

DXA QUALITY ASSURANCE

INTRODUCTION

The purpose of this manual is to describe the dual-energy X-ray absorptiometry (DXA) bone mineral density (BMD) quality assurance (QA) program for the Clinical Centers (CCs) participating in the Women's Health Initiative (WHI) Osteoporosis Substudy using the Hologic QDR-2000. This manual is intended as a supplement to the Hologic User's Manual.

To use this manual effectively, it is essential to have read and understood the entire Hologic User's Manual. The study densitometer operators are required to have participated in the 4-day Hologic training session and should be familiar with all instrument features and procedures discussed in the Hologic User's Manual.

****Unauthorized Hologic software changes during the study must be avoided. If for any reason you think you have to change or update the software or a Hologic technician suggests a change, contact the WHI Bone Density (BD) Center before any changes are made.****

Acknowledgment

Several of the procedures that are specific to the Hologic QDR-2000 Series Bone Densitometer have been designed with the technical assistance of Hologic, Inc.

1. Bone Density Scans

1.1 Measurements

DXA scans will be obtained on the Hologic QDR-2000 scanner provided for use in the WHI studies. No other scanner should be used.

Scans will be acquired according to the schedule in *Vol. 1 – Study Protocol and Policies, Table 1-A1.1 – Frequency of Data Collection*.

1.2 Radiation Doses

The radiation doses presented below for the QDR-2000 are the effective dose equivalent, which weighs the radiation dose according to the volume and type of tissue irradiated and as such provides a better estimate of risk than the surface dose. They are extrapolated from the surface dose values supplied by the manufacturer. The unit is the microSievert (μSv) which is the standard SI unit for the effective dose equivalent. For those who prefer to use millirems (mrem), note that $1 \mu\text{Sv} = 0.1 \text{ mrem}$, or $1 \text{ mrem} = 10 \mu\text{Sv}$. Also given are the effective dose equivalents for lateral thoracic and lumbar spine films based on a standard spine film protocol commonly used in clinical osteoporosis studies.

Table 1
Effective Dose Equivalents

Measurement Site	Effective Dose Equivalent (μSv)
Array AP Spine	5
Array Lateral Spine	15
Array Hip	5
Array Whole Body	15
Lateral Thoracic Spine Film	950
Lateral Lumbar Spine Film	2700

For comparison, an 8-week stay in Denver will give an additional $1 \mu\text{Sv}$ of radiation dose due to the increase of cosmic rays compared to sea level. A round-trip transcontinental flight has an effective dose equivalent of $60 \mu\text{Sv}$. The average effective dose equivalent due to natural background radiation is $3000 \mu\text{Sv}$ per year.

1.3 Blinding

Ideally, WHI CC staff that perform functional, anthropometric, or clinical tasks with participants or collect any clinical information on participants should not also function as the WHI DXA operators for baseline or follow-up studies. Instruct participants not to discuss their Clinical Trial (CT) assignment with DXA staff.

1.3.1 Baseline Scans

A copy of the baseline scan may be given to the participant and the original printout may be kept in the participant's file. Results may be discussed with the participant by the DXA operator or other clinical WHI staff, and she should be encouraged to share them with her primary physician.

1.3.2 Follow-Up Scans

In order to maintain blinding, advise the participants during the consent process and before each follow-up visit that copies of subsequent scans will not be available. Tell participants that they will receive a letter informing them of their results and if the results indicate that they are osteoporotic or have excessive bone

loss. If any significant bone loss (see *Section 10.1.4.2 - Excessive Bone Loss*) or osteoporotic results (see *Section 10.1.4.3 – Osteoporotic Values*) are demonstrated, the letter sent to the participant suggests that she discuss the results with her personal physician. See the Questions and Answers: Bone Mineral Density (for CC Staff) (*Vol. 2 – Procedures, Appendix G.1.4*) for additional guidelines on how to respond to participant concerns about blinding for follow-up scans. Note that if significant bone loss is found on a follow-up scan, do not discuss this with the participant until UCSF Bone Density Center has confirmed the finding. Unblinding of these participants in the event of significant bone loss is not usually necessary.

Subsequent scans should not be kept in the participant's file. A separate bone scan file should be maintained and access to these files should be limited to DXA operators (see *Section 8.3 – Hard Copies of Scans*).

2. Overview of DXA BMD QA Program

High quality bone mineral densitometry requires a broad and rigorous program of QA. The BMD QA program for the WHI has the following components:

1. Densitometer Operator Performance
 - Training requirements and certification procedures. See *Section 4 – Training and Certification of WHI DXA Operators (Required)*.
 - Standardized scanning and analysis procedures. See *Section 9 – [Baseline Scanning and Analysis Procedures \(Required\)](#)*, which are supplemental to the Hologic User's Manual.
 - Central review of BMD scans. See *Section [6](#) – WHI BD Center Review of DXA Scans*.
2. Machine Performance
 - Continuous on-site and central monitoring of machine performance. See *Section 7 – Monitoring Machine Performance*.
 - Daily QA spine phantom scans.
 - Weekly QA hip phantom scans.
 - Three times a week QC whole body phantom scans.
 - On-site and central review of daily QA plots.
 - Central analysis of daily QA database.
 - Circulation of “gold standard” phantoms for cross-calibration. ([See Section 7.2 – Cross-Calibration of Scanners](#))
 - Central review and analysis of cross-calibration data.
 - Software control. See *Section 7.4 – Software Change Control*.
3. Data Management
 - Participant and phantom biographies. See *Section 8.1 – Participant Biographies (Required)* and *Section 8.2 – Phantom Biographies*.
 - Participant data. See *Section 8.3 – Hard Copies of Scans (Required)* and *Section 8.4 – Electronic Scan Archive*.
 - Data transfer to WHI BD Center. See *Section 8.5 – Transfer of Data to the WHI BD Center (Required)*.

Each of these areas is of equal importance and is described in detail in the indicated sections of the manual.

3. Division of QA Responsibilities

3.1 Clinical Center Responsibilities (Required)

The CCs must ensure the overall quality and completeness of the DXA data and that all protocols and procedures are strictly followed. Specific responsibilities include the following:

1. Require that technicians are properly trained and certified. (See *Section 4 – Training and Certification of WHI DXA Operators (Required)*).
2. Identify a chief densitometer operator to train and supervise other operators.
3. Perform and review daily QA phantom scans and scheduled cross-calibration scans of traveling phantoms. (See *Section 7 – Monitoring Machine Performance*).
4. Assure that proper archiving and back-up procedures for participant scans are performed and that archives are stored securely on optical disks until the end of the study. (See *Section 8.4 – Electronic Scan Archive*).
5. Every month, send the following materials to the WHI BD Center (see *Section 8.5 – Transfer of Data to the WHI BD Center*):
 - Copies of monthly printouts of plots of the daily QA phantom data.
 - Updated copies of [machine repair logs](#) and [participant scans](#). (See *Figure 1 – WHI Hologic Repair Log Sheet, and the WHI DXA Scan Logs (Figures 2a to 2c)*).
 - Duplicate original printouts of flagged scans.
 - Duplicate original printouts of other requested scans.
 - Traveling optical disk with flagged scan files for central review.
 - A copy of the current study database [DBARCHIVE] on a floppy disk.

The materials should be sent to:

WHI Bone Density Center
UCSF Prevention Sciences
74 New Montgomery, Suite 600
San Francisco, CA 94105

Phone: (415)597-9100 FAX: (415)597-9213

6. Reanalyze centrally-reviewed scans, as requested by the WHI BD Center ([See Section 8.6 – Return Materials Sent by the WHI BD Center](#)).
7. Assure proper functioning of hardware and service from Hologic ([See Section 7.3 – Machine, Software and Service Problems](#)):
 - Notify Hologic and the WHI BD Center of any machine or software problems.
 - Record machine and software problems and service on the *WHI Hologic Repair Log Sheet* (see *Figure 1*).
 - Perform five QA phantom scans (before, if possible) and after service.
8. Contact the densitometry specialists at the WHI BD Center with any questions or problems that cannot be dealt with in the monthly batch mailings.

3.2 WHI Bone Density Center Responsibilities

The following are the responsibilities of the WHI BD Center:

1. Write and update the QA manual.
2. Promptly review the daily QA phantom scan data received from each CC in order to identify surges or drifts in machine performance.
3. Work with the Clinical Coordinating Center (CCC) to incorporate new participant data into the WHI database.
4. Review certification and flagged scans and return results to each CC. (See *Section 8.6 – Return Materials Sent y the WHI BD Center*).
5. Request and review random samples of scans from each CC.
6. Arrange for cross-calibration of all DXA instruments using traveling phantoms.
7. Prepare QA summary reports for WHI Steering Committee and NIH review.
8. Identify possible sources of error and suggest possible solutions. (*However, the WHI BD Center will not be responsible for the solution of a hardware or software problem; that will rest with the CC and Hologic. See Section 7.3 – Machine, Software and Service Problems.*)

Any questions or correspondence regarding the manual or the technical aspects of the DXA measurements should be directed to:

WHI Bone Density Center
UCSF Prevention Sciences
74 New Montgomery, Suite 600
San Francisco, CA 94105

Phone: (415) 597-9100 FAX: (415) 597-9213

3.3 Hologic Responsibilities

The following are the responsibilities of the Hologic, Inc.:

1. Provide central training sessions for all WHI operators, if previously untrained.
2. Provide hardware/software service within 24 hours, and work with the CC to resolve hardware or software problems.
3. Work with the WHI BD Center in identifying and resolving any QA or measurement problems.

