FRAMINGHAM HEART STUDY
OFFSPRING EXAM 7
VASCULAR FUNCTION MANUAL

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Adapted from CHS, BMC and Conquer Protocols
By Drs. D. Herrington, J. Vita, and M. Corretti, respectively

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Framingham Heart Study Vascular Laboratory

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Appendices

Introduction to Brachial Artery Vascular Reactivity Test

The brachial artery vascular reactivity test is designed to look at the function of the endothelium (the blood vessel lining) using high-resolution ultrasound. We are studying vascular reactivity in the Framingham Study to more fully understand the determinants and prognosis of endothelial function in the community. It is hoped that the test results will help predict incident and recurrent CVD. For a more complete description of the specific aims please see appendix 9.

The examination takes approximately 20 minutes: a few minutes for participant preparation, 10-12 minutes of scanning time and a few additional minutes to enter information and complete forms at the end of the test.

Equipment

- Standard examination table
- Height adjustable sonographer chair
- Height adjustable bed table - as rest for participant's right arm
- Toshiba Ultrasound System, Model # SSH-140A,
- Toshiba Monitor, Model # Model UMCL 262A
- Panasonic SVHS VCR Model # AG-7350 - P
- Gateway Computer. ATX Tower, Model # GP6-450 [manufactured 10/14/98]
- VX1100 19" Gateway Monitor
- Acquisition software provided by Gary Mitchell, MD [Cardiovascular Engineering, Holliston, MA].
- Analysis software from Medical Imaging Applications, Iowa City, Iowa, USA. Brachial Analyzer 3.2.3 sp2 and Brachial Converter – FD 3.2.2
- Critikon Dinamap Vital Signs Monitor, Model #1846 SX
- Hokanson AG 101 Automatic Cuff Inflator Source - with foot pedal
- Pediatric Blood Pressure Cuff - for brachial artery (goes with Hakanson equipment)
- Standard minute timer. Countdown Electronic Timer by Component Design, Northwest Inc. Portland, OR
- For tonometry: Flexible measuring tape (Centimeter); Creative Health Products with cylinder at the end. [800-742-4478]

Supplies

- Transducer gel
- ECG electrodes
- S-VHS Video Cassette Tapes
- CD disks

Examination & Data Cleaning Documentation Materials

- Participant and Sonographer Worksheets
- Participant ID tape labels
- Log book
- Log-In sheets
- Complications log sheet (petechiae)
- Study not completed sheet
- Data cleaning sheet
- Food forms if participant has eaten

Miscellaneous

- Standard pillow - for participant
- Upper arm pillow support - for participant
- Hand pillow support - for participant
- Arm pillow support - for sonographer

Performing the Brachial Ultrasound Test

A succinct **protocol flow sheet** is provided in appendix 4. Below we will expand on the elements of performing the brachial artery test in a standard fashion.

Initial Test Set Up

In the waiting room the participant reads a set of instructions about the **Brachial Artery Vascular Reactivity Test** (see appendix 1) and signs an informed consent form before arriving at the Brachial station. If not, have the participant read the instructions and sign the consent form before proceeding.

The sonographer asks the participant the questions on the **Endothelial Function Participant Worksheet** and fills out the worksheet. (see appendix 2). The reverse side of this form, the **Endothelial Function Sonographer Worksheet**, is then used by sonographer to record blood pressures, etc. (see appendix 2 for exact items).

Acquisition. Enter the participant ID# in the Mitchell acquisition computer. Click on Brachial Reactivity (see appendix 10 for details).

Labeling storage media, log in sheet & ultrasound system. The sonographer should also enter the participant ID # and name, exam date, sonographer ID#, comments, videotape #, CD #, and miscellaneous information regarding interpretation and data management, on the **FHS Brachial Ultrasound Log-In Sheet** in the Log Book (see appendix 3). Put participant ID# and name label on the SVHS cassette tape jacket. Enter the participant ID# and name on the Toshiba

Ultrasound System. Put participant ID# and name label on the video CD disk. Save remaining participant labels for data CD disks.

Verbally preparing the participant

The sonographer then reviews the test with the participant to make sure he/she understands the procedure and to gain his/her cooperation (see appendix 1). Make sure to include specific details not mentioned in the participant description as follows (see also appendix 4 - **FHS Brachial Vascular Reactivity Protocol Flowsheet**):

- *Blood pressure will be taken on the left arm once before the scan and once after the scan with an automated blood pressure machine (Dinamap).*
- *First we will take pictures of the right brachial artery, the blood vessel near your elbow.*
- *Then the right arm BP cuff will be inflated above your blood pressure.*
- *You may feel pins and needles or tingling of the right hand during inflation, as if the hand has "gone to sleep".*
- *The cuff is then deflated for a 2-minute scan.*
- *You will be asked to keep your right arm still and not to move your hand or fingers until I announce that the scan is completed.*
- *I will announce each minute of the 8-minute scan, how many more minutes until deflation, i.e. "4 more minutes, 3 more minutes, " etc.*

It is extremely important to let the participant know that the most critical images during the test are obtained immediately after the cuff is deflated to watch how the artery reacts after the cuff is released. It should be emphasized that the participant not move his/her right arm and hand until sonographer announces that she is finished taking pictures.

