SECTION 12

MAMMOGRAPHY

INTRODUCTION

All Clinical Trial (CT) women are required to have baseline and regularly scheduled mammograms performed by a standard low dose radiation technique. It is recommended, but not required, that these occur at an American College of Radiology (ACR) or FDA-accredited facility and read by a qualified radiologist. Those women in the Hormone Replacement Therapy component (HRT) will have yearly follow-up mammograms. Women participating in the Dietary Modification Intervention (DM) will have follow-up mammograms in years 2, 4, 6, 8 and at close-out. Clinical Centers (CCs) have the choice to make special arrangements with one mammography facility to do all participants' mammograms or to have women continue to get mammograms through their usual source of care.

Breast ultrasounds will not be acceptable substitutes for either baseline or follow-up mammograms.

Mammograms will be classified in the ACR classification system as negative, benign, probably benign, suspicious, or highly suggestive of malignancy on *Form 85 - Mammogram.*

12.1 Timing of Mammogram

Many women interested in participating in the CT will never have had a mammogram or will have had mammograms only infrequently. These participants are likely to require a new baseline mammogram and can then be started on a schedule of annual (HRT) or every two year (DM) mammograms. These studies should precede randomization and annual visits by a period long enough for results to be available at these visits.

Some participants will have been on a regular schedule of annual or every two year mammograms before their initial screening for WHI. To allow participants to keep to their usual schedule and avoid excess radiation exposure at baseline, the protocol allows a mammogram within 12 months before Screening Visit Two (SV2) to be used as the baseline mammogram. Anniversary dates for follow-up mammograms for HRT women should, if possible, coincide with their annual visit.

If an HRT participant has been getting mammograms less frequently than every year, she must start getting annual mammograms for HRT, and they should be done no more than 6 months before the annual visit.

12.2 Scheduling Mammograms

12.2.1 Baseline Mammogram (Required)

If a woman has not had a mammogram within the 12 months before SV2, she will need to have one before Screening Visit Three (SV3). At the end of Screening Visit 1 (SV1) or SV2, schedule a mammogram appointment for her. If a woman completed a washout (which must be completed before SV1), her baseline mammogram must be no more than 12 months before that SV2. Thus, the mammogram can be done before the HRT washout begins, as long as it is not more than 12 months before the SV2.

- If you are arranging mammograms through your CC, schedule the appointment at a time convenient for the participant. It is recommended that you give her a Mammogram Appointment Card with directions to the facility, the date and time of the appointment, and any instructions your mammographer requires. (For example, some mammographers ask that women not use deodorant, talc, or other powders on the morning of their appointment. Some mammographers will supply these instructional materials for you to send or give to participants.) Let the participant know how long the mammogram is likely to take.
- Each CC can establish its own system of tracking mammogram appointments and results. This system will be referred to in this section of the manual as a Mammogram Logbook. (CCs may establish their own automated version of a logbook.)
- It is recommended that you record the date of a scheduled mammogram in your Mammogram Logbook. When a participant arranges her own mammogram appointment, ask her to call the CC when she knows the date of the mammogram. When she does call in with the date, record it in the Mammogram Logbook.

12.2.2 Follow-Up Mammograms (Required)

12.2.2.1 Annual Visit Mammograms

At least two months before an HRT participant's scheduled annual visit, begin arrangements for her to have a mammogram scheduled. Dietary Modification participants' every two year mammograms can be done at anytime during the two year interval (although WHILMA will report it as due before the appropriate biannual visit). Target anniversary dates for mammograms are based on the date of the participant's randomization. This also applies to those women who needed to complete an HRT washout. Each CC can access the *Mammogram Reminder Report* through WHILMA that will list the participants needing a mammogram. Each CC can decide on how soon before the appointment time this report should be produced. The recommended lead time is at least two months.

- Call the participant and inform her that her annual visit will be coming up and that she needs a mammogram before that time. Obtain information on where to request the mammogram report or schedule a mammogram appointment for a time that is convenient for the participant. Instruct her as per *Section 12.2.1 - Baseline Mammogram (Required)* above.
- It is recommended that you record the date of the mammogram in the Mammogram Logbook (or computer, if automated).

