

MESA Exam 6 - ****CONFIDENTIAL****

A Longitudinal Epigenetic Study of Atherosclerosis
Carotid Ultrasound Scanning Manual (v1.1, 01/04/2017)

Ultrasound Reading Center: University of Wisconsin
Atherosclerosis Imaging Research Program (UW AIRP)

Director: James H. Stein, MD
Phone: 608-265-4188
Page operator: 608-262-2122
E-mail: jhs@medicine.wisc.edu

Manager: Claudia E. Korcarz, DVM RDCS
Phone: 608-265-9947
Cell phone: 608-712-6497
Fax: 608-263-1534
E-mail: ck4@medicine.wisc.edu

Assistant Manager: Kristin Hansen, RDCS, RVT
Phone: 608-265-9947
Fax: 608-263-1534
E-mail: khansen@medicine.wisc.edu

Carol Mitchell PhD, RDMS, RDCS, RVT
Phone: 608-262-0680
E-mail: ccm@medicine.wisc.edu

Version Number: 1.1

January 02, 2017

TABLE OF CONTENTS

	PAGE
TABLE OF CONTENTS	1
LIST OF ABBREVIATIONS.....	2
1 MESA EXAM 6 CAROTID ULTRASOUND - PROTOCOL OVERVIEW	3
1.1 Access to Exam 5 Plaque Location Information	3
1.2 Participant Positioning	4
1.3 Electrocardiogram (ECG) Hook-up	4
1.4 Blood Pressure Assessment.....	5
1.5 IMAGING PROTOCOL	5
1.5.1 Transducer Frequency and Preset Settings	5
1.5.2 Entering Participant Information into the Ultrasound System	6
1.5.3 Optimal Gain Value (OGV) determination.....	7
1.5.4 Annotations	7
1.5.5 Imaging Sequence	7
2 PROTOCOL SUMMARY – QUICK REFERENCE	15
3 ALERT VALUES.....	16
4 FORMS AND IMAGE MANAGEMENT	17
4.1 Carotid ultrasound log sheets	17
4.2 MESA Exam 6 Carotid Ultrasound Data Collection Form	17
4.3 Image Transmission to UW AIRP.....	18
4.4 Image Overview Reports form the UW AIRP	18
5 SONOGRAPHER CERTIFICATION AND MAINTAINANCE OF COMPETENCY	19
6 ULTRASOUND PHANTOM SCANS.....	20
SUPPLEMENTAL MATERIALS	21

LIST OF ABBREVIATIONS

CCA	Common Carotid Artery
ECA	External Carotid Artery
ECG	Electrocardiogram
FW	Far Wall
ICA	Internal Carotid Artery
Idno	Participant ID Number
LT	Left
MOP	Manual of Procedures
NW	Near Wall
OGV	Optimal Gain Value
PVCs	Premature Ventricular Contractions
QA	Quality Assurance
QC	Quality Control
RT	Right
TGC	Time Gain Compensation pods

1 MESA EXAM 6 CAROTID ULTRASOUND - PROTOCOL OVERVIEW

The focus of the MESA Exam 6 carotid ultrasound imaging protocol is on plaque imaging to permit offline analysis of plaque presence, quantity, size, and other characteristics related to plaque vulnerability. Therefore, it is important to locate all plaques that were noted at MESA Exam 5 and to identify any new or additional plaques. The MESA Exam 6 carotid ultrasound protocol includes a screening survey to identify all plaques. The initial survey is followed by a dedicated plaque imaging acquisition for offline gray scale analyses.

Additionally, distal common carotid artery (CCA) B-mode loops will be recorded for future analyses.

The scanning protocol is bilateral, beginning on the right side and is repeated on the left side.

Examination Order

The examination should begin on the right side of the neck and proceed in the following order:

1. Annotate the text "RT" on the screen and use for all right-sided images
2. Determination the optimal gain value (OGV) for the study
3. RT screening survey images in transverse imaging plane
4. Distal RT CCA B-mode loops in longitudinal imaging plane
5. RT screening survey images in longitudinal imaging plane
6. RT dedicated longitudinal plaque scans (B-mode and color)
7. Annotate the text "LT" on the screen and use for all left sided images
8. LT screening survey images transverse imaging plane
9. Distal LT CCA B-mode loops in longitudinal imaging plane
10. LT screening survey images longitudinal imaging plane
11. LT dedicated longitudinal plaque scans (B-mode and color)

1.1 Access to Exam 5 Plaque Location Information

Prior to the scan, the sonographer must review the list of plaques detected at MESA Exam 5. The presence or absence of plaque(s) and their location(s) from the MESA Exam 5 carotid ultrasound will be pre-populated in the participant's Carotid Ultrasound Data Collection Form under section 8. The goal of this information is to help the sonographer identify and recognize previously reported plaques.

Figure 1 shows an example of the plaque location list from MESA Exam 5 scans. The list includes the six possible segments for plaque locations. Within each segment, subjects may have had near wall (NW), far wall (FW), or NW and FW plaque at Exam 5. Note: When we indicate plaques in the NW+FW for a given segment, this does not necessarily mean that they can be demonstrated simultaneously in the same imaging plane. Also, ECA plaques are not listed here, but when present, they tend to be a continuation of a Bulb segment lesion. In those cases, please show the full extent of the plaque.

8. Availability of Exam 5 plaque location information:

Not available

No plaque

	NW	FW
Right CCA	<input type="radio"/>	<input type="radio"/>
Right bulb	<input checked="" type="radio"/>	<input type="radio"/>
Right ICA	<input type="radio"/>	<input checked="" type="radio"/>
Left CCA	<input type="radio"/>	<input type="radio"/>
Left bulb	<input checked="" type="radio"/>	<input checked="" type="radio"/>
Left ICA	<input type="radio"/>	<input type="radio"/>

Figure 1. Pre-filled form with plaque location by segment and wall. In this case, 4 plaques were noted.