Participant set up

(See appendix 12, illustration 1, for station layout.) The test is performed with the participant lying down with the head resting on one or two pillows. The appropriate size blood pressure cuff (adult size, pediatric size, or large adult size fitting to the lines demarcated on the inside of the cuff), attached to the Dinamap, is placed on the left upper arm over the brachial artery. A second blood pressure cuff (always pediatric size) is placed on the right forearm, 1-2 cm below the bend in the elbow. Attach this cuff to the automatic cuff inflator. The participant is then asked to slide over as far as possible to the right side of the bed, so that the right upper arm may be placed on the small table. The elbow should be slightly bent, palm facing down and fingers relaxed. Pillow-supports are positioned underneath the arm, above the cuff, and also under the hand, to permit inflation and deflation of the cuff during the test. **Make sure that the right arm inflation cuff does not touch any of the pillows, as this will move the arm and the images will be distorted.**

Three ECG leads are attached to the patient's chest to allow visualization of the participant's heart rhythm during the brachial artery scan. Two ECG leads are placed on participant's chest, left side and right side, and one below the participant's right collarbone (clavicle). The amplitude should be sufficient to trigger the capture of frames for the computer. To adjust the amplitude, turn the (Sensi) knob located under ECG on the Toshiba.

Before the sonographer starts the brachial scan, she presses the green "start" button on the Dinamap to measure blood pressure in the left brachial artery. The systolic, diastolic and mean blood pressures and the heart rate are recorded on the Endothelial Function Sonographer Worksheet. When the right arm blood pressure cuff is inflated, it will be inflated to a pressure of 200 mm Hg or 50 mm Hg higher than the systolic pressure measured by the Dinamap – whichever is higher - or to a maximum of 250 mm Hg. The pressure is set on the Hokanson Automatic Rapid Cuff Inflator.

Ergonomic Concerns

A critical issue in designing and implementing the brachial ultrasound protocol is the ergonomic stress on the sonographer, particularly in research sites performing more than a few studies a day. We have instituted the following measures to minimize ergonomic stress on the sonographer:

- Try to lay out the equipment in the room to minimize the amount of reaching the sonographer has to do (see appendix 12, illustration 1).
- Adjust chair and table height to minimize reaching and elevation of shoulders.
- Arrange pillows to support sonographer's right forearm and elbow (the scanning arm).
- The automatic BP cuff inflator is essential, so the sonographer can focus on the scanning and keeping the transducer still.
- Only do 1-2 studies in a row. It is very important to get up, stretch and walk around for a few minutes between participants.
- Neck, shoulder and back exercises throughout the day are essential. Roll shoulders, stretch upper trapezius, stretch rhomboids, stretch levator scapulae, and stretch the scalleni (neck muscles) to relieve tension.

The Preliminary Scan

Confirm that the computer is ready for **Brachial Reactivity acquisition**. (For Brachial Acquisition Tools, see separate Manual.)

Confirm that the **Brachial Program** has been selected on the Toshiba. The sonographer puts ultrasound gel on the transducer and then places the transducer, black arrow pointing toward participant's right shoulder, on the participant's skin surface at an area 2 – 9 cm [ideal is 3.5-5.5 cm] proximal to the elbow crease, to perform the preliminary scan of the right brachial artery. To verify that vessel is an artery and not a vein, she turns on the color and/or the PW Doppler and verifies pulsatile flow.

To expand image on the screen, press the **Pan Expand** button under the **Track Ball** function, and turn the dial to the right until the image is enlarged to its maximum. The **Gain** knob and **DGC** levels are adjusted until the image is optimal.

As the sonographer starts the preliminary scan, she tries to obtain optimal quality images of the four principal boundaries in the artery wall: the media/adventitia boundaries (also referred to as the M-line) in the near border, and the media/adventitia boundaries on the far border. The brachial artery diameter measurements will be made between the M-line on the near border and the M-line on the far border. The sonographer then finds the long axis of the artery. Aspects of an ideal image include:

- The artery lies horizontal on the screen.
- The artery is vertically centered on the screen.
- The straightest segment of the artery is visualized.
- A clear media adventia hypoechoic line – the 'M-line' is well visualized on both the near and far walls over > 50% of the vessel length.
- The lumen is sonolucent – i.e. without 'schmutz' & shadowing in the center of the lumen.
- A readily identifiable landmark is well seen.

The sonographer can adjust the transducer in four "basic" ways to improve the image: angling the transducer, rotating the transducer, "rocking" (toe/heel) the transducer, and applying more or less pressure with the transducer. The participant's arm may also be repositioned if necessary to obtain higher quality images. Since these images need to be maintained for exactly 8 minutes during the test, the position should be comfortable for the sonographer as well. The pillow supports for the sonographer come in handy for this purpose.

It is essential that optimal quality images are acquired with the M-line visible and the artery steady. Do not move up or down the artery or change the angle, once the test has begun! The Brachial Measuring Software works best when images are steady and show the M-line clearly!

Under Doppler, press **PW Cursor** to acquire **Doppler** signals. Rolling the track ball controls the Doppler cursor on the screen. Then press **Angle** and turn the knob below to 60 degrees. Press **D/M+B** button under the **Mode Panel** to split the screen for a view of the Doppler (6K PRF) and B-mode screens (live) simultaneously. To filter the Doppler and freeze the B-mode screen, press the D/M+B button twice. The PRF then becomes 12K. To go back to the B-mode screen only, press the **B-Single** button.

It is important to remind the participant that talking may interfere with the scan, and that it is critical not to move during the scan, especially the right arm and hand.
The sonographer states to the participant: *"I am now going to take pictures of your brachial artery. Are you comfortable?"* Then the sonographer states: *"I'm placing cold gel on your arm."*

The sonographer now reminds the participant that he/she *may terminate the test if at any time the test becomes too uncomfortable.*

When the sonographer is satisfied with the angle and the location of the images of the artery, two markers are positioned on the image screen to facilitate scanning and making measurements. Under Track Ball Function, press **Annot** for "annotate". Then press **Baseline**.