4. Training and Certification of WHI DXA Operators (Required)

To obtain consistent results, the densitometer operators must be aware of possible sources of error that may affect data collection and analysis. Only those operators who have been certified through Hologic training and the WHI BD Center review are allowed to perform the scanning and analysis for this study.

Anyone performing scans for the WHI study must meet the following requirements:

1. Read and understand both the Hologic User's Manual and this manual.
2. Successfully complete the 4-day Hologic QDR-2000 training course.
3. Have a satisfactory review of initial scans by WHI BD Center.

In order for an individual technician to be certified to perform scans of a given skeletal site, the first 10 scans done on study participants at **each** skeletal site for each operator must be sent to the WHI BD Center for review. Original printouts and floppy disk copies of scans should be sent immediately to the WHI BD Center at the address listed above. See *Section 3.1 – Clinical Center Responsibilities (Required)*.

4. Successfully pass the WHI BD Center scan analysis tests.
5. To ensure a high level of quality for the analysis of the follow-up scans, there will be an additional certification procedure for all BMD operators involved in the study. Each DXA operator will be asked to send in baseline and follow-up scans of the first ten 1st annual visit (“12-month”) participants on which they perform densitometry in order to assess the analysis performance of each DXA operator.
6. Periodically unanalyzed scans will be sent to all sites for independent evaluation by all DXA operators

It is the CC's responsibility to ensure that as new operators are brought into the study, all of the above certification criteria are met. Since the Hologic central training sessions are held only sporadically, there may be several months' delay between when a new operator is hired and when certification is complete (usually no more than 4 months).

Personnel not meeting these requirements may not scan participants without close supervision by a certified operator, unless specifically authorized by the WHI BD Center.

5. Scanning and Analysis Procedures – Overview

Standard scanning and analysis procedures for the hip, AP lumbar spine and whole body bone density measurements are described in detail in the Hologic User's Manual.

Detailed supplemental procedures for WHI are described in *Section 9 – Baseline Scanning and Analysis Procedures (Required)* and *Section 10 – Follow-Up Scanning and Analysis Procedures*. Some of the information from the Hologic User's Manual is repeated in this document for emphasis. Please note, however, that some of the scanning evaluation protocols for this study differ from those detailed by Hologic.

6. WHI BD Center Review of DXA Scans

Scan analysis quality will be ensured by a central review of analyzed participant scans. Whenever scans are to be reviewed centrally:

1. A duplicate original printout of the scan should be sent to the WHI BD Center, along with a copy of the scan image file on the traveling optical disk (using the Hologic COPY command) so that the WHI BD Center can view the scan on the workstation, if necessary.
2. It is the responsibility of the WHI CC site operator to reanalyze the scan according to the WHI BD Center comments and return a printout of the reanalyzed scan to the WHI BD Center for verification.

Procedures for compiling and forwarding scans to the WHI BD Center are outlined in *Section 8 - Data Management* and *Section Section 9.6 - BMD Data Mailing Procedures*.

6.1 Certification Scans

The first 10 scans of each type (Hip, AP Spine, Whole Body) done at baseline on study participants by each operator must be sent to the WHI BD Center for review. In addition, the first 10 follow-up scans (including baseline and follow-up scans) done at the first annual visit must be sent to the WHI BD Center for review.

6.2 Flagged Scans

Any scans that appear unusual or difficult to analyze should be flagged for review by the WHI BD Center. Guidelines for flagging scans are listed in *Section 9.4 - Flagging Scans for Review*.

Flagged scans should be sent to the WHI BD Center every month with the updated participant database. (See *Section 9.6 - BMD Data Mailing Procedures*). Note the reason(s) for flagging on the *WHI DXA Scan Log* (see *Section 9.5 - WHI DXA Scan Log Instructions*) and on the original printout for clarification of the problem.

The printouts will be reviewed for standard positioning and analysis procedures and returned to the CCs with instructions for reanalysis, if appropriate. Often, these problem scans have been analyzed correctly and will not require further action.

6.3 Random Samples of Scans

Periodically during the study, a random sample of scans will be requested for review by the WHI BD Center. In the initial phases of the study, a relatively large number of scans will be checked to verify site performance. The number of scans requested will vary according to the period in the study, the number and training of the technicians, and the results of previous samples.

7. Monitoring Machine Performance

Monitoring of machine performance throughout the study is the joint responsibility of the individual CCs and the WHI BD Center.

7.1 QA Phantom Scans

Perform the QA phantom scans (daily for spine, weekly for hip, and 3 times a week for whole body after the initial 20 scans) as outlined in the Hologic User's Manual. See *Appendix A – Whole Body Phantom Protocol*. Review locally for abrupt changes in machine performance and send the results to the WHI BD Center once a month. Points of procedure to note:

1. Scan and analyze the Hologic spine phantom **daily**. Scan and analyze the Hologic hip phantom **weekly**. Scan and analyze the Hologic whole body **3 times weekly**. Use the array and pencil beam mode for scanning the spine phantom. The hip phantom only needs to be scanned in array beam mode.
2. Create only one participant biography per phantom. * **IMPORTANT: enter the site ID followed by # and phantom serial number, e.g., XX#Q135, as PARTICIPANT ID.** Avoid duplication of phantom biographies by using the Participant Menu to select the appropriate biography before scanning the phantom. (See *Section 8.2 - Phantom Biographies*).
3. Scan the phantom on top of the pad. Ensure alignment with the scanner axis by using the phantom case as a spacer between the ledge on the back of the scanner table and the phantom block **and** by running the laser light up and down the edge of the phantom. **Remove case before scanning.**
4. Analyze the daily phantom scans using the COMPARE feature. Keep the original scan that you use as “baseline” for the COMPARE permanently stored on the hard disk. Additional backup copies of this baseline phantom scan should be stored on your optical disks and on an another floppy disk.
5. Add the scan data to the QA phantom database immediately after scanning **and** analysis are complete, following the procedure outlined in the Hologic User's Manual. Back-up the QA phantom database to floppy (diskette) once a week using the ARCHIVE feature in the Hologic QA menu.
6. Use the PLOT feature daily to verify that the BMD and the BMC of your scanner is within normal limits. To do this, select the PLOT option from the QA menu and then press <F10> to generate a graph with the default settings. If the most recent scan falls outside the limits, **reposition the phantom and repeat the scan. If the second scan also falls outside the limits, contact both Hologic and the WHI BD Center.**
7. Unanalyzed scans will not show up in the QA plot in software versions 6.10 and up. Therefore, unanalyzed scans will not adversely affect the calculated coefficient of variation (CV). However, be sure to add only analyzed scans to the QA database.
8. If the CV exceeds 0.5% contact both the WHI BD Center and Hologic to initiate appropriate action.
9. Check the system drift weekly by pressing <R> while viewing the plot. The slope of the calculated regression line should be within the range of the standard deviation shown. If this is not the case, check for unanalyzed QA phantom data (white dots at the bottom of the plot; this only applies to software versions before 6.10). If the drift is greater than the standard deviation, contact both Hologic and the WHI BD Center.
10. Generate a printout of the QA phantom plots (BMC **and** BMD for hip, spine and whole body phantoms,) once a week on your designated “QA day.” This will facilitate detection of long-term drifts as well as short-term inconsistencies. The daily phantom database should be archived onto a floppy disk once a week on your “QA day” using the ARCHIVE option from the menu and kept as a back-up. Follow the instructions in the Hologic User's Manual.
11. Original printouts of the most recent daily phantom plots (BMC **and** BMD for hip, spine and whole body phantoms) are to be sent to the WHI BD Center for review each month, on a schedule specified by the WHI BD Center.

7.2 Cross-Calibration of Scanners

In order to accurately assess absolute variations in scanner performance between CCs, periodically throughout the study, phantoms will be either mailed or brought to each of the CCs and scanned. Hologic spine, femur, and linearity (block) phantoms will be used. A detailed protocol will accompany the phantoms.

7.3 Machine, Software and Service Problems

If your machine needs to be repaired or if any adjustment has to be made that possibly might affect your data:

1. Contact the WHI BD Center before the repairs or adjustments are made to find out whether additional measures have to be taken.
2. Perform five scans of the Hologic daily QA spine phantom before (if possible) and after the repairs or adjustments are made. Reposition the phantom after each scan.
3. After repairs or adjustments are completed, send the repair technician's notes and a copy of the completed *WHI Hologic Repair Log Sheet (Figure 1)* to the WHI BD Center. The repair log should contain complete information on all repairs done on your machine. Please keep a repair log with your machine.

