMD at the same site.

Besides its potential for assessing bone quality, quantitative ultrasound has several practical advantages over densitometry: it is less expensive, entails no radiation exposure, and portable devices may soon be available. Both ultrasonic velocity and BUA measurement are sufficiently reproducible, generally 0.5-1.0% and 2-4%, respectively, for clinical applications. If ultrasound predicts hip and other types of fractures as well as measurements of bone mass, it would be the best approach to screening women to assess their risks of fracture.

In SOF V5, we will be making ultrasound meaasurements at two sites: the calcaneus (heel) and the tibia.

Calcaneal Ultrasound

1. Equipment:

Quantitative ultrasound (QUS) measurements are carried out using the Walker Sonix UBA 575+ device (Walker Sonix Inc., Worcester, MA 01606). The current software is version 7.1. After taking a baseline reference measurement the subject's foot is placed in a water bath. After a wait period of about 5 minutes which serves to dissolve air bubbles and to thoroughly wet the skin of the heel to optimize coupling, the actual scan is taken. A matrix of 3x3 locations is measured and the final results are obtained by averaging of these 9 measurements which in turn are averages of signals obtained in the left-right and right-left ultrasound propagation directions.

The scanner allows for assessment of BUA as well as velocity parameters. BUA reflects the frequency dependence of ultrasound attenuation. Two different velocity parameters are calculated: Speed of Sound (SOS) and Ultrasound Velocity through Bone (UVB). (In our proposal, we refer to UVB as "velocity"). Whereas SOS measurements include a portion of ultrasonic velocity through soft tissue, UVB solely reflects ultrasound velocity when passing through the largely trabecular calcaneal bone. In addition the Walker Sonix device allows us to store the raw data sampled by means of Fourier analysis from the transmitted ultrasound pulse. These raw data would enable us to calculate and investigate additional ultrasound parameters such as the average attenuation of ultrasound in the frequency range of 228-577 kHz based on the average absorption at 27 equidistant frequencies within that range.

For equipment or repair problems related to the UBA 575 system, the contact at Walker Sonix is Phil Townsend (General Manager). He can be reached at (508) 752-1653.

2. Subject preparation

SOF participants should be informed that a painless, radiation-free measure of heel bone integrity will be done during Visit 5, the same measure that they had at visit 4. The test will require removing the shoe and sock or stocking, placing the heel in a room temperature water bath, and then sitting quietly for approximately 10-15 minutes.

Each participant should be told not to use lotions, creams, powders or ointments on the lower extremities the day of her visit.

3. Measurement Procedure:

The protocol for obtaining BUA measurements is detailed in the Walker Sonix UBA 575+ User's Manual, Section 4. Turn on the UBA 575+ at least 15 minutes before performing any patient scans. Be sure to use only "All" liquid detergent in the water bath. It is preferable to prepare the water bath the day before its use, but at the very least it should be prepared 30 minutes before use. Keep the water bath temperature at room temperature. It is not necessary to use a thermometer, but do check the temperature with your hand.

Deciding which side to scan

We will obtain ultrasound measurements at V5 on the same side as the ultrasound measurement performed at V4. In general, this was the right heel unless the participant had recently injured that extremity.

If ultrasound measurements were not done at V4, follow these guidelines: ask each participant the following:

1) "Have you ever broken your right heel bone?"

2) "Do you have any permanent weakness in your right leg, ankle, or foot from an old injury or stroke? (do not include isolated toe weakness)."

3) "Have you broken any bones in your right leg, ankle, or foot in the last year? (do not include isolated toe fractures)"

If the answer to any of these questions is "Yes," scan the left foot. If the participant admits to weakness from a stroke or injury on both sides, scan the least afflicted side. If a participant has had fractures of both legs, ankles, feet or in the last year, or has broken both heels at some point, scan the side with most remote fracture(s).

