CARRS Cohort:
Proposed Measures
[Precision-CARRS]

MANUAL OF OPERATIONS:
CAROTID ULTRASOUND IMAGING

CAROTID ULTRASOUND

Introduction:

Carotid ultrasound for CIMT and carotid plaque**:** CIMT, the combined thickness of the intima and media layers of the carotid artery, results from hypertrophy of either layer and can be readily measured using ultrasonography.[1-7] Carotid plaque is distinct from CIMT and represents atherosclerosis, predominantly due to intimal thickening with foam cells, smooth muscle cells, macrophages, lipid core, and fibrous cap depending on the stage of development.[8, 9] Both carotid plaque and increased CIMT are independent predictors of adverse CVD events including stroke.[10-19]

Expected prevalence: In a large cohort of Indian subjects age ≥30 years without CVD, men had higher CIMT values than women (0.61±0.12 mm vs. 0.58±0.11 mm, $P < 0.001$).[20] CIMT was higher with older age (0.53mm in men 30-39 years vs 0.73mm at ≥60 years; 0.51mm in women 30-39 years vs 0.65mm ≥60 years) and was higher in those with CVD risk factors.

Equipment: Phillips Affiniti 70G in Delhi and Philips Epiq5G in Chennai using vascular linear probe (12 mHz), with reading by Drs. N Pandey and M Harish, respectively. **Duration of testing:** 20 minutes.

Technique: Briefly, ultrasonography of the common carotid artery (CCA), carotid bifurcation, and internal carotid arteries bilaterally for the evaluation of lumen diameter, CIMT, and presence and extent of plaque will be performed with B-mode ultrasonography as per the American Society of Echocardiography guidelines.[21-25] **CIMT**: With the subject lying in a supine position with the head resting comfortably and the neck slightly hyperextended and rotated in the opposite direction of the probe, ultrasound images will be obtained of the distal 1 cm of the far wall of each CCA using B-mode ultrasound producing two echogenic lines (representing the combined thickness of the intima and media layers). Each CCA will be imaged in three different projections: CCA right side 90-120-150 and CCA left side 210-240-270 degrees as per the Meijer arc. A 3-5 beat cineloop would be recorded and optimized R-wave gated end diastole still frames at each angle will be used for measurement after averaging 6 readings for mean CIMT. **Carotid plaque** will be defined as a focal structure that encroaches on the arterial lumen by at least 0.5 mm or is more than 50% of the surrounding IMT or has a thickness greater than or equal to 1.5 mm.[25]

Manual of Operations: Detailed MOPs will be adapted from the MESA protocol enclosed Pages 5-22.

Reproducibility: Inter- and intra-observer variability for CIMT was 0.03 ± 0.02 mm and 0.02 ± 0.02 mm.[26, 27]

CRF for Carotid Ultrasound Imaging

Family Name: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Given Name: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Sex (Male = 1, Female = 2) ☐

Original Study Number ☐☐☐☐☐☐

Serial Number of Current Study ☐☐☐☐

Date of Examination: ☐☐ ☐☐ ☐☐☐☐
d d m m y yyy

- Overnight fasting ☐ (No = 0, Yes = 1)

- Have you consumed after 9 PM yesterday night
  a. Coffee, chocolate, cold drinks ☐ (No = 0, Yes = 1)
  b. Tobacco (smoking, oral tobacco or snuffing) ☐ (No = 0, Yes = 1)
  c. Alcohol ☐ (No = 0, Yes = 1)
  d. High fat diet ☐ (No = 0, Yes = 1)
  e. Vitamin C ☐ (No = 0, Yes = 1)
  - If on medicines for high blood pressure, have you stopped them for the past 24 hours? ☐ (No = 0, Yes = 1)
  - Have you had any strenuous exercise in the past 12 hours? ☐ (No = 0, Yes = 1)

CAROTID ARTERY MEASUREMENTS

Blood Pressure

Systolic ☐☐☐ mmHg

Diastolic ☐☐☐ mmHg

Pulse/heart rate ☐☐☐ Bpm

CIMT measurements (mm)

Probe position	**Right 1**	**Right 2**	**Right 3**	**Mean**
Anterior				
Lateral				
Posterior				

Plaque ☐ **(Right)** **(Present 1, Absent 0)** **Location**

Probe position	**Left 1**	**Left 2**	**Left 3**	**Mean**
Anterior				
Lateral				
Posterior				

Plaque ☐ **(Left)** **(Present 1, Absent 0)** **Location**

Examination carried out by:

Names (CAPITALS) ____

Signature: ____

MESA

Carotid Artery Intima-Media Wall Thickness (IMT)

Sonographer Manual

1.0 Overview of the Carotid Artery IMT Ultrasound Scanning Protocol

1.1 Introduction to the Carotid IMT Ultrasound Scanning Protocol

The extracranial carotid arteries are the largest arteries in the neck. The right common carotid artery (CCA) originates from the innominate artery on the right and the left CCA originates directly from the aortic arch. Each common carotid artery ascends in the neck lateral to and posterior to the trachea. At the approximate level of thyroid cartilage, slightly below the angle of the mandible, the common carotid artery bifurcates into the external and internal carotid arteries. Proximal to the bifurcation, the common carotid artery dilates to form the carotid bulb. The origin of the bulb can be recognized in most, though not all, subjects. It is defined to be where the common carotid artery begins to dilate slightly and the vessel walls curve out, they are no longer parallel to the skin surface. The bulb is elliptically shaped and geometrically complex in the longitudinal view. Its upper limit is defined by the tip of the flow divider. The tip of the flow divider also marks the origin of the internal and external carotid arteries. The external carotid artery lies anterior and slightly medially to the internal carotid artery in 90% of individuals. In the remaining 10%, the orientation is reversed. The external carotid artery is usually smaller than the internal and it has branches that supply the neck and face. The internal carotid artery has no branches in the neck and ascends into the calvarium to supply the brain.