7.4 Software Change Control

Unauthorized software changes must be avoided. If for any reason you think you have to change the software, or your Hologic service representative recommends a software change, contact the WHI BD Center before any changes are made.

The system software installed on WHI QDR-2000 densitometers should be Version 7.10. You can find your version number at the top of the blue Hologic menu. It will say "Hologic QDR-2000 version 7.10 (A, B or C)". Future software upgrades will be checked by the WHI BD Center in conjunction with Hologic technical support personnel to assure that the upgrade will not adversely affect the study. Authorized upgrades must be cleared by the WHI BD Center before installation at the study sites.

8. Data Management

8.1 Participant Biographies (Required)

*** *WARNING. Failure to follow correct biography procedures will result in loss of BMD data.* ***

The participant biography should be entered as follows at the baseline visit:

NAME: Enter four-digit acrostic: first letter of first name followed immediately by the first three letters of last name. Do not include apostrophes or other punctuation, e.g., Mary O'Conner --> MOCO. If the last name is less than three letters, only enter the first two letters.

SOC SEC: Leave blank.

PAT ID: Use the barcode scanner or manually enter the participant's assigned 8-digit participant ID number. (The first two digits are the CC ID, digits 3-7 are the member suffix number and the 8th digit is a character.)

COMMENT: Leave blank.

SCAN CODE: Enter the 3-digit staff ID of the technician performing the scan.

ZIP: Leave blank.

DOB: Enter month/date/year of birth.

SEX: Enter F.

WEIGHT: Enter approximate weight in pounds.

ETHNIC: Leave blank.

REF MD: Enter "WHI."

8.2 Phantom Biographies

*** *WARNING. Failure to follow correct biography procedures will result in loss of BMD data.* ***

Create only one participant biography for each phantom.

NAME: Enter an appropriate name for your daily QA phantoms including your CC site number (e.g., "Site XX spine phantom"). For the cross-calibration phantoms, follow the instructions that accompany those phantoms.

PAT ID: Enter the number that has been assigned to your site followed by # and the phantom serial number, e.g., XX#Q135. See *Section 7.1 - QA Phantom Scans*. Use capital letters and do not put a space before or after the #-sign. Avoid duplication of participant biographies by using the Participant Menu to select the appropriate biography before scanning the phantom.

REF MD: Enter "WHI."

ALL OTHER FIELDS: Leave blank.

8.3 Hard Copies of Scans (Required)

The CC is responsible for maintaining original hard copies of all scans performed during the study. Use prepunched paper when printing scan reports. Keep the original printouts in the participant's scan printout folder. The following printed reports are needed for each scan:

Proximal Femur: print the standard report.

AP Spine: print the standard AP report.

Whole Body: print the BMD and body composition reports (two pages).

8.4 Electronic Scan Archive

For scan archival, each CC works on a two-optical disk system. (There will also be a “traveling optical” for sending scan images for review at the BD Center.) Both optical disks are continually updated at the **end of each day** using the Optical 1 and Optical 2 options under the Hologic ARCHIVE menu. Please be sure to rearchive any flagged scans that were sent back to you by the WHI BD Center for reanalysis after you have completed the reanalysis. Note that there is a capacity limit of 256 directory entries on each side of the optical disk. This means that you cannot save scans on an optical disk if 256 files have been saved even if there is free disk space available. In order to use the optical disks efficiently, do not save or archive scans individually. Saving scans in batches (e.g., at the end of a day) will ensure the longevity and efficient usage of the optical disk space. Flagged scans should be copied to the “traveling optical” once a week in order to make efficient use of space on this optical. The QDR-2000 software will give a warning message when optical capacity has been reached. Fill side A of the disk first, then fill side B. (See the Hologic User's Manual for detailed instructions.)

Scans to be archived **each day** to the Optical 1 and Optical 2 disks include:

- All new participant scans acquired since the last archive was performed.
- All scans that have been reanalyzed since the last archive. *Note* that if a scan needs to be restored and reanalyzed for any reason, it will need to be rearchived.
- For follow-up scans, archive **both** the baseline scan (that was used for the COMPARE analysis) and the follow-up scan on your optical disk after you have finished your scan analysis. This is the only way to identify the baseline scan and corresponding BMD data, that you used for the COMPARE procedure.

Scans to be copied **each week** to the “traveling optical” include:

- All flagged scans acquired since the last batch of flagged scans were copied to the “traveling optical.”

Optical 1 and Optical 2 will remain at the study site at all times. (The “traveling optical” will be sent back and forth between the study site and the WHI BD Center.)

The CCs are responsible for following the archive schedule and for keeping the optical disk archives safe until the end of the study.

8.5 Transfer of Data to the WHI BD Center (Required)

At the end of each month, the following items are to be sent to the WHI BD Center. See *Section 9.6 – BMD Data Mailing Procedures* for instructions on labeling and mailing batches of BMD data.

1. QA PRINTOUT. Send a **printout** of the most recent plots of the QA database, including spine, hip, and whole body phantom BMD and BMC. The plots are reviewed at the WHI BD Center and problems are reported back to the CC.
2. PARTICIPANT SCAN LOG. Send a copy of the written *WHI DXA Scan Log* (see *Figures 2a to 2e*) listing participants scanned since the last data transfer. Use the log sheets to “flag” individual scans for review at the WHI BD Center. See *Section 9.5 – WHI DXA Scan Log Instructions* on filling out the log.
3. SCANS FOR REVIEW. Send duplicate original printouts of certification scans, “flagged” scans, random sample scans and any scans requested for review by the WHI BD Center. **Please write the reason the scan was flagged, requested or being sent directly on the printout.** These scans will be triaged visually based on the original printouts and analyzed on the Hologic workstation, if necessary. For this reason, both an original printout and an electronic copy of each scan sent in for review must be included.
4. “TRAVELING OPTICAL” DISK WITH SCANS FOR REVIEW. Send electronic copies of the scans detailed in #3 on the “traveling optical.” Archive scans for review in one batch on the traveling optical using the COPY feature. Do not archive the scans individually or at the end of each day as this will use up the disk space rapidly.
5. REANALYZED SCANS. Send original printouts of all scans that have been reanalyzed according to the WHI BD Center instructions since the last data transfer. Attach the annotated printouts sent by the WHI BD Center that indicated the problems requiring reanalysis. You do NOT have to send back the reanalyzed scan images on the traveling optical.
6. DB ARCHIVE participant database (on floppy disk). Please include the following on the disk label:
 - “DB ARCHIVE”
 - Batch #
 - CC name
 - Date (end date of 1-month period)
 - If more than one disk, label each disk as above and then write “1 of 3”, “2 of 3”, etc.

Note: The WHI BD Center will use the **most recent scan data** for participants whenever there are multiple analyzed scans from the same date in the database. Notify us if there are exceptions to this.

7. Copy of the updated *WHI Hologic Repair Log Sheet* (Figure 1).

Ship these items monthly to the following address:

WHI Bone Density Center
UCSF Prevention Sciences
74 New Montgomery, Suite 600
San Francisco, CA 94105

8. Longitudinal scan samples, if applicable.

8.6 Return Materials Sent by the WHI BD Center

The WHI BD Center will return the following items to the CC after review:

1. Annotated printouts of flagged scans, random sample scans, and any other requested scans returned to the study site with explicit instructions for reanalysis, as necessary. The CC reanalyzes the problem scans according to the WHI BD Center recommendations. The reanalyzed scan is then saved and rearchived and the database at the study site is automatically updated. A duplicate original printout of the reanalyzed scan is sent to the WHI BD Center with the next data transfer to verify compliance.
2. Any recommendations for service, additional phantom scans, etc., as necessary, based on the QA database.

9. Baseline Scanning and Analysis Procedures (Required)

Obtain all bone density measurements with the participants wearing gowns only. This will help eliminate possible artifacts due to zippers, bras, etc. Please adjust the room temperature whenever possible so that the participant feels comfortable while wearing a gown.

Before performing any follow-up scans, load the baseline scan into the hard disk and have a printout of the baseline available. Refer to the baseline printout as you go through the positioning of the participant for the follow-up; this is to ensure consistent scanning of the same area. Careful positioning and visual comparison of the current scan with baseline are essential for producing precise measurements. Consistent projection of the femur is more important than the actual angle of the foot rotation. Use the RESCAN feature as soon as any positioning errors are detected during the current scan.

The same scans that were done at baseline should be repeated at the first annual or “12 month” visit (Hip, AP Spine and Whole Body). When completing the scan log sheet, please enter the scan ID #s of the scans being used for the COMPARE analysis.

9.1 Hip Measurements

9.1.1 Participant Set-up (Required)

Complete *Form 87 – Bone Density Scan* for each participant. See *Vol. 3 – Forms* for instructions for completing the form.