Number of scans to obtain

Each participant will have at least two measurements of the same heel. The foot should be removed from the water bath and repositioned between measurements. If the second BUA measurement differs by more than ten units, obtain a third measurement. It is not necessary to obtain more than three measurements on a participant

Intrepretation of results

Some participants will want to know the results of their test and its interpretation. Indicate that low ultrasound measurements may be an indication of poor bone quality, but the exact meaning still is unclear. It is important to emphasize that ultrasound measures of bone are still experimental and that we hope to determine the relationship between ultrasound measures and subsequent fractures in this study. Refrain from discussing the exact meaning of a specific ultrasound values. The vast majority of physicians, even those who are knowledgeable about osteoporosis, will not be able to interpret the meaning of a specific BUA, SOS, or UBV levels.

4. Data storage and backup

a. Participant Identification.

Each SOF participant will be identified by her name (last name, first name, middle initial) and SOF ID (5 digits) number. Participant date of birth and female sex ("F") must also be entered, but the other patient identification fields (height, weight, address, etc.) found under "Patient Record" may be left blank.

b. Data Collection and Storage

If the machine is used for more than one study, be sure to maintain a unique identifier for each study in the patient ID field or some other field. You must be able to sort the participants by study.

Save the hard copy generated at the time the examination is done and place it in the participants folder. The current BUA reading, and any previous readings, are automatically stored in the system computer.

Record the BUA, SOS, and UBV values in the designated place on the participant's Visit 5 exam form.

c. Data Backup

Back up the stored data base on floppy disk once a week. Data backup must be completed in two steps so that both the routine patient files and the ATT files are copied. It is not necessary to backup the bone standard database on a weekly basis (see below)

1) First the routine participant data should be backed using the "Backup/Restore function" described in section 6 ("Database") of Walker Sonix User's Manual

2) Next, back up the ATT files using the instructions outlined in the memo titled "Modified Operating Instructions for UBA Software version 7.0." Each week's ATT backup is "incremental". That is, every week's backup only contains information for that week only. If one of these backup disks is lost, the data is not easily retrievable. Four sets of disks should be used to back up these files, one for each week. At the end of the month, all four disks will be sent to the coordinating center.

Do not use only one disk over and over each week. This will continually erase the previous week's data, and the final set will only consist of one week.

d. Data Transfer

At the end of each month, the complete database should be copied and sent to the coordinating center. Three separate procedures are necessary to accomplish this:

1) Copy the complete existing database in ASCII format using the "All Records to ASCII File" command. This command is described in section 6 of the Users Manual, and is found under "Database" on the main menu.

2) Send the raw data (ATT files). As detailed above under "Data backup," each week the ATT files should be incrementally copied, so that all of the ATT data from that month will reside on four discs (or possibly 5 depending on the month). At the end of each month, simply send all of the ATT discs created that month (since the last data transfer) to the cc.

3) Copy the bone standard database. These files are different than those made when testing a patient or copying the ATT files, so the regular monthly routine does not include them. There are two files:

- File **BONESTD.DB** is small, and includes information about what standards are "registered".
- File **BSTDDATA.DB** can become large with time, because it includes the test results for each standard.
- In DOS, both of these files are referenced at once by using B*.DB as a filename. This allows them both to be backed up using a single command.

To backup the bone standard files, perform the following steps at the end of the monthly data transfer procedures:

- Have at least one disk (eventually two or more) on which to put the files. **Whatever is on this disk will be erased, and replaced with the new backup, so do not use a disk that has useful information on it.**
- Type the following command (start at the DOS prompt):

  backup C:\UBA70\B*.DB A:
- A prompt will appear stating that everything on the disk in drive A: is about to be erased. This refers to files on the floppy, not on the hard disk, and is not cause for alarm. Follow the instructions provided.
- If necessary, switch disks when requested. (The files do not grow rapidly, and it should be a long time before two disks or more are needed.)
- Send the bone standard files to the cc.

5. Quality Control

a. Training and Certification of Operators

Although BUA measurements are relatively simple, to obtain reproducible results considerable attention must be paid to preparing the participant and positioning the foot.

