

Manual 6B

Ultrasound Assessment

The National Heart, Lung, and Blood Institute of the National Institutes of Health

Atherosclerosis Risk in Communities Study Protocol

Manual 6

Ultrasound Assessment

Part B: Ultrasound Reading

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1. INTRODUCTION

The participant data acquired at the ultrasound area work station within each ARIC field center are analyzed at a central reading facility located at the Ultrasound Reading Center (URC) in Winston-Salem, North Carolina. The data include B-mode images, arterial distensibility waveforms, and postural change results. The data are forwarded to the URC from each field center at weekly intervals in the form of 3/4" video cassette tapes and 5" floppy disks. After analyses, data summaries are sent from the URC to the ARIC Coordinating Center in Chapel Hill, North Carolina.

This protocol describes the detailed procedures used in reading the ultrasound B-mode images at the URC. Figures referred to in each section are numbered to correspond with sections in which they are cited.

2. SUMMARY OF DATA FLOW WITHIN THE URC

Data flow within the URC is summarized in Figure 2A. The video cassettes (VC) and floppy disks (FD) received from each of the four Field Centers are checked in upon their arrival at the URC, with verification of package contents. The video cassettes containing the participant ultrasound scans and the floppy disks containing participant identification information, arterial distensibility data, and postural change exam data are then logged into the computer.

When this has been completed, the floppy disks and the video cassettes are routed to the transcription station. Video cassette B-mode images are transcribed onto the optical disks which are used at the reading stations. Once the cassettes are transcribed, they are stored at the transcription station for two to three weeks where they are readily accessible for additional viewing by the URC staff. Following temporary storage at the transcription station, the video cassettes are transferred to long-term storage. The floppy disks are forwarded to the arterial distensibility and postural change exam workstation.

Each optical disk can store 24,000 B-mode image frames. The number of participant studies on each disk to maintain daily availability to readers and to ensure that each reader receives approximately the same number of studies to read is regulated. Approximately one-half of the total space on each optical disk is used during the initial session at the transcription station. The disks are then sent to the reader station where they are read by an assigned reader. Once read, the optical disks are returned to the transcription station to store additional participant studies on the unused space of the disk. The disks are again sent to the reader station where the newly added material is read. Each optical disk cycles through the transcription station and the reader station twice. All ultrasound studies on the disk will have been read by this time, and the optical disks are then assigned to long-term storage.

On occasion it will be necessary to review data on a stored video cassette or optical disk. The cassettes, optical and floppy disks in long-term storage are available for review and can be checked out for additional studies by authorized personnel.



Figure 2.A Ultrasound Reading Center Flow Chart ARIC PROTOCOL 6. Part B: Ultrasound Reading.

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3. READER TRAINING AND MONITORING

All readers receive intensive training from the URC staff in order to become certified to perform ultrasound readings in ARIC. This training includes lectures and work station activities which cover the following topics: arterial anatomy, pathology of atherosclerosis, gross dissection (cadaver), acoustical physics, ultrasonic instrumentation, ultrasonic scanning, problems associated with B-mode image acquisition, common artifacts arising in B-mode images, operation of work station instrumentation, and detailed performance of the ultrasound reading protocol. Each reader establishes his own intra-observer reliability statistics to use as a baseline for assessing future performance by performing blinded repeat readings on randomly selected studies. Inter-observer statistics are also developed for the entire group of readers to determine achievable and acceptable criteria for certification. After completion of the training program, each reader is examined by a member of the URC staff to assess satisfactory performance of the reader protocol from the perspectives of proficiency and efficiency of performance.

Inter- and intra-observer measurement statistics are reviewed monthly to monitor the performance of individual readers as well as the entire reader group. Trends suggesting a deterioration in performance levels are promptly discussed with the individuals concerned in order to correct deficiencies as soon as possible. Sustained high performance levels during the studies are recognized and commendation and incentives provided to the individuals involved.

4. READER WORK STATION INSTRUMENTATION

4.1 General Description

The instrumentation provided at each B-mode image analysis work station includes a personal computer (PC) (Leading Edge Model M, IBM-XT equivalent) with computer monitor, a color TV monitor and an optical disk player. The reader selects specific image frames from an optical disk provided by the Chief Reader and acquires these image frames using the PC. The detailed reader protocol for making measurements is completed on these frames, and a data file on each participant is stored on the 20 Mb hard disk of the PC. After participant data have been stored on the PC hard disk, these data are transmitted to the central URC Masscomp computer for storage, analyses, and preparation of data summaries which are forwarded to the ARIC Coordinating Center in Chapel Hill, North Carolina.

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4.2 Operation of Instrumentation

4.2.1 Color TV Monitor Cabling and Adjustments

The switch positions on the front control panel of the color TV monitor are as follows:

Switch	<u>Position</u>
Line A	Out
Line B	Out
VTR	Out
RGB	In
CMPTR	Out
Power	On

The <u>BRIGHT</u> and <u>PICTURE</u> controls are used to adjust image brightness during reading. Cable hook-ups for the color monitor listed below are located in the rear.

<u>Color Coded Cable</u>	Connector	Position 75 OHM
Red	R	Up
Green	G	Up
Blue	В	Up
Black	Ext Sync	Up

4.2.2 Computer Monitor Cabling and Switches

The switches and controls located in the front and rear of the computer monitor are listed below with their correct settings.

<u>Located in Front</u>	<u>Correct_Setting</u>
Power switch	ON
Color & brightness controls	Adjusted to preference

Located in Rear

Mode I/Mode II SwitchMode II positionInput labeled "SIGNAL IN"Large cable connects here

Correct Setting

4.2.3 Computer Cabling

For a diagram and explanation, see figures 4.2.3.A and 4.2.3.B.

4.2.4 Optical Disc Player Control Panel and Rear Panel Terminals

For a diagram and explanation, see figures 4.2.4.A and 4.2.4.B.

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Figure 4.2.3.A - Front Panel of Computer

- 1. Keyboard connector IN
- 2. Power switch ON
- 3. Hard Drive

The figure below shows the switch and the possible connections you may have already present in your System Unit. Depending upon your selection of options, your rear panel may be configured in a different way.



- 1. Monitor cord cables to large monitor
- 2. Power cord to electric source
- 3. Targa Board Connector ~ cables to optical disc player allowing operator to "grab"
- frames to read 4. RGB (4 wire cable) - cables to back of large color monitor
- 5. Video Out cables to small computer monitor and sends video signals out to be viewed on the small monitor

Figure 4.2.3.B Rear Panel of Computer ARIC PROTOCOL 6. Part B: Ultrasound Reading.

NOMENCLATURE AND FUNCTIONS of the CONTROL PANEL.



Figure 4.2.4.A - Front Panel of the Optical Disc Player

- 1. Pover switch DOWN
- 2. Load/Eject located on draver for disc
- 3. Play

REAR PANEL TERMINALS . . . ۰. (2) VIDEO Signal Output Terminal (7) Connector for Interface 6 VIDEO Signal Input Terminal (8) FUNCTION SWITCH Fuse Holder (2A) (4) External Synchronizing Signal Terminal -----(NIIII) 1 P 0 0 0-0 0 Subcarrier Q Terminal Ô **DPOWER SOCKET** (3) Audio Signal Output Terminal (9) Audio Signal input Terminal

Figure 4.2.4.B - Rear Panel of the Optical Disc Player

- 1. Pover Source to electric source
- 2. Video Signal Output Terminal cabled to Targa Board on the computer

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5. OPERATION OF THE READER STATION

- 5.1 EQUIPMENT START-UP AND LOGIN
- 1. Turn on the optical disk player (ODP), Sony TV monitor, computer monitor and computer in that order. Peripheral devices should be turned on before the computer to prevent a power surge to the personal computer.
- 2. Follow the instructions on the computer monitor. Use either upper or lower case:
 - a. Type in the date: month-day-year <enter>. Example: "12-5-88".
 - b. Type the hours and minutes in military time <enter>. Add zeros when there is only one digit. Hours equal 24 per day: 7:30 a.m. is 07:30; 1:30 p.m. is 13:30. When figuring military time, add 12 to your hours after 12 Noon. The minutes are always 01-60 preceded by a colon.
 - c. A "C>" will appear on the computer monitor. You are now at the PC system level.
- 3. Log-in with the central URC MassComp computer:
 - a. At C> type "sy mass" <enter>.
 - b. At login type your three initials (first, middle, last) <enter>.
 - c. At <u>password</u> type your first initial and your date of birth, entering zeros where the number is only one digit, <enter>. The password does not appear on the computer monitor as it is typed. If an incorrect password is entered, the screen goes back to <u>login</u>.
 - d. An ARIC# prompt will appear when the reader's password is accepted.
 - e. The keyboard is now a terminal to communicate with the MassComp (Synchrony program).

5.2 Transfer of Participant Files from MassComp

The reader obtains a study code sheet from the chief reader for each participant study that will be done during the reading session. The average number of participant studies read during a reading session is four; therefore, a reader would transfer at least four participant studies from the MassComp to the reader station PC before beginning the reading session. The participant ID # is located in the upper right hand corner of the study code sheet.

- At ARIC# on the computer monitor, type MTOR (space), the participant number including the prefix X (space), the study number (space), and the study type <enter>. Upper or lower case may be used. (example: "MTOR x123456 1 1" <enter>). The study number and the study type are obtained from the chief reader.
- b. A "SUCCESSFUL TRANSFER" message will appear when the transfer is complete. If incorrect entries are made, error messages will appear, and information may be re-entered.

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- c. Repeat steps a. and b. for each participant to be read.
- d. Exit the Synchrony program by simultaneously typing the <ALT> and the <F9> keys.
- e. At the next screen, type T to return to DOS. Type Y to affirm instructions. It is not necessary to <enter>. The C> prompt will appear on the computer monitor, and there is no longer any communication with the MassComp.

Files do not have to be retrieved again from the MassComp if readers do not read them that same day. They will remain on the computer's hard disk until the reader deletes them. They are deleted when the chief reader notifies the readers to do so.

5.3 The ARIC Image Measurement System

- 1. Access the ARIC image measurement system program as follows:
- a. At C> type CPS <enter> (Upper or lower case).
- b. The Main Menu appears.
- c. Move the highlighted box on the Main Menu with the arrow keys to ACQUIRE <enter>.
- d. Move the highlighted box on the Main Menu with the arrow keys to CAMERA <enter>.
- e. A blue screen will appear on the computer monitor with instructions to enter the participant number identifying the study to be read.
- f. Select a participant number from one of the study code sheets. Type in that six digit participant number excluding non-numeric characters and <enter>.
- g. The computer monitor will prompt the reader with the message, "Put optical disk #..... in optical disk holder.
- h. Carefully load the optical disk listed in this message. This disk contains B-mode images for the participant number chosen.
- i. When "DISK IN" message appears on the Sony TV monitor, <enter>.
- j. Wait for the ODP to initialize, at which time a B-mode image <u>OR</u> a calibration frame will appear on the Sony TV screen. <enter>.
- k. The Optical Disk Player Control Menu is present on the computer monitor.
- 5.4 The Optical Disk Player Control Menu

A brief explanation of each command follows:

NC:	Move	to	the	<u>n</u> ext	study	<u>c</u> od	e

- PC: Move to the previous study <u>c</u>ode.
- SR#: Return to a selected frame number.**
- FR#: Play forward from the present frame to a selected frame and then return to present frame.**
- TF: Move forward one frame.
- RETURN: By pressing the RETURN or <enter> key, any command on the command line will be repeated.
- ** NOTE: To use this command, a specific frame number must be entered. This frame number must be within limits of the selected study code. (EXAMPLE: SR1234 or FR2811)

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The upper left corner displays the participant ID#. The left side of the menu displays each study code with its corresponding start and stop frames.

There will be three asterisks (***) beside the stop frame of the code which the optical disk player is presently displaying on the Sony TV screen. At the bottom of the screen is a rectangular box displaying a blinking cursor where menu commands are entered. On the right side of the screen is a list of optical disk player commands. Each time an "NC" and <enter> is typed at the blinking cursor, the three asterisks move down to the next study code, and the Sony TV monitor displays the first frame of that particular study code. The "NC" and <enter> command is used to move from study code to study code after each site has been read.

Movement through this menu with its commands allows the reader to view frames, choose frames to be captured, and to get an overall view of the study codes present on the participant scan.

5.5 The Calibration Frame

The calibration frame is usually the first frame measured. (See Figure 6.6.A). If a calibration frame is present on the participant study, and the asterisks are in place next to this calibration study code, do the following:

- a. Enter Q at the Optical Disk Player Control Menu blinking cursor command box <enter>.
- b. The calibration frame appears inside a colored border on the Sony TV monitor. It is "captured" by the computer and measurements can be made.
- c. The Main Menu is present on the computer monitor.
- d. Using the arrow keys, move the highlighted box to MEASURE <enter>.
- e. The Measurements Screen appears. Use any arrow key until POINT appears and is highlighted at AOI TYPE in the upper left corner and <enter>. The crosshair appears on the Sony TV image.
- f. "DO YOU WISH TO CALIBRATE" appears in the lower portion of the Measurements Screen. Answer Y and <enter>.
- g. To measure the calibration line, use the arrow keys to move the crosshair up or down, right or left until the vertical leg of the crosshair touches (1) the start of the calibration line; press <enter> and then (2) the end of the calibration line; press <enter>. The ODP Menu will return when the second crosshair is entered.

5.5.1 No Calibration Code

When a calibration code is not present, the first valid code listed on the ODP Control Menu will be a B-mode image, which will also be displayed on the Sony TV screen. Using the ODP Menu and the TF command, view the frames of the first study code, and choose the best systolic frame to be measured. (See Section 6.7). Do the following when the first site present is anything other than a calibration code.

a. Enter Q to capture this frame; it will appear on the Sony TV monitor.b. The Main Menu is present on the computer monitor.

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- c. Use the arrow key to move the highlighted box to MEASURE <enter>.
- d. The Measurements Screen appears. Use any arrow key until POINT appears and is highlighted at AOI TYPE in the upper left corner and <enter>. The crosshair appears on the Sony TV image.
- e. "DO YOU WISH TO CALIBRATE?" appears in the lower portion of the Measurements Screen. Answer N and <enter>. Proceed to measure the B-mode image.

5.6 Measuring B-Mode Images

5.6.1 The Popliteal Study Code

The study code following the calibration frame is usually the popliteal. Readers will recognize the image on the Sony TV monitor. After choosing the best frame for measuring the popliteal (from the ODP menu), capture it by entering Q at the blinking cursor command box. If a command is already present in the command box, and if the cursor is in the first space, that command may be overwritten, and extra letters do not have to be deleted.