When performing hip scans, the following guidelines must be adhered to:

1. If the participant answers “yes” to any of the items in *Question 7 – “Tests in the Past Ten Days,” Form 87 – Bone Density Scan*, have the WHI CC physician confirm the response and reschedule her bone density measurement for a date at least 14 days later.
2. No metal or plastic object should remain in the scanning area. Check for jewelry, coins or other objects in the hip pockets, zippers, buttons, rivets, belts or any other clothing fasteners, as well as hip and back braces. See *Question 6 – “Metal Objects,” Form 87 – Bone Density Scan*.
3. Lower any thick clothing that might obscure the scanning area.
4. Keep the participant’s hands out of the scanning area by placing them well away from the hips.
5. Whenever possible, scan the **left** hip. Ask the participant whether she has ever fractured that hip or had a total hip replacement in that hip (*Question 5 – “Fracture or Replacement,” Form 87 – Bone Density Scan*). If she has, scan the other hip. If both hips are affected, scan the one with the least hardware. If the participant has had bilateral hip replacement, do not obtain a hip scan. Note that people often do not know what kind of hip surgery they have had, so it is usually a good idea to confirm that the prosthesis prevents a hip measurement by attempting a scan.

Scan the right side if you cannot rotate the left foot inward due to pain.

6. Ensure rotation of the hip by holding the knee and the ankle when positioning the leg. Optimum positioning of the leg is most important to achieve a consistent projection of the femur.
7. After proper rotation, attach the foot to be scanned to the angled block supplied by the manufacturer.
8. The participant should be made as comfortable as possible to reduce the chance of unwanted movements. Use a pillow for the head and a small pillow under the knee of the leg not being scanned. Maintain the participant at a comfortable body temperature for the duration of the scan.
9. Instruct the participant to remain still until the end of the measurement. Make sure that the leg is not moved during the scan. Flag any scans in which the participant has moved and has not been rescanned.

9.1.2 Hip Scan Acquisition (Required)

1. Use the **array left hip** or **array right hip** mode as appropriate. Also use the default settings for the hip scan.
 - Length: 6.0040 inches
 - Width: 4.2445 inches
 - Spacing: 0.03950 inches
 - Resolution: 0.03735 inches
2. If the scan shows a “short” neck with little space between itself and the ischium, this could be due to poor rotation of the leg. **Check the participant's leg positioning and, if needed, reposition the participant and rescan.**
3. In order to obtain the best position for the measurement, the RESCAN option (F3 key) should be used freely. When restarting a femur scan, place the repositioning marks so that the intersection of the two lines touches the most lateral aspect of the greater trochanter.
4. Interrupt scanning about 1.5 cm (15 lines) beyond the medial extent of the acetabulum if scan width limit has not yet been reached.

9.1.3 Baseline Hip Scan Analysis Procedures (Required)

High quality data analysis is strongly dependent on the ability to duplicate the placement of each of the four subregions of the hip. The Hologic analysis software calculates and displays all four regions using default values without any required operator interaction. The default size and location of these regions is usually not altered by the operator. However, to adapt them more closely to the optimal anatomic location for an individual participant, changes can be made as detailed in the sections that follow.

In a given population, large variations in weight, hip conditions and hip anatomy can result in scans that are difficult to analyze. Adjustment of the brightness and contrast will frequently be necessary to improve the appearance of the image so that regions of interest (ROI) can most easily be placed.

Global Region of Interest (ROI): The procedures outlined in the Hologic User's Manual are to be followed. The points listed below are for emphasis.

1. The left side of the global ROI should be at least 5 mm (five lines) beyond the outer edge of the greater trochanter to provide sufficient soft tissue for analysis, although it should not extend outside the participant's body.
2. The bottom edge of the global ROI should be at least 1 cm (10 lines) below the lesser trochanter to provide sufficient soft tissue for analysis.
3. In the event that the global ROI must be expanded to allow complete filling of the bone edges (see below) in low BMD participants, all edges must be at least two steps away from the border of the scan field. This will be important when the baseline scan is used with the COMPARE feature on the follow-up scan analysis.

Bone Edges: If the bone edges are not properly determined by the analysis program, increase the size of the global ROI by first moving the top border up ten lines further from the femoral head and then moving the medial border ten lines further out, if possible, to include more soft tissue in the analysis. Repeat as needed. Do not move the bottom or lateral border. Do not fill in bone edges manually unless absolutely necessary. The software will automatically fill any “holes” within the bone. Occasionally, the bursa or tendons surrounding the greater trochanter can be calcified. This will produce “knobs” that can merge with the trochanter and throw off the automatic placement of the four regions. Expanding the global ROI will not always separate these from the trochanter and they will have to be excluded manually. Flag for review by the WHI BD Center any cases in which you manually alter the bone edge.

Femoral Midline: Unevenness (notches) in the upper or lower edge of the femoral neck can throw off the femoral midline so that it does not run down the center of the neck. This will in turn cause the femoral neck box to twist. If the midline looks like it might be off or the box is twisted, it may be necessary to adjust the bone mask (e.g., filling in neck notches) in order to obtain appropriate positioning of the midline. The position of the midline itself should not be altered. If you have made changes to the scan, such as filling in bone in order to alter the midline, or if the midline still seems off, please flag these cases for review by the WHI BD Center (see *Section 9.4 - Flagging Scans For Review*).

Femoral Neck Box: If the default neck box provided by the Hologic program looks reasonably placed, leave it unchanged.

1. The femoral neck region (the area of the neck covered by the neck box as listed on the scan analysis) should be at least 2.5 cm². Whenever possible, use the maximum width of the neck box (default). The neck box should be perpendicular to the neck axis. If the maximum area of the neck that can be covered by the femoral neck box is less than 1 cm², the participant should be rescanned with special care taken to improve the rotation and degree of adduction of the leg. Since such a narrow neck box would be only two to three lines wide, you will only rarely have a problem with this constraint.
2. If the area of the neck region is less than 2.5 cm², attempt to increase the width of the neck box to the maximum possible while still avoiding inclusion of the trochanter, ischium or femoral head, and acetabulum. In order to obtain maximum size of the neck box, the ischium may be deleted (see item 4 below).
3. If the default neck box partially extends into the trochanter or femoral head and acetabulum, adjust its location or size while maintaining the maximum possible area.
4. The Hologic software is sometimes unable to provide an appropriate placement of the neck box and other regions. This can occur if the projected neck axis is too short or the neck is too close to the ischium. Soft tissue between the neck and ischium will be read as bone, and the automatic placement of the femoral midline will fail. If this happens, use the procedure in Chapter 4 of the Hologic User's Manual for deleting the bone of the ischium. Deleting this will not adversely affect the analysis, as this bone is not included in the reported regions of interest.

Ward's Triangle The Hologic software should place the square, marking Ward's triangle, adjacent to the femoral neck box. In participants with low BMDs or short femoral neck projections, the Ward's Triangle box may be misplaced considerably. If this happens, follow the instructions in the Hologic User's Manual to modify the search region.

Trochanteric Line The trochanteric line should intercept the bone edge just below the lateral aspect of the greater trochanter. There is no need to correct minor deviations of up to about three pixels.

9.1.4 Reanalysis of Hip Scans (Required)

It may be necessary to reanalyze hip scans. Always use <Control> <End> to confirm the general ROI of a hip scan for reanalysis of a baseline scan. All regions of interest will be recalculated. Ward's triangle and trochanteric line will be placed independently from the previous analysis. This procedure is absolutely necessary when you reanalyze your scans, for example, after deleting ischium or filling in notches. After accepting the general ROI, proceed in the analysis of the hip scan as you did before.

9.2 AP Spine Measurements

Note the following important points when performing AP spine scans.

9.2.1 Participant Set-Up (Required)

1. No metal or plastic object should remain in the scanning area. Check for jewelry, zippers, buttons, rivets, belts or any other clothing fasteners, as well as hip and back braces.
2. Lower any heavy clothing so that nothing obscures the scanning area.
3. Follow the instructions for participant positioning outlined in the Hologic User's Manual. Verify that the participant's spine is aligned with the **DOTTED** line on the scanner table (slightly to one side of the table center).
4. Use a knee-elevating pad to reduce lordosis. Always use the same pad for all participants.
5. Keep the participant's hands out of the scanning area.
6. The participant should be made as comfortable as possible to reduce the chance of unwanted movements. Use a pillow for the head and elbows if necessary. Ask the participant if she will be able to lie comfortably for the duration of the examination.
7. Instruct the participant that she must not move from the beginning of the AP scan through the end of the scan. If the participant does move, rescan if possible. Flag scans that cannot be repeated.

9.2.2 AP Spine Scan Acquisition (Required)

1. Use the **array spine** mode with the default acquisition parameters:
 - Length: 8.2160 inches
 - Width: 4.2445 inches
 - Spacing: 0.03950 inches
 - Resolution: 0.03735 inches
2. Include five to ten lines of the iliac crest in the AP scan. Terminate the scan if positioning is incorrect; reposition the participant and restart the scan. If necessary, perform a preliminary scan to verify participant position.
3. Observe the scan acquisition on the screen. Use the RESCAN feature (F3 key) as needed, following the instructions in the Hologic User's Manual for repositioning the scan starting point (blue arrow) and realigning the scan center line within the red limits. It is **imperative** that the spine be well centered and that part of the iliac crest be clearly visible.
4. Scan from the middle of L5 (include a portion of the iliac crest for reference) up to the middle of L1, so that you will include all vertebrae from L2 to L4. Scans for some of the older women in our population can be difficult to interpret, so be sure to collect sufficient data for accurate identification of vertebral levels. If you are unsure of the levels, acquire data through T12, which is usually (but not always) identified as the first vertebra with visible ribs.
5. After acquisition and post processing, the system will automatically proceed to the AP ANALYSIS menu.