1.2 Participant Positioning

The participant should rest supine without a pillow during the exam. Their head should be slightly rotated to the side opposite of the side being imaged, approximately 30-45 degrees from midline. All scans start with the right carotid artery and end on the left side. The sonographer scans from the head of the bed, with sufficient room to rest their elbows on the bed to gain stability. Discourage the participant from looking at the monitor, which in most cases will result in an overextended neck position. The sonographer may gently place his/her hands on the subject's head to rotate the head into the correct position. The sonographer should emphasize the importance of not moving or talking. To improve the subject's comfort and reduce low back tension, have the subject bend their knees and place a pillow under their legs, if they desire.

1.3 Electrocardiogram (ECG) Hook-up

The ultrasound system has a standard 3 lead ECG set-up. Electrodes are placed on the skin. In general, there is no need to prepare the skin as long as you use good quality ECG electrodes. On rare occasions, it might help to wipe the skin with alcohol to improve electrode contact. The ECG tracing will display at the bottom of the ultrasound system monitor. This signal is used by the reader to choose image frames at different time points of the cardiac cycle for offline measurements. For example, all plaque measurements are performed at the time of the "R wave", at end-diastole. The sonographer should ensure that the signal is of good quality, with appropriately magnification (gain), a clear QRS complex deflection with minimal respiratory wandering and minimal baseline noise. The P and T waves should be discernible.

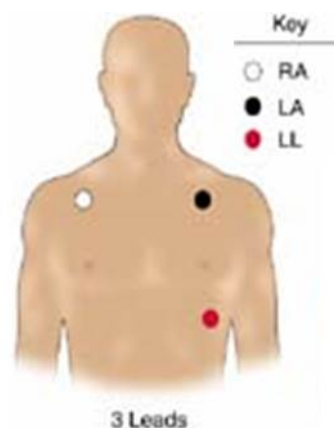


Figure 2. ECG Electrodes placement

1.4 Blood Pressure Assessment

An appropriate-sized BP cuff is connected to an automated sphygmomanometer (Dinamap) and placed over the right and then left upper arms. **It is very important to use the appropriate cuff size for each subject.** Each field center should have the following cuff sizes available: small adult (17-25 cm), adult (25.1-33 cm), large adult (33.1-40 cm), and thigh (40.1-50 cm). **The subject is placed supine and should rest for 5 minutes prior to measurements, preferably 10 minutes.** Other study set-up procedures should be completed while the subject is resting. The arms are positioned slightly abducted from the body, but resting comfortably on the table. BP measurements will be obtained from both arms to verify that there are no significant differences. During BP assessment the MESA participant should remain quiet. Start by measuring the right arm BP twice, each obtained one minute apart followed by two left arm blood pressures also recorded one minute apart. All 4 systolic and diastolic blood pressures and heart rates should be recorded on the case report form (CRF). In rare cases where only right or left BP can be obtained, note this in the carotid ultrasound CRF.

BP and heart rate alerts should follow the same criteria as for the seated procedures. Immediate alerts should be initiated if the systolic BP is >210 mmHg, the diastolic BP is >120 mmHg or the heart rate exceeds 130 beats/minute. Urgent alerts should be initiated when the systolic BP is between 180-210 mmHg or the diastolic BP is between 110-120 mmHg (see section 3).

Summary of Blood Pressure Measurement Protocol

Initial BP measurements, performed after a 5-10 minute rest in the supine position.

- a. Right arm BP measured twice obtained one minute apart
- b. Left arm BP measured twice obtained one minute apart
- c. Enter values in Carotid Ultrasound Data Collection form

While you are recording BPs and setting up for carotid imaging, ask the subject if they had any carotid artery intervention (i.e. carotid endarterectomy or carotid stent placement). If a single side was operated on, perform your ultrasound scan only on the contralateral side. If both sides were intervened or operated on, you will not collect US images from either side. Complete the US CRF and document this finding.

BP PROTOCOL MODIFICATION: If the arterial stiffness protocol was performed less than 2 hours prior to the start of the carotid ultrasound study, the blood pressures recorded with the VaSera VS-2000 device (Fukuda Denshi USA, Redmond, WA) can be used to fill the carotid data collection form. Please indicate the time of BP recording in the Carotid Ultrasound Form

1.5 IMAGING PROTOCOL

1.5.1 Transducer Frequency and Preset Settings

MESA Exam 6 ultrasound scans will be performed with Mindray M9 ultrasound machines using the L12-4s probe. A MESA 6 preset has been pre-programmed and should be used for all studies. The sonographer should become familiar with the MESA 6 preset and confirm the correct preset and settings are selected for all Exam 6 studies.

MESA 6 Preset

B-mode	B
Frequency (F):	H9.0 (Hgen)
Depth (D):	4.0 cm*
Gain (G):	Determine OGV per subject
TGC location	All 8 pods vertical and centered
Focus location	preset starts at 2.0 cm depth**
Frame Rate (FR):	46
Dynamic Range (DR)	170 dB
Persistence	1
iBeam	1
iClear	OFF (does not show on the screen)
Tint	OFF (does not show on the screen)
Gray Scale Map	1 (does not show on the screen)
Horizontal scale	ON

* Deeper arteries might need to be scanned at 5 cm depth, but this change in preset should be a rare exception

** The focus is placed at mid-vessel level when scanning the CCA or at the level of the plaque

1.5.2 Entering Participant Information into the Ultrasound System

The following information should be entered on the “Exam Management” screen and be displayed on the images throughout the scan (example on **Figure 3**). Select "Patient Info", then:

- Under the Last Name field, enter: **MESA6** (no spaces)
- Under the First Name field, enter: **Idno** (7 digits)
- Under the Patient ID field, enter: **Idno-6** (no spaces)
- Under the Operator field, enter: **Sonographer ID number**