- a. If the popliteal is the first study code for this participant, the Main Menu appears on the computer monitor. (See previous section to explain the steps necessary when there is no Calibration Code.) Continue with step c.
- b. If the popliteal follows the Calibration Code: when Q is entered, the Measurements Screen will appear on the computer monitor, and the popliteal frame with a crosshair appears inside a colored border on the Sony TV screen. Do the following for the POPLITEAL only:
- c. "LOCATE AND ENTER CURSOR" is present at the bottom center of the Measurements Screen.
- d. Using any arrow key to move left, right, up or down, move the crosshair to the point where the horizontal crossbar touches the cursor. The cursor is the Y coordinate. When a cursor is not present, or if in the reader's judgment it is placed in error, the reader will locate the approximate vertical center of the B-mode image. (Section 6.5). This serves as a reference point for the next step.
- Look at the Measurements Menu on the computer monitor. The Y coordinate is listed in the upper right side as a value, example Y = 125. Move the crosshair with the UP arrow until that value increases by 75, example Y = 200.
- f. After the crosshair is moved <enter>. This marks the Y coordinate from which the measurements will begin. Proceed measuring the boundaries, starting from Step d. in the following section.

5.6.2 Other Study Codes

After choosing the best systolic frame for measuring, capture it by entering Q at the blinking cursor command box. If a command is already present in the command box, and if the cursor is in the first space at the command box, that command may be overwritten, and extra letters do not have to be deleted.

If this is the first code for this participant, the Main Menu appears on the computer monitor. See Section 5.5.1 for appropriate steps when no

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calibration code is present.

If a calibration code was present: when Q is entered, the Measurements Screen appears on the computer monitor, and the chosen frame with a crosshair appears inside a colored border on the Sony TV screen.

- a. "LOCATE AND ENTER CURSOR" appears at the bottom center of the Measurements Screen.
- b. When a cursor is present: using any arrow key to move left, right, up or down, move the crosshair to the point where the horizontal crossbar touches the cursor and <enter>,
- c. When a cursor is not present, or if in the reader's judgment it is placed in error: locate the appropriate anatomical reference for that study code and <enter>. (Section 6.5).
- d. Proceed to measure the boundaries, which can be measured in any order. Move the crosshair with the left or right arrow keys, taking care to place the center of the crosshair on the boundary edge, to the first boundary to be measured and <enter>. Each time <enter> is pressed, a crosshair remains at that site, and the X and Y coordinates for that boundary are registered in a temporary file. Another crosshair will appear 15 pixels up or down at the next Y coordinate.
- e. Move each crosshair with the left or right arrow keys along the selected boundary and <enter> at each measurement point until that interface can no longer be recognized. A maximum of 11 points are possible, and they may or may not be continuous.
- f. When eleven measurements on a boundary are registered, the crosshair automatically returns to the beginning measurement area. Press <F4> to register information for interface 2, <F5> for interface 3, <F6> for interface 4, or <F7> for interface 5.
- g. Measure the remaining three boundaries in a similar manner.
- h. Press <F9>, which brings up the ARIC DATABASE SCREEN on the computer monitor and stores measurements to the hard disk.

5.6.3 Measuring Study Codes with Unrecognizable Points

It is possible to measure a maximum of eleven points on each boundary. When the <u>first</u> of these possible eleven points is not recognizable, use the up or down arrow and, watching the Y coordinate measurement in the upper right hand corner of the computer monitor, move the crosshair 15 pixels. (This adds or subtracts a value of 15 to that number). Determine if a boundary can be measured at that point. If it can, measure it and <enter>. A crosshair remains at this point, and another crosshair appears 15 pixels down. Move along the interface and measure each recognizable boundary. (Step d. in Section 5.6.2).

5.6.3.1 The <Home> Key

If the first point was measured, but the second point is not measurable, use the <Home> key to move up or down to the next potential point. No crosshair remains at the second point, but a crosshair appears at this next potential measuring point. If that point is recognizable, measure the boundary using the left or right arrow keys to move the crosshair, and <enter>. A crosshair remains at the measured point, and another crosshair appears 15 pixels above or below.

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If that point is not measurable, use the <Home> key; if it is measurable, measure it and use the <enter> key.

Continue to move along the boundary using either the <Home> key or the <enter> key until the interface can no longer be recognized. When all possible points are registered, the crosshair automatically returns to the beginning measurement area. Press <F4> to register information for interface 2, <F5> for interface 3, <F6> for interface 4, or <F7> for interface 5.

In some instances, all eleven sites may be unacceptable, and no points are measured. Press the appropriate "F" key for that boundary, and all measurements will be registered as "000". This can be qualified by viewing the printout of coordinates, which appear after the Comment Screen. (Section 5.7).

5.6.4 The <F8> Key

The $\langle F8 \rangle$ key is used to escape the reading process after an image has been captured. It may ONLY be used before the measurements are stored to the hard disk using the $\langle F9 \rangle$ key. Use the $\langle F8 \rangle$ key:

- a. to choose a systolic frame other than the current captured frame;
- b. to look at arterial motion in other frames to determine a boundary location.

When the $\langle F8 \rangle$ key is pressed, data for all boundaries that have been read on a chosen frame are erased. The reading process for that site MUST be started over, beginning with choosing a systolic frame and capturing that image (Refer to Sections 5.6.1 or 5.6.2.). When the $\langle F8 \rangle$ key is pressed, the ODP Menu appears on the computer screen.

5.6.5 The Toggle Key

While measuring boundaries, crosshairs from previous measurements may interfere with your line of sight. Use the <F3> key to toggle previous crosshairs from your vision.

5.7 The ARIC Database Screen

The ARIC Database screen on the computer monitor is a list of questions concerning the frame which the reader has just read. Appropriate answers are entered with the keyboard. The last question asks if all the questions were answered correctly. If it is answered Y, these data are stored along with the coordinate data in the computer. If the last question is answered N, any information on the ARIC Database screen may be corrected. Shown below is the Database Screen.

ARIC DATABASE SCREEN Reader Number Lesion? Y or N Shadow? Y or N Alert Value? Y or N Quality of Interfaces: Correct? Y or N

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Explanation: Alert value - lumen diameter may be 2 mm or less Quality of each interface (A total of 4 must be entered). 0 - not readable 1 - poor 2 - fair

- 3 good
- 4 excellent

Upon completion of these questions, a printout of coordinates and responses appears for the current study code. Check for obvious errors, such as Lesion or Alert. If no measurements for any boundary were entered, check for "000" on that boundary. If anything is incorrect, the site must be read again. When the last question on this menu is answered Y, the Optical Disk Player Menu appears on the computer screen and the asterisks are still at the image just read. Type "NC" <enter> in the command box to move the asterisks to the next code to be read. View the frames in this code with the TF <enter> command to choose the best frame. Capture that frame, and make the appropriate measurements. The reading process will repeat until all sites are read.

5.8 Ending the Reading Session

After all sites have been successfully read, the reading session for one participant is complete. To end the reading session after each participant study:

- a. Enter Q at the command line on the ODP Menu and <enter>.
- b. Press <Fl> several times until the C> prompt appears. (The Main Menu will appear before you come to the C> prompt.) Be certain to push ONLY the <Fl> key and no others. If you hit any other key, you may erase the file you have created.
- c. Data on each participant should be sent to the MassComp upon completion of the reading process.
- 5.8.1 Sending Data to the MassComp

In order to transfer the reading data to the MassComp database, the synchrony program must be accessed. Once in the synchrony program, the MassComp can retrieve files from the reader station. Listed below is the transfer process.

- a. At the C> prompt, type "Sy Mass" and <enter>.
- b. The Synchrony program will appear. If ARIC# does not appear press <enter>.
- c. Type in "rtom (space) participant # (without alphabetical symbols)"
 <enter>.
- d. After a pause of several seconds, there should be a "successful transfer" message followed by ARIC#. If the data transfer was not followed by a "successful transfer" message on the computer monitor, consult with the chief reader and/or the computer programmer to determine the problem.
- e. Press <ALT>, then <F9> to return to C>.

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- f. A printout of the data collected will be in the computer room. This should be checked for errors, stapled to the study code sheet and handed in to the chief reader. If errors are found, they should be pointed out to the chief reader so that he/she can correct them.
- g. The next participant file transferred from the MassComp may be done. At C> prompt, type CPS <enter>. Refer to Section 5.3, which explains the reading process from that point.
- 5.8.2 Log Out
- a. When reading is complete for the day, log out by typing "bye" or "logout" after the ARIC # and <enter>.
- b. Simultaneously press <ALT> and <F9>.
- c. Press T, then Y to return to the C> prompt

Turn off computer, and then peripheral devices in order to prevent a power surge to the PC. Turning off the computer will also mean that you are logged out.

- 6. READING OF ULTRASONIC B-MODE IMAGES
- 6.1 Orientation to the Biosound B-Mode Image

The B-mode image appearing on the Biosound video screen shows a rectangular segment of the tissues at and below the skin surface having the dimensions shown in Fig. 6.1.A. The transducer in contact with the skin surface is located along the left side of the rectangle. Deeper structures are located at successively greater distances from left to right across the image. The deepest structures which can be imaged are located 4cm from the skin surface. The width of the tissue segment visible is 2cm.

6.2 Arterial Sites to be Examined

6.2.1 Introduction

B-mode images are obtained at one anatomical site in the popliteal artery in the leg and at three anatomical sites (the distal common, the bulb, and the internal carotid) in each of the left and right carotid arteries in the neck. Simplified diagrams of the anatomical sites and the various images which are obtained on each participant are shown in figures 6.2.1.A and 6.2.1.B.

When possible, each distal common carotid artery is scanned at three different transducer angles defined as follows:

 Optimal Angle - orientation of transducer handle at which the two principal anatomical landmarks (the origin of the bulb and the most superior portion of the arc of the flow divider as shown in Fig. 6.2.1.A) are visualized. This angle is normally between 10-20 degrees above the horizontal in a supine subject.

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Figure 6.2.1.B Simplified Diagrams of the B-Mode Images to be Read

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- 2. Anterior angle orientation of the transducer handle at 55 degrees above the horizontal.
- Posterior angle orientation of the transducer handle at 10 degrees below the horizontal.

6.2.2 Popliteal Arteries (Frame 1 in Figure 6.2.1.B)

The popliteal artery in the leg is normally located between 3cm and 4cm below the skin surface when the transducer center is placed on the skin crease located directly behind the knee. Since a distinguishing internal arterial anatomical landmark is not normally visible on the image, the cursor is placed in the vertical center of the image which is directly under the skin crease, an external landmark. Measurements are made on the arterial segment located from a point 5mm above the cursor to a point 5mm below the cursor. Either the right or left popliteal will be imaged on each participant using a single angle of interrogation.

6.2.3 Carotid Arteries (Frames 2-11 in Figure 6.2.1.B)

The right and left carotid arteries are located between the clavicle and the base of the skull on each side of the neck. The common carotid normally bifurcates (divides) into two arteries (the internal carotid and external carotid) at or near the level of the larynx.

6.2.3.1 The Right Common Carotid Artery (Frames 2-4 in Figure 6.2.1.B)

After the popliteal image, the right common carotid image is obtained. Whenever possible, the three transducer angles defined in Section 6.2.1 will be used to interrogate the vessel and obtain these separate images. The origin of the crest of the bulb is the principal anatomical landmark to be identified in this image. The cursor should always be placed at the level of the origin of the bulb by the sonographer who is able to define this point, even when the origin cannot be seen on the reader's image. Measurements are made on the lOmm segment of the common carotid artery immediately below this landmark on the image. This arterial segment is usually located between 2cm and 3cm below the skin surface and is generally shallowest when imaged from the anterior angle and deepest when imaged from the posterior angle.

6.2.3.2 The Right Carotid Artery Bulb (Frame 5 in Figure 6.2.1.B)

The next image acquired is that of the right carotid bulb, using only the optimal transducer angle. The superior arc of the flow divider separating the internal and external carotid arteries is the principal anatomical landmark to be identified in the image. The cursor should be located by the sonographer at this position in the image also. Measurements are made on the 10mm segment of the bulb directly below this landmark on the image. The segment is generally located about 2cm - 3cm below the skin surface.

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6.2.3.3 The Right Internal Carotid Artery (Frame 6 in Figure 6.2.1.B)

The next image acquired is that of the right internal carotid artery, using only the optimal transducer angle. The superior arc of the flow divider is again the principal anatomical landmark identified and marked with the cursor. Measurements will be made on the 10mm segment of the internal carotid directly above this landmark on the image. The segment is usually nearer to the skin surface than the external carotid and has a larger diameter.

6.2.3.4 The Left Common Carotid Artery (Frames 7-9 in Figure 6.2.1.B)

The left common carotid is studied in a manner identical to that of the right common carotid. The image is inverted compared to the right side, with the participant's head located at the bottom of the image. Measurements are made on the 10mm segment of the artery <u>above</u> the origin of the crest of the bulb, as seen on the image monitor.

6.2.3.5 The Left Carotid Bulb (Frame 10 in Figure 6.2.1.B)

The left carotid bulb is studied in a manner identical to that of the right carotid bulb. Again, the image is inverted compared to the right side, with the participant's head located at the bottom of the image. Measurements are made on the 10mm segment of the bulb directly <u>above</u> the origin of the flow divider as seen on the image monitor.

6.2.3.6 The Left Internal Carotid Artery (Frame 11 in Figure 6.2.1.B)

The left internal carotid artery is studied in a manner identical to that of the right internal carotid. This image is also inverted compared to the right side, as discussed in 6.2.2.4 and 6.2.2.5. Measurements are made on the 10mm segment of the artery directly <u>below</u> the superior arc of the flow divider as seen on the image monitor.

6.3 Definition of Important Tissue Interfaces Within the Normal Arterial Wall

6.3.1 Tissue Layers Within the Normal Artery Wall

Three distinct anatomic layers are identified in the walls of normal arteries: the tunica intima, tunica media and tunica adventitia. A simplified diagram of these layers is shown in Fig. 6.3.1.A for a <u>normal</u> arterial wall.

The innermost of the three layers which is directly adjacent to the blood is the intima. In a normal artery, this is a relatively thin region measuring less than 0.10mm. This is less than one-tenth of the total arterial wall thickness. With the development of lesions, this layer may expand greatly and become the thickest layer within the artery wall.

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Figure 6.3.1.A Diagram of the Arterial Wall Layers

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Generally, over 90% of the normal intima plus media thickness is composed of the media. The media varies widely in thickness, depending on the arterial segment, and in composition, depending on whether the components are primarily characterized by elastic tissue, smooth muscle cells, or a combination of these tissues. With the development of lesions, the intima may involve the media and significantly modify its thickness and characteristics.

The outermost portion of the arterial wall is the adventitia. The adventitia begins at the outermost region of the media, defined anatomically as the external elastic lamina, and is composed principally of collagen, a dense form of connective tissue, with small nerve fibers, vessels and elastic fibers also being present. The thickness of the adventitia varies, depending on the particular artery segment and its location within the cardiovascular system. The outermost portion of the adventitia is bounded by periadventitial adipose tissue which may vary in thickness. It gradually merges into the surrounding tissue (periadventitial tissue). Its outer boundary is not generally well-defined. With severe disease present, plaque may protrude into and involve the adventitia.

