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## QUANTITATIVE ULTRASOUND OF BONE

### 1. Introduction/overview of ultrasound measurements in Health ABC

Bone mass explains 30 to 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 directly with its connectivity.

Quantitative ultrasound (QUS) may be a useful measure of both the quality and quantity of bone. Two 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 to 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 ( $r=0.4$  to  $0.6$ ), nor are they highly correlated to each other.

Although QUS is not a good surrogate measurement for bone density, it does have clinical utility because it appears to assess bone strength. In the Study of Osteoporotic Fractures we have demonstrated that low calcaneal QUS is associated with a variety of fractures, and more importantly, QUS is strongly associated with the risk of future hip fractures. The relationship between QUS and hip fractures is similar to that observed with hip BMD. Other large prospective studies have found similar relationships. There is little data on the relationship between QUS and weight loss, inactivity or major medical illness.

Besides its potential for assessing bone strength, quantitative ultrasound has several practical advantages over densitometry: it is quicker, less expensive, entails no radiation exposure, and is portable. Both ultrasonic velocity and BUA measurements are sufficiently reproducible, generally 0.5 to 1.0% and 2 to 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 Health ABC we will be measuring QUS with the Hologic Sahara. This device has recently been approved by the FDA and will be widely available soon. Compared to other available devices, the advantages of the Sahara include reduced scan time, improved precision, dry coupling to the heel (no water bath), and importantly, an established and reliable service network.

## **2. Equipment**

Quantitative ultrasound (QUS) measurements will be carried out using a Hologic Sahara. A matrix of 3x3 locations is measured and the final results are obtained by averaging 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. Speed of Sound (SOS) measurements are also obtained with the Sahara. Lastly, the Sahara combines both BUA and SOS measurements into a single parameter called the Quantitative Ultrasound Index (QUI).

Details regarding the initial set up, including room requirements, unpacking, set up, printer operations and system calibration are in Chapter 2 of the Sahara User's Guide.

For equipment or repair problems related to the Sahara system, please contact Hologic directly after contacting the Coordinating Center (see section 2.1). They may be reached at (800) 321-4659.

### **Equipment list**

- Sahara Clinical Bone Sonometer
- Laptop PC with Research Software Version 1.2
- Sahara ultrasound coupling gel
- Baby wipes
- QC phantom
- Positioning aid

- Power module

## 2.1 Equipment maintenance and repair

Routine maintenance of the Sahara is discussed in detail in the User's Guide, Chapter 6. Do not use other brands of coupling gel.

### When Problems Arise

In order to track calibration changes within your Sahara unit, UCSF has CIRS phantoms that should be scanned before and after some system repairs. If you encounter a problem with your Sahara unit that requires repair, replacement of transducer pads and/or recalibration, please follow these steps:

1. Contact Michaela Rahorst (415-597-9318) to inform her of the problem.
2. Then contact Hologic for service.
3. Immediately report back to Michaela what action Hologic has suggested. Do nothing to the scanner until you have talked to Michaela.
4. UCSF will then decide if the CIRS phantoms should to be sent to your site before the scanner is repaired. You will be informed of the decision and given instructions.
5. Detailed instructions of how to scan the phantoms will be sent with the phantoms themselves.

### Sahara Maintenance Logs

The UCSF Coordinating Center would like to keep track of repairs, upgrades and equipment replacement. Please use the attached Sahara Repair/Service Log Sheet to document any equipment, hardware (including the computer), or software problems and their resolution. These should be sent to Russell Scott at the UCSF Coordinating Center. Be sure to record (with dates) all scheduled and unscheduled maintenance performed on your device, as well as any change in hardware or software. Please make copies of the Sahara Repair/Service Log as needed.

## 3. Safety issues and exclusions

A small proportion of participants will have very large heels because of foot edema or other problems. If the heel does not fit easily into the Sahara, do not attempt to scan the participant. Also, do not scan a heel that has ever been broken, or a foot that has an open sore or cast.

## 4. Participant and exam room preparation

Health ABC participants should be informed that a painless, radiation-free measure of heel bone integrity will be done during their Year 5 Health ABC clinic visit. The test will require removing the shoe and sock or stocking, placing the heel into the ultrasound device (no water) and then sitting quietly for approximately 5 to 10 minutes.

Each participant should be told not to use lotions, creams, powders or ointments on the lower extremities the day of their visit. The foot must be completely dry before the measurement is made!

### **5. Measurement procedures**

The protocol for obtaining Sahara measurements is detailed in Chapter 3 of the Sahara User's Guide. Be sure that the device is kept at room temperature for at least 1 to 2 hours prior to use. Follow this procedure:

For each transducer pad, squeeze out about an inch bead of gel.