12.2.2.2 Annual Visit Mammograms Following a Mammogram Requiring Follow-Up in Less Than a Year

Many women, who require a 6-month follow-up mammogram after baseline, have a normal follow-up mammogram (e.g., mammogram report recommends follow-up in 12 or more months). The need for a follow-up mammogram in 6 months does not change the target date for the follow-up mammogram. For these participants, their mammogram anniversary date will remain their target annual visit date (yearly from date of randomization for HRT; dietary modification participants can maintain a flexible 2-year schedule).

12.3 Requesting and Receiving Mammogram Results

A normal mammogram report (or a normal follow-up to an abnormal mammogram) is required before you can randomize a woman into the CT or continue her study pills in the HRT. It is important to follow-up on mammogram results in an organized and timely manner, so that you do not delay randomization and can regularly address safety issues. Recommendations for timely follow-up on mammograms include:

- Provide participants with a stamped, self-addressed envelope with which the mammographer can mail results back to the CC.
- One week after the date of the participant's scheduled mammogram, check to see if a report has been received.
- If no report has been received, call the participant's mammographer and ask to have a copy of the report mailed or faxed to the CC. If you do not receive the report within one week, call the mammographer again.
- When the report arrives at the CC, log it into the Mammogram Logbook.

Complete *Form 85 - Mammogram* for each regularly scheduled mammogram report you receive. If this is a follow-up mammogram for a previous breast exam or mammographic abnormality, complete a new *Form 85 - Mammogram*. If you receive a report addendum which incorporates the review of previous films and changes the results of the original report, edit the already completed *Form 85* as needed and attach the updated mammogram report.

12.3.1 Receiving Mammograms at Unscheduled Times

If you receive a mammogram report that is not required by WHI in a particular time frame, do not fill out a *Form 85 - Mammogram* or enter it into the database. Only reports for mammograms done at the required time intervals (annually for HRT participants, follow-up studies as indicated for abnormalities found in HRT participants, and every 2 years for DM participants) should be recorded on a *Form 85* and entered into WHILMA. If, however, an unsolicited mammogram shows an abnormality and the woman is in HRT or OS (this does not apply to DM), monitor the findings closely and report them as an outcome of cancer (as appropriate) only after receipt of a final pathology report (see *Volume 8 - Outcomes*).

12.3.1.1 Lay Mammogram Reports

Data on *Form 85 – Mammogram* should be based on an actual radiology report. In October 1999, the Steering Committee approved limited use of written “lay” mammogram reports because mammographers are now required to send these more-standardized lay reports to all women. A participant may come to clinic visits with a “lay” mammogram report as proof of her mammogram. These lay reports are acceptable if they include all of the following:

- Date
- Participant’s name
- Institutional letterhead
- Normal or benign findings
- Recommended mammogram follow-up is 12 months or more

If you are completing *Form 85 – Mammogram* from data on a lay report, be careful to complete only those data items that the report describes. Attach the lay mammogram report to *Form 85*.

.

12.4

12.5 Actions Based on Baseline Mammogram Reports (Required)

After reviewing the mammogram report, decide if you need to take any action based on the findings. *Table 12.1 - Eligibility Based on Mammogram Results* offers recommendations for determining whether or not a woman's mammogram report makes her eligible or requires further follow-up before randomization. Clinical Centers may adopt more conservative guidelines if they wish, and, as always, clinical judgment should be used in the final decision.

12.5.1 Negative or Benign Mammogram Findings

Any descriptive findings on mammogram that do not require repeat within 12 months or referral for evaluation will be considered normal and thus eligible. Results of "mammary dysplasia," "adenosis," "fibrocystic breast tissue or disease," "coarse calcifications," or "fat-containing lymph" should be considered normal. Reports of fluid-filled cysts that are greater than or equal to 5 mm in size (and are demonstrated on ultrasound to be smooth-surfaced) or walled simple cysts can be considered normal. If there is any question regarding the nature of the cyst, even after ultrasound, a fine needle aspiration (FNA) should be performed by the woman's private physician.

Negative or benign reports may also recommend a follow-up or repeat mammogram in less than one year to assess stability. This will not exclude the woman from entering the CT or continuing with enrollment pills. However, you will need to review a report of her repeat mammogram and complete a new *Form 85 - Mammogram*, if appropriate.