Using the track ball, the sonographer then moves the cursor to the middle of the vessel at the center of the segment of the artery, called the "**Area of Interest**" or **AOI.** The area with optimal quality of the near border and the far border and positioned as close to the center of the screen as possible is chosen as the AOI. Try to place the AOI in the portion of the artery where you are most likely to want to measure the artery. Press the key with the degree ^{0} symbol to mark the AOI.

Next, place the cursor on an identifiable "**landmark**" anywhere on the image. Use one of the various directional arrows, → ← ↓ ↑, to point the arrow to the landmark chosen. Criteria for choosing a landmark include: a) an unusual or distinctive area; b) preferably an area relatively near the center of the screen; c) good landmarks include a small branch off the artery or bright echoes ("ridges") or hollow black spaces. If the artery is scanned consistently during the test without the sonographer moving, the degree marker and the arrow marker will be in the same location at the beginning of the baseline scan until the end of the deflation scan.

The duplex images on the screen during the examination also help the sonographer to consistently scan the same segment of the artery during the entire test. After the baseline scan, the baseline images stay on the screen to guide the sonographer. Anytime during the deflation scan, she can look at the baseline image on the screen and double check that she is scanning the artery at the same segment and with the same angle during the deflation scan. The baseline images will be there for comparison to all subsequent images.

During the preliminary scan, the sonographer also makes a mental note of the transducer location and angle relative to the participant's upper arm. The angle closest to 10, 30, 45, 60, or 90 degrees is selected for the probe angle and recorded on the Endothelial Function Sonographer Worksheet at the end of the test.

The Baseline Scan

The beginning of the baseline scan is indicated by the appearance of the word **Baseline** at the top of the image screen. Sonographer verifies that the participant is comfortable. She also verifies that she is getting high quality images before starting to acquire and record images. When the timer on the Toshiba shows _:00, the sonographer presses **Start** on the VCR and starts recording. The sonographer will be recording baseline images for a period of 1 minute**,** maintaining high quality images throughout.

At _:20, during this 1-minute pre-inflation scan, she will click **Baseline** on the Computer to start acquiring B-single images.

At _:40, the sonographer will press **PW Doppler** on the Toshiba**.** Then she will press **D/M+B** to get a duplex image on the screen at 6K PRF. Immediately thereafter, she presses **D/M+B again,** to switch to 12K PRF (the images will be frozen). After recording 3-5 Doppler signals, she hits **Save Doppler** on the computer and switches back to Doppler at 12K PRF. The duplex images on the screen will be live.
At _:50, she presses the **Start** button (pre-set to 5 minutes) on the **manual timer** and also annotates **Inflation** on the Toshiba.

The baseline images will stay on the screen, in a duplex format, to guide and help the sonographer during the deflation scan. During the baseline sequence, measurements of the brachial artery diameter from a minimum of 10 cardiac cycles will be made for comparison with the brachial artery diameter of the corresponding segment during the two-minute deflation period.

The Inflation Scan

A few seconds before 1:00, the sonographer warns the participant that *"the cuff will inflate suddenly"* and that the participant will feel a lot of pressure on their arm. The sonographer reminds the participant not to move his/her arm. **At 1:00** exactly, the sonographer inflates the cuff by stepping on the foot pedal connected to the Automatic Cuff Inflator. Immediately thereafter, she presses **Stop** on the VCR on the Toshiba and hits **Save Images** on the computer. It is important to capture 3-5 triggers of Doppler signals @ 6K PRF on the computer to note the **Trigger of Inflation.** She then returns to B-single and continues to obtain 2-D images of the brachial artery during the 5-minute occlusion period.

The occlusion cuff is inflated to 50 mm Hg above the participant's baseline systolic pressure or at least 200 mm Hg for a maximum of 250 mm Hg. The occlusion systolic measurement is recorded on the work sheet.

The cuff remains inflated for 5 minutes and the sonographer stays focused on obtaining optimal quality images. It is crucial to keep arm and transducer steady, and also to keep AOI and landmark in the same position throughout this period. In some participants, the artery will move as the cuff is inflated. Since the two markers placed on the image are frozen on the screen, they will also appear to have moved slightly relative to the artery. **The two markers need not be repositioned**. Often, the artery will return to its original position at the end of the exam, which will be confirmed by the markers reappearing in its original position.

Great care must be taken to image the same arterial segment during the occlusion period as during the baseline period, to help sonographer continue to image the same arterial segment during the deflation period to the greatest extent possible.

During this 5-minute occlusion period, the sonographer announces to the participant: *"4 more minutes until deflation,... 3 more minutes,... 2 more minutes, etc."*

At 15 seconds before deflation, the alarm on the manual timer will sound. The sonographer then presses **Start** on the VCR on the Toshiba, and starts acquiring PW Doppler images on 6K PRF with duplex imaging. She also hits **Deflation** on the Annotation menu.

At 10 seconds before deflation, she clicks on **DEFLATION** on the Computer, to start acquiring the deflation sequence of images on the computer, while announcing to the participant that the cuff will be deflated in 10 seconds. The sonographer also reminds the participant that he may feel pins and needles or a warm or cold feeling in the hand.

The Deflation Scan

The sonographer deflates the cuff at exactly :00 by stepping on the foot pedal of the automatic cuff inflator. It is important to acquire images with PW Doppler on the computer to capture **the trigger # of deflation.** Immediately thereafter, she switches the PW Doppler from 6K PRF to 12K PRF and captures 3-5 beats on 12K PRF as well as hits **Save Doppler** on computer. She then immediately switches to B-single and records optimal quality 2-D images of the brachial artery for the remaining 2 minutes on the computer as well as on the VCR on Toshiba.