All trained staff who wish to be certified to perform BUA measurements on SOF participants must complete the following:

- Carefully read this section and the Walker Sonix operations manual
- Receive training from the SOF QC Officer or the designated staff who attended the central training session at the coordinating center
- Practice scanning with the acoustic phantoms, then on other staff or volunteers
- Perform at least one scan on a participant while being observed by the SOF QC Officer or designate

b. Phantom Scans

Each site will receive a set of acoustic phantoms from Walker Sonix. Phantom scans must be done in duplicate. Turn on the UBA 575 at least 15 minutes before performing the QC scans. Keep the water bath temperature roughly constant, preferably at room temperature. It is not necessary to use a thermometer, but do check the temperature with your hand.

Both phantoms should be scanned on a weekly basis (two scans for each phantom each week) and the results recorded in the QC log maintained at the site. Follow the instructions detailed in the User's Manual, section 10, "System maintenance." Note that the phantoms are referred to as "bone standards" in the User's Manual, and the results of the phantom scans are in a separate database when the instructions are followed correctly.

c. Cross Calibration

A study wide ("gold standard") phantom will be circulated to each site with instructions on its use. The phantoms will be circulated periodically during the course of the study as well.

d. Reproducibility

In our cohort, long-term reproducibility obtained on 12 subjects with 5-8 measurements each over a period of 1 week to 1 month was 5.8% for BUA and 2.8% for UVB. Averaging the 2-3 measurements obtained on the same day improved precision to 4.0% for BUA and 2.0% for UVB. Reproducibility errors were defined as root mean square average of standard deviations (SD) of repeated measurements with interim repositioning.

6. Equipment maintenance

Routine maintenance of the UBA 575 is discussed in detail in the Walker Sonix UBA 575 Operations Manual, Sections 9 and 10.

7. General remarks

Unlike bone densitometry, ultrasound scanners are fairly new devices and there is not much knowledge about what kind of problems will be encountered. Therefore, we encourage you to call not only Walker Sonix, but also the coordinating center when problems arise. Both Claus Glueer (415) 476-5551 and Doug Bauer (415) 597-9289 will be available to help you.

8. Quality control checklist

☐ Water bath preparation

- ☐ • Preparation the day before use
- ☐ • Uses "All" liquid detergent
- ☐ • Bath maintained at room temperature

☐ Participant preparation

- ☐ • Shoe, stockings removed
- ☐ • Chair, leg positioned properly

☐ Foot positioning

- ☐ • Uses same side as Visit 4 measurement
- ☐ • Heel/transducers wiped with hands
- ☐ • Restraint applied

☐ Patient information entered

☐ Scanning of participant

- ☐ • Scanning system self test
- ☐ • Scan results obtained

☐ Print results

☐ Results given to participant, placed in chart

Calcaneal Examiner ID:_____

Side scanned at V4 ☐ Right ☐ Left ☐ N/A

Side scanned at V5 ☐ Right ☐ Left ☐ Refused

If V5 side is different than V4 side, why?_____

BUA 1:____ ____ ____ ____ units

UVB 1:____ ____ ____ ____ units

SOS 1:____ ____ ____ ____ units

BUA 2:____ ____ ____ ____ units

UVB 2:____ ____ ____ ____ units

SOS 2:____ ____ ____ ____ units

If BUA scan 1 and 2 differ by more than 10 units, repeat scan.

BUA 3:____ ____ ____ ____ units

UVB 3:____ ____ ____ ____ units

SOS 3:____ ____ ____ ____ units

☐ Unable to obtain values

Tibial Examiner ID:_____

Side scanned: (same as calcaneal US) ☐ Right ☐ Left ☐ Refused

Distance between malleolus and patella: _____ cm

Midpoint: _____ cm

Distance between probe and bone (mm): ☐ < 12 mm

☐ ≥ 12 mm

SOS 1:____ ____ ____ ____ m/sec

☐ Unable to obtain values