9.2.3 Baseline AP Spine Scan Analysis (Required)

Analyze the AP scan immediately according to the instructions in Chapter 3 of the Hologic User's Manual, along with the following guidelines.

9.2.3.1 Analysis Procedures

Global Region of Interest (ROI): The global region of interest (large, yellow box surrounding all vertebrae to be analyzed) should be created according to the following guidelines:

1. The ROI should be no narrower than 113 pixels and be tall enough to include the L2-L4 region.
2. The ROI should be aligned symmetrically around the spine.
3. The ROI must be large enough to include at least 5 mm of soft tissue outside the most extreme aspects of both the right and left bone edges of the spine. Special care must be taken with extremely scoliotic individuals to achieve this goal.
4. The above constraints must produce an ROI with all edges at least two steps away from the border of the scan field. This will be important when the baseline scan is used with the COMPARE feature for follow-up scan analysis.
5. Do not angle the top or bottom borders or the intervertebral markers. For participants with scoliosis, the intervertebral space markers should be adjusted so that inclusion of adjacent vertebrae is kept to a minimum. Flag cases of moderate to severe scoliosis.

Labeling of Vertebrae: Label the vertebrae using the iliac crest (and the ribs, if visible) as landmarks. Most individuals have only five lumbar vertebrae, though it is not uncommon to see six in some participants; L5 will be at or below the iliac crest, which is why the iliac crest is used as a landmark.

Exclusion of Vertebrae: According to the protocol, crush fractures are to be excluded from the analysis. Lumbar fractures identified from the spine film should be noted and excluded for each participant. In the absence of a current lumbar spine film, fractured vertebrae can usually be identified for exclusion if there is a reduction in height by more than a few scan lines relative to the vertebra above it or especially below; this is usually accompanied by an increase in density compared to the other vertebral bodies. Confirm that your intervertebral spaces are adjusted properly. If the vertebra seems to be decreased in height with respect to adjacent vertebrae, exclude it from the analysis and flag it for the attention of the WHI BD Center.

Filling and Deleting Bone: After the software has calculated the bone mask (yellow area), fill in remaining obvious gaps or holes in the contours of the vertebral body. This may sometimes require altering the bone edges. Please flag the scans where you altered bone edges for review.

Bone Edges: If there are no obvious gaps or holes, do not alter the bone edges. Sometimes the transverse spinous processes or closely adjacent ribs can alter the appearance of the bone edge. To achieve optimal precision, most of the time it is best to let the computer define the bone edges.

9.3 Whole Body Measurements

9.3.1 Participant Set-Up (Required)

When performing whole body scans, attention has to be paid to the following points:

1. Have the participant remove all clothing, including shoes, and dress them in a hospital gown. Check that no metal or plastic objects remain in the scanning area. This includes hair clips and pins, underwire bras, snaps, zippers and buttons. Have participant remove any jewelry, earrings, bracelets, watches, or rings.
2. Position the participant in the center of the scanning table with her head just below the head of the table. The arms should be separated from the sides of the body with the hands placed palm down within a few centimeters of the table edge.
3. You may loosely tape the ankles together to avoid motion during the scan. Inversion of the feet will bring the femoral neck into better position.
4. Verify that the participant is aligned with the scanner axis (solid line on the table). If during scanning it is apparent that part of the participant's body lies outside the scan field, restart the scan.
5. The participant should be positioned as comfortably as possible; this reduces the chances of unwanted movements. In general, try to avoid using any pillows or blankets. If the participant feels uncomfortable in that position, you may use pillows for the head only after the upper half of the scan is done. You may

then carefully place a pillow under the head of the participant without causing motion artifacts. This procedure should be practiced with the participant before scanning.

6. When using the soft tissue bar, please make sure that it is completely surrounded by air. No body part should be in contact with the soft tissue bar; this will adversely affect the analysis procedures.
7. Instruct the participant not to move until the end of the measurement. If movement occurs, rescan if possible. Flag scans that cannot be repeated.

9.3.2 Whole Body Scan Acquisition (Required)

Use the whole body scan mode (fan beam).

9.3.3 Baseline Whole Body Scan Analysis

High quality data analysis depends critically on the reproducible placement of the regions to be analyzed. For whole body studies, bone mineral content (BMC) of 11 areas is evaluated:

- Head
- Left arm
- Right arm
- Left ribs
- Right ribs
- Thoracic spine
- Lumbar spine
- Pelvis
- Left leg
- Right leg
- Total body

Unlike other analysis programs, the Hologic whole body analysis software requires that the operator align the default regions to the participant's anatomy. The following general rules should be followed:

9.3.3.1 Analysis Procedures

1. Locate the horizontal shoulder line just below participant's chin.
2. The vertical shoulder lines should bisect the shoulder joints and separate the arms from the trunk. Avoid including any body soft tissue in the arm ROI.
3. Align the spine ROI with the curvature of the spine, if possible. Divide the spine at the T12-L1 disc space.
4. The horizontal line above the pelvis should be just above the iliac crest. The angled lines defining the pelvic triangle should bisect the femoral necks.
5. The vertical line between the legs should run between the participant's feet. The lateral leg lines should be moved to include as much of the thigh soft tissue as possible without crossing the hands.

9.4 Flagging Scans for Review

Guidelines identifying which scans warrant flagging are outlined below and described in the area-specific follow-up scanning and analysis sections as well.

9.4.1 General Guidelines for Flagging Scans

- Scan has unusual appearance or is difficult to analyze.
- Any of the following in scan field (either in the bone or soft tissue):
 - Unusual anatomical variations
 - Surgical hardware
 - Participant motion during scan
 - Superimposed buttons, pins, zippers, pacemakers, vitamin pills, etc.
- ROI used on follow-up is different size than used at baseline.
- Bone edges have been altered in any way.
- Follow-up scans cannot be reasonably matched to baseline analysis.

9.4.2 Guidelines for Flagging Hip Scans

- Femoral midline misaligned and cannot be corrected by following the analysis procedures as outlined in *Section 9.1.3. – Baseline Hip Scan Analysis Procedures*.
- Neck box width reduced from default.
- Ward's region persistently located outside of Ward's triangle - difficulties in redefining search region.
- Analysis program fails repeatedly to place regions appropriately - major operator interaction required for analysis.
- Excessive bone loss.

9.4.3 Guidelines for Flagging Spine Scans

- Excessive scoliosis, either indicated by a warning from the Hologic software during AP analysis or in the opinion of the operator.
- Vertebral height and/or density inconsistencies, indicating presence of crush fracture.
- Questionable vertebral levels - difficulties in identifying L2-L4 region.
- Excessive bone loss.

9.4.4 Guidelines for Flagging Whole Body Scans

- Participant motion without rescanning (these scans are extremely susceptible to motion artifacts).
- Significant changes in positioning between baseline and follow-up scan.

9.5 WHI DXA Scan Log Instructions

The *WHI DXA Scan Log Sheet (Figures 2a to 2e)* is used to document information about scans performed since the last data transfer.

DATE	Enter date of scan. One entry per individual is sufficient.
PAT ID	Enter assigned participant ID number. One entry per individual is sufficient.
ACRO	Enter participant acronym. One entry per individual is sufficient. This is the first letter of the first name plus the first three letters of the last name. Example: Mary Smith = MSMI

If a participant changes her last name for any reason, please be sure to retain her original name and acronym in the DXA biography.

SCAN TYPE Place a check mark beside all scans completed.

FLAG Indicate that this scan is flagged for review by the WHI BD Center by checking the box.

FLAGGING

COMMENTS The comment should indicate the specific reason for flagging.

9.6 BMD Data Mailing Procedures

This section contains procedures for sending BMD data and scans to the WHI BD Center.

1. "Batches" of BMD data and scans should be sent to the WHI BD Center at the end of each month according to the schedule provided by the WHI BD Center. Send the batches to:

WHI Bone Density Center/BMD
UCSF Prevention Sciences
74 New Montgomery, Suite 600
San Francisco, CA 94105

Pack the materials carefully. The optical disk should be placed in a plastic bag and then wrapped in plastic bubble wrap to avoid damage.

2. Assign a number to each batch of BMD data, beginning with the first batch of BMD materials sent. Start with batch number 001. The batch number should be the CC identifier followed by this 3-digit number. Thus the batch number should be a 5-digit field: e.g., for CC XX, batch number 1, the number should be XX001.
3. Complete a *WHI BMD Batch Check List (Figure 3)*, indicating the number and which materials are included in the batch, and send it along with the batch materials.
4. The materials in the batch should be bundled separately by type, as listed below, and the bundles securely bound (clips, rubber bands, etc.) and labeled with a "post-it" or piece of paper securely attached to the bundle or written on the diskettes.