The two minutes immediately following cuff deflation is the most critical time of the entire exam. This is when the flow-mediated dilation occurs. Every effort should be made to avoid movement of sonographer transducer or the participant's arm. The sonographer should therefore announce to the participant: *"It is critical that you not move your arm for the next two minutes."*

The artery should be horizontally displayed on the screen. Adjust transducer by doing toe or heel, if artery is displayed diagonally. Every attempt should be made to have artery vertically centered with the anterior and posterior intima parallel to each other. The artery will be in the focal zone, and the lumen should be free of echoes as much as possible. Fine-tune the image by rotating and/or angling transducer to optimize near wall and far wall. Ideally the artery will "look like a railroad track" with intima, M-line, and adventia fully visible!

At end of scan, the sonographer announces *"End of scan – you may move your arm, hand and fingers!"* Click on **Save Images** on the Computer. Press **STOP** on the Toshiba VCR Control Panel.

Test Wrap Up

A final blood pressure determination is made in the left brachial artery by pressing the Start button on the Dinamap. Write down blood pressure, pulse and mean arterial pressure on the **Endothelial Function Sonographer Worksheet.** Determine the probe placement distance on the participant's arm. Recheck the probe angle. Record information on the work sheet. Also record the start and ending times of the video recording. Write any additional comments on the **Log-In Sheet.** Remove the electrodes, the BP cuff on the left arm, and the cuff on the right arm.

Before participant leaves the room, have him fill out the Discomfort Survey at the bottom of the Endothelial Function Participant Worksheet (see appendix 2).

He/she should also be told the following: *"You should be aware that about 0.5% of participants develop painless red spots on the arm after the test, which resolve on their own within a few days. This is harmless, but if it occurs, you should call the sonographer, so that we can track the frequency and the time to resolution".*

Thank the subject for participating.

Appendix Item 1

The Vascular Function Tests – Handout for Participant

The Framingham Study's Vascular Testing Station

The Brachial Artery Vascular Reactivity Ultrasound Test

For this test you will be asked to do the following:

- Have an ultrasound picture taken of the artery located in your upper arm.
- Have a blood pressure cuff inflated on your lower right arm for 5 minutes.
  When the cuff is inflated your arm may feel like it is going to sleep or numb.
- After the cuff is released we will take pictures of your artery for 2 more minutes.
  When the cuff is released your arm may feel pins & needles, warm or cold.
- At a later date we will make computer measurements of the amount that your artery expands after the cuff was released. The changes are very small, so we cannot tell you the results while we are doing the study.
- ***To get the best information it is very important that you not move when we are taking the ultrasound pictures.***
- This noninvasive test has been performed in thousands of research participants safely.
- Approximately 0.5% of participants develop painless red spots on the arm after the test, which resolve on their own within a few days. This is harmless, but if it occurs please call the sonographer (508-935-3445 or 508-935-3406) so we can track the frequency & the time to resolution.

Why are we doing this test?

- This test is designed to look at the function of the blood vessel lining.
- We are doing the test to understand if the results relate to risk factors for heart disease and to understand if the results will help predict the development of heart disease and stroke.

The Arterial Pressure Waveform Test (tonometry)

How is the test performed?

- Measurements are made by gently pressing the blunt tip of a pencil-like device (the tonometer) against the superficial pulses in the arm, leg and neck for approximately a minute at each of four sites. This device records the pressure waveform that is associated with each pulse or heartbeat.
- Next, the distance from the base of the neck to each of the pulse sites is measured.
- You will be asked to lie quietly during this phase of the testing. There should be no discomfort. This test has been performed safely in thousands of patients.
- At a later date, using a computerized analysis, we will examine the shape of the pressure waveforms and calculate the speed at which pressure waves travel through the large arteries.

Why are we doing this test?

- The arterial pressure waveform test is a noninvasive method to evaluate the stiffness of the large arteries.
- This test will allow us to evaluate the relationship between cardiac risk factors, arterial stiffening and the development of cardiovascular disease.

These tests are solely used for research purposes.
We will not be sending the results to your physician
because the tests' clinical significance are yet to be determined.

Thank you for your support of the research at The Framingham Study.

If you have further questions about the brachial reactivity or tonometry test please contact Dr. Emelia Benjamin by leaving a message at 508-935-3445 or 617-638-8968.

Appendix Item 2

FHS Vascular Function Participant Worksheet

&

FHS Vascular Function Sonographer Worksheet

Exam 7
Framingham Study Vascular Function Participant Worksheet

Keyer 1: ___________________

Keyer 2: ___________________

|__|__|/|__|__|/|__|__|	**Date of brachial artery scan?**
0 1 9	**Exam Date?** (0=No, 1=Yes, 9=Unknown)
0 1 9 If yes, ☞ discontinue procedure	**Do you have active Raynaud's disease, as manifested by daily attacks of Raynaud's currently blue fingers or ischemic finger ulcers?** (0=No, 1=Yes, 9=Unknown)
0 1 8 9 If yes, ☞ discontinue procedure	**Women Only: Have you had a radical mastectomy on either side?** A radical mastectomy is the removal of the breast, associated lymph nodes, and underlying musculature. Does NOT include lumpectomy or simple mastectomy. (0=No, 1=Yes, 9=Unknown)
0 1 9	**Have you had any caffeinated coffee, caffeinated tea, or other caffeinated drinks in the last 6 hours?** (0=No, 1=Yes, 9=Unknown)
|__|	If yes, how many cups?
0 1 9	**Have you had a fat free cereal bar in clinic?** (0=No, 1=Yes, 9=Unknown)
0 1 9	**Have you smoked cigarettes in the last 6 hours?** (0=No, 1=Yes, 9=Unknown)
|__|__|:|__|__|	If yes, how many hours and minutes since your last cigarette?
0 1 9	**Today, have you already had your six-minute walk test?** (0=No, 1=Yes, 9=Unknown)
0 1 9	**Today, have you already had your oral glucose tolerance test?** (0=No, 1=Yes, 9=Unknown)
|__|__|mm	**Discomfort scale (mm) – brachial.**
|__|__|mm	**Discomfort scale (mm) – venipuncture.**