Select the "OK" key when you are done to exit and begin scanning

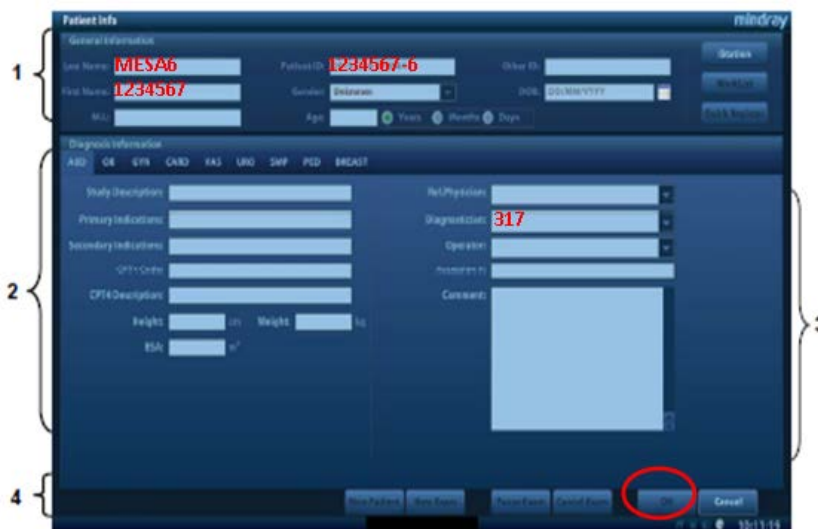


Figure 3. Example of Patient (Participant) Information screen with data entry

1.5.3 Optimal Gain Value (OGV) determination

Because gray scale analysis of the plaques is an essential component of this protocol, special attention is paid to the overall gain settings for plaque delineation. This optimal gain value (OGV) is established at the beginning of the study, before any image acquisition occurs. Step-by-step instructions for the OGV determination for a given MESA participant are listed below:

Begin imaging, without recording, using the MESA 6 preset:

- Start with a longitudinal view of the right common carotid artery, advancing to the bulb, followed by ICA segment covering the entire artery.
- Ensure that all TGC pods are in the center of the pod field. For this protocol TGC pods are kept constant, in a vertical and centered position (see Figure 4) to maintain an even gain amplification across the full scan field.
- Adjust focus to the level of interest (i.e. level of plaque (if present) or the far wall of the distal CCA).
- Adjust the overall gain so that the lumen of the artery is completely black and a plaque-free segment of the adventitia wall is white. The overall gain settings should not be adjusted beyond seeing a very small amount of noise in the blood (black area in vessel) (see Figure 6). **NOTE on the screen this OGV value. After the participant specific OGV has been established, the goal is to keep it as constant as possible while obtaining the best images of the plaque.**



Figure 4. TGC pods

When scanning the left side, try to keep the same OGV selected for the right side. If this is not ideal for plaque border definition and needs to be adjusted, try to remain between +5 /- 5 dB from the originally selected setting between sides and/or segments.

1.5.4 Annotations

Select the “*ABC Comment*” key next to the keyboard arrow keys, and type RT or LT to indicate the side being scanned in the upper left corner of the screen. The only additional annotation will be the originally assigned OGV.

1.5.5 Imaging Sequence

Before starting a scan, review the MESA Exam 5 plaque location information provided by the Reading Center. Always start with the right carotid artery (annotate RT) and only image the left side after the right-sided scan has been completed (annotate LT).

1.5.5.1 Imaging Sequence Screening Survey: Transverse Imaging Plane

For both right and left-sided carotid scans, the probe is oriented with the notch towards the right of the subject and the carotid artery is imaged transversely, in a cross section. The purpose of transverse scan is to:

- 1 Characterize the orientation the carotid arteries and locate the site of bifurcation and branches orientation
- 2 **Identify areas of plaque previously noted in Exam 5, or any new plaques,**
- 3 **Demonstrate the entire length (extent) of each plaque identified.**

Before recording the transverse scan, perform a brief, initial overview to:

- 1 Become familiar with the orientation of the carotid artery and branches
- 2 Locate the bifurcation and distinguish the ICA vs. the ECA
- 3 Adjust transducer to achieve full probe contact
- 4 Identify the site of maximal plaque on the near or far wall
- 5 Color and pulsed-wave Doppler can be used as identification aids

The transverse plaque screening scan is obtained at 4 cm depth without magnification in 3 separate (or more if needed) acquisitions to demonstrate the transverse carotid anatomy from the clavicle to the mandible using the initial OGV setting (remember to note this gain value on the screen):

1. Transverse CCA acquisition scan

Record a 4-beat loop showing the proximal CCA, starting just above the clavicle, proceeding superiorly until its transition into the bulb (denoted by the change in shape from a circular to a more oval cross sectional image). This sweep should be performed slowly to show the artery in the center of the screen, at an ideal 1.5-3 cm depth, and with clear double lines on the near and far walls screening for any possible plaque. Plaques that are in the proximal or mid-CCA also are imaged in this protocol.

2. Transverse Bulb acquisition scan

The next 4-beat loop starts at the level of the distal CCA and advances slowly through the bulb until the bifurcation is seen. Try to maintain imaging with the initial OGV setting. Do not vary this setting – if absolutely necessary, do not adjust more than -5 or +5 dB from OGV.

3. Transverse Distal acquisition scan

The next 4 beat loop starts from the middle of the bulb and advances distally to show the first 2 cm of the ICA and ECA branches.



Figure 5. Examples of the transverse loops to acquire of the (A) CCA, (B) carotid bulb, and (C) carotid bifurcation into the ICA and ECA.

1.5.5.2 Distal CCA Loops

The purpose of these longitudinal scans is to demonstrate the anatomy of the distal CCA before it transitions onto the carotid bulb to evaluate the distal CCA wall thickness, grayscale composition, and diameter changes during the cardiac cycle. **Because of the dynamic nature of these analyses, translation artifacts should be avoided.**

From a lateral approach, the sonographer will obtain 2 consecutive 4-beat loops showing the distal portion of the CCA including at least 0.5 cm of the bulb transition. For the second recording the sonographer might adjust the pressure applied, focus location or make slight changes in angle of incidence to clearly demonstrate the near and far wall double lines, adjusting for any respiratory variations. These images are being acquired for future analyses and are not part of the specific aims of MESA Exam 6.