6.3.2 Tissue Boundaries Associated With the Normal Artery Wall

The ARIC ultrasound study uses the four interfaces marked with a (*) below, that serve as boundaries and which are most easily identified in straight segments of longitudinal B-mode ultrasound arterial images. The overall goals of the ultrasound component of ARIC are the valid and reliable measurement of distances between these interfaces, including lumen diameter and (intima + media) thicknesses, as well as other linear and area measurements.

- 1 Boundary between the periadventitia and adventitia of the near wall
- *2 Boundary between the adventitia and media of the near wall
- *3 Boundary between the intima of the near wall and the blood
- *4 Boundary between blood and intima of the far wall
- *5 Boundary between media and adventitia of the far wall
- 6 Boundary between adventitia and periadventitia of the far wall

The following sections discuss procedures for identifying these boundaries from B-mode images and measuring their locations. Pay particular attention to the difference in the interpretation of boundary 2 relative to boundaries 3, 4 and 5, in terms of the physical principles involved in obtaining B-mode images of closely spaced interfaces.

6.4 Physical Principles of B-Mode Image Formation

6.4.1 The Pulse-Echo Principle

Ultrasonic B-mode images are obtained by sending out short, narrow bursts of acoustical energy and receiving echoes which arise from the environment. The energy is assumed to travel in a straight line until encountering a reflecting object. Echoes received are assumed to originate from reflectors located in a specific direction defined by the

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direction of the ultrasonic beam. After echoes arrive, the time between the transmission and reception is electronically measured and assumed to be proportional to the distance of the reflector from the source of the energy. Assuming an average sound velocity along the propagation path, an absolute distance to the target can be calculated. After converting the acoustical echoes into electrical signals, the amplitudes of these signals are used to modulate the brightness of an electron beam on a video display. This process produces an image of the plane through which the sound transducer scans. This image is referred to as a B-mode (Brightness mode) image. Figures labeled 6.5 (A-N) are examples of B-mode images.

6.4.2 The Origin of Echoes

Reflections originate, in general, whenever an acoustic wave passes from one material into another. If the mechanical properties (stiffness x mass density) of the two materials differ greatly, a strong reflection occurs at the boundary and only a small amount of energy passes through. If the mechanical properties are very similar, a very weak reflection occurs and most of the energy passes through. It is possible for rather different materials to have very similar mechanical properties so that the amplitude of the reflection is negligible. In such a case, a pulse-echo system would not detect the presence of the boundary. Consequently, B-mode images may fail to visualize certain boundaries located within the scan plane.

An optical analogy exists. When a first quality plate glass window is very clean, it is difficult to see its surfaces even when bright daylight is available to be reflected from these surfaces. This situation has on rare occasion resulted in a person injuring himself attempting to walk through such a plate. The mechanical properties of glass and air are very different but the factors producing optical reflection are such that the surfaces are invisible to the eye. Interpretation of anatomical information contained on B-mode images should be approached with a similar healthy skepticism.

6.4.3 Reflection From Smooth, Flat Boundaries

When a narrow beam of energy strikes a smooth flat boundary perpendicular to its path, it returns along the same path. In a pulse-echo imaging system, an echo is received from such a boundary, assuming that the mechanical properties across the boundary are sufficiently different. However, if the angle of incidence differs by only a few degrees from being perpendicular, the reflection may be missed. Consequently, <u>the</u> <u>slightly oblique or curvilinear smooth boundary may not be seen</u> on the image even though it is present.

6.4.4 Reflection From Rough Boundaries

When a ray of energy strikes a rough boundary from almost any direction, energy is scattered over a broad range of angles. Such a boundary is normally visualized on pulse-echo images since the source is likely to receive at least a small portion of the scattered energy. Rough boundaries are relatively insensitive to slight changes in ultrasonic propagation angle.

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6.4.5 Imaging of Arterial Wall Boundaries

A boundary is located on a B-mode image as a <u>dark to bright transition</u> going from shallow to deep structures. This transition identifies the BEGINNING of the return echo and its position is relatively insensitive to the echo strength or instrument gain setting. The bright to dark transition at the end of the echo is determined by other factors including the echo strength and system gain settings. This is discussed in detail in section 6.4.8.

When sound is traveling from the center (lumen) of a normal artery outward through a wall, it passes through several principal boundaries: the blood-intima boundary; the intima-media boundary; the media-adventitia boundary, and the adventitia-periadventitia boundary. In the absence of disease, the blood-intima boundary is rather smooth. Thus reflections are very angle dependent. In addition, the mechanical properties of the media are quite similar and the reflections are relatively weak. Consequently, it is not uncommon for the blood-intima boundary to be very faint or nearly invisible on pulse-echo images.

As the surface becomes irregular (rougher) due to disease development, the sensitivity to angle diminishes. Also, the mechanical properties of lesions may become significantly different from the blood and therefore result in larger amplitude echoes. Consequently, this boundary is more likely to be visible on the image after disease develops. Inability to visualize the boundary tends to suggest a normal artery if considerable effort has been made by the sonographer to visualize the boundary.

Since the normal intima is generally considerably thinner than 0.10 mm, the echoes from the blood-intima and intima-media interfaces tend to overlap when they are present. Consequently, the location of the intima-media boundary cannot usually be resolved in normal artery walls. As the intima thickens as a result of disease, the location of the intima-media boundary may be visualized. Generally this occurs when thickness is greater than 0.20 mm; although, should the mechanical properties of the intima and adjacent media be very similar, this interface may still not be seen.

The normal media in the carotid arteries is between 0.6-1.0 mm in thickness, and the media-adventitia boundary can generally be resolved with a high resolution ultrasound system. This boundary is usually rougher, produces strong reflections and is readily visualized on pulse-echo images.

The adventitial tissue is generally heterogeneous, containing collagen, nerve fibers, vessels, etc., and normally in the order of 0.2mm thick. Many relatively rough boundaries are present within this region and consequently the adventitia-periadventitia boundary may be difficult to resolve. Echoes from within the adventitia overlap echoes which arise at this boundary on the far wall. The location of the adventitiaperiadventitia boundary can on occasion be estimated by observing the apparent end of the echoes arising from this interface and then subtracting an echo pulse length from it.

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In summary, when imaging from the blood outward, i.e., far wall, in normal vessels, the normal blood-intima (boundary 4) and media- adventitia (boundary 5) interfaces are seen with clarity and are generally resolvable. The former is often nearly invisible in young, normal subjects, whereas the latter is usually seen. With the development of disease, both tend to be readily visualized.

If we now consider the boundaries encountered by a sound pulse as it enters an artery from the outside, we can expect the following differences. The periadventitia-adventitia interface on the near wall appears highly reflective, and therefore can on occasion be demonstrated in B-mode images even when gain settings are relatively low. The easiest angle for reliably identifying this boundary is anterior. As the angle of interrogation becomes more lateral, the internal jugular vein is seen in front of the carotid artery, with the far wall of the vein adjacent to the near wall of the artery. When this vein-artery relationship is present, it is often difficult to reliably identify the arterial periadventitial-adventitial interface. Strong echoes from the adventitia tend to overlap the adventitia-media boundary. The boundary which is relatively easy to identify in the normal near wall is the media-intima interface. Because the normal intima is very thin, this is an excellent approximation of the intima-blood boundary. The media-intima boundary is again relatively smooth in the normal vessel and often invisible or nearly so due to a sensitivity to sound interrogation angle. Also, the mechanical properties across the boundary are similar, resulting in weak echoes.

One can get an estimate of the location of the adventitia-media boundary by observing the end of the echoes from this boundary and subtracting an approximate echo pulse length; although this depends on echo strength and system gain setting. As disease develops, and the intima thickens, it may be possible to see a rougher media-intima interface, and the actual intima-blood interface, if the echoes from within the intima are not particularly strong. With significant lesions present, a close estimate of the intima-blood boundary can be made by marking the end of the echoes from this boundary and again subtracting the echo duration.

In summary, when sound travels from outside to inside of the arterial wall, only the intima-lumen boundary (boundary 3) is well defined although it may often be invisible or nearly so due to similar mechanical properties across the boundary and sensitivity to angle. With disease, it is more readily seen and inability to visualize tends to suggest absence of disease. With significant disease, the intima-blood boundary may be approximated by identifying the bright-dark transition after this echo. Similarly, the adventitia-media boundary (boundary 2) may be approximated by identifying the correct bright-dark transition.

6.4.6 Effects of Arterial Geometry

> 6.4.6.1 Transverse Cross-Section.

The transverse cross-section of a vessel segment which is nonbranching is normally considered to be nearly circular. However, the high sensitivity to interrogation angle of boundaries 3 and 4 in B-mode images can result

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in a high frequency of invisible boundaries when opposite sides of the artery differ only a few degrees from being parallel. For example, if the blood-intima boundary on the far wall is visualized, there is a good chance that the intima-blood boundary on the near wall will be invisible and vice versa. Rough boundaries, such as the media-adventitia boundary on the far wall (boundary 5) and the adventitia-media boundary on the near wall (boundary 2), are relatively insensitive to these deviations from circular cross-section and are more often visualized.

6.4.6.2 Longitudinal Cross-Section (Curvature)

In a similar manner, if the artery curves within the scan plane, or bends outside of the scan plane, there may be only a small segment of (smooth-weak) boundaries which satisfy the sound angle requirement at one time. Consequently, unless a segment is very straight, only a small portion of a boundary such as the far wall blood-intima boundary will be visible. The rougher boundaries are not as sensitive to curvature, and are visualized more frequently.

6.4.7 Effects of Blood Flow and Respiration

Arterial geometry may be altered during both the cardiac and respiratory cycles by the regular changes in blood pressure during systole, diastole and respiration. Some interfaces may be visualized during part of the cardiac cycle and not at others, particularly smooth-straight- weak interfaces. Capturing such frames at systole or diastole must contend with these problems. <u>Careful attention should be paid to wall motion in</u> <u>attempting to identify the several boundaries</u>.

6.4.8 Simple Arterial Models

An ultrasonic B-mode image of an artery differs significantly from an optical image of the same vessel. A significant amount of artifact (false or misleading information) is present in the B-mode image, and a reader must be aware of the fundamental limitations inherent in interpreting such images. In this section, several simple idealized models are discussed to help identify some of these situations. Readers should also refer to recent papers entitled, "Artifacts in Ultrasound Imaging" by Dr. F. W. Kremkau and "Intimal Plus Medial Thickness of the Arterial Wall: A Direct Measurement with Ultrasound Imaging" by Dr. P. Pignoli. Copies of these articles are included in Appendix 1.

In Figure 6.4.A. (Real Boundary), a sound pulse traveling from left to right and encountering a single boundary is considered. If the acoustic impedances of the two media are different, an echo arises and is received by the sending transducer. In Figure 6.4.A. (High Gain), the appearance of this single boundary on the B-mode image is illustrated when the ultrasound system gain is high. A "literal" interpretation of this B-mode image would lead one to believe that a thin "layer" (the bright region) of material was present in the path of the ultrasound beam; however, in reality only one boundary is present. The apparent thin "layer" arises because of the finite time duration of the ultrasound pulse which is launched from the transducer. The apparent thickness of this "layer" has

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Figure 6.4.B Idealized B-mode Image of Two Boundaries

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Figure 6.4.C Idealized B-mode Image of Boundaries Simulating Arterial Walls



Figure 6.4.D Idealized B-mode Image of Boundaries Simulating Arterial Walls

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no physical relationship to the dimensions of the boundary. The real information presented in this image is the location of the boundary on the left side of the thin "layer".

In Figure 6.4.A. (Low Gain), the appearance of this single boundary model on a B-mode image is illustrated when the ultrasound system gain is low. Note that the thin "layer" is now less thick than in Figure 6.4.A. (High Gain). The left side, i.e., the location of the boundary of this thin "layer", is essentially at the same location. The right side, however, has moved substantially, suggesting an apparent decrease in thickness of this boundary, when in fact, the boundary has not changed. Thus <u>gain</u> settings do affect the ultrasound echo duration significantly, but do not alter position of the left boundary in the B-mode image. <u>Measurements</u> <u>made on the left side of a boundary are essentially gain (brightness)</u> independent.

Figure 6.4.B.(Real Boundaries) shows a sound pulse again moving from left to right, now through two simple boundaries. With high gain setting, the B-mode image arising from each of these boundaries is shown in Figure 6.4.B.(High Gain). If the relative strength of the echoes at the two boundaries is different, the effective differences in pulse durations will make the corresponding thin "layers" appear to have different apparent thicknesses. To measure the distance between the boundaries on the B-mode image, the left side of each thin "layer" is located and the measurement of the distance is made between those two lines. As seen in Figure 6.4.B.(Low Gain), the distance between these two lines is essentially unchanged when the system gain is lowered even though the apparent thicknesses of the thin "layers" has been reduced. Consequently, <u>separation distances between real boundaries measured from B-mode images are essentially independent of system gain.</u>

In Figure 6.4.C. (Real Boundaries), two sets of three boundaries are shown to simulate a simple interface model of two normal "arterial walls" consisting of a relatively thick "media", a relatively thin "intima" and a homogeneous "adventitia".

With high gain, the corresponding B-mode image is shown in Figure 6.4.C. (High Gain). Note that the interfaces of the "intima" are so close that the pulse length of the ultrasound system prevents them from being resolved. The greater thickness of the dark region, i.e., "media", however, permits this region to be identified in this interface model of the left wall.

On the right wall, the distance between the "intimal" boundary and the "media-adventitia" boundary is clearly delineated, and the thickness defined by these interfaces is readily measured on this wall. When the gain is lowered, these two distances are not significantly altered as shown in Figure 6.4.C. (Low Gain).

If we add to this simple interface model a relatively homogeneous "adventitia", the boundary between the "adventitia" and "media" on the left wall is obscured by echoes arising within the "adventitia", adjacent to the "media" boundary. This is illustrated in Figure 6.4.D. When this occurs, direct measurements of the "media" thickness on the left side are

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no longer possible. The "intima plus media thickness" on the right side can, however, be measured as shown previously in Figure 6.4.C.

In general, echoes arising within the adventitial tissues are relatively strong and remain bright when the system gain (brightness) is dramatically reduced.

THE SPECIFIC BOUNDARIES, LABELED BY 2, 3, 4 and 5 ON FIGURE 6.4.D. (High Gain) ARE THE ONES TO BE IDENTIFIED AND MEASURED ON EACH OF THE IMAGE FRAMES SELECTED.

Please note that while boundary 3 is actually located at the dark-tobright (left side) transition of the echo shown, the bright-to-dark (right side) transition marked 3, permits a better determination of the near wall (intima plus media) thickness for a wide range of arterial conditions.