1.2 Participant Position

The subject is supine during the carotid artery examination and is made comfortable in a position that allows head rotation to either side. The sonographer stands or is seated at the end of the exam table near the participant's head. The top of the head is about three inches from the end of the exam table and the head is rotated 10^{o} away from the side examined. Participants may wish to turn their heads to look at the screen. This should be discouraged. This is best achieved by the sonographer using his hands at the start of the study to rotate the head while stressing to the participant the importance of not moving.

1.3 Anatomical Sites of Interest

The extracranial carotid arteries are divided into four anatomically defined segments:

- Distal common carotid artery
- Carotid bulb
- Internal carotid artery
- External carotid artery

The lateral extent of each segment is defined relative to the tip of the flow divider, which is typically the most clearly defined anatomical reference in the carotid system. The three segments of interest are the distal common carotid artery, the carotid bulb, and the internal carotid artery. No external carotid images will be recorded.

Anatomical Definitions

Distal common carotid: this is the segment of the common carotid artery immediately proximal to the origin of the carotid bulb, where the near and far walls of the artery are parallel to one another. The end of the distal common carotid artery is marked by the dilatation of the vessel walls, which is the carotid bulb.

Carotid bulb: the inferior extent of the bulb is the beginning of dilatation or 8 mm below the tip of the flow divider. The superior extent of the bulb is defined by the very tip of the flow divider.

Internal carotid artery: the caudal, or inferior, extent is defined by the tip of the flow divider. The vessel then ascends in the neck and enters the base of the skull. For the purposes of this protocol, the ultrasound study will be limited to the initial 10 mm of the internal carotid artery.

1.4 Initial Scan

The purpose of the initial scan is to orient the sonographer to the subject's carotid anatomy; to locate the bifurcation and distinguish which vessel is the internal and which is the external carotid artery. The site of maximal wall thickening in the near or far wall, in the bulb or internal carotid artery should also be identified during the initial scan. Color and pulse-wave Doppler can be used as identification aids.

1.5 Standard Carotid Ultrasound Images

One *real time* transverse (short-axis) scanning sequence and five longitudinal images and are taken from both the right and the left carotid arteries for each subject. The *real time* transverse (short-axis) scanning sequence is a sweep of the carotid from the base of the common, up through the bulb into the internal and back down to the base of the common. The cine loop enables the reader to distinguish artifact from true anatomical structure. The first of the five longitudinal images is a pulse-wave Doppler measurement of the peak systolic velocity in the internal carotid. Next is a standard lateral view of the common carotid. And the other three longitudinal images are of the internal carotid artery or bulb. The frozen images of the common carotid and the internal or the bulb are videotaped as both frozen images and as part of a cine loop.

In summary, the sonographer first videotapes a transverse (short-axis) scanning sweep of the common through the bulb. Hr then finds the site of peak systolic velocity as measured by pulse-wave Doppler. The common carotid is then imaged. And finally the site of maximal thickening in the internal artery or in the bulb is then imaged from three different angles, anterior, lateral and posterior, to obtain as much circumferential information at this site as possible.

The carotid ultrasound images are collected and videotaped in this order:

IMAGE DESCRIPTION	TO BE VIDEOTAPED
RIGHT SIDE	
1. Transverse (Short-axis) sweep	15 second *real time* scanning sweep
2. Pulse Wave Doppler	5 seconds of frozen, measured image
3. Common Carotid	5 seconds of frozen image followed by 5 seconds of cine loop
4. Anterior Internal/Bulb	5 seconds of frozen image followed by 5 seconds of cine loop
5. Lateral Internal/Bulb	5 seconds of frozen image followed by 5 seconds of cine loop
6. Posterior Internal/Bulb	5 seconds of frozen image followed by 5 seconds of cine loop
LEFT SIDE	
1. Transverse (Short-axis) sweep	15 second *real time* scanning sweep
2. Pulse Wave Doppler	5 seconds of frozen, measured image
3. Common Carotid	5 seconds of frozen image followed by 5 seconds of cine loop
4. Anterior Internal/Bulb	5 seconds of frozen image followed by 5 seconds of cine loop
5. Lateral Internal/Bulb	5 seconds of frozen image followed by 5 seconds of cine loop
6. Posterior Internal/Bulb	5 seconds of frozen image followed by 5 seconds of cine loop

Image 1: Transverse (Short-Axis) Sweep

The transverse sweep begins at the base of the common carotid and smoothly travels up through the bulb, into the internal and back down to the common. Videotape in *real time* the full sweep, up from the common, into the internal and back, for 15 seconds.