An ideal distal CCA image will have:

- Clear near and far wall interfaces, perpendicular to the beam,
- The original OGV determined for that subject, adjusted to show walls well without saturating the lumen
- Focus adjusted to be at the level of the far wall or the center of the artery lumen
- The distal CCA segment horizontal on the screen
- A recording obtained **at end-expiration**. To avoid translation artifact, wait a few beats after the subject stops breathing and the jugular vein reaches a stable distension.
- The jugular vein stacked over the CCA while trying to avoid respiratory translation

artifact

- CCA lumen should not taper off at either end, assuring that the probe is aligned with the vessel course and scanning through its true center
- A clear ECG signal with clear QRS complex. Avoid PVC's if possible.

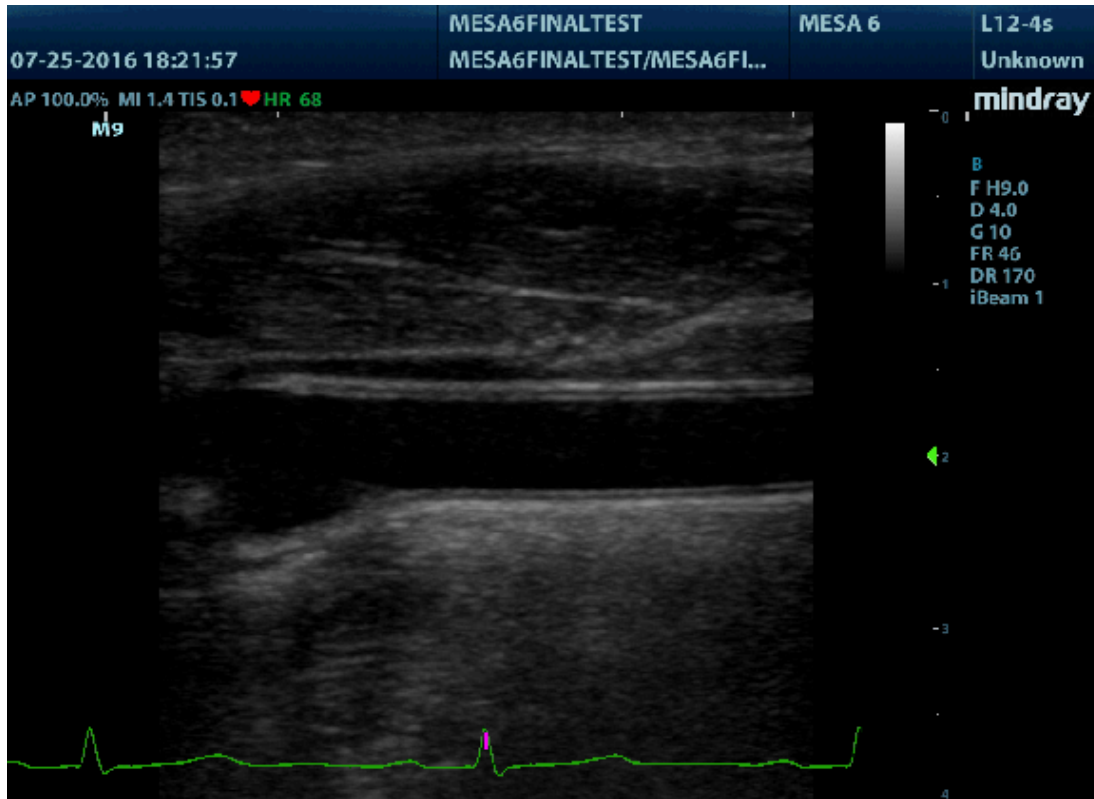


Figure 6. Example of longitudinal distal CCA image. Notice clear near and far wall double lines, appropriate overall gain, focus position and vessel perfectly horizontal on the screen, showing the transition onto the bulb segment

1.5.5.3 Plaque Screening Survey: Longitudinal Imaging Plane

The purpose of these scans is to confirm the presence of plaques identified during the transverse screening; either lesions already noted in MESA 5 exam or new ones. Plaques are defined as discrete, **focal areas of wall thickening ≥ 1.5 mm or focal thickening at least 50% greater than the surrounding intima-media thickness (i.e., wall thickening, not obstruction)**. These scans are a series of slow longitudinal 4-beat cine loop recordings acquired at 4 cm depth, without magnification. Three longitudinal screening cine clips should be obtained:

- one from the clavicle through the bulb
- one from the bulb to the origin of the ICA (Figure 7 A)
- one from the bulb to the origin of the ECA (Figure 7 B).

During the screening acquisition, the sonographer should identify the imaging approach and view that demonstrates the best plaque borders, the longest and the thickest dimensions of the plaque. This longitudinal screening acquisition is used to find the best imaging approach to be used for each dedicated longitudinal plaque image.