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6.5 Identification of Principal Boundaries from the B-mode Images

Representative B-mode images of the carotid and popliteal arteries are shown in the figures labeled 6.5 (A-N). The location (or estimate) of each of the four boundaries (2,3,4 and 5) within the middle lOmm of the image is sketched in the enlarged second image of each pair. This is the segment which is read and which has the least geometric image distortion.

Beginning readers should carefully study these figures before beginning the reading process. Particular attention should be paid to the identification of these boundaries when lesions are present. <u>Wall motion</u> is an important tool which should be routinely used to identify the important wall boundaries. Individual image frames recorded between diastole and systole should be carefully analyzed to clearly distinguish between vein wall and artery wall, to select the frame-closest to systole, and to identify artifacts which are clearly not associated with the principal boundaries being read. Images having unusual features (e.g. boundaries which are difficult to identify and possible artifacts) should be discussed with the chief reader before performing the measurements. If the reader deems it necessary, the video cassette tape may be reviewed after reading an image.

6.5.1 Exercise for Reading B-Mode Image of Right Common Carotid: Figures 6.5.A(1) and 6.5.A(2)

<u>Site</u>: Right Common Carotid Artery

Anterior Wall Depth: X = 1.2cm

Posterior Wall Depth: X = 2.2cm

<u>Cursor</u>: The cursor is correctly placed at y = +0.3 cm. This is the origin of the bulb.

<u>Anatomical Landmark</u>: The origin of the bulb is clearly visible at y = +0.3cm. This is the correct vertical placement of the image since it positions the area of measurement in the vertical center of the screen.

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Figure 6.5.A(1) B-mode Image of Right Common Carotid

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<u>Posterior Wall</u>: B4 is clearly visible from y = -0.3cm to y = +0.1cm and then again at y = +0.2cm. This interface is fairly distinct and continuous except for the gap which appears between y = +0.1cm and y =+0.2cm. B5 is also fairly distinct and continuous and is identified with relative confidence from y = -0.8cm to y = +0.3cm. Although there are some diffuse echoes immediately to the left of B5, a "dark" to bright transition can be seen and indicates the location of B5. These diffuse echoes also indicate the presence of non-homogeneous tissue located within the media.

Anterior Wall: B3 is visible in the range of y = -0.4cm to y = +0.3cm. Although it is not as smooth and distinct as B4, it can be identified with a fair amount of confidence. The bright to dark transition characteristics of B2 is clearly visible from y = -0.6cm to y = +0.3cm and B2 can be easily identified in this range.

Significant Artifact: There is an apparent gap in B4 located at approximately y = +0.3 cm. This does not represent discontinuity of the interface, but is an artifact which may be caused by a number of phenomena. For example, the characteristics of this image suggests that the gap may be due to mild shadowing arising from strong reflectors or scatterers located on the anterior wall.

6.5.2 Exercise for Reading B-Mode Image of Right Common Carotid: Figures 6.5.B(1) and 6.5.B(2)

<u>Site</u>: Right Common Carotid Artery

Anterior Wall Depth: X = 1.4cm

Posterior Wall Depth: X = 2.7cm

<u>Cursor</u>: The cursor is correctly positioned at y = +0.4 cm.

<u>Anatomical Landmark</u>: The origin of the bulb is visible in this image at the location of the cursor on the posterior wall. (The origin of the bulb can not be seen as well on the anterior wall.) The origin of the bulb is properly positioned so that the common carotid is in the middle third of the screen.

<u>Posterior Wall</u>: B5 is clearly visible from y = -1.0cm to y = +0.3cm. The thin, dark band to the left of B5 provides for a smooth, distinct interface, and measurements of this boundary can be made with relative confidence. B4 is also easily identified from y = -1.0cm to y = +0.3cm. This boundary is distinct and continuous, and measurements of B4 may confidently be made. In between B4 and B5 there appears to be some non-homogeneous structure which is producing echoes in this area. These echoes, which appear within the media (which is most often echo-free), suggests that the instrument gain may have been relatively high. Another possibility is that the intima is beginning to thicken.

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Figure 6.5.B(1) B-mode Image of Right Common Carotid

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Figure 6.5.C(1) B-mode Image of Right Common Carotid

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<u>Anterior Wall</u>: B2 is clearly visible from y = -1.0cm to y = +1.0cm, the entire length of the artery. This is a very good interface since rarely will a boundary be so clear and continuous. The absence of a dark band to the right of B2 makes it difficult to make confident measurements of B3. However, by turning down the monitor brightness, B3 may be identified in the range from y = -1.0cm to y = -0.1cm. The most confident area of measurement would be at y = -0.2cm where B3 appears the brightest. The diffuse echoes which appear within the media in the lower half of the image are similar to those in the posterior wall media and may be explained in a like manner (for explanation, see Posterior Wall).

Significant Artifact: B3 only appears in the lower half of the image which might suggest that there is no intima-lumen interface in the region above y = -0.1cm. B3 is probably in that portion of the artery even though it doesn't appear on the image. The "missing" interface may be the result of a slight artery curvature which would cause echoes to be bounced off the boundary in many different directions and missed by the signal receiving transducer.

6.5.3 Exercise for Reading B-Mode Image of Right Common Carotid: Figures 6.5.C(1) and 6.5.C(2)

<u>Site</u>: Right Common Carotid Artery

Anterior Wall Depth: X - 1.0cm

Posterior Wall Depth: X = 2.2cm

<u>Anatomical Landmark</u>: The origin of the bulb is not easily identified on the image. It should have been placed adjacent to the cursor at y = +0.5 cm.

<u>Posterior Wall</u>: Lesion appears to be present. B4 is clearly identifiable over y = -0.5cm to y = +0.5cm. The lesion occupying the region to the right of B4 contains much speckle texture. B5 is preceded by a dark band from y = -0.2cm to y = +0.5cm and is readily identified over this range. Reduction in brightness may help in identifying a more distinct dark to bright transition characteristic of B5.

<u>Anterior Wall</u>: B3 is not readily identifiable, probably due to improper alignment of the anterior wall with the ultrasound beam. B2 is fairly clear and should be marked with reduced brightness on the monitor. The structures appearing within the lumen are discussed below.

<u>Significant Artifacts</u>: The diffuse echoes appearing within the lumen to the right of B2 may be reflections from the lateral walls due to misalignment of the ultrasound or significant disease as suggested by the lesion on the posterior wall. Careful viewing of adjacent frames in the cardiac cycle is necessary to confirm an interpretation.

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6.5.4 Exercise for Reading B-Mode Image of Right Common Carotid: Figures 6.5.D(1) and 6.5.D(2)

<u>Site</u>: Right Common Carotid Artery

<u>Anterior Wall Depth</u>: X = 1.5cm

Posterior Wall Depth: X = 2.8cm

<u>Cursor</u>: In this image the cursor is placed almost in the vertical center of the screen at X = 1.2 cm. This is an incorrect placement. The cursor should be placed at the origin of the bulb which appears to be located at y = +0.3 cm.

<u>Anatomical Landmark</u>: The origin of the bulb is visible and is located at approximately y = +0.3 cm. This is an ideal vertical placement as it positions the area of measurement in the middle third of the screen.

<u>Posterior Wall</u>: B4 is identifiable from y = -0.1cm to y = +0.2cm and is fairly smooth and continuous except for the gap which is present in the middle third of the screen. B5 is not quite as smooth and distinct as B4, but can still be identified with relative confidence from y = -0.7cm to y = +0.3cm. Turning down monitor brightness can help in identifying a more distinct dark to bright transition characteristic of B5.

Anterior Wall: The anterior wall is not very clear, and the measurements taken there will not have a high quality rating. Because of the diffuse patches of echoes preceding B3, there is no dark, echo-free band, and identification of B3 and B2 is difficult. Nevertheless, B3 may be identified in two regions along the anterior wall from y = -1.0cm to y = -0.3cm and from y = +0.2cm to y = +0.7cm. Lowering of the monitor brightness may eliminate a significant amount of the diffuse echoes between B2 and B3 and make identification of these interfaces easier.

Significant Artifact: Speckle adds apparent texture to both walls, particularly the posterior wall in the area of B5. The "gap" in B4 is either a result of transducer misalignment or shadowing from strong reflectors on the anterior wall. The echoes in the region between B2 and B3 seem to indicate heterogeneous tissue in the media; however, the echoes are probably the result of ultrasound beam-arterial wall misalignment.

6.5.5 Exercise for Reading B-Mode Image of Right Common Carotid: Figures 6.5.E(1) and 6.5.E(2)

<u>Site</u>: Right Common Carotid Artery

Anterior Wall Depth: X = 2.0cm

Posterior Wall Depth: X = 2.9cm

<u>Cursor</u>: Improperly placed. It should be located at the origin of the bulb located at y = +0.5 cm.

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Figure 6.5.D(1) B-mode Image of Right Common Carotid ARIC PROTOCOL 6. Part B: Ultrasound Reading. Version





Figure 6.5.E(1) B-mode Image of Right Common Carotid

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<u>Anatomical Landmark</u>: The origin of the bulb is located at y = +0.5 cm. This is the proper vertical screen placement.

<u>Posterior Wall</u>: B4 can be easily identified from y = -0.5cm to y = 0.0cm. There is a smooth, distinct dark to bright transition in these ranges. In the interval from y = 0.0cm to y = +0.4cm, the dark to bright transition is not as distinct. In this range, B4 appears to have a few gaps in it; however, measurements could still be made with a fair confidence. Along the interval y = -0.2cm to y = +0.4cm, B5 is easily identified by the continuous dark band following B4 and the distinct dark to bright transition.

Anterior Wall: B3 can be identified from y = -0.5cm to y = 0.0cm. Along this interval, there are diffuse bright patches within the dark band preceding B3, but this interface may be identified with confidence by lowering the monitor gain. B3 may be identified along the interval y =0.0 cm to y = +0.3 cm, although the dark to bright transition is not as distinct. B2 can be identified from y = -0.5 cm to y = +0.8 cm with a fair amount of confidence and with the aid of low gain. Although the bright to dark transition in this range is not as distinct, it is adequately visible.

<u>Significant Artifact</u>: The diffuse patches within the lumen from X = 2.0 cm to X = 2.5 cm are the result of reverberations from the bright reflectors to the left of this area. The apparent gaps in B4 at y = 0.0 cm to y = +0.4 cm probably do not represent actual "holes" in the interface, but are probably the result of a misaligned transducer. Gain settings could be considerably lower and if so, would probably reduce the multiple reverberations present within the lumen.

6.5.6 Exercise for Reading B-Mode Image of Right Common Carotid: Figures 6.5.F(1) and 6.5.F(2)

<u>Site</u>: Right Common Carotid Artery

Anterior Wall Depth: X = 1.2cm

Posterior Wall Depth: X - 2.0cm

<u>Cursor</u>: The cursor should be located at y = +0.5 cm, rather than y = +0.8 cm.

<u>Anatomical Landmark</u>: Origin of the bulb is not identifiable. This suggests an interrogation angle other than the optimal (anatomical) angle, most probably the anterior angle. Origin of the bulb should be located at y = +0.5cm and marked at this vertical location by the sonographer.

<u>Posterior Wall</u>: B4 is well visualized from y = -0.5cm to y = +0.5cm. The dark band to the right of B4 is moderately good and permits B5 to be easily identified over this interval. By reducing the brightness of the image monitor when marking B5, this boundary will be more clearly delineated. Sonographer alignment is excellent for the posterior wall.

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Figure 6.5.F(1) B-mode Image of Right Common Carotid

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Anterior Wall: B3 is well visualized from y = -0.5cm to y = 0.0cm. Above this segment, reasonable estimates of the location of B3 can also be made. The ark band which frequently appears to the left of B3 is fairly clear from y = -0.5cm to y = 0.0cm, but becomes diffuse when moving upward. B2 can be approximated fairly well from y = -0.5cm to y = 0.0cm, but becomes less certain as one moves upward. The anterior wall <u>appears</u> to be considerably thicker than the posterior wall.

<u>Significant Artifacts</u>: Diffuse bright regions located within the lumen between y = 0.0 cm and y = +0.8 cm and near y = -1.0 cm are due to weak reflections of side lobes of the ultrasound beam from the lateral walls of the vessel.

Speckle adds apparent texture to both the posterior and anterior walls.

6.5.7 Exercise for Reading B-Mode Image of Right Common Carotid: Figures 6.5.G(1) and 6.5.G(2)

<u>Site</u>: Right Common Carotid Artery

Anterior Wall Depth: X = 2.5cm

Posterior Wall Depth: X = 3.5cm

<u>Cursor</u>: The cursor is correctly positioned at Y = +0.5cm.

<u>Anatomical Landmark</u>: The origin of the bulb in this image is not distinct, but it appears to be located slightly below the cursor position at y = +0.1cm. The fact that the landmark is not clearly visible suggests that the transducer was not held at the optimal angle.

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<u>Posterior Wall</u>: B5 is clearly visible from y = +1.0cm to y = -1.0cm. Although there is not an echo-free region preceding B5, there is a distinct "dark" to bright transition making it possible to make measurements of B5 with confidence. In this image, the intima + media region, which is typically dark, is filled with echoes -- some of which are fairly bright. Although there is not a thin, bright line representative of B4, B4 can be identified as the left edge of this echogeneous region from y = +0.8cm to y = -1.0cm. These echoes between B4 and B5 and the fact that the distance between B4 and B5 appears greater than usual suggests the presence of material not typically found within the artery wall. For example, the image may indicate some beginning stages of disease.

Anterior Wall: B2 and its characteristic bright to dark transition is clearly visible from y = +0.6 cm to y = -1.0 cm. Measurements of this interface may be made with confidence. There is a distinct, bright line and a dark to bright transition representative of B3 from y = +0.6 cm to y = 0.0 cm. The brightness of this interface compared to typical images of B3 is the result of some apparently highly reflective matter within the intima layer. There is also much echogenic matter between B2 and B3 within the intima + media layer. Measurements for B3 may be made on the right edge of this echogenic layer from y = 0.0 cm to y = -1.0 cm. In this region, measurements of B3 are made on the right side of an echo because

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Figure 6.5.G(1) B-mode Image of Right Common Carotid Version 1.0, 1/89 ARIC PROTOCOL 6. Part B: Ultrasound Reading.



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of the absence of the typical dark to bright transition. The highly reflective nature of the tissues in this wall suggest (as was the case for the posterior wall) the possibility of beginning disease in this artery.

6.5.8 Exercise for Reading B-Mode Image of Right Internal Carotid: Figures 6.5.H(1) and 6.5.H(2)

<u>Site</u>: Right Internal Carotid Artery

Anterior Wall Depth: X = 1.7cm (at y = 0.0cm)

<u>Posterior Wall Depth</u>: X = 2.4cm (at y = 0.0cm)

<u>Cursor</u>: The cursor is properly placed at the superior arc of the flow divider located at y = -0.5 cm.