12.5.2 Probable Benign Findings

A woman whose mammogram report shows a probable benign finding such as calcification with benign features, stability unknown, circumscribed mass, or cyst less than 5 mm or with irregular walls, will be considered eligible. Clinical Centers are cautioned that within this group up to 10% of these findings may represent a malignancy and should be reviewed. The CP or CC gynecologist may elect to follow participants with these results more closely and refer the participant to their private physician for further evaluation after randomization. Examples of assessing which cases may benefit from further evaluation include:

- A report of calcifications with benign features, stability unknown. In this case you have the choice of determining stability through:
  - comparing with old films or repeat the films in 6 months,
  - making a definitive diagnosis through tissue analysis, or
  - using clinical discretion to determine that the participant is indeed clear to participate in DM or HRT.
- A report of circumscribed masses. For these masses, you can:
  - refer the participant back to her primary MD to determine definitive diagnosis through tissue analysis,
  - determine stability over time by comparing with old films or by repeating the study in 6 months, or
  - use clinical judgment to determine if there would be a safety issue for this woman to participate in WHI.

If ultrasound or tissue sampling is done to confirm a benign status, document findings and procedures in the participants file. The woman may then continue in the screening process.

Table 12.1
Eligibility Based on Mammogram Results

Mammogram Results	Initial Eligibility Determination	Description	Ultrasound Requirement	Final Eligibility Determination (Enter on *Form 85 - Mammogram*, question 9 or 12, as appropriate)
1. Negative	Eligible	---	---	Eligible
2. Benign findings	Eligible	- Coarse calcification or fibroadenoma	- None	Eligible
		- Fat-containing lymph	- None	Eligible
		- Fluid-filled cysts (≥5 mm)	- Smooth-surfaced cyst walls	Dependent upon ultrasound results. May consider FNA.
3. Probably benign	Eligible	- Calcification with benign features, stability unknown	- None	Tissue diagnosis to determine benign status. (FNA may be used.) *OR* repeat mammogram in 6 months for stability.
		- Circumscribed masses	- CC discretion	Tissue diagnosis to determine benign status. FNA may be used.
		- Any cysts < 5 mm or irregular borders	- Smooth-surfaced cyst walls	Tissue diagnosis to determine benign status. FNA may be used. OR Clinical judgment by PI/MD
4. Suspicious	Temporarily ineligible		- CC discretion	Tissue diagnosis to determine benign status.
5. Highly suggestive of malignancy	Temporarily ineligible		- CC discretion	Tissue diagnosis to determine benign status.

FNA = Fine Needle Aspiration

Note: These are guidelines for results #1-3. For suspicious or high probability of malignancy results, tissue diagnosis is needed to determine eligibility.

12.5.3 Suspicious or Highly Suggestive of Malignancy Findings

A woman whose mammogram report shows suspicious or highly suggestive of malignancy results should not be randomized to the CT and should be immediately referred to her primary physician for follow-up. When the CC receives a mammogram report requiring referral, the Clinical Practitioner (CP) should notify the participant of the results and advise her to contact her primary physician. In addition, a copy of the report should be mailed or faxed to either the participant or her primary physician. It is recommended that CCs follow-up with these participants within one month to ensure that they have seen their physician.

If tissue sampling made by either FNA or open biopsy determines that there is no possible malignancy, it is recommended that the CP discuss the evidence with the PI or physician designee for concurrence. If the PI and CP agree that the abnormality is benign, complete the follow-up section of *Form 85 - Mammogram* and the woman may continue in the screening process.

12.5.4 Mammograms Requiring Short-Term Follow-Up

If a mammogram report requires a repeat film in 6 months or less, the eligibility window for baseline screening tasks may be extended for potential HRT participants only from 6 to 9 months. Since there is no safety issue for potential DM participants, those participants in whom there is a request for a short-term follow-up but are not suspicious or have a high probability of malignancy are considered eligible.

If an "Immediate/ASAP" repeat mammogram is requested on the report, the participant will be considered ineligible until cleared either by another mammogram or definitive diagnostic test (needle aspirate, ultrasound, or tissue biopsy).