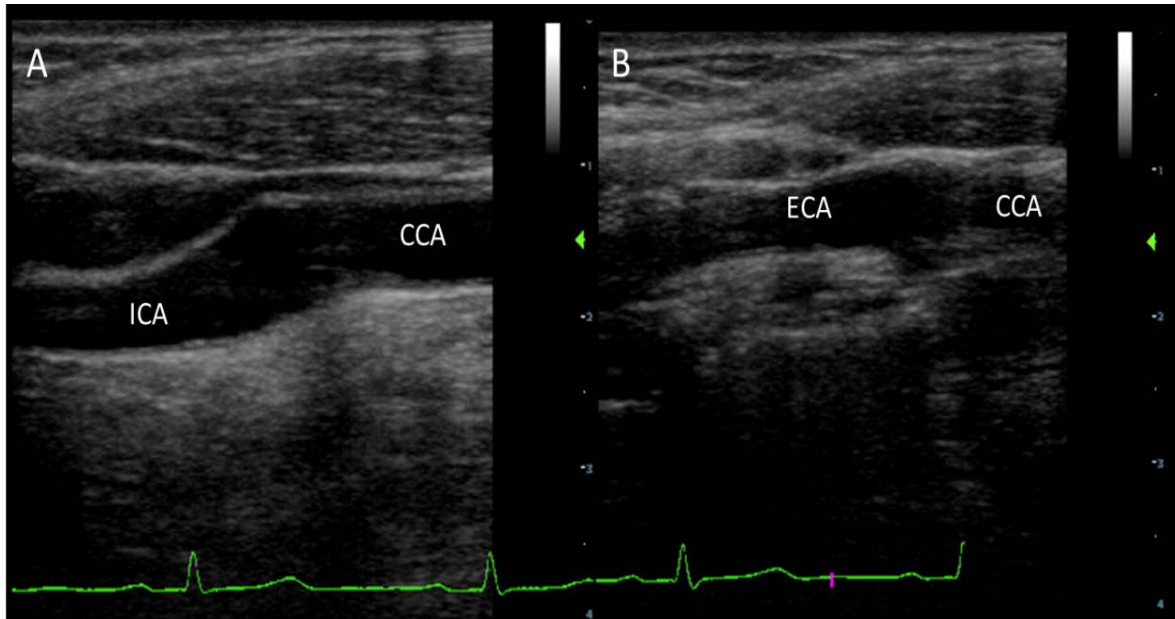


Figure 7. Examples of screening survey in the longitudinal plane where the sonographer toggles from the ICA (A) to the ECA (B) trying to demonstrate plaque presence.

1.5.5.4 Dedicated Plaque Scan for Gray Scale Analysis: Longitudinal Imaging Plane Survey

The purpose of the dedicated longitudinal plaque scans is to provide the most representative image of the plaque for offline plaque grayscale and texture analysis.

After completing the screening survey scans, the sonographer should acquire the following images for **each plaque** identified;

1. **Gray scale longitudinal image of the plaque** where it demonstrates the best delineated borders, longest and thickest plaque dimension, and narrowest lumen. Align the ultrasound beam perpendicular to the plaque. Acquire 4-beat cine clip.
2. **Color Doppler longitudinal image of the plaque** from the exact same imaging plane as longitudinal grayscale image but with color Doppler turned on. Optimize the color Doppler to fill vessel lumen to help delineate plaque borders without over saturation. Acquire a 4-beat loop.

To optimize the color Doppler flow:

- Set the color Doppler region of interest (ROI) to the length of the vessel segment and the height of the vessel walls,
- Steer the color Doppler ROI to be parallel with the vessel wall
- Adjust the color Doppler scale (PRF) to the highest setting appropriate for carotid scanning (MESA 6 preset starts at +/-32.1 cm/s)
- Turn the gain all the way up until it appears to bleed outside the vessel borders and slowly bring down the color Doppler gain until the color flow fills the lumen up to the vessel wall and plaque borders.

Note: if color Doppler does not reach the vessel wall and/or plaque borders, the sonographer will need to slowly adjust down the color Doppler scale (PRF) while adjusting the color Doppler gain to demonstrate **complete filling of the vessel lumen** without color aliasing and bleeding of color outside the vessel wall).

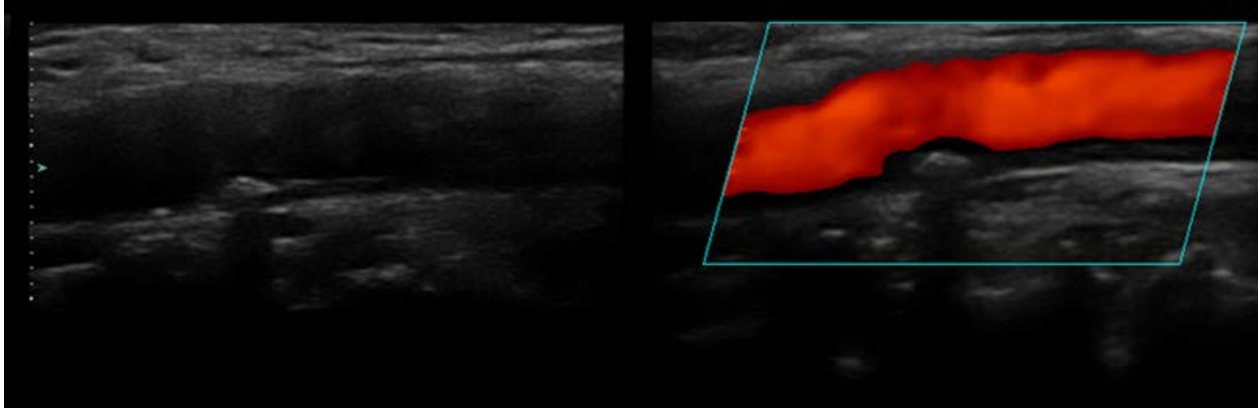


Figure 8. A plaque in the right bulb far wall in gray scale followed by the same image with color Doppler ON.

The protocol requires a combination of transverse and longitudinal views, first using B-mode followed by color Doppler imaging to help the reader identify the plaque/blood interfaces (Figure 8 example). Plaques will be traced from longitudinal views, but the transverse images are used to corroborate plaque size and provide an orthogonal confirmation of maximal plaque encroachment.

Note: For longitudinal images, if the sonographer believes that more than one image is needed to demonstrate the “best” view of a plaque, the sonographer may take an additional longitudinal grayscale (still and loop) followed by a color Doppler image (loop).