<u>Anatomical Landmark</u>: The superior arc of the flow divider is visible and located at y = -0.5cm. This is the proper vertical placement.

<u>Posterior Wall</u>: The internal carotid begins at y = -0.5cm and extends upward. Although the posterior wall is visible from y = -0.5cm to y = 0.0cm, the characteristic bright line for B5 is not present. Lowering the monitor brightness may give a smooth dark to bright transition from which a few measurements of B5 may be made. There is no B4 visible within the area of measurement except at the vertical position of the cursor, y = -0.5cm. B4 is visible below the area of measurement because of an apparent lesion which is located just below the tip of the flow divider in the bulb. It should be noted that cases may arise where lesions appear outside the site of measurement as it does in this image.

Anterior Wall: As with B5, there is not a distinct bright line representative of B2. There is a rough boundary which separates the anterior wall from the lumen and measurements of B2 may possibly be made along this interface from y = -0.5cm to y = +0.1cm. These measurements, however, may be of a low confidence level. B3 is not visible in this image of the interval.

Significant Artifact: Speckle adds much texture to both B2 and B5. Both walls appear to be missing above y = 0.0 cm. This is because the artery begins to curve away from the skin surface at this point, and sound is greatly attenuated in this region.

6.5.9 Exercise for Reading B-Mode Image of Left Common Carotid-Posterior: Figures 6.5.1(1) and 6.5.1(2)

<u>Site</u>: Left Common Carotid-Posterior

Anterior Wall Depth: X = 1.5cm

Posterior Wall Depth: X = 2.5cm

<u>Cursor</u>: The cursor's vertical screen placement is correct at y = -0.5 cm.

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Figure 6.5.H(1) B-mode Image of Right Internal Carotid ARIC PROTOCOL 6. Part B: Ultrasound Reading. Version 1.0, 1/89





Figure 6.5.I(1) B-mode Image of Left Common Carotid-Posterior ARIC PROTOCOL 6. Part B: Ultrasound Reading. Version 1.0, 1/89



<u>Anatomical Landmark</u>: The origin of the bulb is visible not in the anterior wall, but on the posterior wall. The origin appears to be located at y = -0.2 cm.

<u>Posterior Wall</u>: B5 is clearly visible from y = -0.4cm to y = +0.4cm. Within this range, the interface is distinct and continuous, and measurements by be made with confidence. Above the range B5 is less distinct; (y = +0.4cm to y = +0.8cm); however, measurements may still be made. B4 is also visible, although this boundary is not as distinct. B4 could be identified from y = 0.0cm to y = +0.4cm.

Anterior Wall: B2 can be identified from y = -0.5cm to $y = \pm 0.5$ cm. Although there is not a continuous dark bank to the right of B2, there is a distinct bright to "dark" transition along the interface and these measurements may be made with a fair amount of confidence. B3 is visible, although not continuous, from y = -0.7cm to $y = \pm 0.3$ cm. In the middle of the image, B2 and B3 appear to be adjacent (no dark band between). Turning down the monitor gain may make it easier to identify B3 at this point.

<u>Significant Artifact</u>: There appear to be gaps in B3, although this is probably not the case. This is probably the result of slight angle changes in the transducer. At the top of the image in the middle of the artery is an echo which suggests that there is some structure within the lumen. This is probably caused by misalignment of the transducer.

6.5.10 Exercise for Reading B-Mode Image of Left Common Carotid-Optimal: Figures 6.5.J(1) and 6.5.J(2)

<u>Site</u>: Left Common Carotid-Optimal

Anterior Wall Depth: X = 1.5cm

Posterior Wall Depth: X = 2.5cm

<u>Cursor</u>: The cursor is correctly placed in the lower third of the screen at y = -0.5 cm, and ideally positioned in the center of the artery.

<u>Anatomical Landmark</u>: The origin of the bulb is visible on the posterior wall and appears to be located at y = -0.2cm. Ideally, it should be placed a little lower (y = -0.5cm); however, the vertical screen placement is adequate for proper measurement of the common carotid artery.

<u>Posterior Wall</u>: B5 is clear and distinct and may be easily identified from y = +1.0cm to y = -0.3cm. Below this region, from y = -0.3cm to y = -1.0cm, B5 is slightly visible, and with the aid of low monitor gain, identification of the interface may be made in this area as well. Although there isn't a characteristic dark band to the left of the boundary, B5 is adequately bright and distinct so that confident measurements may be made. B4 is clearly visible and, except for an apparent gap (located at y = -0.3cm), it is smooth and continuous. Confident measurements may be made of B4 from y = +1.0cm to y = -0.6cm.



Figure 6.5.J(1) B-mode Image of Left Common Carotid-Optimal ARIC PROTOCOL 6. Part B: Ultrasound Reading. Version 1.0, 1/89



The echoes which appear within the media suggest that the sonographer's gain may have been relatively high. (Structure within the media is being picked up by the ultrasound system because of the higher gain.)

Anterior Wall: A thin bright line is visible from B2 from y = +0.6cm to y = +0.1cm and again from y = -0.2cm to y = -0.5cm. Above, below, and in between these two regions, the location of B2 is unclear. Because of the apparent "smear" of B2, measurements of the interface may be made more confidently by lowering the monitor gain. Although B3 appears jagged and discontinuous, measurements may be made with a fair amount of confidence from y = +0.6cm to y = -0.5cm.

Significant Artifact: The apparent gaps in B2, B3 and B4 are probably the result of slight angle changes between the transducer beam and the artery wall.

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6.5.11 Exercise for Reading B-Mode Image of Left Carotid Bulb: Figures 6.5.K(1) and 6.5.K(2)

<u>Site</u>: Left Carotid Bulb

Anterior Wall Depth: X = 0.8cm

Posterior Wall Depth: X = 1.8 cm

<u>Cursor</u>: The cursor is correctly placed at y = -0.4cm. Anatomically, it is positioned at the superior arc of the flow divider. The cursor's vertical position on the screen is ideal since it locates the area of measurement in the middle third of the screen.

<u>Anatomical Landmark</u>: The tip of the flow divider is clearly visible and is located at y = -0.4 cm.

<u>Posterior Wall</u>: B5 is not very distinct; however, turning down the monitor brightness may aid in making measurements from y = -0.3 cm to y = +0.5 cm. B4 is not visible in this image.

Anterior Wall: B2 can be fairly well identified at the point of a bright to dark transition from y = -1.0cm to y = +0.6cm. As with B5, turning down the brightness may cause B2 to appear smoother and more distinct and allow measurements to be made with a greater degree of confidence. B3 can not be seen in this image.

<u>Significant Artifact</u>: Speckle, as well as the curvature of the bulb, add apparent texture to both B2 and B5.

6.5.12 Exercise for Reading B-Mode Image of Left Carotid Bulb: Figures 6.5.L(1) and 6.5.L(2)

<u>Site</u>: Left Carotid Bulb

<u>Anterior Wall Depth</u>: X = +0.5cm

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Figure 6.5.K(1) B-mode Image of Left Carotid Bulb ARIC PROTOCOL 6. Part B: Ultrasound Reading. Version





Figure 6.5.L(1) B-mode Image of Left Carotid Bulb ARIC PROTOCOL 6. Part B: Ultrasound Reading.



Posterior Wall Depth: X = +2.2cm

<u>Cursor</u>: The cursor is located at a correct vertical position of y = -0.5 cm, at the tip of the flow divider.

<u>Anatomical Landmark</u>: The tip of the flow divider is visible and is located vertically at y = -0.5cm and horizontally at X = 2.0cm.

<u>Posterior Wall</u>: B5 can be measured with relative confidence along two different intervals: from y = +1.0cm to y = +0.3cm and from y = -0.1cm to y = -0.8cm. Measurement along these intervals is aided by turning down monitor brightness. In the center of the image, from y = +0.2cm to y =-0.1cm, the posterior wall is not visible because of an artifact known as shadowing. B4 is visible from y = +0.2cm to y = +0.7cm. Although there is not a distinct, thin echo for B4, the band of low level echoes preceding B5 suggests the presence of material different from the lumen and it is possible to measure B4. The overall image gain appears low, and because these low level echoes are visible, it suggests the presence of something abnormal (i.e., beginning lesion, fatty streak, etc.). In the lower portion of the image, B4 is not clearly visible.

Anterior Wall: There is a thin, bright echo followed by a slightly visible bright to dark transition representing B2. By turning down the monitor brightness, this bright to dark transition may be more visible and B2 may be identified from y = +1.0cm to y = -0.7cm. As with the posterior wall, the typically dark band between B2 and B3 (or B4 and B5 on the posterior wall) contains some low level echoes suggesting the presence of matter not normally visible within this intima + media layer. Even though these low level echoes are present, a dark to bright transition for B3 is still slightly visible from y = +1.0cm to y = +0.2cm. In the center of the image from y = +0.2cm to y = -0.1cm, an apparent lesion and its echogenic substance make it difficult to visualize a dark to bright transition for B3. In this area, B3 should be marked just to the right of the lesion as this is a good approximation of the intima-blood interface. Below the point y = -0.1cm, B3 cannot be visualized.

Significant Artifact: This image is a good example of an artifact known as shadowing. The posterior wall appears to have a large gap in it making it impossible to measure B4 and B5 in that particular area. Shadowing is typically the result of highly reflective or absorptive tissues through which very little or no sound passes. The effect is a blocking out or shadowing of any subsequent tissues in that path of the sound. In this case, the lesion on the anterior wall has apparently reflected (or absorbed) most of the sound energy so that no sound reaches the posterior wall. Therefore, neither the posterior wall, nor the tissue following it, are visible. Shadowed areas often indicate the presence of possible lesions preceding them, but nothing can be concluded about the shadowed tissues. 6.5.13 Exercise for Reading B-Mode Image of Left Internal Carotid: Figures 6.5.M(1) and 6.5.M(2)

<u>Site</u>: Left Internal Carotid Artery

Anterior Wall Depth: X - 1.6cm

Posterior Wall Depth: X = 2.7cm

<u>Cursor</u>: The cursor is improperly placed. It should be placed at the superior arc of the flow divider which is located at y = +0.4 cm.

<u>Anatomical Landmark</u>: The tip of the flow divider is clearly visible at y = +0.4 cm. This is the proper vertical screen placement.

<u>Posterior Wall</u>: B4 is visualized from y = -0.5cm to y = 0.0cm. The dark band following B4 is distinct, and therefore, permits B5 to be easily identified from y = -0.5cm to y = +0.4cm. Lowering the monitor brightness will eliminate the fuzziness in the dark band from y = -0.5cm to y = -0.1cm, making it even easier to identify B5.

Anterior Wall: B3 is not easily identified. Although some diffuse patches appear just to the left of the artery lumen, there is no distinct dark band following B2. Therefore, B3 could not be identified with much confidence. It should be noted, however, that turning down the monitor brightness may eliminate some of the diffuseness leaving brighter portions of B3 which may then be identified. B2 is easily identified from y =-0.3cm to y = +0.4cm. Just above and below this range, it may be identified fairly well by turning down the monitor brightness.

<u>Significant Artifact</u>: The weak echoes appearing within the lumen around X = 2.0 cm are artifact resulting from multiple reverberations between the two bright lines located at X = 1.3 cm and X = 2.7 cm.

6.5.14 Exercise for Reading B-Mode Image of Popliteal Artery: Figures 6.5.N(1) and 6.5.N(2)

<u>Site</u>: Popliteal Artery

Anterior Wall Depth: X = 1.8cm

Posterior Wall Depth: X = 2.5cm

<u>Cursor</u>: The cursor is properly placed at approximately y = 0.0 cm, the vertical center of the image. It is also ideally positioned in the center of the artery.

<u>Anatomical</u> <u>Landmark</u>: Not applicable in the popliteal artery.

<u>Posterior Wall</u>: B5 can be seen fairly well from y = -0.7 cm to y = +0.2 cm.

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Figure 6.5.M(1) B-mode Image of Left Internal Carotid ARIC PROTOCOL 6. Part B: Ultrasound Reading. Version 1.0, 1/89






Although this boundary is rather rough in places (i.e., in the region located in the center of the image), measurements of B5 may be made with a fair amount of confidence. Lowering the monitor gain may make identification of the interface easier. B4 is visible from y = -0.8cm to y = -0.4cm. Within this range, B4 is rather smooth and continuous. Above this range, B4 is not visible.

Anterior Wall: The anterior wall interfaces are not as easily identifiable as the posterior wall. It is not immediately clear which lines represent B2 and B3. There is a bright line characteristic of B2 located from y =-0.8cm to y = -0.5cm and again at y = -0.2cm. Turning down the monitor gain may result in a more distinct bright to dark transition in this region, and if so, a few measurements of B2 may possibly be made. B3 is also hard to identify primarily since there is no dark band preceding a thin bright line, which usually identifies B3. However, there is a thin, bright line from y = -0.5cm to y = -0.2cm which resembles B3 and perhaps measurements can be made within this range.

<u>Significant Artifact</u>: Speckle adds apparent texture to B5 and B2. B3 and B4 appear to be missing in certain areas. This latter phenomena is due to the curvature of the artery.

6.6 Calibration of Image Pixel Size

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At the beginning of each participant study, a calibration frame is read. An example is shown in Figure 6.6.A.

The length of the cursor line in millimeters is given on the upper right portion of the image. By successively placing the crosshairs at first the left and then the right ends of the cursor, the number of pixels in the image corresponding to 20mm is determined. Typically, the calibration factor is one pixel = 0.067mm. This factor is automatically calculated in the computer and used in computing arterial wall dimensions.

6.7 Selection of Image Frames

Twenty-four frames of each view at each arterial site are stored on the optical disk. The frame to be read is selected by the reader as the systolic frame (largest lumen diameter) which best visualizes the four principal boundaries. These boundaries are then marked as described in the next section. Be certain to use <u>wall motion</u> as a tool in convincingly identifying these arterial wall boundaries.

6.8 Placement of Crosshairs on Principal Boundaries

A crosshair is used on each of the identifiable boundaries to mark its location at 11 specific locations as shown in Fig. 6.8.A. The coordinates of these locations are stored in the central computer and used to compute dimensions of arterial lumens and wall layers. A maximum of 44 locations is recorded if all boundaries are clearly visible. In many cases, between 25 and 35 locations are the number actually marked, due to lack of sufficient information in the image.







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Figure 6.8.A Placement of Crosshairs on B-mode Image Boundaries ARIC PROTOCOL 6. Part B: Ultrasound Reading. Version 1.0, 1/89

Based upon the discussion in section 6.4., if a sonographer has made every effort to visualize the four boundaries being measured, missing data are generally (the shadowing artifact being the exception) an indication of the absence of disease within the arterial walls. Whenever data are missing due to shadowing, this should be noted in the comments discussed in the next section. An example of shadowing is given in figure 6.5.M.