Each bundle should be labeled as indicated below (and sent to the WHI BD Center according to the schedule in parentheses).

- "QA database printout." (Printout of plots: every month.)
- "Certification scans." (Printouts: when applicable.)
- "Flagged scans." (Printouts, scan log sheet: every month.)
- "Random sample scans." (Printouts: as requested.)
- "Special request scans." (Printouts: as requested.)
- "Reanalyzed scans." (Printouts: when applicable.)
- "DB archive." (Floppy disks: every month.)
- Traveling optical disk with scans for review (already labeled).

FLAGGED SCAN LABELS: Please write the reason the scan was flagged directly on the printout.

Include a copy of the *WHI DXA Scan Log (Figures 2a to 2e)* for the period covered by the flagged scans.

DB ARCHIVE DISK LABELS: Please include the following on the disk label:

- "DB ARCHIVE"

- Batch #
- CC name
- Date (end date of 1-month period)
- **If there is more than one disk, label each disk as above and then write “1 of 3”, “2 of 3”, etc.**

10. Follow-Up Scanning and Analysis Procedures

The schedule for follow-up scans is described in *Vol. 1 - Study Protocol and Policies Table 1-A1.1 - Frequency of Data Collection*. Follow-Up Scanning & Analysis procedures include comparisons between current and early bone density scans.

Before performing any follow-up scans, load the baseline scan into the hard disk and have a printout of the baseline available. Refer to the baseline printout as you go through the positioning of the participant for the follow-up; this is to ensure consistent scanning of the same area. Careful positioning and visual comparison of the current scan with baseline are essential for producing precise measurements. Consistent projection of the femur is more important than the actual angle of the foot rotation. Use the RESCAN feature as soon as any positioning errors are detected during the current scan.

The same scans that were done at baseline should be repeated at the 1st annual "12-month" visit (Hip, AP Spine and Whole Body). When completing the scan log sheet, please enter the scan ID #s of the scans being used for the COMPARE analysis.

10.1 First Annual Visit

10.1.1 Hip Scan Analysis Procedures (Required)

Load the baseline scan into the hard disk. Display this baseline evaluation using the COMPARE feature along with the current scan to be analyzed. It is important to realize that proper comparison of a follow-up hip scan to its baseline depends upon maintaining the identical size and relative position of the region markers. Vertical or horizontal shifts of these regions by one or more pixels can greatly alter the final values of the analysis.

Global Region of Interest

1. The width and height of the global ROI **must** be the same as that used on the baseline.
2. The dotted lines from the baseline defining the bone region should overlay the follow-up as closely as possible. Occasionally there are small changes in adduction and rotation of the leg which were not eliminated by rescanning. The region surrounding the neck should have the best fit.
3. If the global ROI cannot be moved to the appropriate position because it is too large, the baseline scan will have to be reanalyzed with a properly reduced global ROI. Then the follow-up should be analyzed comparing it to the reanalyzed version of the baseline. Flag cases in which the baseline had to be reanalyzed.
4. Use <Control> <End> to accept the global ROI and bone mask.

Bone Edges: If the bone edges do not fill in properly on the follow-up analysis, first the baseline will have to be reanalyzed with a larger ROI, and then the comparison analysis may proceed.

Femoral Midline: Unevenness (notches) in the upper or lower edge of the femoral neck can throw off the femoral midline so that it does not run down the center of the neck. This will in turn cause the femoral neck box to twist. If the midline looks like it might be off or the box is twisted on either the baseline or follow-up scan, it may be necessary to adjust the bone mask (e.g., filling in neck notches, deleting the ischium) in order to obtain appropriate positioning of the midline. The position of the midline itself should not be altered. If you have made changes to the scan such as filling in bone in order to alter the midline, or if the midline is still off, flag these cases for review by the coordinating center.

Femoral Neck Box: If the current location is optimally matched to the location of the neck box of the baseline analysis, use it unchanged.

1. If the current location is not optimally matched to the location of the neck box on the baseline, adjust the current region to achieve maximum correspondence. The size of the neck box must be the same on both baseline and follow-up.
2. If the current location cannot be satisfactorily adjusted while maintaining the same sized neck box, reanalyze the baseline within the constraints outlined above.
3. It is most important to have the neck box location and size correspond as closely as possible. If you cannot get the neck boxes to match, flag the scan for review by the CCC.

Ward's Triangle: If the Ward's triangle box appears on the follow-up scan in a significantly different position than on the baseline, or if after reanalysis of the baseline its location is different than that of the original baseline placement, flag the scan for review by the CCC.

Trochanteric Lines The trochanteric line should intercept the bone edge at the same point on all scans. Matching is easily done during the COMPARE analysis, especially since you will have the baseline to consult during the COMPARE.

10.1.2 AP Spine Scan Analysis Procedures (Required)

Load the baseline scan into the hard disk. Display this baseline evaluation using the COMPARE feature along with the current scan to be analyzed.

Brightness and Contrast: The WHI population exhibits notable variations in weight, spine condition, and spine anatomy, any of which can result in scans which are difficult to analyze. Adjustments to the brightness and contrast will frequently be necessary to improve the appearance of the image.

Global Region of Interest: Use the same global region of interest as used on the baseline scan. If the yellow global region of interest box cannot be adjusted from the baseline to follow-up scans, it may be necessary to reanalyze the baseline examination. Be certain that the vertebral levels correspond between baseline and follow-up; mismatched levels can give the appearance of shortening or lengthening of the spine on follow-up. Flag any alterations. **Never change the width of the global ROI on the follow-up scan.**

Intervertebral Spaces: It is most important that the intervertebral space markers of the follow-up scan correspond as closely as possible to those of the baseline. The COMPARE feature will generate the baseline vertebral spacing automatically. A slight manual adjustment may be necessary to place the line markers at the same level between the vertebrae. Large discrepancies in spacing may indicate that either the baseline or follow-up scan has had its intervertebral spaces misinterpreted or that a crush fracture has occurred.

Labeling Vertebral Levels: Match corresponding vertebral levels from baseline to follow-up. Look carefully at the darker low density features at the intervertebral spaces and count up from the pelvic girdle to determine levels. If levels were mislabeled on the baseline (e.g., L2 was called L1) and the baseline must be reanalyzed for another reason, correct the level numbers. Otherwise, flag any scans with uncorrected levels for review by the WHI BD Center.

Crushed Vertebrae: If a vertebra appears to have crushed since the baseline scan, both the crushed follow-up vertebra and the normal baseline vertebra must be excluded from these analyses. This will require reanalysis of the baseline scan.

Bone Edges: If there are noticeable gaps or holes that were not present at baseline, fill in the bone edges so that the follow-up scan matches the baseline as closely as possible and flag these scans for review by the WHI BD Center.

10.1.3 Whole Body Scan Analysis Procedures (Required)

For evaluations of follow-up measurements, display the baseline evaluation using the COMPARE feature and compare it to your current image on the screen.

Match the location of the region markers as closely as possible to the baseline measurement. Optimally matched in this context means that the markers should be at the same position between the body regions as on the baseline image.

If adjustment cannot be done satisfactorily, it will be necessary to reanalyze the baseline scan. Again, it is most important that the region markers of all measurements do correspond as closely as possible. If it is necessary to reanalyze the baseline measurement, all subsequent follow-up measurements should also be reanalyzed using COMPARE.

10.1.4 Changes in Bone Mineral Density

CCs must send a Bone Mineral Results letter to all participants after a scan is performed. (See *Appendix B – Protocol for the Bone Mineral Results Letters to Participants.*) The WHI BD Center helps in the interpretation of scans **before** the participant is sent a letter. To determine the annual loss or gain of bone mass, it is necessary to compare the results of the previous and the recent bone scans. The Hologic software provides a very convenient option to calculate the annual bone loss from two or more scans. The AP lumbar spine and the total hip are the regions of interest where DXA measurements can be performed with a very high precision. Therefore, use these regions for the determination of the annual individual rate of change.

10.1.4.1 Determining Rate of Change

Determine the rate of change of all scans directly after the COMPARE analysis of the participant's scans.

1. At the Hologic Main Menu, select <Select>.
2. Highlight the most recent, analyzed hip or spine scan and press the <return> or <enter> key.
3. Choose <Normals> at the Hologic Main Menu screen and see a list of the participant's scans.
4. Use the <+> key to mark the baseline and most recent visit scan and press the <return> or <enter> key.
5. Choose <Rate of Change>.
6. A graph is displayed showing the data points and the normal age range. This graph also shows the annualized percentage change in BMD. On the HIP graph, use the TOTAL under the “% change/yr” column as the value for calculation. On the SPINE graph, use the value under “% change/yr.” Multiply this figure by the number of years since the baseline visit (3, 6, or 9).

10.1.4.2 Excessive Bone Loss

An excessive bone loss at the first annual visit is defined as:

- Decrease of 10% or more of the AP spine bone mass, or
- Decrease of 10% or more of the TOTAL hip bone mass

An excessive bone loss at the third or sixth annual visit is defined as:

- Greater than a 10% loss from baseline to AV3.
- Greater than a 12% loss from baseline to AV6.