For women requiring follow-up during the HRT enrollment period, dispense a second bottle of pills if needed, or stop the enrollment pills and initiate a second enrollment period when the abnormality is cleared (see *Section 15.4.1.3 - Repeat HRT Enrollment Period* for details).

12.6 Actions Based on Mammogram Reports for Randomized Women

Women randomized in the CT are required to have either yearly mammogram follow-up (HRT) or follow-up in years 2, 4, 6, 8 and at close-out (DM). Required documentation based on the reports are similar to those for baseline mammograms with the following exceptions.

12.6.1 Negative or Benign Findings

Participants who receive these findings on their follow-up reports should be informed that their mammogram was within the normal range and requires no action. They may continue with their CT activities without interruption.

12.6.2 Probable Benign Findings

HRT participants with probable benign findings should be considered on an individual basis. Most participants should be able to continue with their study pills while undergoing evaluation of the findings. However, this decision is left to each CC CP and PI or physician designee's discretion, and the option of stopping study pills during this time is available. If the study pills are temporarily discontinued, complete a *Form 54 - Change of Medication* at the time of stopping and resumption.

Call the participant to discuss the findings. If it is clinically indicated, refer her to her primary physician for evaluation. Complete *Form 85 - Mammogram* to record the probable benign findings and if a referral has been made. If follow-up studies have been performed, complete the follow-up section on *Form 85 - Mammogram.*

12.6.3 Suspicious or Highly Suggestive of Malignancy Findings

HRT participants with suspicious or highly suggestive of malignancy findings should be considered on an individual basis by each CC CP, in consultation with the consulting gynecologist and PI or physician designee, with regard to the option of stopping HRT study pills. Complete a *Form 54 - Change of* if study pills are stopped or resumed.

Call the participant to discuss the findings. Refer her to her primary physician for evaluation. Complete *Form 85 - Mammogram* to record the suspicious or highly suggestive of malignancy findings and document that a referral has been made. Call the participant within a month to confirm that she has made contact with her primary physician. If appropriate documentation is obtained confirming benign status, complete the follow-up section on *Form 85 - Mammogram.*

If a participant refuses any diagnostic follow-up tests and/or exams for an abnormal breast finding, stop her study pills. Study pills may be resumed if the participant does have the required test or exam and abnormal findings are not cancerous. Complete *Form 54 – Change of Medications* when you make such study pill changes.

If investigation of a mammogram abnormality leads to the diagnosis of carcinoma in-situ or cancer, initiate the following steps:

- Contact the participant and refer her to her primary physician for evaluation.
- Advise HRT participant to permanently discontinue HRT study pills immediately and return the bottles at the next possible visit or provide her with a stamped self-addressed mailing envelope.
- Complete *Form 85 - Mammogram* to indicate initial report findings and follow-up findings.
- Initiate outcomes investigations for both HRT and DM participants. (See *Volume 8 – Outcomes.*)
- Complete *Form 7 - Participant Status* to indicate the reason for change of status in the intervention.

Section 12
Mammography

Table of Contents

Contents		Page
INTRODUCTION		**12-1**
12.1	**Timing of Mammogram**	**12-2**
12.2	**Scheduling Mammograms**	**12-3**
12.2.1	Baseline Mammogram	12-3
12.2.2	Follow-Up Mammograms	12-3
	Annual Visit Mammograms	12-3
	Annual Visit Mammograms Following a Mammogram Requiring Follow-Up in Less Than a Year	12-3
12.3	**Requesting and Receiving Mammogram Results**	**12-4**
12.3.1	Receiving Mammograms at Unscheduled Times	12-4
	Lay Mammogram Reports	12-4
12.4	**Actions Based on Baseline Mammogram Reports**	**12-5**
12.4.1	Negative or Benign Mammogram Findings	12-6
12.4.2	Probable Benign Findings	12-6
12.4.3	Suspicious or Highly Suggestive of Malignancy Findings	12-8
12.4.4	Mammograms Requiring Short-Term Follow-Up	12-8
12.5	**Actions Based on Mammogram Reports for Randomized Women**	**12-9**
12.5.1	Negative or Benign Findings	12-9
12.5.2	Probable Benign Findings	12-9
12.5.3	Suspicious or Highly Suggestive of Malignancy Findings	12-9

Tables

12.1	Eligibility Based on Mammogram Results	12-7