6.9 Subjective Comments on the B-Mode Image Frames

Following each frame selected for measurement from the optical disc, readers record the following information: (to be stored along with other computer data on each frame.)

- 1. Their reader identification number
- 2. Presence of lesions (within the measurement area)
- 3. Presence of shadowing (within the measurement area)
- 4. Alert value (lumen diameter ≤ 2 mm) present
- 5. Quality of each interface
 - 0 not readable
 - 1 poor
 - 2 fair
 - 3 good
 - 4 excellent

The menu is shown below:

Reader Number Lesion? Y or N _____ Shadow? Y or N _____ Alert Value? Y or N _____ Quality of interfaces: ______ Correct? Y or N ______ (Any information entered from the menu may be corrected if the response is NO; a YES response routes this information to computer memory.)

This information that is entered by the reader is shown in Figure 6.9.A along with other data that is stored in the computer.

6.10 Procedure for Reporting Alert Values

Procedures for reporting possible alert values to the Ultrasound Director at the field centers are initiated when the minimum residual lumen in the carotid artery is $\leq 2mm$. Identification of these possible alert values is carried out by the sonographers performing the scans at the field centers or by the readers at the Ultrasound Reading Center. When a field center sonographer suspects one or more sites on the carotid artery meet the possible alert value criterion, the back-up copy of the participant's tape is sent to the field center's Ultrasound Director for reading, in addition to the regular data transfer procedures to the Ultrasound Reading Center.

When an Ultrasound Reading Center reader measures or suspects that the distance between boundaries 3 and 4 is $\leq 2mm$ (readings at the URC are limited to ARIC protocol sites), the Chief Reader is notified immediately to visually confirm the reading. The alert value variable in the database

ARIC PROTOCOL 6. Part B: Ultrasound Reading.



Figure 6.9.A B-Mode Image Data Stored in Computer ARIC PROTOCOL 6. Part B: Ultrasound Reading.

(see Section 6.9) is recorded as "Yes" for storage in the ultrasound database. An electronic mail message is sent to the field center the same day identifying the ARIC participant and the site(s) in the carotid artery in which a possible alert value(s) has been measured or is suspected. The participant's ARIC ID and the date of the e-mail alert value transmission to the field center is logged in the URC Alert Value Log for future reference.

Upon receipt of an e-mail message of a possible alert value, the procedures in the field center become identical to those followed if an alert value is suspected by the sonographer. The resolution of possible alert values is the function of the field centers; at the recommendation of the field center Ultrasound Director in accordance with local community standards, a statement documenting the possible abnormal findings of the ultrasound scan may be included in the Summary of Results for ARIC Participants and their Physicians. Field centers keep a log of actual alert values.

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REVIEW

Artifacts in Ultrasound Imaging

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Ultrasound imaging artifacts of acoustic origin relating to resolution, propagation path, and attenuation are reviewed. Lateral and axial resolution limitations are artifactual in nature since a failure to resolve means a loss of detail and two adjacent structures may be visualized as one. Apparent resolution close to the transducer (speckle) is not directly related to tissue texture but is a result of interference effects from the distribution of scatterers in the tissue. Reverberation produces a set of equally spaced artifactual echoes distal to the real reflectors. The mirror image artifact is the presentation of objects that are present on one side of a strong reflector, appearing on the other side as well. Shadowing and enhancement are useful artifacts for determining the nature of masses. Enhancement results from low attenuation objects in the sound path while shadowing results from strongly reflecting or strongly attenuating objects. Additional artifacts include section thickness, refraction, multipath, side lobe, grating lobe, focal enhancement, comet tail, ring down, speed error, and range ambiguity. (Key words: ultrasonography; artifacts; resolution; shadowing; enhancement; reverberation)

The word artifact comes from the Latin arte (by skill) and factum (to do). Webster's Ninth New Collegiate Dictionary states that the earliest recorded use of this word in English occurred in 1821. Definitions include 1) a characteristic product of human activity, and 2) a product of artificial character due to an extraneous agency. The use of the word in this review relates to the second definition. Imaging artifacts are display phenomena not properly representing the structures to be imaged. They are of various types, as follows:

- 1. acoustic: error in presentation;
- 2. optical illusion: error in perception;
- 3. anatomic: error in interpretation (often called a pitfall);
- 4. other: electrical noise, dust in photographic system, etc.

In this review, only artifacts of acoustic origin are

Table 1. Ultrasound Imaging Artifacts of Acoustic Origin

Resolution Group

- 1. Axial Resolution
- 2. Lateral Resolution
- 3. Speckle
- 4. Section Thickness

Propagation-Path Group

- 1. Reverberation
- 2. Refraction
- 3. Multipath
- 4. Mirror Image
- 5. Side Lobe
- 6. Grating Lobe

Attenuation Group

- 1. Shadowing
- 2. Enhancement
- 3. Refraction (Edge) Shadowing
- 4. Focal Enhancement

Miscellaneous Group

- 1. Comet Tail
- 2. Ring Down
- 3. Speed Error
- 4. Range Ambiguity

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discussed. These acoustic artifacts cause errors in presentation of anatomic structures. Some are useful and desirable while others are not. For example, enhancement beyond an echogenic fluid collection permits its true cystic nature to be appreciated. Automatic correction of this artifact would preclude perception of this important information and is, therefore, not desirable. The unde-

sirable artifacts that hinder correct interpretation must be avoided or at least recognized as such in order to make the correct diagnosis.

Acoustic artifacts in ultrasound imaging occur as presentations on the display that, with respect to the anatomy in question, are added (not real), are missing, or are of improper location, brightness, shape, or size. They result when the assumptions



Figure 3 (left). A pelvic cyst (C) showing internal section-thickness artifact (T) and distal enhancement (E). (Courtesy of J.J. Sivo, Yale-New Haven Hospital)

Figure 4 (right). Reverberation (R) and section-thickness artifact (T) in the bladder (B). (Courtesy of J.J. Sivo, Yale-New Haven Hospital)



Figure 5 (left). Short-range reverberation (R) from an air gun BB (B) adjacent to the testicle (T). (Courtesy of A.T. Rosenfield Yale University)

Figure 6 (right). Long-range reverberation causes bladder (B) to be imaged a second time (A).

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Figure 7. An echoic mass (M) in the liver is also artifactually represented (A) superior to the diaphragm. (Courtesy of J.J. Sivo, Yale-New Haven Hospital)

made by the ultrasound imaging instrument are incorrect and lead to errors in imaging. These assumptions include:

- 1. sound travels in straight lines;
- 2. echoes originate only from objects located on the transducer axis;
- intensity of returning echoes is directly related to the scattering strength of imaged objects; and
- distance is proportional to the round-trip travel time—13 microseconds per centimeter of depth.

Some artifacts are produced by improper equipment operation (e.g., improper transducer location or orientation information sent to the display) or settings (e.g., incorrect receiver compensation setting). Some are caused by improper scanning technique (e.g., allowing patient or organ movement during scanning with a static imaging instrument). These could be included in category 4 of the list above. Others are inherent in the ultrasound diagnostic method (such as categories 1 and 2 in the list above) and can occur even with proper equipment and technique. The acoustic artifacts reviewed here are of that nature. They are listed in table 1, grouped as they are considered in this review. The physical principles underlying the occurrence of these artifacts are presented elsewhere,¹ as are discussions of acoustic artifacts.¹⁻⁴

RESOLUTION GROUP

Spatial resolution limitations are artifactual in nature, since they cause closely spaced objects to appear merged together and tiny objects to be presented larger than they are. A sagittal scan of a normal liver is shown in figure 1. Axial resolution is seen to be relatively constant with depth. However, lateral resolution varies with depth, being optimum in the focal region of the transducer. Axial resolution is equal to half the pulse length and lateral resolution is equal to the pulse width (beam width) in the image plane. Since pulse width is normally larger than pulse length, axial resolution is better than lateral (fig. 2).

The apparently excellent resolution close to the transducer is artifactual in nature. This parenchymal echo pattern, normally interpreted to be "tissue texture," does not represent a one-to-one correspondence of scatterers to brightness dots, but rather patterns of constructive and destructive interference of returning echoes from a scatterer distribution in the interrogated tissue volume. This interference pattern, called acoustic speckle,⁵⁻⁹ is a major source of ultrasound image degradation. It can be viewed as a form of acoustic noise. Lack of correlation between apparent and actual resolution in an image has been shown to be caused by speckle.¹⁰ Smith and Lopez have shown that detection of high-contrast and low-contrast objects is limited by spatial resolution and image speckle, respectively.¹¹ Morrison et al. have described and explained speckle motion in real-time imaging.¹² This motion bears no simple relation to tissue or transducer motion and may be very misleading. Digital and photographic averaging¹³ and deconvolution¹⁴ have been used to reduce speckle and improve images.

The section thickness artifact within a pelvic cyst and the urinary bladder is shown in figures 3 and 4. This weakly echoic region might suggest the presence of solid material but is more likely artifact. It results from the finite width of the imaging pulse in the direction perpendicular to the scan plane. This produces an imaged section of tissue (through the scanning process) with some thickness, but the echoes in that slice are compressed into an infinitely thin slice for presentation. The artifactual region in this scan represents echoes received from the edge of the interrogated slice either toward or away from the viewer. Scattering from the cyst or bladder boundary there has been received and placed on the image (as if within the cyst or bladder). Goldstein and Madrazo described this artifact and demonstrated its effects in gallbladder, cysts, and ascites.¹³ Filling in of images of cysts^{16,17} and cardiac septal defects¹⁸ and mimicking of gall-

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Figure 8. A (*left*), an unusual presentation of mirror-image artifact around the diaphragm (D). The shape of the artifact (A) is not the same as that of the object (O) (probably bowel). The explanation of this result is shown in *B* (*right*). (Courtesy of J.J. Sivo, Yale-New Haven Hospital)

bladder sludge¹⁹ have been attributed to this artifact.

PROPAGATION-PATH GROUP

If two or more reflectors are encountered in the sound path, multiple reflections (reverberation)



Figure 9. Side lobe artifact (A) appears in a scan of a corpus luteal cyst but not in other scans of the same cyst. The reflector generating this artifact is likely bowel gas (G). (Courtesy of A. Carter, Yale University)

will occur. These may be sufficiently strong to be detected by the instrument and to cause confusion on the display. An example of this artifact in the urinary bladder is shown in figure 4. The internal echoes presented should not be there. They represent subsequent (later, presented deeper) echoes from traversing the path between two reflectors several times.¹ This results in additional reflectors that are not real being placed on an image. They will be placed behind the second real reflector at separation intervals equal to the separation between the first and second real reflectors. Each subsequent reflection is weaker than prior ones, but this will be at least partially compensated for by the compensation function (TGC) of the receiver. The first of the two reflectors is usually the transducer face. An exception to this, reverberation from within metal objects^{20,21} (fig. 5), is quite pronounced and makes them easy to locate and identify. They usually produce a series of closely spaced echoes because of their small dimensions and high sound speed. This has been called the 'comet-tail artifact" and is discussed in the "Miscellaneous Group" section. An extreme example of reverberation is shown in figure 6, where the urinary bladder is imaged twice.

Refraction can cause a reflector to be improperly positioned on the display. The change in direction of sound as it crosses a boundary where a speed change occurs causes lateral error in reflector positioning.¹ Such improper lateral repositioning of structures has been demonstrated in phantoms.²² Several effects of in vivo refraction have been reported.²³⁻²⁹ KREMKAU AND TAYLOR-JOURNAL OF ULTRASOUND IN MEDICINE



Figure 10 (*left*). Shadowing (S) from a gallstone (G) and enhancement (E) from the gallbladder. (Courtesy of J.J. Sivo, Yale-New Haven Hospital)

Figure 11 (below, left). Scattering from particles in hematocele (H) simulates a solid mass surrounding the testicle (T). Shadowing from the testicle (or enhancement from hematocele) indicates the cystic nature of this collection.

Figure 12 (*below*, *right*). Edge shadowing (S) from the gallbladder (G). (Courtesy of J.J. Sivo, Yale-New Haven Hospital)





The term, multipath, describes the situation in which the paths to and from a reflector are different.¹ The longer path that the sound takes traveling to or from a reflector results in an axial error in reflector positioning (increased range). Refraction and multipath positioning errors are normally relatively small and contribute to general degradation of the image rather than to gross errors in structure location.

The mirror-image artifact³⁰ is most commonly seen around the diaphragm^{31,32} although it occasionally occurs elsewhere.³³ Since the air in the lungs acts as a total reflector of sound, imaging superior to the diaphragm³⁴ is not expected. Yet tissue appears to be routinely imaged above the diaphragm. This is because the sound is reflected off the diaphragm on its way to another reflector and back. The instrument assumes a straight line path and places the reflector superior to the diaphragm.¹ An echoic mass correctly located in the liver and also artifactually presented superior to the diaphragm is shown in figure 7. An example of a more unusual case of mirror image in which the artifactual object looks substantially different than the real one is given in figure 8.

Side lobes (from single-element tranducers) and grating lobes (from arrays), beams in addition to the primary sound beam, cause objects that are not directly in front of the transducer to be displayed incorrectly in lateral position (fig. 9).^{1,4,33}

ATTENUATION GROUP

Shadowing is the reduced amplitude of echoes caused by intervening structures with high attenuation.³⁶ A pronounced shadow distal to a gallstone is shown in figure 10. The stone shows brightly, indicating a strong reflection. This, in addition to the likely larger absorption in the stone, causes the sound passing through it to be weak. This results in weak echoes (dark presentation) of tissues distal to the stone.³⁷ The greater the amount of the beam cross-section attenuated, the greater the shadowing. Therefore, the location of the attenuating object relative to the focus determines how much shadowing occurs for a given object.36-40 Stone shadowing has been discussed extensively.41-44 Loss of femur shadowing between 20 and 32 weeks' gestation is suggestive of osteogenesis imperfecta.45

Enhancement is the increased relative amplitude of echoes caused by an intervening structure of low attenuation. Enhancement distal to the gallbladder is shown in figure 10; an example of enhancement distal to a pelvic cyst is given in figure 3. As with shadowing, small cyst location relative to the focus is important in producing observable enhancement.¹⁷

Shadowing and enhancement help to determine the cystic nature of echogenic fluid collections (fig. 11).

Shadowing from the edge of a curved object can



Figure 13. A case of reverberation mimicking enhancement. An anechoic mass is located at the diaphragm. The apparent enhanced transmission distal to the mass (into the lung) is a result of two reverberations within the anechoic mass. (Courtesy of S.R. Schwimer, Lebovic and Schwimer, P.C.)

occur as a result of refraction.⁴⁶⁻⁴⁶ In figure 12, such edge shadowing from the gallbladder is shown. The shadow results from reduced intensity as the beam spreads after refraction through a curved surface.⁴⁷ Edge enhancement (also due to refraction) can also occur,⁴⁷ although edge shadowing is the more common occurrence.