Apply a bead of gel along the face of each pad, from the tip to the bottom. The tip of the pad should be covered with gel.

Select the OPEN button on the <Measure the Patient's Heel> window. This will open the transducer pads to the fully open position.

Please refer to pages 5-7 to 5-9 of the Sahara Clinical Bone Sonometer Advanced Clinical User's Guide by Hologic for additional details.

#### *Deciding which side to scan*

We will obtain ultrasound measurements at Year 5 on the same side as the ultrasound measurement performed at Year 2. To see which side was scanned at Year 2, look at the Data from Prior Visits Report. In general, this was the right heel unless the participant had recently injured that extremity. Only switch to the other side in an extreme situation, including open sore on the foot/ankle, heel fracture, or cast making positioning impossible.

1. Answer Question #1 on the Ultrasound data collection form (page 11 in the Year 5 Clinic Visit Workbook) regarding whether or not the participant has a cast or open sore on either foot; with the follow up question regarding whether or not they've

ever broken their heel. Follow the directions on the form regarding which heel to scan.

2. If the participant does not have a cast or open sore on either foot, ask:
  - a) (Question #2, page 11) “Have you ever broken your heel bone?” (note, we are NOT interested in any other fractures, such as foot, ankle, or leg fractures.)

If the answer is “Yes,” and they have fractured their right foot, scan the left foot; if they have fractured their left foot, scan the right foot. If they have fractured both, do not scan.

- b) (Question #3, page 12) “Which heel was scanned at Year 2?” (refer to Data from Prior Visits Report.) Scan the same foot that was scanned at Year 2.

3. If ultrasound measurements were not done at the Year 2 visit, follow these guidelines: ask each participant the following:

- a) (Question #4, page 12) “Have you broken any bone in your leg, ankle, or foot in the last 12 months?” (Do not include isolated toe fractures.)  
If they answer, “Yes.” ask them: “Which ankle, leg, or foot?”  
If the answer is “Right,” scan the left foot; if the answer is “Left,” scan the right foot; if the answer is “Both,” ask: “Which side was most recently broken?” If the answer is “Right,” scan the left foot; if the answer is “Left,” scan the right foot; if the answer is “Both,” scan the right foot.
- b) (Question #5, page 13) “Do you have any permanent weakness in your legs, ankles, or feet from an old injury or stroke?”  
If the answer is “Yes,” ask: “Which side is weaker?” If the answer is “Right,” scan the left foot; if the answer is “Left,” scan the right foot. If the answer is “Right and left are equally weak,” scan the right foot.

#### *Number of scans to obtain*

Each participant will have at least two measurements of the same heel. The foot should be removed from the device and repositioned between measurements. If the second BUA measurement differs by more than ten units obtain a third measurement. Do not obtain a third measurement unless the first two BUA measurements differ by 10 or more units, or one or more of the scan results have an asterisk (see next paragraph). It is not necessary to obtain more than three measurements on a participant, even if they all differ by more than 10 BUA measurements.

#### Asterisk results.

Asterisk results indicate a non-linear BUA result which may be inaccurate. They may occur with unusual-sized or shaped heels.

If asterisks are obtained on the first scan, pay special attention to positioning of the heel when repeating the measurement. If an asterisk is obtained on a scan, obtain a third measurement.

*Special problems*

- a. Bunions. The centering device for the Sahara assumes normal foot anatomy. Some participants will have significant bunions (outward deviation of the toes) which complicates positioning of the foot. If a bunion is present, do not use the centering line (normally placed between the participants second and third toes), simply position the foot as best as possible so that the long axis of the proximal foot is perpendicular to an imaginary line drawn between the two heel transducers.
- b. Swollen/big feet. A small proportion of participants will have very large heels because of foot edema or other problems. If the heel does not fit easily into the Sahara, do not attempt to scan the participant.
- c. Sores on shin. A small number of participants may have sores on their shins. If this is the case, place a paper sheet between the participant's shin and the positioning device.

## **6. Data collection**

All data collected for the Sahara measurements will be stored and transmitted to the Coordinating Center electronically. Results will also be recorded on the Health ABC Clinic Visit Workbook.

### a. Participant Identification.

Each Health ABC participant will be identified by their name (last name, first name, middle initial) and Health ABC ID number. Participant date of birth, sex, height, weight, etc., do not need to be recorded on the ultrasound forms.

### b. Health ABC Ultrasound Data Collection Form

Record the Staff ID # and participant's Health ABC ID # on the form. For each Sahara measurement, record on the Ultrasound Data Collection Form the BUA, SOS, and QUI values as they appear on the Sahara print out.