Please indicate on the scale below, the level of discomfort you experienced while the blood pressure cuff was inflated and deflated for the brachial artery endothelial function test?

|____|

0 No pain — 10 Worst pain imaginable

Please indicate on the scale below, the level of discomfort you experienced with blood drawing today?

|____|

0 No pain — 10 Worst pain imaginable

|__|__|__|	**S-VHS Brachial scan tape ID Number**
|__|__|__|	**Brachial Video CD number**
|__|__|b / |__|__|t	**Brachial Sonographer ID / Tonometry Sonographer ID**
|__|__|:|__|__|	**Time of day scan started** (Military time)
|__|__|	**Room temperature** (Celsius)
0 1 2	**Left arm cuff size – blood pressure** (0=Adult, 1=Pediatric, 2=Large Adult)
Baseline blood pressure and pulse:	**systolic** |__|__|__| **diastolic** |__|__|__| **pulse** |__|__|__| **mean** |__|__|__|
|__|__|:|__|__|:|__|__|	**Tape start time**
|__|__|__|	**Cuff inflation pressure** (Baseline SBP + 50 or 250)
|__|__|:|__|__|:|__|__|	**Tape stop time**
Post blood pressure and pulse:	**systolic** |__|__|__| **diastolic** |__|__|__| **pulse** |__|__|__| **mean** |__|__|__|
0 1 2 If no (0) or incomplete (2), ☞	**Was brachial scan protocol completed?** (0=No, 1=Yes, 2=Incomplete) 1: Equipment problem, specify ______________________ 2: Subject refusal 3: Subject discomfort 4: Other, specify ______________________
|__|__|mm	**Distance from the antecubital crease to the probe?**
10 30 45 60 90	**What was the probe angle?** (degrees)
1 2 3	**What was the quality of the scan?** (1=Good, 2=Fair, 3=Poor)
0 1 2 If no or incomplete ☞	**Was tonometry completed?** (0=No, 1=Yes, 2=Incomplete) Comment: ______________________ **brachial** |__|__|__| **radial** |__|__|__| **femoral** |__|__|__| **carotid** |__|__|__|
|__|__|	**Interpreter ID**
|__|__|/|__|__|/|__|__|	**Interpretation date**
0 1 9	**Baseline measurable?** (0=No, 1=Yes, 9=Unknown)
0 1 9	**Deflation measurable?** (0=No, 1=Yes, 9=Unknown)
0 1 9	**OK to calculate FMD?** (0=No, 1=Yes, 9=Unknown)
|__|__|__|-|__|__|__|	**Measurement Video CD#**
|__|__|__|-|__|__|__|	**Brachial data floppy #**

Appendix Item 3

FHS Vascular Function Log-In Sheet

Framingham Heart Study
Brachial Noninvasive Laboratory

Cycle 7 – Offspring Cohort

No.	FHS ID # Name	Exam Date	Sono. ID #	Comments	Video Tape #	Video		Reading			Data Clean		
						CD #	Burn Date	Read Date	CD # with line on	FDD #	Clean Date	FDD#	CD#

Appendix Item 4

FHS Vascular Station Flowsheet

With Succinct Description of

Vascular Reactivity & Tonometry Tests

FHS Brachial Vascular Protocol Flowsheet

Phase	Time, mins Total	Phase	Worksheet & Dynamap	Toshiba	Computer	Verbal	Cuff, Timer, Light, Table
Set up	0-4	4	• Hand participant description sheet • Fill out participant worksheet • Place BP cuff on LA	• Machine on, Select Brachial • Enter name, ID • Apply 3 ECG leads (R collarbone, L & R ribcage) • Verify ECG is appropriate amplitude	• Machine on, [Register] • Enter pt ID type & ID # • **Double check the subject ID against the subject's FHS Heart ID** • Study date (default) • Study type • Sonographer #	• Ask eligibility questions • Ask subject to lie supine & rest • Ask other work-sheet questions	• If wearing shorts, have subject remove shorts in dressing room • If dressing gown tight, remove sleeves
Acquire Tonometry	4-12	8			• Click [Waveforms] on toolbar • Click [Bra], Record pulse, R click to freeze screen • Find BA & keep L finger on pulse • Place tonometer over artery, adjust pressure, maximize image • Repeat for radial, femoral & carotid [Rad] [Fem] [Car] • Close	• 'Now I'm checking your pulses with a blunt instrument' Before Femoral • 'I'm going to check the pulse at the top of your leg'	• Put on gloves
Tonometry Wrap up	12-14	2	• Take BP/P in LA • Measure distances to pulse sites • Record on worksheet		• Click [distances} on toolbar • Enter distances to pulse sites • Close • Click [waveforms] on toolbar • Click [BP] and enter BP • Close	• 'Now I'm going to take your BP' • 'Now I'm going to measure the distances to your pulses'	Take off gloves