Figure 14 (*ieft*) Hyperechoic hemangioma (H) with distal enhancement (E). (Reprinted with permission from Taylor KJW: Allas of Utrasonography. New York, Churchill-Livingstone, 1985, ch 2)

Figure 15 (r ght). Anechoic breast carcinoma (C) with distal shadowing (S).

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Figure 16 (left). Comet tail from the diaphragm.

Figure 17 (below, left). Ring down from air in the bile auct. (Reprinted with permission from Taylor KJW: Atlas of Ultrasonography. New York, Churchill-Livingstone, 1985. ch 2)

Figure 18 (below, right). Adrenal myelolipoma with 11-cm axial dimension on ultrasound scan. The distal diaphragm is displaced 2 cm. (Reprinted with permission from Richman TS, Taylor KJW, Kremkau FW: Propagation speed artifact in a fatty tumor (myelolipoma): significance for tissue differential diagnosis. J Ultrasound Med 2:45, 1983)



Increased brightness can also occur in the focal region of the transducer as a result of the higher intensity present there. Such banding or focal-region "enhancement"(not strictly enhancement according to the definition presented above) is seen in the liver in figure 1. In extreme cases of this, a nonexistent mass might be suspected.

Apparent enhancement can occur where unexpected. The liver and an anechoic mass within or adjacent to the diaphragm are shown in figure 13. Enhancement appears to be present in the lung. On closer inspection it is seen that this apparent enhanced transmission is, rather, presentation of two reverberations from within the anechoic mass. The strong echo from the air boundary superior to the diaphragm appears distal to the mass (as it should). This boundary is then imaged two more times (superior to the diaphragm) as a result of reverberation.

All four combinations of high and low echogeni-

city and high and low attenuation in lesions (resulting in distal shadowing and enhancement, respectively) occur. This is because absorption is the dominant contributor to attenuation in tissues (scattering is a minor contributor). Thus, scattering level (echogenicity) and attenuation are not correlated. High echogenicity with shadow (gallstone) and low echogenicity with enhancement (gallbladder) are shown in figure 10. These are the commonly occurring combinations. Examples of high echogenicity with enhancement (low absorption hemangioma) and low echogenicity with shadowing (high absorption breast carcinoma) are given in figures 14 and 15. In these cases it is clear that attenuation and echogenicity are uncorrelated.

MISCELLANEOUS GROUP

An example of a particularly well-localized "enhancement" phenomenon which has been termed



Figure 19. A (*left*), Apparent pelvic collection. B (*right*), a second view of the collection shown in A that indicates its artifactual nature. The distended urinary bladder compresses the empty rectum and completely fills the pelvis (the patient had a hysterectomy). The outer margin of the patient (determined by measurement) is indicated by the arrows. The coccyx (C) produces a distal shadow. Reverberation (R), i.e., a second image of the coccyx, and enhancement from increased gain (TGC) on the second round-trip fill in the shadow posteriorly. The combination of shadowing, reverberation, and enhancement produces the convincing but totally artifactual mass seen in A. (Reprinted with permission from Taylor KJW: Atlas of Ultrasonography. New York, Churchill-Livingstone, 1985, ch 2).

comet-tail artifact is shown in figure 16.^{49,50} It appears to be a series of closely spaced discrete echoes similar to the short-range reverberation in figure 5. The example in figure 17 appears to be fundamentally different from this. Discrete echoes cannot be identified because they are too close to-

Table 2. Artifacts	Listed by	v Manifestation
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Added Objects	Missing Objects	Incorrect Object Brightness
Speckle Section Thickness Reverberation Mirror Image Comet Tail Ring Down	Resolution	Shadowing Enhancement
Incorrect Object Location	Incorrect Object Size	Incorrect Object Shape
Refraction Multipath Side Lobe Grating Lobe Speed Error Range Ambiguity	Resolution Refraction Speed Error	Resolution Refraction Speed Error

gether or, rather, a continuous emission of sound from the origin may be occurring. The mechanism for such a continuous effect (termed ring-down artifact⁵¹) is not well understood but may be caused by a resonance phenomenon associated with gas bubbles.⁵¹

Propagation speed error^{52,53} occurs when the assumed value for propagation speed by the instrument is incorrect. If the actual speed is greater than that assumed, the calculated distance to a reflector is too small and the display will place the reflector too close to the transducer. If the actual speed is less, the reflector will be displayed too far from the transducer. A recent report has shown that at least some of this artifact is due to refraction.²⁵ Refraction and propagation speed error can also cause a structure to be displayed with incorrect size and shape. An example of these effects is shown in figure 18, where an adrenal myelolipoma measuring 9 cm in diameter on a computed tomographic (CT) scan appears larger on an ultrasound scan because of the low sound speed within it.

In ultrasound imaging, it is assumed that for each pulse produced, all reflections are received before the next pulse is sent out. If this is not the case, ambiguity can result.⁵⁴ This is because the instrument calculates the distance to a reflector from the echo arrival time assuming that all echoes were

Table 3. Artifacts and Their Cal	USes
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Artifact	Cause
Axial Resolution	Pulse Length
Lateral Resolution	Pulse Width
Speckle	Interference
Section Thickness	Pulse Width
Reverberation	Reflection
Refraction	Refraction
Multipath	Reflection
Mirror Image	Reflection
Side Lobe	Side Lobe
Grating Lobe	Grating Lobe
Shadowing	Attenuation
Enhancement	Attenuation (low)
Refraction Shadowing	Refraction
Focal Enhancement	Focusing
Comet Tail	Reverberation
Ring Down	Resonance
Speed Error	Speed Error
Range Ambiguity	High Pulse Repetition Frequency

generated by the last emitted pulse. The maximum depth to be imaged unambiguously by an instrument determines its maximum pulse repetition frequency. In dynamic imaging, the maximum depth imaged unambiguously (cm) multiplied by the lines per frame and by frame rate (frames per second) cannot exceed 77,000. Otherwise, distant reflectors will be placed at distances too close to the transducer. This observation has been reported in echocardiography.³³

CONCLUSION

We conclude with an interesting and sobering case. In figure 19A, a pelvic collection in a patient in whom we were searching for an abscess is shown. This pelvic collection is completely artifactual! Another view with the distended urinary bladder completely filling the pelvis (the patient had a hysterectomy) is shown in figure 19B. The coccyx (C) produced a distal shadow. Reverberation in the bladder images the coccyx a second time (R). Distal filling (in figure 19A) occurs this time because time-gain-compensation has over-increased the gain (relatively low attenuation in the urine). This deceiving image resulted from the combination of three artifacts-shadowing, reverberation, and enhancement. The artifactual mass is totally located outside the patient, whose outer margin is indicated by the arrows in figure 19B.

In this review we have discussed 18 ultrasound imaging artifacts of acoustic origin. They are listed in Table II according to the ways in which they are manifested. Explanations of how these artifacts occur are listed in Table III. In some cases, artifact names are identical to their causes. Some artifacts are useful in interpretation and diagnosis (e.g., shadowing and enhancement), while some can cause confusion and error (e.g., section thickness and reverberation). A proper understanding of artifacts and how to deal with them when encountered enables sonographers and sonologists to use them in diagnosis while avoiding the pitfalls which they can cause.

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Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging

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ABSTRACT A study in vitro of specimens of human aortic and common carotid arteries was carried out to determine the feasibility of direct measurement (i.e., not from residual lumen) of arterial wall thickness with B mode real-time imaging. Measurements in vivo by the same technique were also obtained from common carotid arteries of 10 young normal male subjects. Aortic samples were classified as class A (relatively normal) or class B (with one or more atherosclerotic plaques). In all class A and 85% of class B arterial samples a characteristic B mode image composed of two parallel echogenic lines separated by a hypoechoic space was found. The distance between the two lines (B mode image of intimal + medial thickness) was measured and correlated with the thickness of different combinations of tunicae evaluated by gross and microscopic examination. On the basis of these findings and the results of dissection experiments on the intima and adventitia we concluded that results of B mode imaging of intimal + medial thickness did not differ significantly from the intimal + medial thickness measured on pathologic examination. With respect to the accuracy of measurements obtained by B mode imaging as compared with pathologic findings, we found an error of less than 20% for measurements in 77% of normal and pathologic aortic walls. In addition, no significant difference was found between B mode-determined intimal + medial thickness in the common carotid arteries evaluated in vitro and that determined by this method in vivo in young subjects, indicating that B mode imaging represents a useful approach for the measurement of intimal + medial thickness of human arteries in vivo.

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ERIMENTAL STUDIES on nonhuman primates¹ on human subjects²⁻⁴ indicate that atherosclerotic ns may progress without a reduction in luminal because of dilatation of the arterial wall. The corestimation of the size of atherosclerotic lesions fore requires the simultaneous measurement of ial wall thickness and residual luminal size. rosclerotic lesions in peripheral and carotid arterre generally evaluated by the measurement of lual size by invasive methods such as contrast ography or by noninvasive ultrasound techniques. is and microscopic pathologic examination allows surement of arterial wall thickness in tissue specis only. In our laboratory the measurement of the intimal + medial thickness has been attempted by the use of the noninvasive technique of B mode real-time imaging. This approach is currently used to measure organ dimensions^{5, 6} as well as atherosclerotic lesions.⁷ A multicenter validation trial is now being conducted to determine the accuracy of B mode imaging vs that of angiography and histology.⁸ However, the potential of B mode imaging for direct measurement (i.e., not that from residual luminal size) of arterial wall thickness has not been assessed as yet.

In a previous study⁹ we found a significant correlation between results of gross pathologic evaluations and measurements by B mode imaging of arterial wall thickness. This study, however, was conducted on a limited number of normal or moderately diseased arterial segments.

The objectives of this study were (1) to determine the anatomic structures involved in ultrasound energy reflection in the arterial wall, (2) to determine the accuracy of intimal + medial thickness measurements by B mode imaging by comparison with findings of gross and microscopic pathologic examinations in nor-

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mal and pathologic arterial segments, and (3) to assess the feasibility of the measurement of intimal + medial thickness of arterial walls not only in vitro but also in vivo in human subjects.

The investigations were carried out in vitro with specimens of human aortas and common carotid arteries and in vivo in common carotid arteries of normal human subjects.

Materials and methods

Selection and procession of autopsy material. Abdominal aortas and common carotid arteries were removed at autopsy from 18 male subjects (age range 20 to 74 years), 12 to 20 hr after death.

Processing of aortic tissue. Aortic tissue was processed as previously described.⁹ Briefly, after longitudinal opening, rectangular strips $(2 \times 4 \text{ cm})$ of washed aortic tissue were longitudinally distended with a Plexiglas holder and fixed with formalin (10% for 10 hr). The segments to be studied were held in place with two metallic pins.

Processing of the common carotid artery. Common carotid arteries from young subjects (age range 20 to 25 years) were cannulated and perfused under pressure (90 mm Hg) with 10% buffered formalin for 10 hr.² After ultrasound interrogation, arteries were longitudinally opened and processed for gross and microscopic examination.

For experiments in situ common carotid arteries were cannulated during autopsy (24 to 30 hr after death) with a Foley catheter (Rusch-Gold Balloon catheter, SILKOLATEX, West Germany) and flushed under pressure (\approx 120 mm Hg) with saline. The arteries were processed as described for aortic tissue.

Gross and microscopic pathologic evaluation and classification. The specimens were cut longitudinally between two metallic pins previously fixed 10 mm apart to define the segment of interest. After ultrasound interrogation the specimens were stained for 12 hr in a supersaturated Sudan IV 38% isopropyl alcohol solution¹⁰ and then washed for 1 hr. After lipid staining, gross pathology of the artery was evaluated by a Zeiss operative microscope at 10× magnification. The media was differentiated from the adventitia on the basis of the color and consistency. The calibration of the ocular graduate scale to be used for thickness measurements was performed with a Zeiss test microobject. The resolution of the miscroscope was 20 paired lines per millimeter. After gross pathologic evaluation the specimens were cut, decalcified with a Standard Cal Ex Solution (Fisher Inc.) for 4 hr, and embedded in paraffin after dehydration. The histologic slices were stained with Verhoeff-Van Gieson and with hematoxylin-eosin stains and evaluated by optical microscopy.

Each sample was classified into one of two arbitrarily defined categories (A or B) on the basis of gross and microscopic characteristics. Class A included aortic segments that were macroscopically normal or had fatty streaks. Microscopically these samples showed homogenous intima with varying amounts of intimal thickening, intimal fibrosis, internal elastic lamina fragmentation, and duplication. The arterial segments included in class B showed a fibrous/muscular cap with a lipid and/or necrotic core. Microscopically, the intima showed focal areas of fibrotic smooth muscle cell proliferation, microcalcification, and necrosis.

The intimal + medial thickness of the arterial specimens was determined by gross pathologic and histologic examination. The thickness of adventitia and of the overall complex intima +

media + adventitia was measured by gross pathologic evaluation, whereas the intimal and the medial thicknesses were determined by histologic examination only.

Ultrasound instrumentation. A high-resolution small-part real-time scanner (Biosound, Biodynamics Inc, Indianapolis) was used. This instrument generates a wide-band ultrasonic pulse with a midfrequency of 8 MHz. The measured pulse length at 6 dB is $0.5 \,\mu$ sec, corresponding to an axial resolution of approximately 385 μ m for an ultrasonic speed of 1540 m/sec. The reported¹¹ dynamic range is at least 70 dB. The lateral resolution is 0.5 mm. A standard 15 inch television monitor allowed magnification of the objects by $10 \times$. Marker lines were present on the display for depth measurements, which were performed with a mechanical caliber.

Experiments in vitro were carried out by placing the aortic tissue specimens in a Plexiglas tank filled with water at room temperature (22° to 25° C). A mechanical system allowed optimal positioning of the ultrasound incident beam with respect to the area under evaluation. The intimal surface was exposed to the incident incoming pulse. Common carotid arteries were perfused with saline under pressure and ultrasound interrogation was carried out along their longitudinal axes. For each carotid artery four longitudinal measurements were obtained by rotating (90 degree increment) the vessels along the axis.

Experiments in situ were performed on common carotid arteries during autopsy (n = 3). B mode evaluations were carried out in situ on the same carotid arteries with and without the tissues located between the outer side of the vessels and the ultrasound probe (skin, subcutaneous tissue, and muscles). Scans were carried out in the anteroposterior and laterolateral planes of the lower and higher third of the common carotid arteries. After ultrasound interrogations the carotid arteries were removed and processed.

Experiments in vivo were carried out in 10 young subjects (age range 20 to 29 years) with no clinical sign of atherosclerotic disease.

The subjects were kept supine with the head slightly extended. Two longitudinal scans were performed in the anteroposterior and coronal planes of the lower and higher third of the right and left common carotid arteries. In both studies in vitro and in vivo only the far (deeper) wall image was evaluated.