Image 2: Pulse-wave Doppler

The critical information is the peak velocity in the internal carotid artery at peak systole at the point of maximum flow acceleration. To locate it a 2-mm Doppler sample gate should first be place in the center of the distal common carotid artery. The sample gate is then moved from the common through the bulb to the proximal internal. If there is no site of disturbed or turbulent flow, the Doppler measurement should be taken from the first centimeter of the internal carotid artery. The audible signal can be used to facilitate placement of the Doppler sample gate. Angle correction must not exceed 60°. The frozen image of the measurement is videotaped for approximately five seconds.

Image 3: Common Carotid

Image 1 is a view of the distal 10-mm of the common carotid artery in the lateral projection. The carotid bulb is displayed on the left side of the monitor (when facing the screen). If the bulb cannot be identified, but the tip of the flow divider can, this may substitute as the internal landmark on this view. After locating the tip of the flow divider and centering it on the screen, the probe is rotated into the lateral plane and moved downward 2 cm. The probe is then centered on the upper 1 cm of the common carotid.

Images 4, 5 and 6: Internal or Bulb at the site of maximum wall thickness

Images 4, 5 and 6 are images of the internal artery or the bulb are centered on the site of maximum wall thickness in the internal carotid artery. The objective is to image the segment of the internal that contains the single largest wall abnormality, on either near or far wall, in any one view. THE IMAGES SHOULD NEVER BE CENTERED ON THE COMMON CAROTID EVEN IF IT IS THE SITE OF MAXIMUM DISEASE**.** The location of the site of maximum wall thickness is determined during the initial scan. It is not the site of average maximum wall thickness, but rather it is the single site of maximum wall thickness in any single view. The sonographer can use any available technique to make this decision including long axis or short axis views, color or pulse-wave Doppler.

The three internal carotid images are taken from three different scanning angles, the anterior-oblique, the lateral and the posterior-oblique. The point of maximal wall thickness should be centered in the middle of the screen for each image. The sonographer should adjust the probe to maximize the lesion and wall interfaces in each projection to not exaggerate the size of the focal plaque by scanning across the vessel on an oblique axis. The Ultrasound Reading Center readers are completely dependent upon the sonographer to provide a legitimate display of a plaque.

The anterior-oblique, the lateral and the posterior-oblique scanning angles are defined as follows:

- Anterior-oblique: the arch on the surface of the neck from the midline (trachea) to 55° to a line drawn from the mid-trachea to the center of the back of the neck.
- Lateral: the arch along the lateral surface of the neck, from 55 ° to the perpendicular to 100 ° (hence 45 °). The sternomastoid muscle can be palpated beneath this portion of the skin's surface.
- Posterior-oblique: the arch from 100 ° to the perpendicular to 145 °. The probe almost always lies just behind the posterior margin of the sternomastoid muscle.

If the artery is normal, the study will be centered on the initial 10 mm of the internal carotid artery. The tip of the flow divider is used as the point that identifies the most caudal portion or inferior boundary of the internal carotid artery. It will not always be possible to identify the tip of the flow divider in the frozen image. The priority is to display the wall interfaces of the proximal internal artery, not the tip of the flow divider.

A cine loop of each of the four images described above, one of the common carotid and three of the internal carotid arteries, is captured by selecting the freeze button. The sonographer then cycles through the 32 cine loop images to select the one that best displays the intimal walls. It is videotaped for five seconds. The cine loop is then set in motion and it is videotaped for five seconds.

1.6 Criteria for Satisfactory Images

The criteria for optimal B-mode ultrasound image of the carotid arteries is defined as the clear visualization on long axis views of arterial interfaces, internal arterial landmarks, and lesions.

1. Near wall - arterial wall nearest the probe

    a) adventitial - medial boundary
    b) intima - lumen boundary
2. Far wall - arterial wall furthest from probe
    a) lumen - intimal boundary
    b) medial - adventitial boundary

The area of interest will be centered in the middle of the image and the probe will be aligned to show as much of the vessel cephalad and caudad as possible. The sonographer should optimize the visualization of the interfaces by adjusting the gain settings, beam steering and probe placement.

It is expected that the lumen of a good carotid ultrasound study image will contain a significant amount of artifact. To clearly visualize the intimal linings the gain setting will need to be set considerably higher than it is for a typical clinical study.

1.7 Imaging Priorities

Some participants will not have vascular lesions or easily visible intimal linings. For these cases the sonographer will prioritize the far wall intimal linings over the near wall intimal linings. For the more difficult cases, where there is some disease, the top priority is to provide a quality image of disease. Disease located in the carotid bulb presents a special case. When a lesion is detected in the bulb and the internal is normal capture images to characterize the bulb disease. Instead of capturing an anterior, a lateral and a posterior view of the internal image the bulb disease from these three perspectives.