FHS Brachial Vascular Protocol Flowsheet

Brachial Setup	14-18	4		*If subject eligible* • Annotate baseline • Find artery long axis, find straightest segment of the artery • Color Doppler verify artery • PAN Expand, turn dial right • **Find best image** • Adjust FOCUS closest to near wall • Adjust UF5 & UF6 • **Annotate AOI & landmark** • Set up pw Doppler • Note transducer distance from antecubital fossa & angle with arm	*If subject eligible* • Click [Brachial Reactivity]	*If eligible* • 'I'm placing cold gel on your arm' • Describe test • **'To enhance test, during scan it's critical that you not move'** • **If at any time the test becomes too uncomfortable ask terminate test**	*If subject eligible* • Reposition side table parallel • Apply cuff R forearm 3 cm distal to antecubital fossa • Turn off room light • Set timer for 5 mins
Baseline	18-20	2		• **Verify that you are comfortable** • Record B single from _:00 • Pw Doppler ~ @_:40 verify position • Switch to 12K PRF, record Doppler for 3-5 beats & save • Switch to imaging Doppler (6K) till after inflation • **Annotate inflation**	• Verify good image quality before acquiring • Hit [Baseline] to acquire @ _:20 • 15 triggers B mode • 5 triggers Doppler at 12K PRF • Hit [Save Doppler]	• **Verify 'Are you comfortable?'** • 'I'm taking pictures of your artery'	• Start timer 10 seconds before inflation
Inflation	20-25	5		• Note exact time of inflation :00 • **Return to B single,** keep AOI & landmark steady for 5 minutes • **Keep arm & transducer in same position** • Before deflation, imaging Doppler with 6 K PRF @ _:45	• 3-5 triggers after inflation hit [Save images] • No images are acquired during occlusion • Hit [Deflation] @ _:45-50	• 'Now I'm going to inflate the cuff on your arm for 5 mins' • Announce minutes • 'Your arm will feel like it is going to sleep'	• **Footpedal inflate @:00** cuff to 200 mm, or 30 mm above pt's SBP • Timer rings 10 secs pre-deflation
Deflation	25-27	2		• **Keep transducer in same position** • **Annotate deflation** • **Deflate cuff @ _:00** • Switch to 12 K PRF • Record 5 beats of pw Doppler • Turn off Doppler; go to B single • Record B single till 2 minutes post • Stop recording SVHS	• 5 triggers Doppler at 12K PRF • Hit [Save Doppler] • Record for 2 minutes • Hit [Save Images] 2 minutes __:00 post deflation	• 'I'm about to deflate the cuff, you will feel pins & needles warm/cold' • **'It's critical that you not move your arm for 2 minutes**	• **Footpedal deflate cuff @:00**
Finish	27-30	3	• Take BP/P in LA • Record on w.sheet • Subject fills out discomfort survey • Fill out sonographer worksheet	• Wipe gel off subject • Measure probe placement	• Hit [Distances] • Enter distances & hit [OK] • Hit [tonometry] [BP] • Hit [clear all], enter SBP, DBP • Hit [Add], Hit [OK] • Hit [close]	• 'I'm going to take BP in LA' • Ask subject to fill out discomfort survey • **Review rare 'red spots'** • **Thank subject for participation**	• Turn on room light • Take BP in LA • Remove BP cuff • Reposition side table perpendicular
Change gloves & wash hands after each subject **At end of clinic save to 2 CDs - Verify image CD ok on brachial**							

Appendix Item 5

FHS Petechiae Log Sheet

&

FHS Incomplete Vascular Study Log Sheet

&

FHS Participant Food Intake Sheet if Non-Fasting

Brachial Reactivity Test – Skin Reaction – Petechiae

N	Name & ID	Date Clinic Visit Mo/day/yr	Abnormality Location: Hand 0=no 1=yes	Forearm 0=no 1=yes	Up. Arm 0=no 1=yes	Time Course Onset: Date Time	Offset: Date Time	Pain? 0=no 1=yes 0=no 1=yes describe	Patient upset? 0=no 1=yes 0=no 1=yes describe	P = Prior Occurrence E = Easy bruising? 0=no 1=yes describe	Comments
		Describe									
		___/___/___	0 1	0 1	0 1 Describe	___/___/___ ___ ___:___ ___	___/___/___ ___ ___:___ ___	0 1	0 1	P 0 1 E 0 1	
		___/___/___	0 1	0 1	0 1 Describe	___/___/___ ___ ___:___ ___	___/___/___ ___ ___:___ ___	0 1	0 1	P 0 1 E 0 1	
		___/___/___	0 1	0 1	0 1 Describe	___/___/___ ___ ___:___ ___	___/___/___ ___ ___:___ ___	0 1	0 1	P 0 1 E 0 1	
		___/___/___	0 1	0 1	0 1 Describe	___/___/___ ___ ___:___ ___	___/___/___ ___ ___:___ ___	0 1	0 1	P 0 1 E 0 1	
		___/___/___	0 1	0 1	0 1 Describe	___/___/___ ___ ___:___ ___	___/___/___ ___ ___:___ ___	0 1	0 1	P 0 1 E 0 1	

	Name & ID	Date	Mastectomy	Raynaud's	Pain		Left Early	Other Reason	Computer
					Fear *1	Interupt *2			

*1 Refuse because of fear of pain.

*2 Interupt the test because they experience pain.

OFFSPRING EXAM 7 - DIETARY FAT ON DAY OF EXAM

ID
NAME
DATE

(place sticker here)

Please list ALL food and beverages that you ate or drank TODAY. Include descriptions of combination dishes. Also list the approximate amount and time it was eaten.