What to do if the bone loss exceeds the allowable limits:

1. If the RATE-OF-CHANGE indicated in the list below the graph exceeds the allowable limits, inform your Supervisor. The analysis of the follow-up scan should be repeated by the head QDR operator.
2. If, after reanalysis, the bone loss remains greater than allowed, rescan the participant with repositioning, and analyze the repeat scan using the Compare with the baseline scan.
2. Recompute the annual RATE-OF-CHANGE as described above, marking with the <+> key the baseline and both first annual scans.

The RATE-OF-CHANGE value will then be the average for the two scans.

4. If, after repeating the scan and recomputing the RATE-OF-CHANGE, the average BMD loss still exceeds the allowable limits, complete the *WHI Bone Loss Scan Review* sheet (*Figure 6*) and send the specified scans and printouts to the WHI BD Center. These scans should be separated from other flagged scans and marked "EXCESSIVE BONE LOSS." Note that participants should not be told about excessive bone loss until **after** confirmation is received from the WHI BD Center.
5. Even if the value drops below the threshold after rescanning, baseline and follow-up scans should be flagged and sent to the WHI BD Center for review. Please complete the *WHI Bone Loss Scan Review* sheet (*Figure 6*) and send the specified scans and printouts to the WHI BD Center. These scans should be separated from other flagged scans and marked "SUSPECTED EXCESSIVE BONE LOSS".
6. The WHI BD Center will review these scans and confirm the excessive bone loss findings. If such confirmation is received, mark the "excessive bone loss" box on the BMD Results letter. If bone loss is not confirmed, mark the "no excessive bone loss" box on the letter (see WHI BMD Results letter in *Appendix B*).

10.1.4.3 Osteoporotic Value

WHO (World Health Organization) developed guidelines to interpret the result of bone mineral density scans. These guidelines suggest osteoporotic values are more than 2.5 standard deviations (SD) below young adult values at either the hip or the spine. For WHI, osteoporotic values are based on the National Osteoporosis Foundation's (NOF) guidelines, which incorporate WHO's guidelines. NOF guidelines are based on bone densitometer scans of the hip, using the femoral neck measurements. This measurement is retrieved via the Hologic software (see *Appendix B – Protocol for the Bone Mineral Results Letter to Participants*).

10.2 Third, Sixth, and Ninth Annual Visit

The same scans that were done at baseline should be repeated at the 3rd, 6th and 9th annual visit (Hip, AP Spine, and Whole Body). Use the COMPARE analysis function with the baseline scan. When completing the *WHI DXA Log - Third Annual Visit Sheet (Figure 2c)*, *WHI DXA Log – Sixth Annual Visit Sheet (Figure 2d)*, and *WHI DXA Log – Ninth Annual Visit Sheet (Figure 2e)*, enter the scan ID #s of both the current and baseline scans.

10.2.1 Archiving of Follow-Up Scans

Please archive both the baseline scan (that was used for the COMPARE analysis) and the 3rd, 6th, and 9th annual visit scan on your optical disk after you have finished your scan analysis. This is the only way to identify the baseline scan and corresponding BMD data that you used for the COMPARE procedure.

10.2.2 Determination of Changes in Bone Mineral Density at the Third, Sixth, and Ninth Annual Visit

CCs must identify and appropriately counsel participants who lose a significant amount of bone mass during the study. To determine the annual loss or gain of bone mass, it is necessary to compare the results of the previous and the recent bone scans. The Hologic software provides a very convenient option to calculate the annual bone loss from two or more scans. The AP lumbar spine and the total hip are the regions of interest where DXA measurements can be performed with a very high precision. Therefore, WHI uses these regions for the determination of the annual individual rate of change.

Determine the rate of change of the spine and hip directly after the COMPARE analysis of the participant's scans. Examine the following two RATE-OF-CHANGE plots per each anatomical site (total of 4) to determine excessive bone loss (EBL): current to baseline and current to 1st annual (12-month). Note that OS participants will not have a 1st annual visit (AV1) scan.

1. Select the participant's current visit scan (lumbar spine or femur) using the SELECT menu.
2. After you have selected the scan, go to the NORMALS menu (use arrow keys or type <N> or <F7>). The program will then show you a list of participant scans available for your analysis.
3. Use the <+> key to mark the baseline and the current visit, or the 1st annual (AV1) and current visit scans, that you will use to calculate the RATE-OF-CHANGE.
4. After you have chosen the scans, press the <Enter> key. The screen now shows a new menu.
5. Using the arrow keys, select the menu option RATE-OF-CHANGE and then press <Enter>. A graph is now shown using the data points selected and the normal age range. Please notice that the RATE-OF-CHANGE plot will show an annualized percentage change in BMD. For the current visit to baseline percentage, multiply the value by the visit # to get the percent change since baseline. For the current visit to 1st annual visit (AV1) percentage, multiply the value by visit # -1 to get the percent change since the 1st annual visit (AV1). On the hip RATE-OF-CHANGE graph, use the TOTAL under the '% change/yr.' column as your value for calculations. On the spine RATE-OF-CHANGE graph, use the **value** under '% change/yr.'. Use these calculations at the current visit to determine if the participant has had excessive bone loss since the baseline or the 1st annual visits (AV1).

10.2.3 What to Do If the Bone Loss Exceeds the Allowable Limits

An excessive bone loss at the hip and/or spine at the 3rd, 6th, and 9th annual visit is defined as:

- Decrease of 10% or more between the 1st annual and 3rd annual visits (annual loss of 5% or more)
 - Decrease of 12% or more between baseline and the 3rd, 6th, and 9th annual visits (annual loss of 4% or more)
1. If the percent rate of change on the graph exceeds the allowable limits at any one time frame, please inform your Supervisor and have the head QDR operator repeat the analysis of the follow-up scan.
 2. If, after re-analysis, the bone loss remains greater than allowed, re-scan the participant with repositioning, and analyze the repeat scan using the COMPARE with the baseline scan.
 3. Recompute the annual RATE-OF-CHANGE as described above, marking with the <+> key both current visits and whichever scan produced the EBL, baseline, or 1st annual. Then average the rate of change value for the two current visit scans.

4. If, after repeating the scan and re-computing the rate-of-change, the average BMD loss still exceeds the allowable limits, please complete the *WHI Bone Loss Scan Review* form (*Figure 6*) and send the specified scans and printouts to the WHI BD Center. Separate these scans from other flagged scans and mark them "EXCESSIVE BONE LOSS".
5. Even if the value drops below the threshold after re-scanning, flag and send the baseline and follow-up scans to the WHI BD Center for review. Please complete the *WHI Bone Loss Scan Review* form (*Figure 6*) and send the specified scans and printouts to the WHI BD Center. Separate these scans from other flagged scans and mark them "SUSPECTED EXCESSIVE BONE LOSS".
6. The WHI BD Center will review these scans and confirm the excessive bone loss findings. After the WHI BD Center reviews the scans, the CC can send the participant a results letter with the appropriate box marked either "no excessive bone loss" or "excessive bone loss."

Figure 1
WHI Hologic Repair Log Sheet

CC name and site #: Date:

1. Describe problem (incl. dates): _____

2. Did problem affect scans or BMD data?
 Yes No
If yes, describe: _____

Over what time period were the scans affected? _____

3. Did problem cause down time of scanner? If yes, for how long? _____

4. Describe the action taken by you (including repair by Hologic)? _____

5. Was the problem resolved?
 Yes No
If not, please specify: _____

6. Was a recalibration of the device necessary?
 Yes No

7. Were phantom scans performed after the repair or the recalibration?
 Yes No
If yes, did you notice a change in the phantom BMD values?
 Yes No

Please fill in the form thoroughly. Send one copy to Michael Jergas at the WHI BD Center. Keep one copy with your scanner in your own repair log.