Identification of the anatomic structures generating the B scan pattern. To define the anatomic structures generating the B scan pattern 10 of the 116 aortic specimens (five from class A and five from class B) were examined in dissection experiments. A 1.5 to 2.0 mm deep excision of the intima was performed in five class B arteries. These specimens were then interrogated by ultrasound and evaluated by microscopy. The findings on the B scan images obtained in the region of the inlay were compared with the structural changes induced by dissection in the arterial wall. To define the anatomic structures generating the outer line, arterial segments with and without the adventitia and the periarterial tissues were interrogated by ultrasound and evaluated by light microscopy.

Quantitative ultrasound and pathologic measurements were also made to determine the correlation between the B mode image and the anatomic structures. The distance separating the inner and outer lines shown in figure 1 was measured in 45 class A aortic specimens and defined as the B mode image of intimal + medial thickness. Without prior knowledge of ultrasound data, gross pathologic and histologic evaluations of the different tunicae were performed in all the aortic specimens (45 class A and 49 class B), and the results were correlated with those obtained by B mode imaging of the intimal + medial thickness.

To ensure that B mode, gross pathologic, and histologic evaluations were performed in the same location, the following criteria were used. (1) From each arterial specimen a segment

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INTIMA + MEDIA ADVENTITIA

FIGURE 1. The typical B scan pattern (the double line pattern) of a normal class A arterial wall. The A to B line represents the distance between the inner and the outer echogenic lines and corresponds to the B mode image of intimal + medial thickness.

showing homogenous thickness was selected, and a distance of 10 mm was delimited with two metallic pins. This procedure was undertaken to avoid the error that might result from making measurements with the three methods at slightly different points. (2) B mode and gross pathologic evaluations were carried out in the middle of the segment under study, which was identified by the metallic pins. (3) Histologic measurements were obtained in the middle of longitudinal sections identified by the holes left by the pins.

The overall error in the identification of the site at which the different measurements (B mode, histologic, and gross pathologic) were made was estimated to be ± 0.5 mm. For all the aortic specimens showing a characteristic B scan pattern (45 class A and 49 class B), the absolute and percent differences between results of B mode and gross pathologic evaluations of intimal + medial thickness were determined.

Intimal + medial thickness values obtained in vitro in common carotid arteries with B mode imaging were compared with those determined in vivo in common carotid arteries of young living subjects.

Statistical analysis of the experimental data. The data are expressed as the mean \pm SD. Statistical analysis was carried out by paired two-tailed t test. Correlation coefficients were calculated by plotting the values obtained with B mode imaging against those obtained by pathologic techniques.

Results

Gross pathologic and histologic evaluations of aortic specimens and common carotid arteries. One hundred sixteen aortic segments were studied. Fifty of the 116 segments (43%) were grouped in class A (mascroscopically normal or with fatty streaks), whereas 66 (57%) were grouped in class B (aortic segments with atherosclerotic lesions). Histologic evaluations of these segments showed that intimal thickness of class A and class B arteries was 0.25 ± 0.12 and 1.11 ± 0.27 mm, respectively, whereas intimal + medial thickness was 1.03 ± 0.27 and 1.72 ± 0.71 mm, respectively. Results of gross pathologic evaluations were comparable (class A intimal + medial thickness 1.13 ± 0.26 mm and class B 1.93 ± 0.84 mm). The mean intimal + medial thickness measured by histologic examination of common carotid arteries in vitro (n = 44) was 0.48 ± 0.06 mm. The gross pathologic evaluation resulted in comparable data (0.50 ± 0.06 mm).

The typical B mode image of the arterial wall and its prevalence in class A and class B aortic specimens. In all the class A and in 85% of class B aortic specimens a similar B scan pattern was found. This pattern was characterized by two parallel echogenic lines separated by an hypoechoic or anechoic space (figure 1). This B scan pattern was defined as the "double line pattern." The inner (luminal) line was generally more regular, smooth, and thin than the outer one. In 20% class B

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aortic segments (12 of 61) the double line pattern was absent, whereas it was present but more complex in 9% and in 31% of class A and B aortic segments, respectively. The characteristic double line pattern was found in the far wall of all the common carotid arteries evaluated in vitro (figure 2).

Identification of the structures generating the double line pattern. Five class B aortic specimens were prepared to identify the structures generating the inner echogenic line of the double line pattern. A small portion of the arterial wall was excised from the luminal side. The excision was found, by light microscopy, to be confined within this tunica. In these specimens the intimal/medial transition and the more peripheral layers were unchanged (figure 3). The B scan image generated by the five dissected arteries showed the disappearance of the inner line at the level of the inlay. This finding demonstrates that the inner line is generated by the intimal surface. In all of the five class A arteries the adventitia was completely removed from the media as confirmed by histologic examination (figure 4). The B scan image of each of these specimens showed the disappearance of the outer line in the region without adventitia, indicating that this line was generated by the adventitia.

To determine the anatomic structures delimited by the inner and the outer lines of the double line pattern, the distance between these two lines was measured



FIGURE 2. B mode image of a water pressure-perfused normal longitudinally scanned human common carotid artery in vitro. NW = near wall; FW = far wall. The double line pattern within black and white arrows is visible only on the FW.



FIGURE 3. B mode image of a class B arterial wall with an inlay of dissected intima. Space between long bars in panel B is equal to 1 mm. The magnification of panels B and C is twice and 20-fold, respectively, that of A. M = media. Arrows are pointed opposite the bottom of the inlay.

with the use of B mode imaging. Values for intimal + medial thickness determined by B mode imaging were correlated with histologic and gross pathologic thickness values for the different tunicae. The B mode measurements of intimal + medial thickness showed a significant correlation with values obtained by gross pathology and by histology in both class A and class B aortic samples (figure 5). In contrast, B mode intimal + medial thickness values appeared to correlate less well with the values for other components of the vessel wall, alone or in combination (intima + media + adventitia and adventitia alone as measured by gross pathology and intima and media measured by histology; figure 6).

It should also be noted that evaluations of intimal + medial thickness by B mode imaging and gross pathologic examination did not significantly differ in either class A or class B aortic samples (class A: B mode intimal + medial thickness, 1.22 ± 0.37 vs $1.13 \pm$ 0.26 by gross pathology, NS; class B: B mode, $2.06 \pm$ 1.02 vs 1.93 ± 0.84 by gross pathology, NS).

Accuracy of B mode measurements. To determine the

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FIGURE 4. B mode image (top) and histologic section (bottom) of a class A arterial wall with a region without adventitia (wa). Magnification in both images (\times 10). P = pin; H = hole.

absolute and percent error in B mode measurements of aortic tissue specimens in vitro vs an accepted reference standard (results of gross pathologic examination), the absolute and percent differences between intimal + medial thickness values obtained by the two methods were evaluated. The absolute difference between B mode and gross pathologic findings was 0.19 \pm 0.23 mm and the percent difference was 11.5 \pm 10.4% for the whole group of aortic specimens (n = 94).

The accuracy of the determinations in class A samples was significantly different from the accuracy in class B samples (absolute error 0.12 ± 0.09 and 0.25 ± 0.30 mm for class A and B samples, respectively, p < .001), whereas percent error (10.9 \pm 7.7% and 11.9 \pm 11.4% for class A and B, respectively) was similar.

In addition, the absolute and the percent differences were significantly lower when the ultrasound images were typical as opposed to complex (absolute error 0.12 ± 0.09 and 0.47 ± 0.38 mm for typical and complex ultrasound images, respectively; percent error $8.8 \pm 5.7\%$ and $22.1 \pm 16.0\%$ for typical and complex ultrasound images, respectively).

Common carotid intimal + medial thickness: comparison between measurements in vitro in situ and those in vivo. The mean intimal + medial thickness in common carotid arteries (n = 44) as evaluated in vitro by B mode imaging was 0.52 ± 0.08 . This value did not differ significantly from those found on histologic and pathologic examinations.

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To assess whether intimal + medial thickness measured in vitro in arterial specimens was similar to that in situ, experiments were carried out during autopsy on carotid arteries that had been cannulated and flushed with saline. For this purpose common carotid arteries were cannulated with an inflatable balloon catheter, and the position of the balloon was verified on the monitor of the instrument. The catheter was kept in the same position during all the experiments, working as a position marker. A clip was placed on the anterior wall of the artery, just over the balloon, to allow the correct identification of the scanning plane after the excision of the artery.

Measurements of intima + media in situ obtained with intact superficial tissues yielded values not significantly different from those obtained in exposed carotid arteries (1.11 \pm 0.14 and 1.08 \pm 0.19 mm for in situ and exposed arteries, respectively, n = 3; absolute error 5.25 \pm 1.65%). Thickness data obtained in vitro in pressure-fixed vessels on the arterial segment identified by the balloon and the clip were 10% lower than those obtained in situ or in the exposed arteries (0.99 \pm 0.29 mm, n = 3). This difference could be attributable to an effect of fixation.

B mode experiments to evaluate intimal + medial thickness of common carotid arteries in 10 living subjects showed that the double line pattern was present at the far wall of all the common carotid arteries considered (n = 20). B mode intimal + medial thickness measured in vivo was 0.53 ± 0.05 mm (n = 20). No significant difference was found between the mean values in common carotid arteries evaluated in vitro and in vivo by B mode imaging.

Discussion

Our investigations show that a characteristic B mode image is consistently generated in vitro at the far wall level by most arterial walls (100% of class A and 85% of class B arteries).

It is relevant to note that, most likely due to the different order in which the interfaces of the intima/lumen and media/adventitia are exposed to the incoming ultrasound beam, the B mode images of the near (more superficial) and far (deeper) walls are different. Our experiments were performed only on far walls because they could be more constantly and repeatably visualized, and therefore our conclusions can be applied only to far walls.

The characteristic B scan pattern of class A arterial walls shows two parallel echogenic lines separated by a relatively hypoechoic space (the double line pattern) (figure 1). A similar acoustic behavior of the arterial

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wall has been previously reported in vitro9, 12-20 and in vivo^{21, 22} in normal and diseased human carotid arteries. In experiments in which a disection confined to the intima was produced in class B aortic specimens the luminal intimal transition was profoundly modified, but the intimal medial transition remained unmodified (figure 2). The inner line change found on the B mode image must be caused by an alteration in the generating structure: this line can thus be identified as the luminal/intimal transition. These experiments were performed only in class B arteries, since the intimal thickness of class A specimens did not allow a careful dissection. On the other hand, the removal of the adventitia from the media resulted in the disappearance of the outer line, indicating that the adventitia was responsible for the echoes representing this line.

strument may influence the appearance of the hypoechoic space between the two lines, the double line pattern of each arterial specimen was evaluated over a large range of time-gain compensation settings. In our experience, however, the typical double line pattern was easily recognizable in the same class A arterial specimens over a large range of time-gain settings. Thus, a time-gain compensation in the usual range does not appreciably influence the distance between the two echogenic lines.

In class B arteries, however, even with optimal adjustment of the time-gain compensation setting, highamplitude echoes were frequently present between the inner and outer lines. In 12 of 61 arterial specimens (19.7%) these echoes, sometimes followed by acoustic shadows, did not allow the identification of the typical double line pattern.



Since the time-gain compensation setting of the in-

FIGURE 5. Correlation of intimal + medial thickness measured with B mode imaging (BMIMT) and that evaluated by histology (HIMT) in class A and B arterial specimens. The correlation coefficients and the regression lines are shown. GPIMT = intimal + medial thickness measured by gross pathology.

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FIGURE 6. Correlation of B mode intimal + medial thickness (BMIMT) with intimal thickness (HIT) and medial thickness (HMT) measured by histology and with intimal + medial + adventitial (GPIMAT) and adventitial thickness (GPAT) measured by gross pathology. The combination of medial thickness measured by histology and adventitial thickness evaluated by gross pathology (HMT + GPAT) is also correlated with B mode intimal + medial thickness. All these measurements were carried out in class A aortic specimens. The correlation coefficients and the regression lines are shown.

In class A and B aortic specimens a good correlation between gross pathologic and histologic intimal + medial thickness (r = .77) was found. In addition, these data were very similar to those obtained by B mode imaging. The difference between intimal + medial thickness measured by B mode imaging and gross pathology was not statistically significant, indicating that B mode measurements represent the distance between the luminal surface and the inner part of the adventitia. This distance represents the intimal + medial thickness (figure 1). In contrast, the difference between B mode intimal + medial thickness and that measured by histology in class A and B specimens was highly significant (p < .001). This discrepancy was due to artifacts introduced during procession of tissue for histologic evaluation.^{2,23}

The B mode image pattern may be complicated by the presence of additional echoes between the two echogenic lines and/or by a fuzzy appearance or discontinuites in the outer line. The B mode image was complex in 15 of 61 class B (25%) and in four of 45 class A (9%) specimens and these arterial wall measurements were less accurate. The absolute and percent errors in B mode measurements, as compared with gross pathologic findings, in class A and B arteries with a complex ultrasound image were significantly different from those for arterial specimens with a typical ultrasound picture.

Therefore, evaluation of intimal + medial thickness can be carried out more precisely in the early stages of atherosclerotic disease, when other available methods (Doppler ultrasound and contrast angiography) cannot be used. All the normal young subjects studied in vivo and most of the patients with angiographically and surgically proven atherosclerotic lesions had the characteristic double line pattern at the level of the common carotid artery. The results of experiments in situ indicate that the presence of superficial tissues does not influence the B mode image of the arterial wall or the thickness of the intima + media. In addition, B mode measurements of intimal + medial thickness of common carotid arteries obtained in vivo were almost identical to those obtained in vitro with both B mode imaging and histologic techniques. We may therefore

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conclude that the results in vitro reported in this study can be extended to conditions in vivo.

The present study demonstrates that: (1) a characteristic B mode image (the double line pattern) is consistently generated in vitro by the far walls of most of the arteries, (2) the distance between the transducer-facing edges of the inner and outer lines of the B mode image correlates with and does not differ significantly from the intimal + medial thickness, (3) regarding the accuracy of B mode imaging, a percent error of less than 20% has been found in 77% of the arterial specimens of both classes (normal and pathologic), and (4) the accuracy of B mode imaging depends on the presence of a typical B scan image. In 85% of class B arterial specimens a characteristic B mode image was found and in 59% of specimens of the same class the image was typical and easy to interpret.

We conclude that B mode imaging represents a useful tool for the detection and monitoring of changes in intimal + medial thickness, allowing the evaluation of changes in the arterial wall in areas without localized plaques. At the present time, it is difficult to determine whether this information will be of clinical relevance. It is possible that early changes in vascular thickness will later result in atheroma; they could on the other hand evolve only in a diffuse intimal thickening and have no hemodynamic relevance. It is also not known whether a relationship exists between the morphologic changes in the vessel wall detected by our method (thickening) and local damage to the endothelial layer, which can induce alterations of potential clinical relevance. The noninvasive nature of this new approach is a recommendation for its use in the preclinical diagnosis and follow-up of patients with atherosclerosis.24, 25

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