[Example: omelette: 2 slices cheese, 2 eggs,1 tablespoon margarine 8:30 am]

MEAL	FOOD OR BEVERAGE / DESCRIPTION OF COMBINATIONS	AMOUNT	TIME	FOR OFFICE USE	
BREAKFAST					
SNACKS / CANDY					
LUNCH					
VITAMINS	(circle one) YES NO				
VITAMIN C	(circle one) YES NO				

FOR OFFICE USE CIRCLE VALUE

1. |__| FASTING	0= NO	1 = YES	9 = UNK					
2. |__| FAT CONTENT	0= NONE	1=SOME	9 = UNK					
3. |__| VITAMINS	0= NONE	1=YES	9 = UNK					
3. |__| VITAMIN C	0= NONE	1=YES	9 = UNK					

Appendix Item 6

FHS List of Rules for

Measuring Brachial Artery Ultrasound Images

FRAMINGHAM HEART STUDY

List of Rules for Measuring Brachial Artery Ultrasound Images
Milan Sonka's Program

Conversion

- Review the images and decide which will be the first and last image. Enter the frame numbers in appropriate boxes. Do the same for both **baseline** & **deflation** images.
- Annotate baseline versus deflation sequence.
- Include **"Inflation trigger"** and **"Deflation trigger"** in the sequence you save.
- **"Inflation trigger"** frame is the frame where Doppler signal first demonstrates reduced flow. "**Deflation trigger"** frame is the frame where Doppler signal first demonstrates augmented flow.

Training

- Reader should sit straight in front of the screen, not at an angle!
- Open baseline images as well as deflation images simultaneously and place them next to each other, baseline images to the left on the screen, deflation images to the right on the screen.
- **Baseline study and deflation study should be measured on the same day.** (Only exception is during data cleaning, if only baseline study or deflation study needs to be remeasured.)
- **Check calibration!!!** The latest calibration result is always memorized. If you need to change the calibration, click Define Starting Marker and Define Ending Marker and identify the points. Then input or edit the distance in millimeters in the appropriate spot.
- Review the images first, before you decide which image you want to train on.
- Try to choose **one of the first 5 best frames for training** - for **baseline** images.
- Choose **one of the first 5 best frames at 1:00 post deflation** - for **deflation** images.
- When all frames are equal, train on the first of the "good" frames.
- If results are not accurate when training on the first few frames, go several frames forward (5-10) and train on frame that will give the most accurate results.
- Try to have "training box" include AOI (area of interest), if possible.
- However, if reader decides that another segment is more accurate, train on this segment.
- Try to keep the "training box" between 6-11 mm lengthwise, if possible.
- **DO NOT reject the frame you have trained on.**
- Train on an image where "confidence level" is 70% or higher.
- When reviewing or playing, change the speed of the frames playing to 1 FPS or 2 FPS. (Default is 10 FPS.)
- Retrain if you have less than 70% of frames measured correctly.

- Always adjust the measuring lines to measure the "M-line", the line between the adventia and the intima.
- If measuring line jumps to the intima, adjust "near border" or "far border". Only measure from inside the intima when you can consistently measure the intima throughout the baseline and the deflation studies, and the M-line is not measurable.
- "Launch" the measuring program and watch carefully the measurements and the lines. Then review once and look for accuracy and confidence level.
- If results will improve, make "training box" longer (lengthwise), or move it right to left or left to right, particularly if the edge detection is jumping because of a bifurcation or "gap" in the intima.
- **Train on the same segment for baseline & deflation images. This is extremely important!**
- The average of the baseline diameters and the first five frames of the deflation diameters should measure within 0.20 mm.
- **Flow-mediated dilation is calculated from baseline images and peak dilation of deflation images.**

Measuring

- "Launch" the measuring program when satisfied with training. **DO NOT STOP** during the launch! Adjust speed to 1FPS or 2 FPS. Watch measuring lines carefully.
- Then look at the summary and the outliers. Reject all Doppler frames.
- Go back to frame 1 and play the program frame by frame. Reject outliers or remeasure, if frames are measurable. (Use Control X on the keyboard to reject. Control Z will undo rejection.)
- If more than 70% of frames seem to be measured accurately, reject frames with "wrong" lines.
- If less than 70% of frames seem to be measured accurately, retrain (= too many outliers!).
- **Measure at least 10 frames for baseline sequence.** It is OK to reject "bad" frames and not edit them, if you already have 10 measured frames.
- If you have lots of frames with wrong measurements, reject them. Then manually (black person icon) edit every third frame, if they are measurable.
- When done measuring, look at report. Make sure 70% of frames are measured, either by program or manually.

Rejecting

- When reviewing or playing, keep mouse on STOP button and write down frame numbers of the frames you want to reject. i.e. frames with Doppler images.
- Reject all frames where Doppler is turned on.
- Before rejecting a frame, decide whether the "lines" are measuring accurately or not.
- Do not reject "outliers" where the measuring lines are accurate.

- Do not reject a frame because the diameter is different from other frames. Always go back and look at the accuracy of the measuring lines.
- Do not reject the frames with confidence level less than 70% if the measuring lines look accurate. (Let in-house statistician make this decision later.)
- The diameter of the artery on the first few frames after deflation should measure within 0.20 mm of the averages of baseline diameters.
- If more than 5 continuous frames are rejected, measure manually (black person) every third frame.
- **DO NOT** reject more than 30% of frames.

Manual measurements

- Manual measurements are made by clicking on the black person icon.
- It is preferable to go with the computer generated lines. However, if it is more efficient to measure manually 10-15 frames than to retrain multiple times, do so.
- For intermittently rejected isolated frames, there is no need to measure manually.
- When multiple frames in a row have been measured by the computer in an unsatisfactory way, manually measure every third frame.

Training box – ROI

- Training box should preferably measure 9-10 millimeters lengthwise.
- However, if it is obvious while training that there is a segment where the computer lines "jump" off the appropriate borders, it is reasonable to narrow the ROI.
- The default ROI is 155 pixels long and therefore measures 115 diameters. It is reasonable to narrow the ROI to as little as 55 pixels (approx.1/2 of default ROI).