In summary the imaging priorities are,

1. Lesion – if there is a focal lesion in either the distal 10 mm of the common or in the proximal 10 mm of the internal, focus on the lesion.
2. Bulb lesion – if there is a lesion in the bulb and the internal is normal, focus on the bulb lesion.
3. Far wall interfaces – if there is no disease the clear visualization of far wall is more important than that of the near wall
4. Near wall interfaces

1.8 Sonographer Response to a Significant Stenosis – ALERT

Some participants will have significant carotid stenoses, which are discovered, perhaps for the first time, during this examination. An ALERT is defined as an 80% or greater stenosis in the common carotid, the bulb or internal carotid artery. The only criteria used to estimate stenosis is the peak systolic pulse-wave Doppler. An 80% or greater stenosis is indicated by a pulse-wave Doppler measurement of 2.0 m/s. Imaging data should **not** be used in arriving at this conclusion; its role is limited to determining the site of the abnormality.

If a sonographer believes a significant vascular abnormality is present, he should double-check this finding by repeating the Doppler measurement. Under no circumstances should this impression be conveyed either directly or indirectly to the participant by the sonographer. **The clinic coordinator should be told immediately after the participant has left the scanning area.** An inquiry is thereby triggered at the field center regarding the presence of relevant symptoms in the participant. It will be determined whether he is under care for the vascular abnormality and if necessary appropriate referrals will be provided.

The responsibility of the participant's health care is completely with the field center. Whenever a participant presents with what the sonographer suspects is a problem he is to communicate it immediately to the field center medical personnel. **Do not wait for confirmation from the Ultrasound Reading Center.** The scan will not be reviewed until at least a week later. The readers and the project manager are not qualified to provide any sort of diagnostic report.

1.9 A *Good* Carotid Ultrasound Image

Wall boundaries can be demonstrated with high resolution ultrasound imaging. They appear as as two parallel echogenic lines separated by a hypoechoic space in longitudinal views of the carotid arteries and are usually best observed in the common carotid artery where the vessel courses parallel to the skin surface and thus presents a target which is at a right angle to the ultrasound beam.

The first echo along the far wall is derived from the lumen-intima interface and the second, normally brighter, echo along the far wall originates from the media-adventitia interface. Between these interfaces lies the media, which appears as an echolucent zone. The distance between the first two lines corresponds to the combined thickness of the intima and media. Because of its collagen content the adventitia is quite echogenic and appears as a bright zone highlighted along its inner margin by the media. However the periadventia, depending on location, is composed of loose areolar tissue and in most instances is echolucent.

It is more difficult to image the interfaces when the near and far walls of the vessels are curvi-linear and not at right angles to the ultrasound beam. Beam steering can help to improve the image. In the carotid bulb, where the walls flare, only short wall segments may be seen on any single frame. This same phenomenon is observed in the proximal portion of the internal carotid artery when the walls are not parallel and hence sub-optimally visualized. Other causes for loss of wall interfaces that are not related to scanning technique are the presence of plaques and the presence of fat in the arterial wall. The interfaces can also be seen along the near wall but the lines may be disrupted and the echoes weaker because the ultrasound beam is passing from tissue to fluid. At times, it is impossible to maximize both the near wall and far wall interfaces on the same image. On such occasions the priorities are to first optimize lesion, second the far wall, and third the near wall. *Lesion* refers to the site of maximum single wall thickness, near or far wall.

The very earliest changes that can be seen in the arterial wall indicating the onset of atherosclerosis are fatty streaks. It is not clear that this finding can be detected by ultrasound. Fat is weakly echogenic and would not be expected to generate a signal. Picano et.al. pointed out that the gaps seen in the lumen-intima interface, the "first interface" of the double line echo pattern along the far wall in a study of 75 fresh human aorta specimens might be a reflection of the presence of fatty plaques. However, such breaks may be present for multiple other reasons, including less than optimal scanning technique.

The first definite abnormality that can be detected by B-mode is intimal-medial thickening. As progressive development of atherosclerotic lesions occur, there is an increase in the error of estimating anatomic abnormalities because acoustical shadowing is often present with large lesions. Doppler, on the other hand, becomes progressively more accurate with increasing levels of disease. The Ultrasound Reading Center uses both grayscale imaging information and Doppler to compile a complete lesion profile for each carotid artery. It is important that both portions of the examination be done well.

2.0 Overview of Carotid Ultrasound Analysis Protocol

The first thing the reader does when analyzing a carotid ultrasound scan is to read the sonographer's comments on the log sheet and preview the videotape of the entire study. Through the preview process the reader learns of any unusual situations specific to the study, such as images videotaped out of the standard order. Carotid system structures are identified: the common carotid artery, the carotid bulb, the internal carotid artery, and if visible the external carotid artery. The site where the interfaces are most clearly imaged is identified in both the common carotid and non-diseased internal/bulb images. If there is disease in the internal/bulb, the site of the largest lesion is determined. In addition, the pulse wave Doppler measurements are assessed.