Ideal Image Acquisition Settings for Plaque Grayscale Analysis

1. Use MESA 6 study preset. It was created to optimize grayscale setting for this ultrasound system. DO NOT change the dynamic range and DO NOT change the gray scale map. Low persistence and high frame rate to improve temporal resolution also are part of the preset.
2. The TGC curve is set to the center of the pod field. For this protocol it is very important that the TGC pods are not adjusted (**figure 1**).
3. **The overall gain is adjusted at the beginning of the scan and the OGV is determined by imaging in the longitudinal plane the RT CCA, bulb to ICA segments. If plaque is noted, the OGV should be set based on the plaque images.** The OGV is determined by turning down the overall gain so that the lumen is completely black with no noise visible, then slowly turning up the overall gain until there is a little bit of noise in the vessel lumen and the adventitia is completely white on both the near and far walls. **The selected OGV should be used throughout the study and not changed unless necessary to improve plaque delineation.** In instances where the OGV truly needs to be adjusted to best demonstrate the plaque, the change in overall gain setting should not be more than +5 or -5 dB from the original OGV setting.
4. The ultrasound beam is perpendicular to the arterial wall showing the largest plaque encroachment into the lumen from each orthogonal plane (transverse and longitudinal views respectively). See **figure 9, panel C**.

5. For the dedicated plaque scans, plaques are imaged in the longitudinal plane, with the focus positioned at the level of the plaque.
6. If the same plaque could be displayed in the near or far wall depending on the angle of incidence, we recommend showing the plaque on the far wall.
7. If there are plaques on the near and far walls that can be displayed within the same imaging plane that option is preferred, unless presenting them in the same imaging plane compromises the image resolution of either one.
8. Color Doppler is used to define the plaque/blood borders and residual lumen, especially useful in cases where the plaque surface is echo lucent or image quality is limited. See **Figure 9 panel C and D** for ideal gain settings and color confirmation of plaque borders.

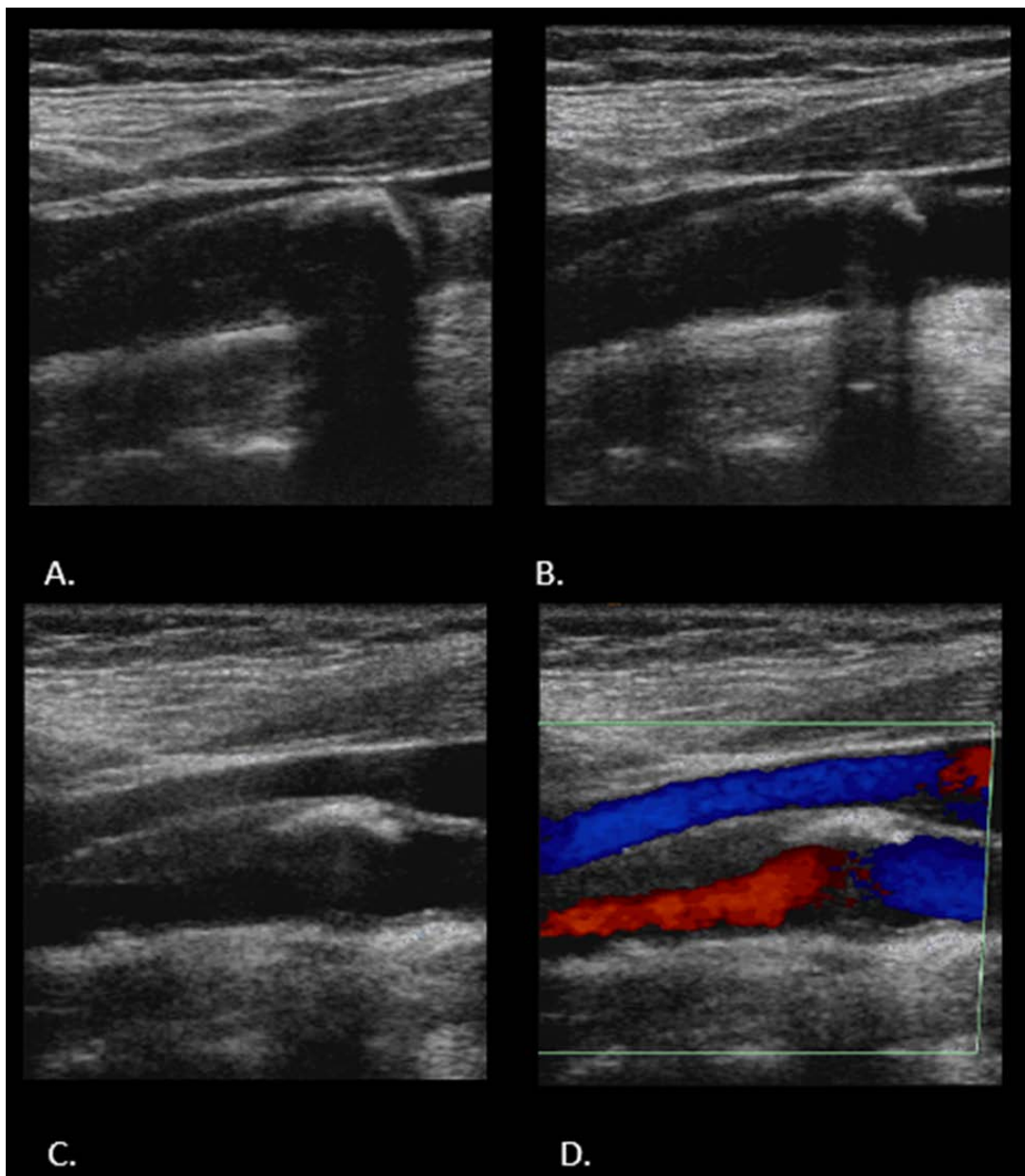


Figure 9. Panels A-D are from the same plaque. Panel A shows dense acoustic shadowing from the near wall plaque however; the distal borders of the plaque continuing into the ICA are

not shown. Panel B demonstrates less acoustic shadowing from the near wall plaque and some of the borders of soft plaque in the distal ICA (arrow). Panel C demonstrates the “best” view of the plaque with the best delineation of all plaque borders, thickest and longest dimension. Note there is a calcific proximal portion of the plaque with acoustic shadowing and the distal soft plaque borders are well delineated. D demonstrates the color Doppler image of the plaque in its “best” view.

1.5.5.5 Left Side Sequence

Repeat the same acquisition sequence of transverse, distal CCA loops, and longitudinal plaque scan, dedicated plaque gray scale analysis, on the left side. End the study and send the images and completed paperwork to reading center for review.