**Figure 2a
WHI DXA Scan Log**

Clinic: _____

Date	Pat ID	ACRO	Scan Type	Flag	Flagging Comments
			Hip		
			AP Spine		
			Whole body		
			Hip		
			AP Spine		
			Whole body		
			Hip		
			AP Spine		
			Whole body		
			Hip		
			AP Spine		
			Whole body		
			Hip		
			AP Spine		
			Whole body		
			Hip		
			AP Spine		
			Whole body		
			Hip		
			AP Spine		
			Whole body		
			Hip		
			AP Spine		
			Whole body		
			Hip		
			AP Spine		
			Whole body		
			Hip		
			AP Spine		
			Whole body		
			Hip		
			AP Spine		
			Whole body		

Figure 2b

Clinic: _____

WHI DXA Log- First Annual (“12 Month”) Visit

Date	Pat ID	ACRO	Scan Type	Scan #	Flag	Flagging Comments
			Hip (12 month)			
			Hip (baseline)			
			AP Spine (12 month)			
			AP Spine (baseline)			
			Whole body (12 month)			
			Whole body (baseline)			
			Hip (12 month)			
			Hip (baseline)			
			AP Spine (12 month)			
			AP Spine (baseline)			
			Whole body (12 month)			
			Whole body (baseline)			
			Hip (12 month)			
			Hip (baseline)			
			AP Spine (12 month)			
			AP Spine (baseline)			
			Whole body (12 month)			
			Whole body (baseline)			
			Hip (12 month)			
			Hip (baseline)			
			AP Spine (12 month)			
			AP Spine (baseline)			
			Whole body (12 month)			
			Whole body (baseline)			
			Hip (12 month)			
			Hip (baseline)			
			AP Spine (12 month)			
			AP Spine (baseline)			
			Whole body (12 month)			
			Whole body (baseline)			
			Hip (12 month)			
			Hip (baseline)			
			AP Spine (12 month)			
			AP Spine (baseline)			
			Whole body (12 month)			
			Whole body (baseline)			

Figure 2c
WHI DXA Log - Third Annual Visit

Clinic: _____

Date	Pat ID	ACRO	Scan Type	Scan #	Flag	Flagging Comments
			Hip (3rd Annual)			
			Hip (baseline)			
			AP Spine (3rd Annual)			
			AP Spine (baseline)			
			Whole Body (3rd Annual)			
			Whole body (baseline)			
			Hip (3rd Annual)			
			Hip (baseline)			
			AP Spine (3rd Annual)			
			AP Spine (baseline)			
			Whole Body (3rd Annual)			
			Whole body (baseline)			
			Hip (3rd Annual)			
			Hip (baseline)			
			AP Spine (3rd Annual)			
			AP Spine (baseline)			
			Whole Body (3rd Annual)			
			Whole body (baseline)			

Figure 2d
WHI DXA Log – Sixth Annual Visit

Clinic: _____

Date	Pat ID	ACRO	Scan Type	Scan #	Flag	Flagging Comments
			Hip (6th Annual)			
			Hip (baseline)			
			AP Spine (6th Annual)			
			AP Spine (baseline)			
			Whole Body (6th Annual)			
			Whole body (baseline)			
			Hip (6th Annual)			
			Hip (baseline)			
			AP Spine (6th Annual)			
			AP Spine (baseline)			
			Whole Body (6th Annual)			
			Whole body (baseline)			
			Hip (6th Annual)			
			Hip (baseline)			
			AP Spine (6th Annual)			
			AP Spine (baseline)			
			Whole Body (6th Annual)			
			Whole body (baseline)			

Figure 2e
WHI DXA Log – Ninth Annual Visit

Clinic: _____

Date	Pat ID	ACRO	Scan Type	Scan #	Flag	Flagging Comments
			Hip (9th Annual)			
			Hip (baseline)			
			AP Spine (9th Annual)			
			AP Spine (baseline)			
			Whole Body (9th Annual)			
			Whole body (baseline)			
			Hip (9th Annual)			
			Hip (baseline)			
			AP Spine (9th Annual)			
			AP Spine (baseline)			
			Whole Body (9th Annual)			
			Whole body (baseline)			
			Hip (9th Annual)			
			Hip (baseline)			
			AP Spine (9th Annual)			
			AP Spine (baseline)			
			Whole Body (9th Annual)			
			Whole body (baseline)			

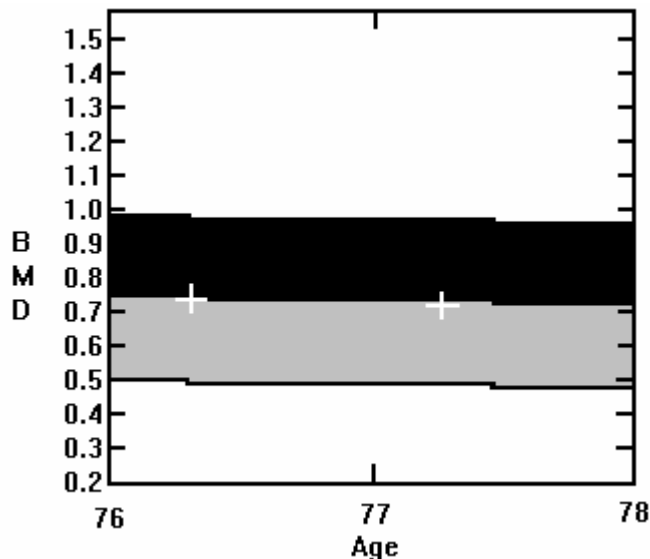
Figure 3
BMD Batch Check List

(See I:\MOPVOL6\1.PM4)

Figure 4
Example of Rate of Change Plot for the Hip

KAISER: CHR/FIT STUDY/PORTLAND

A Right Hip
Reference Database



P11299417 Tue Nov 29 17:28 1994
 Name:
 Comment:
 I.D.: Sex: F
 S.S.#: Ethnic: W
 ZIP Code: Height: 5' 3"
 Scan Code: Weight: 107
 BirthDate: 08/19/17 Age: 77
 Physician:

Date	Age	BMD Neck	BMD Troch	BMD Inter	BMD TOTAL	BMD Ward
12/13/93	76.3	0.512	0.604	0.833	0.722	0.411
11/29/94	77.3	0.544	0.555	0.731	0.655	0.373

Region	Rate of Change/yr.	± SD**	% Change/yr.	± SD
Neck	+0.0333	0.0153	+6.51	2.99
Troch	-0.0512	0.0093	-8.48	1.54
Inter	-0.1068	0.0132	-12.82	1.59
TOTAL	-0.0693	0.0142	-9.59	1.96
Ward's	-0.0400	0.0237	-9.72	5.76

**1.96 x SD = 95% Confidence Interval

◆ Age and sex matched

T = peak bone mass

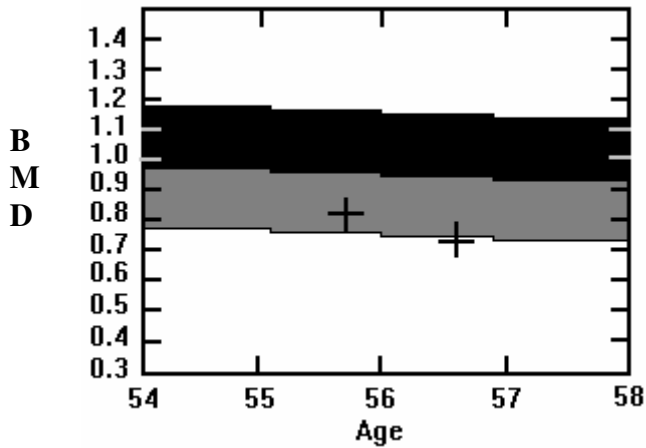
Z = age matched

TK 10/25/91

Figure 5
Example of Rate of Change Plot for the AP Spine

FIT CLINIC - U/M MIAMI, FL

**A Lumbar Spine
 Reference Database**



G1028930E Thu Oct 28 16:07 1993
 Name:
 Comment:
 I.D.: Sex: F
 S.S.#: Ethnic: W
 ZIP Code: Height:
 Scan Code: Weight
 :
 BirthDate: 02/06/37 Age: 56
 Physician:

Date of Scan	Age	BMD (L2-L4)
10/29/92	55.7	0.801
10/28/93	56.7	0.701

L2-L4

Rate of Change/yr.	± SD**	% Change/yr.	± SD
-0.1005	0.0114	-12.55	1.43

**1.96 x SD = 95% Confidence Interval

◆ Age and sex matched

T = peak bone mass

Z = age matched TK 10/25/91

Figure 6
WHI Bone Loss Scan Review

Be sure to follow all procedures for participants with suspected bone loss detailed in *Vol. 6, Section 10.1.4 - Changes in Bone Mineral Density*.

Clinical Center: _____

WHI Participant ID: _____

BMD operators: _____

Scan date(s): _____

Site of excessive bone loss Spine Femur

Your Comments: _____

Excessive Bone loss checklist

Please make sure that this form is accompanied by all the items listed below!

- printouts of the baseline and follow-up scans of the hip and spine. Be sure to include printouts of all follow-up scans done at the site of suspected excessive bone loss (follow- up scan, reanalyzed scan, repeat scan)
- printouts of the compare report you created for the spine and the hip (gives annualized % bone loss)
- copies of baseline and follow-up scans of the hip and the spine on floppy disk

(continued next page)

Figure 6 (continued)
WHI Bone Loss Scan Review

To be filled out by the WHI BD Center:

- Yes, we can confirm an excessive bone loss. The scans are technically correct and the analyses are performed appropriately. Please send the participant a results letter with the “excessive bone loss” box checked.
- Yes, we can confirm an excessive bone loss. However, the scans were not analyzed properly. Please reanalyze the scan(s) following our instructions and send the participant a results letter with the “excessive bone loss” box checked.
- The scans provided indicate an excessive bone loss. However, a second scan of the site was not performed in this participant. An excessive bone loss can only be confirmed after you have obtained a second scan of the region where a bone loss is suspected. Please schedule the participant for a repeat measurement.
- After scan review we cannot confirm an excessive bone loss.

Comments: _____

DXA Quality Assurance

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