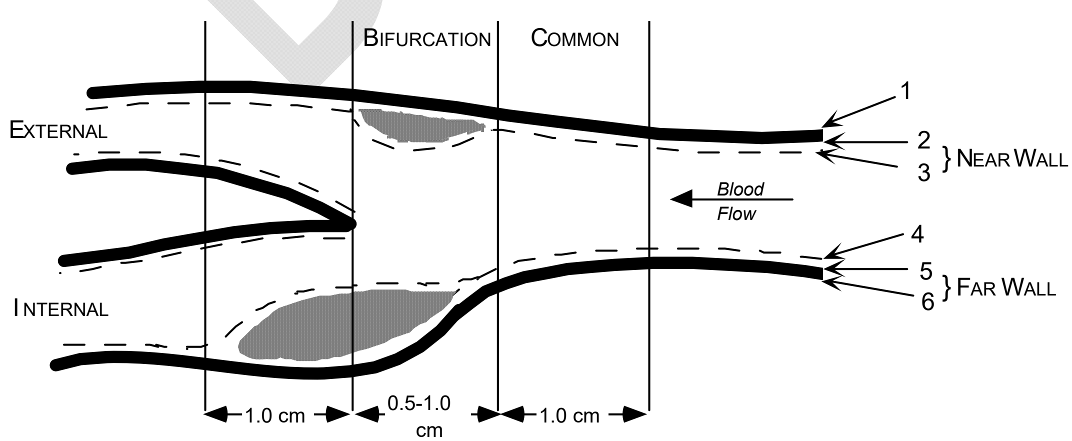
After previewing the videotape, the images are digitized. The computer-based ultrasound image analysis system combines the digitization and analysis functions. The program is designed to permit the user to immediately proceed with the analysis after digitizing a study.

2.2 Calibration

The first step in carotid image analysis is calibration. It is necessary to calibrate each ultrasound image in order to convert the computer unit, pixels, to "real world" units, centimeters. Toshiba ultrasound machines images have calibration marks at the far left and top edges. To calibrate an image the reader positions the calibration tool such that it demarcates the 1-cm distance between two calibration marks

2.3 The Interfaces

The reader's goal is to draw all six of the lines as shown on the each carotid artery image. The figure below demonstrates the anatomy of the carotid artery in the longitudinal perspective and the correspondence of the vessel layers to the line numbers used by the ultrasound image analysis program.



The correspondence between the line numbers and the interfaces are defined:

Wall	Line Number	Interface
Near Wall	Line 1	Adventitia –
	Line 2	Media – Adventitia
	Line 3	Lumen – Intima
Far Wall	Line 4	Lumen - Intima
	Line 5	Media – Adventitia
	Line 6	Adventitia – Periadventitia

Measurements from carotid study images are made from the six lines drawn on the image. The lines are drawn with the stylus pen and are approximately 1-cm long. In the common carotid view, the measurements are taken in the 1-cm segment proximal to the bulb. The common carotid view is the only view from which measurements are made in the common carotid artery. It is a relatively simple task for a trained reader to draw the lines on a high quality image of a healthy artery. It is more difficult to analyze diseased arteries.

The measurements are that are made are of the near wall, far wall, vessel width and lumen. The measurement algorithm calculates the distance between pairs of lines and reports the minimum, maximum and average (and standard deviation) values. The vessel structures are defined by the lines pairs as follows:

Vessel Structure	Line Pair
Near Wall	2 – 3
Far Wall	4 – 5
Vessel Width	1 – 6
Lumen	3 – 4

2.4 Priorities

The goal is to draw six lines on each carotid image. Due to varying degrees of image quality, which is highly dependent upon sonographer skill and subject anatomy, it will not always be possible to draw all six lines. It is, therefore, necessary to set priorities. The physics of ultrasound make the far wall is easier to image. The far wall interfaces will typically be more distinct than those of the near wall. Thus the far wall data set will be more complete and therefore be considered most important. Wall thickness is of greater importance than vessel thickness because this is a study of atherosclerosis.

The carotid ultrasound analysis priorities in order of importance are:

Measurement	Line Pair
Far Wall	4 – 5
Near Wall	2 – 3
Vessel Width	1 – 6

2.5 Image Quality Scores

An image quality score is assigned to every analyzed image. This score is based on the quality of the image and the reader's confidence that the lines drawn represent the true interfaces. Although the score is subjective, the following is a loose guideline for scoring the common and non-diseased internal carotid arteries. Note that the criterion used to assign a quality score to a diseased vessel differs slightly from that of a healthy vessel

<u>Common & Healthy Internal Arteries</u>

1. Unacceptable: only one or no lines drawn.
2. Poor: only two lines, one pair, drawn, giving a lumen measurement (i.e.. 3&4, or 2&5) or vessel width (i.e.. 1&6)
3. Acceptable: only two or three lines on either near or far wall with an opposing line (lumen measurement).
4. Very Good: all six lines drawn, all measurements made.
5. Excellent: all six lines clearly visualized and easily drawn, with good gain and positioning.

<u>Atherosclerotic Carotid Arteries</u>

1. Unacceptable: only one or no lines drawn.
2. Poor: only two lines, one pair, drawn, yielding a lumen measurement (i.e.. 3&4, or 2&5) or vessel width (i.e.. 1&6) or can draw lines on wall opposing the lesion but no lesion measurement can be made.
3. Acceptable: four to five lines drawn, lesion traceable but not clearly defined, with at least one posing line.
4. Very good: all six lines drawn, lesion clearly defined, with opposing line.
5. Excellent: lesion clearly defined, with opposing wall measurement, lines are easily drawn and the image has good gain and positioning.