2 PROTOCOL SUMMARY – QUICK REFERENCE

1. Review plaque location information from MESA Exam 5
2. ECG lead placement
3. Blood pressure assessment (if stiffness protocol performed within 2 hours, those BPs may be used instead; enter time on Carotid Ultrasound Form)
4. Complete initial portion of study forms
5. Enter participant information in ultrasound system
6. Select MESA 6 preset and settings
7. Determine OGV
8. Begin image acquisition
9. Fill Carotid Ultrasound Data Completion form
10. Transmit images to Reading Center

Table 1. Ultrasound Scanning Protocol

Image Sequence	Number of 4-Beat Loops to Be Stored	Description
Set OGV	None	Before recording, adjust overall gain to determine the subject's specific OGV by scanning the CCA, bulb and ICA segments with plaque (if present) while adjusting the focus. The initially set OGV ideally should remain constant throughout the study, but only adjusted +/- 5 dB if needed.
Right Side		
Transverse plaque screening scan	3 or more	<ul style="list-style-type: none"> • Slowly advance from the clavicle to the mandible in transverse • Show CCA, bulb and ICA anatomy and plaque presence
Distal CCA Loops	2	<ul style="list-style-type: none"> • Stable longitudinal views of the distal CCA including transition into the bulb
Longitudinal plaque screen	3 or more	<ul style="list-style-type: none"> • From the clavicle to the mandible • Show transition to ICA and ECA • Identify plaques reported in MESA 5 and any new lesions
Dedicated plaque scan	1 or more for each plaque (start with CCA, followed by bulb and ICA)	<u>Longitudinal B-mode</u> <ul style="list-style-type: none"> - Proper OGV and focus - Maximize display of plaque - No sweeping while recording <u>Longitudinal color Doppler</u> <ul style="list-style-type: none"> - Steer, adjust color scale and gain to fill lumen and highlight plaque borders - No sweeping while recording
Left Side		Repeat sequence from right side above

3 ALERT VALUES

MESA alert procedures should be followed if any of the findings listed in Table 2 are identified during the carotid ultrasound which may have adverse health consequences to the participant if untreated. **These values should be brought to a physician's attention and appropriate follow-up, determined by local policies, should be assured.**

Table 2. Alerts

Carotid US: carotid artery dissection	Immediate
Carotid US: atherosclerotic plaque visually >70% occlusive	Urgent (Immediate if symptomatic)
Carotid US: occluded carotid artery or color Doppler "String sign"	Urgent (Immediate if symptomatic)
Carotid US: thyroid pathology (nodule > 1.0 cm or severe enlargement)	Urgent
Carotid US: mass > 1.0 cm	Urgent
Carotid US: Jugular vein thrombosis	Immediate
Carotid US: systolic BP >210 mmHg, or diastolic BP >120 mmHg or heart rate exceeds 130 beats/minute	Immediate
Carotid US: systolic BP between 180-210 mmHg or the diastolic BP between 110-120 mmHg	Urgent

4 FORMS AND IMAGE MANAGEMENT

There are two forms that the MESA sonographers will complete: (i) the Carotid Ultrasound Log and (ii) a Carotid Ultrasound Data Collection Form

The MESA Carotid Ultrasound Case Report Forms are entered into the MESA web database at the field center.

4.1 Carotid ultrasound log sheets

The Carotid Ultrasound log is kept at each site to help catalogue the back-up copies of all the local studies. A copy of this log is faxed to the UW AIRP (608-263-1534) after uploading the images to the server. The Carotid Ultrasound Log will help sonographers keep track of local copies of the carotid ultrasounds from exam 6.

Organize your log sheets by date in your study binder filing the most recent one on top. Double check the dates and identification number (Idno) entries in this log before faxing and filing it, this will help minimize errors and follow up queries.

MESA Exam 6 Carotid Ultrasound Log Sheet Example

Site: _____ Page number: _____

	Scan Date	Idno	Sonographer ID	Comments
1	4/2/2015	3551212	317	<i>Nice scan</i>
2	4/2/2015	3899223	316	<i>Extra plaque images</i>

Fax copy to UW AIRP 608-263-1534 as soon as finished with MESA 6 scans for the day and images have been transmitted to the UW AIRP via internet. File this form in the study binder.

4.2 MESA Exam 6 Carotid Ultrasound Data Collection Form

All MESA Data Collection Forms require entry of the MESA participant ID, date of scan, and the sonographer ID at the top right of the form. The sonographer is responsible for completion of the mentioned items and to verify the participant ID, and date are correct. The original forms are to be returned to the clinic coordinator who will be responsible for entering them into the MESA database system. The site is responsible for faxing the form to the ultrasound reading center the same day of the study, **(608-263-1534)**.

As an alternative to fax, the site can e-mail or upload via ftp the 2 forms (log sheet and data collection forms). If these are sent via e-mail, enter in the subject line "MESA 6-site#- date (mm/dd/yyyy)-forms". Send e-mails to:

ck4@medicine.wisc.edu

khansen@medicine.wisc.edu

4.3 Image Transmission to UW AIRP

Ultrasound scans should be transmitted to the UW AIRP server via the internet for review and analysis on the same day they are recorded. Field Centers will use WinSCP client software to connect to the University of Wisconsin, Department of Medicine network

After study completion, a backup copy is “sent to” an external hard drive via USB connection. This encrypted 4 TB external hard drive uses a Padlock system to enter your assigned password. The drive is recognized by the M9 ultrasound system or by your computer only after the password has been entered. The M9 system recognizes it as a USB drive that you can send the study images to in DICOM format. To eject the drive, just press Cancel on the external HD keypad. Based on standard file sizes, we expect each site to only use one external drive to back up all the studies. Additional hard drives will be provided if necessary. Each HD will be labeled as MESA 6 Site# and range of dates of recorded data. After completion of the study, hard drive/s should be stored in a secure safe, locally.