If Sahara measurements are not obtained for any reason, write an explanation in the space provided on the Ultrasound Data Collection Form (Question #6 on page 13 in the Year 5 Clinic visit Workbook).

If a scan is completed, but not recorded on the computer, note this in the “Comments” section of the Health ABC Monthly Ultrasound (Sahara) Data Transfer form, and attach page 14 of the completed ultrasound data collection form (Year 5 Clinic Visit Workbook). At the top of this attached page, record the date of the exam, and the participant’s acrostic and Health ABC Enrollment ID#. In addition, call Hologic for Sahara repair service and record the problem and service in the Health ABC Sahara Repair/Service form. Send the form and copy of any paperwork from Hologic (if provided) with the monthly Sahara data transfer. Be sure to record which foot was scanned on Question #6 in the Year 5 Clinic Visit Workbook; i.e., do NOT choose the “scan not completed” response option.

### c. Sahara Printed Results

Although the Sahara is capable of printing results, this is not required in Health ABC as the data will be captured electronically and on the Health ABC workbook.

## **7. Data backup and transfer**

During the Health ABC study it is expected that the database on the Sahara will become very large. This situation would require many floppy disks in order to archive completely. In order to save clinic time during the archiving process and facilitate the transfer of data to the Coordinating Center, each clinic has been asked to purchase and install an external 'zip' drive onto the laptop computer that is used for the Sahara. The data back-up and transfer procedures will require several zip cartridges: we recommend that each site purchase at least four cartridges. Each cartridge should be clearly labeled with the clinic name. The zip drive will probably occupy either the 'e' or 'f' drive on the laptop. Whoever does the installation of the zip can tell you which drive has been assigned to the zip function. In order to set the archive path to the zip drive (the default is the 'a' drive) the following directions should be followed:

At the Sahara main menu, click on the <Utilities> pull down menu on the menu bar at the top of the screen. Select <Set Program Defaults> on the pull down menu. See the box labeled 'Directories' and select <Change Directory>. See <Choose Archive Path>. The current archive path probably reads **a:\arch\_dat\**. Highlight the current drive letter (the 'a') and change the current drive letter to the zip drive letter. The zip will probably be 'e' or 'f'. Then close the window.

This is a one-time set-up and need only be re-set when it is necessary to change the archiving media.

### **7.1 Archiving the Sahara database**



To prevent data loss from computer or other system failures, we are requesting that each Health ABC clinic archive the entire Sahara database at the end of each week. We recommend that each field center devote two zip cartridges to the weekly archiving of data (although both zip cartridges do not have to be used every week). The zip cartridges that are used for the weekly back-ups should be rotated every other week.

To archive the database, open the Sahara main menu. Put a zip cartridge into the zip drive. Click on the <Database> pull down menu on the menu bar at the top of the screen. Select <Archive Database>.

Keep the archived database in a safe location in the clinic.

## **7.2 Monthly transfer of Sahara data to the Coordinating Center**

Starting immediately and then on or about the first of every month, please make an additional zip cartridge using the instructions for archiving described above and send it by Federal Express (2-day delivery is sufficient) to the Coordinating Center. Complete a Health ABC Sahara Data Transfer Log and enclose it with the zip cartridge. Please make copies of the Health ABC Sahara Data Transfer Log as needed. Also send a copy of the Quality Control Log (Hologic form P/N 080-0606 Rev A). Also, if any repairs were performed during the month, include a copy of the Sahara Repair/Service Log and any repair log provided by Hologic.

Send the zip disk to:     Russell Scott  
                                  UCSF Prevention Sciences Group  
                                  74 New Montgomery Street, Suite 600  
                                  San Francisco, CA 94105  
                                  (415) 597-9312

The disks will be downloaded onto computers at the Coordinating Center and then the zip cartridges will be returned to each clinic for re-use.

Please designate one examiner and a back-up examiner, to serve as the local Sahara data contact. This person should be familiar with the weekly back-up and monthly data transfer procedures, and will be contacted by the Coordinating Center or Hologic for Sahara-related data issues.

## **8. Procedures for performing the measurement at home**

The same procedures are used in the home as in the clinic.

## 9. Alert values/follow-up/reporting to participants

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 is unclear. It is important to emphasize that ultrasound measures of bone are less well established than bone densitometry, particularly for African-American men and women, and that we hope to further study the relationship between ultrasound measures and skeletal health in this study. Refrain from discussing the exact meaning of specific ultrasound values. Keep in mind that the vast majority of physicians, even those who are knowledgeable about osteoporosis, will not be able to interpret the meaning of specific BUA, SOS or QUI levels.