2.6 Subjective Assessment

In addition to obtaining measurements of wall thicknesses, vessel width and lumen the reader characterizes the internal/bulb disease. Lesions in the common carotid artery are not characterized. Assessments are made of the surface, morphology, percent stenosis, location and density. Each characteristic and the categories the Ultrasound Reading Center uses to qualify them are briefly described.

2.6.1 Surface

The surface of the artery or lesion is categorized as <u>one</u> of the following:

1. Smooth - no lesion is present in the artery and the lumen-intima surfaces (lines 3 & 4) are free of irregularities. If there is a lesion present then this category is applicable when the lumen-intima surface (lines 3 & or 4) of the lesion is smooth and free of irregularities.
2. Mildly irregular - the lesion has minute surface irregularities.
3. Markedly irregular - the lesion has noticeable surface irregularities. This can be best described by saying that the surface is “bumpy” but without a prominent pit or crater.

4. Ulcerated - the lesion surface has prominent ulceration, pit(s)or crater(s) that is at least 1mm in depth and is at least 1mm in width. The "back wall" of the lesion, defined as the media-adventitia interface, can be clearly seen at the point of ulceration.
5. Can't tell - the surface characteristics of the artery/plaque cannot be determined due to insufficient information (images are unclear or missing).

2.6.2 Morphology

The morphology, the form and structural characteristics, of the lesion are categorized as:

1. No lesion - no lesion present in either the internal or bulb
2. Homogeneous - a lesion that demonstrates an echogenicity that does not vary across its width and thickness.
3. Heterogeneous - a lesion with have a mixture of lucent and echogenic zones.
4. Can't tell - the morphology of the plaque cannot be determined due to insufficient information (images are unclear or missing).

2.6.3 Percent Stenosis

All available information is used to determine the percent stenosis. Information sources include digitized images, cine loops and Doppler values. The degree of stenosis is crudely estimated from the images and cine loop as a ratio of artery width. The Doppler value (velocity) which is known to be a more reliable measure is incorporated to refine the estimate. It may not be evident from the images the images that there is a 100% occlusion. In some cases, there may not be a Doppler value because the sonographer was unable to produce a Doppler signal. When Doppler values are nonexistent and the images are unclear, the reader must rely on comments from the sonographer to determine the degree of stenosis.

% Stenosis	Doppler Values
0-49%	<1.5 m/sec
50-74%	> 1.5 m/sec but < 2.5 m/sec
75% -99%	> 2.5 m/sec
100% (occlusion)	0.0 m/sec

The categories from which the percent stenosis must be chosen are more specific:

1. Normal - no lesion present in either the internal or bulb.
2. 1-24% - Doppler values that are <1.5 m/sec and reader's estimate.
3. 24-49% - Doppler values that are <1.5 m/sec and reader's estimate.
4. 50-74% - Doppler values that are ≥ 1.5 m/sec but <2.5 m/sec.
5. 75-99% - Doppler values that are ≥ 2.5 m/sec.
6. 100% - Doppler values that are 0.0 m/sec.

7. Bad image/Nl (normal) Doppler - the images are so unclear that % stenosis can't be estimated by looking at them <u>but</u> Doppler values fall within normal range, < 1.5 m/sec.
8. Can't tell – the percent stenosis cannot be determined due to insufficient information (images are unclear or missing).

2.6.4 Location

The plaque location describes the site of the lesion. The categories are:

1. No lesion - no lesion is present in either the internal or bulb
2. Can't tell - cannot determine the location of the plaque cannot be determined due to insufficient information (images are unclear or missing).
3. Internal - the lesion is located in the internal carotid
4. Bulb - the lesion is located in the bulb
5. Can't tell - cannot determine the location of the plaque cannot be determined due to insufficient information (images are unclear or missing).

2.6.5 Density

The lesion density qualifies the compactness of the plaque. The categories are:

1. No lesion - no lesion is present in either the internal or bulb
2. Hypodense - a plaque that appears darker than the surrounding tissue.
3. Isodense - a plaque that has same level of brightness as the surrounding tissue.
4. Hyperdense - the plaque appears brighter than the surrounding tissue and <u>some</u> of the tissue beneath the plaque is shadowed.
5. Calcified - the plaque appears much brighter than the surrounding tissue and all of the tissue beneath the plaque is shadowed.
6. Can't tell - cannot determine the density of the plaque cannot be determined due to insufficient information (images are unclear or missing).

3.0 Data Transmission

3.1 Videotape

Carotid ultrasound images are transmitted to the Ultrasound Reading Center on videotape. The Toshiba ultrasound machines are equipped with Super VHS videocassette recorders. **Super VHS tape must be used.** It can be purchased at Radio Shack or through the field center's vascular lab or radiology department. Standard, non-Super VHS, tape is not acceptable.

When the image displayed on the ultrasound machine monitor is optimal, "Freeze It". Page through the cine loop of saved images and select the image that best demonstrates the intimal linings. Videotape five seconds of the frozen image, start the cine loop on *free run* and videotape it for five seconds. It is important to wait for the mechanical delay of the VCR mechanism to engage when timing recordings. A few seconds of over-recording is infinitely more desirable than a non-recording. If at any time during an examination a better image than that previously recorded is obtained, **do not** erase or tape over the previous recording. Add the new images to the videotape and make a note in the *Comments* section of the log sheet to inform the reader.