For data transmission to the UW AIRP Ultrasound Reading Center, the site will install WinSCP client software in a local PC (either laptop or workstation) that is accessible to Field Center sonographers and coordinators. The UW AIRP will provide a username and password for each sonographer and study coordinator to access their site specific folder on our network to permit secure ftp upload of ultrasound images recorded that day plus, if they desire, the scanned study forms.

4.4 Image Overview Reports form the UW AIRP

All studies sent to the UW Ultrasound Reading Center (UW AIRP) will be reviewed within 5 working days. Any studies with alerts will be reviewed as quickly as possible, usually within 24 hours. The sonographer and study coordinator will receive an email with comments about the scan. Sonographers will receive feedback on protocol adherence, image quality, and completion of paperwork, as well as praise and constructive tips for improving future images. During the overview and check-in process, a quality score is generated based on the over-read form.

5 SONOGRAPHER CERTIFICATION AND MAINTAINANCE OF COMPETENCY

- **Sonographers must complete online training provided by the UW AIRP even if they had been certified previously to scan for MESA 5.** This will include didactic presentations, case examples, review of study logistics (MESA exam 5 plaque list, MESA exam 6 forms and image management) followed by a live video demonstration of the scanning protocol using the M9 system.
 - After online training, in-person training will be provided at the field centers.
 - After training, sonographers will be required to complete at least 3 sets of paired mock exams of passing quality, using the M9 ultrasound system following all study procedures. Mock scans can be performed in any volunteer willing to be scanned twice for practice following local policies. Ideally, it would be good to identify at least one volunteer with known carotid plaques. Each pair will consist of part 1, a protocol-defined scan, which will be sent to the UW AIRP for overview and selection of images to match on part 2, which will be completed per the study protocol, as if the plaques to match came from a returning MESA participant. A sonographer will not be certified to scan subjects for MESA exam 6 until they have successfully completed 3 pairs of mock scans.
 - Sonographers will retain their certification by performing at least one passing scan every 60 days after they have achieved initial certification. After 45 days, the sonographer will receive a reminder of this process. If they do not plan on scanning a study subject in the next 2 weeks, they should perform a single mock exam and send it for review. It must achieve a passing score of 90%. Sonographers also must maintain a passing score of over 85% in over 95% of their scans and may not have more than two consecutive scans fail. Sonographers may be decertified if these criteria are not met, or at the discretion of the reading center if their performance is determined to be substandard.
 - Designated subjects from each field center will have a repeat carotid ultrasound study to evaluate sonographer reproducibility. A reproducibility exam may be performed on the same day as the initial exam, as long as the subject leaves the room for a minimum of 30 minutes before returning for a reproducibility exam. They may perform other MESA Exam 6 activities during this time, such as completing questionnaires. If not performed on the same day as the initial exam, repeat exams must be performed within 28 days of the initial exam. Each sonographer at a field center must complete at least 10 reproducibility exams. Therefore, sites with more than 2 sonographers will complete at least 20 reproducibility exams. Scans of subjects selected for a reproducibility (QA) study will be labeled differently in the US system. See example below for participant 3551212.
- Under the Last Name field, enter: **MESA6-QA** (no spaces)
 - Under the First Name field, enter: **ldno**
 - Under the Patient ID field, enter: **ldno-6B** (no spaces)
 - Under the Operator field, enter: **Sonographer ID number**
 - Select the "OK" key to exit to begin scanning

Patient Info		
General Information		
Last Name: <input type="text" value="MESA6-QC"/>	patient ID: <input type="text" value="3551212-6B"/>	Other ID: <input type="text"/>
First name: <input type="text" value="3551212"/>	Gender: <input type="text"/>	DOB: <input type="text"/>
M.I.: -----	Age:-----	
Diagnosis Information		
	Operator: <input type="text" value="317"/>	

6 ULTRASOUND PHANTOM SCANS

A small parts gray scale phantom (Gammex 404GS LE-0.7) will be used by each field center to detect changes in the ultrasound image calibration, transducer performance, and overall image quality throughout the course of the study. Phantom scans will be performed every 6 months starting before subjects are scheduled, to determine the baseline M9 system performance at each field center.

During the data collection period, sonographers will be instructed to repeat the phantom scan twice a year, reproducing the initial equipment settings. They will submit the images to the UW AIRP lab. Measurements of axial and lateral resolution will be performed. A subjective assessment of overall image uniformity and objective measurements of distance calibrations, (vertical and horizontal) and gray scale will be reported.

The ultrasound phantom form will assist the sonographer in setting up the equipment correctly for the phantom scan exam. The sonographer will record 5 still frame images following the protocol and preset provided during the face-to-face training:

1. Axial/lateral Resolution (4 cm) of the near field pins with overall gain set at 10 dB and focus at 2 cm depth
2. Axial/lateral Resolution (4cm) of the far field pins with overall gain set at 10 dB and focus at 2 cm depth
3. Depth and horizontal Calibration
4. Near zone Vessel Simulation (3.5 mm diameter) at overall gain of 10 dB (OGV) with focus at 1 cm depth (NOTE: TGC's vertical in the middle, **figure 10** left panel)
5. Far zone Vessel Simulation (7.5 mm diameter) at overall gain of 15 dB (OGV) with focus at 3 cm depth (NOTE: TGC's vertical in the middle, **figure 10** right panel)

Phantom images should be transmitted to the UW AIRP for review. Upon review and approval of the scan, a shipping slip will be sent via e-mail if the site shares a phantom with another MESA site.



Figure 10. Phantom images showing the near (left) and far field (right) gray scale calibration

SUPPLEMENTAL MATERIALS

These documents are relevant to the protocol, but they are not considered part of the protocol. They are stored and modified separately. As such, modifications to these documents do not require protocol amendments.

- 1) MESA Exam 6 Carotid Ultrasound Data Collection Form (with prefilled list of plaques noted in MESA Exam 5)**
- 2) MESA Exam 6 Carotid Ultrasound Log Sheet**
- 3) MESA Exam 6 Phantom Form**
- 4) MESA Exam 6 Overread Form**