## 10. Quality assurance

### 10.1 Phantom scans

1) Each site will receive acoustic phantoms from Hologic. Phantom scans must be performed daily. As phantom results are very temperature dependent, we recommend that the phantoms be kept at room temperature (to the extent possible), and that daily phantom scans be performed after the ambient temperature of the room and machine have been stable for several hours (for example, during the noon hour or early afternoon).

A single phantom scan should be performed each day the machine is used, and the results recorded in the Hologic QC Log (see attached) maintained at the site. Follow the instructions detailed in the User's Manual, Chapter 3, "Quality Control."

### 2) 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.

### 3) Reproducibility

We plan to assess the reproducibility of the Sahara units in the near future. Detailed descriptions of these in vitro (phantom) and in vivo (staff or participants) studies will be distributed.

## 10.2 Training and certification of operators

Although BUA measurements are relatively simple compared to BMD measurements, 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 Health ABC participants must complete the following:

- Carefully read this section and the Sahara User's Guide
- Receive training from the Health ABC QC Officer or the designated staff who attended the central training session
- 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 Health ABC QC Officer or designate

## 10.3 Quality control checklist

### QC scans

- Phantom maintained at room temperature
- Proper placement of phantom
- Results recorded on QC log

### Participant preparation

- Shoe, stockings removed
- Foot is completely dry
- Chair, leg positioned properly

### Foot positioning

- Correctly assesses side to scan

- Gel applied correctly
- Positioning/restraint applied correctly
  
- Scanning of participant
  - Two measurements of the same heel performed
  - Third measurement performed if second BUA measurement differs by more than ten units.
  - Third measurement performed if either the first or second BUA measurement is asterisked.
  
- Results properly transcribed and attached to Ultrasound Data Collection Form
  - Participant's Health ABC Enrollment ID # properly recorded
  - BUA, SOS, and QUI values are recorded as they appear on the Sahara printout or computer screen



Quality Control Log

QUALITY CONTROL LOG

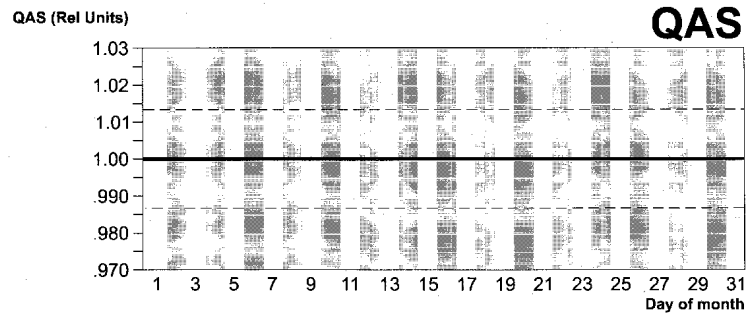
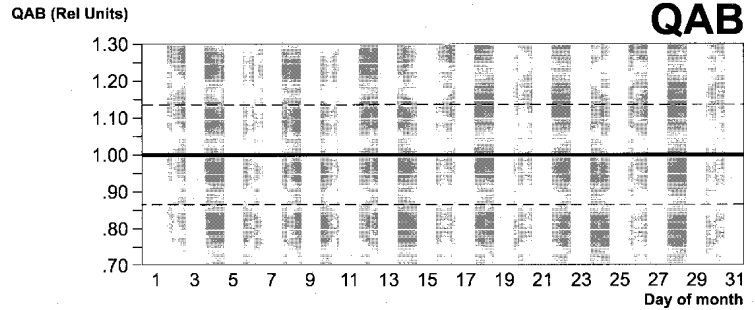
Month: \_\_\_\_\_ Year: \_\_\_\_\_

Clinic: \_\_\_\_\_ Operator: \_\_\_\_\_

System S/N: \_\_\_\_\_ Phantom S/N: \_\_\_\_\_

Phantom BUA: \_\_\_\_\_ Phantom SOS: \_\_\_\_\_

Day	QAB (Rel Units)	QAS (Rel Units)
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Monthly Ultrasound Data Transfer



MONTHLY  
ULTRASOUND (SAHARA) DATA TRANSFER

To: Russell Scott  
UCSF Prevention Sciences Group  
74 New Montgomery, Suite 600  
San Francisco, CA 94105  
415.597.9312

From: \_\_\_\_\_

Staff ID #:

Field Center:  Memphis  Pittsburgh

Telephone #: ()  -

Date data backed-up on Zip cartridge:  /  /   
Month Day Year

Comments: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

UCSF Coordinating Center Use Only:

Date Zip cartridge received:  /  /   
Month Day Year

Date Zip cartridge mailed back to field center:  /  /   
Month Day Year

Zip cartridge mailed back to: \_\_\_\_\_  
(Name of Field Center Staff)

Comments: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_