At the Ultrasound Reading Center the readers digitize (computerize) and analyze the images from the carotid ultrasound videotapes. The computer-based system to accomplish these tasks was developed by the Ultrasound Reading Center.

3.2 Labels and Log Sheets

At the training session the sonographers will be given sets of labels and master copies of a log sheet. These items make it possible to track and organize the numerous videotapes that arrive at the Ultrasound Reading Center. It is of utmost importance that the sonographers carefully label the videotapes and the corresponding log sheets. The labels contain the study name, field center name, exam number and tape number. See the label illustrated in the upper right corner of the sample log sheet below. The log sheet enables the reader to quickly locate each study on the individual videotapes and to obtain pertinent information regarding particular cases.

The sonographer completes the appropriate sections of the log sheet for each subject he scans. The necessary items are relatively obvious.

- Scan Date – the date of the carotid scan,
- Sonographer ID – theMESA Technician ID assigned to the sonographer
- Subject ID – the ID number assigned to the participant (no names please)
- VCR Start – the VCR counter/timer that indicates where the particular study is located on the tape
- Comments – the place for the sonographer to tell the reader about the case
- URC Use – is for the reader to indicate that the study has been analyzed

Sample of Typical Videotape Log Sheet Entries

	Scan Date	Sonog ID	Subject ID	VCR Start	Comments	URC Use
1.	11/13/98	819	612345	0:00	Good study, an easy subject	
2.	11/13/98	819	612222	5:30	Bulb lesion	
3.	11/13/98	819	613333	11:20	Wrong id typed on study, 13333 is correct not 13445	
4.						
5.						

Use the Comment section of the log sheet to communicate any abnormalities, problems or difficulties encountered. For example, if a scan is canceled or if there are images missing or out of order, **write it down**. The importance of this communication cannot be stressed enough. The readers must base all of their decisions on the information the sonographer provides. It is not always easy for a reader who is not medically trained, to distinguish plaque from artifact. Efforts by a sonographer to assist the reader in the analysis process are greatly appreciated.

4.0 Sonographer Quality Control

Following initial certification sonographers will be evaluated continuously to monitor and assure quality control. Since reliable data is the essential element in studies that seek to monitor arterial change over time, great effort must be expended upon all aspects of quality control. The Ultrasound Reading Center has found it best to minimize the number of sonographers and to maintain the same reader thereby limiting problems prospectively rather than retrospectively adjusting data.

4.1 Field Center Sonographers

If possible, two sonographers should perform all examinations at each field center on the same ultrasound machine. Ideally, these individuals would be an experienced vascular sonographer, preferably RVT certified or equivalent. If not the sonographers should have experience in an ICAVL accredited laboratory. The sonographers do not necessarily have to have experience performing research protocols. The Ultrasound Reading Center Carotid IMT protocol is such that it can be quickly taught to someone who routinely performs high quality clinical ultrasound examinations.

The Ultrasound Reading Center assumes that at most of the six field centers there will be two sonographers performing all of the carotid studies. If necessary, the Ultrasound Reading Center can assess inter-sonographer variation. Intra-sonographer variability measurements, which will involve the replicate scanning of twenty subjects by the same sonographer on two different occasions, are highly recommended.

4.2 Ultrasound Reading Center – Sonographer Communication

Experience with prior studies demonstrated the need for rapid and possibly frequent communication between the Ultrasound Reading Center and the sonographers. The project manager and readers will periodically call each of the field centers. Problems encountered by the sonographers and sonographer performance will be discussed and the importance of sonographer compliance with the protocol will be stressed. Examples of the kind of problems that required immediate attention in the past include the apparent non-recording of images on videotape and discordance between Doppler and imaging data. Sonographers are asked to keep notes when problems are recognized so that they may provide direction to the Ultrasound Reading Center when necessary. Sonographers are encouraged to call the project manager to discuss problems or questions as they arise. If necessary, a member of the Ultrasound Reading Center staff will visit field centers. The execution of the carotid protocol will be observed and equipment function evaluated. The purpose of the visits is to be a direct assistance to the sonographers and the field centers.

If a sonographer submits unacceptable or un-analyzable studies, the reader will alert the project manager. An unacceptable study is one from which very little or no data can be obtained. Unusable studies can be the result of poor images or failure to follow the protocol (incorrect images). Poor performance by a sonographer will result in a telephone call to the sonographer and the clinic coordinator from the project manager. Severe cases will warrant a memo to the field center and Ultrasound Reading Center Director documenting the persistent poor quality.

Throughout the exam period, the sonographer will receive sets of *Reader Comments.* The *Reader Comments* are written by the reader at the time of study analysis. Typically, the comments contain constructive criticisms and suggestions for improving the study images, i.e., gain adjustments, check the Doppler gate angle or position. More often than not, the *Reader Comments* include such positive feedback as "Great images, thanks".

4.3 Ultrasound Reading Center Report on Sonographer Performance

In addition to the *Reader Comments,* sonographers will receive feedback from the Ultrasound Reading Center in the form of a sonographer performance quality control report. The maintenance of high performance requires immediate and direct feedback. The reports, which will be published bi-monthly, quantitatively track each sonographer's performance. Copies of the reports will be distributed to the field centers, the Ultrasound Reading Center PI and the coordinating center. Cumulative summaries will be published periodically to serve as an ongoing benchmark against which to judge individual results.

The report will include the number of studies, average image quality scores and percentages of possible lines drawn and Doppler velocity measurements tabulated for all of the field centers, and then by each individual field center, by sonographer and reader. A one page summary report that highlights the overall study results as well as the best and the worst field center and sonographers will accompany each report. Consistently poor performance by a sonographer will initiate a call of encouragement and investigation by the project manager. Continued poor performance will result in the sonographer being re-trained or replaced.

4.4 Performance Standards During Examination Period.

A baseline quality control score, derived from the score assigned to each image and the number of lines drawn for each image, will be established after analysis of pilot and pre-pilot data, below which sonographer performance will be considered unacceptable if maintained for three consecutive weeks. A sonographer must perform a minimum of five studies every two weeks to remain certified. The readers will be monitored to ensure uniform scoring throughout the exam period. Additional training may be required of sonographers and/or readers in the event of any significant temporal drift in accuracy or precision of sonography study performance and/or reading. In terms of the analysis of the actual measurements produced, we will subscribe to those suggested by echocardiography - namely, a goal of mean variability of 10%, with a cut-off point of 15% acceptable variability.

4.5 Replacement or Retraining of a Sonographer

If a sonographer resigns or is replaced due to poor performance, a replacement must be trained and certified prior to performing scans on research subjects. The Ultrasound Reading Center must conduct all sonographer training. A new sonographer can be introduced to the protocol by a certified sonographer, but the new sonographer will not be certified to conduct participant exams until he attends an Ultrasound Reading Center training session. Contact the Ultrasound Reading Center Project Manager immediately when the need to train a new sonographer becomes apparent. Due to the Ultrasound Reading Center's involvement in numerous national multi-center research studies, it may be possible to identify a local sonographer who is certified to execute the carotid ultrasound protocol to assist with the training.

4.6 Within Sonographer Variability Assessment

Intra-sonographer variability during the examination period will be assessed from the data obtained by repeating complete carotid ultrasound studies on a number of subjects. Each sonographer will complete two scans on a subset of approximately twenty participants distributed throughout the exam time period. The videotapes will be sent to the Ultrasound Reading Center for analysis coded with random number assigned by the Coordinating Center. The reader be blinded – he will not know that a study he is analyzing is a standard or a sonographer intra-variability quality control study. Subjects for the replicate studies will be recruited during the exit interview. They will not be recruited by the sonographer. The repeat scan should be scheduled to occur no sooner than one week and no later than one month after the initial scan. On the return visits, each volunteer will be scanned once by each sonographer.

4.7 Achieving and Maintaining Quality Ultrasound Data

High quality carotid ultrasound data begins with the sonographer. The sonographer produces the images from which the readers extract the date. A poor set of images results in a poor and sometimes incomplete set of data. The readers are entirely dependent upon the sonographers to provide clear images and to explain any conditions, anatomical or procedural that vary from the norm.

A. Acquire nothing but clean images that clearly display the intimal linings and the lesions. The intimal linings and the lesions are the top priority, they are what is measured by the reader. It is expected that in order to clearly display the intimal linings the lumen will contain more artifact than the typical clinical study. Review Section 3.8 Imaging Priorities.

B. Videotape the images in the order stated by the protocol. A study that is videotaped out of order is not as easy for the readers to analyze.

    1. Right pulse wave Doppler measurement
    2. Right common carotid
    3. Right internal/bulb anterior oblique
    4. Right internal/bulb lateral oblique
    5. Right posterior/bulb oblique
    6. Right transverse sweep of common and internal
    7. Left pulse wave Doppler measurement
    8. Left common carotid
    9. Left internal/bulb anterior oblique
    10. Left internal/bulb lateral oblique
    11. Left internal/bulb posterior oblique
    12. Left transverse sweep of common and internal

C. Annotate the images with the following information:

    1. EDIC

2. Subject ID
3. Subject Acrostic
4. Sonographer ID
5. Image acronyms

RPW, RCC, RAO, RLO, RPO, LPW, LCC, LAO, LLO, LPO

D. Annotate the images and use arrows to distinguish the vessels when the images are atypical. Don't force the reader to guess which vessel is the internal and which is the external carotid.

E. **Use the Comment section of the log sheet to communicate** any abnormalities, problems or difficulties encountered. For example, if a scan is canceled or if there are images missing or out of order, **write it down**. The importance of this communication cannot be stressed enough. The readers are not medically trained and must base their decisions on the information the sonographer provides.

F. Videotape the frozen images and the cine loops for 5-10 seconds. Any shorter than 5 seconds makes the image difficult to capture and any longer than 10 seconds reduces the reader's efficiency.

G. Take the time to verify subject ID's. Check the ID typed into the ultrasound machine and written on the log sheet. If an incorrect ID is videotaped because the wrong ID was typed into the ultrasound machine, tell the Ultrasound Reading Center about it with a note in the Comments section of the log sheet. After the videotape leaves the field center sorting out erroneous ID's can be a very difficult, if not impossible task. Watch for transpositions.

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