Saving

- **Save study, with measuring lines** on the frames, to D:drive. (@ FHS: Shuxia's folder, Birgitta's folder, and Eva's folder. After 10 studies, burn to a video CD, for back-up and for data cleaning.)
- **Save data in a separate data file,** on D:drive. (@FHS: Birgitta or Shuxia or Eva; then Data; then Sonka data. Also save on a floppy on A:drive, to give to data people. Make an extra Floppy of Data for back-up.)

Measuring difficult studies

- When measuring difficult studies, measure manually. Click on the black person icon, and manually draw the measuring lines on the near border and the far border.
- Only measure images that are measurable. If baseline images are measurable, but deflation images are **NOT** measurable (participant moved, sonographer moved, artery

moved, etc.), measure the baseline sequence and **DO NOT** measure the deflation sequence. **Baseline diameters alone may be prognostic**. (Make a note to data people that deflation sequence is missing.)

- Repeat measuring manually every 3-5 frames throughout the study where diameter is measurable.
- If possible, try to measure as many frames as possible around 60 seconds post deflation (5 frames before 1:00 post deflation, and 5 frames after 1:00 post deflation).
- When measuring studies with arrhythmias average all the beats between 55 and 65 seconds irrespective of the RR interval.

Appendix Item 7

FHS Data Cleaning Procedures

Brachial Cleaning at Exam 7:

This is documentation on how to clean the brachial data. Each brachial record is made up of two components: a quantitative part and a qualitative part.

- The **quantitative** part consists of brachial diameter measurements made offline by the sonographers using automated edge detection software. The measurement data includes information about the diameter and time because the brachial diameter is measured at baseline and for two minutes post-deflation.
- The **qualitative** part includes subject data recorded by the sonographers at the time of the test on paper forms entitled the *"Endothelial Function Participant and Sonographer worksheets."* The qualitative data is entered into the Ingres database by two keyers. The qualitative information includes subject eligibility criteria, the temporal relation of the brachial test to other FHS tests [walk test, oral glucose tolerance test], subject blood pressure, subject discomfort and test timing.

Joining together these two parts forms a complete record. It is challenging to clean this data because each record has multiple lines of data, and this makes it very difficult to manage the datasets.

Step 1- Clean the Brachial Worksheets:

This is an explanation of how to clean the brachial worksheets. The cleaning programs are located in /home/brachial/michelle/worksheets. These programs allow you to get a single keying of the worksheets so they can be hooked up to the measurement data.

First, run prelim1.sas and see how many single/double/multiple keyings there are and decide if you want to key all sheets up to this point or just take the id's that are double keyed. Then run prelim2.sas and prelim3.sas. Prelim2.sas outputs keyings into two different data sets and prelim3.sas makes sure the keyers are not equal.

IMPORTANT: At this point, make sure to run the before.sas program. This program takes a snapshot of the tables before any changes are made to them.

Run the compare.sas program. You should be comparing prelim3a.ssd01 to prelim3b.ssd01- this is comparing the two keyings. Print this out and look up what the appropriate answers should be. Also, look for any sheets the keyers may have flagged and also make the necessary changes- I tend to write those down on an additional sheet if they do not pop out on the compare.

Once the compare and flags are all set, then you can begin making the changes in the table. Make sure to make corrections to BOTH keyings. Once this is done, run the after.sas program. This outputs the after.ssd01 dataset and now you can compare before.ssd01 to after.ssd01 and make sure that all your changes made it into the table.

Prelim4.sas takes in the after.ssd01 data set and just outputs a single keying. Then prelim5.sas outputs prelim5.ssd01 and changes -1's, 9's, etc. to .'s.

<u>Step 2- Process the Data:</u>

1. Take all floppy disks from technicians and use WS_FTP to transfer them from floppy to UNIX. Put all Birgitta's studies into /home/brachial/michelle/data/curdatbl, all of Shuxia's studies into /home/brachial/michelle/data/curdatsf, and all of Eva's studies into /home/brachial/michelle/data/curdateo. If a study is a remeasured study (on a floppy disk of numbered 500 or higher) then it should go into one of the following directories: /home/brachial/michelle/data/remeasbl (Birgitta), /home/brachial/michelle/data/remeassf (Shuxia), and /home/brachial/michelle/data/remeaseo (Eva).
2. Use the bprocess.sas (for Birgitta's data), sprocess.sas (for Shuxia's data), and eprocess.sas (for Eva's data) to create sas datasets from the text files stored in /home/brachial/michelle/data/curdatbl, /home/brachial/michelle/data/curdatsf, and /home/brachial/michelle/data/curdateo respectively. If the study is a remeasured study, use the following programs instead to process the text files into sas datasets: remeasbl.sas (Birgitta), remeassf.sas (Shuxia), and remeaseo.sas (Eva). IMPORTANT: In these programs, you must change the dataset name that you want to get outputted. For example, if Birgitta has remeasured studies that are being processed on 1/22/2001, change the name to b012201r in the program anywhere there is a dataset getting outputted. Note that there is a variable called "pdate" created in these programs. This variable is the process date and should get changed to the date that the date gets processed.
3. Print out the .lst files for each tech. At this point the id's need to get checked against the logbook. Place a check mark next to each id once it is found on the printout and use a yellow highlighter to place a check mark in the logbook for that id. This is a very important step.
4. The programs listed above in (2) put the sas datasets into the directory /home/brachial/michelle/data/ouput. The programs output the datasets named as bmonthly.ssd01 (Birgitta), smonthly.ssd01 (Shuxia), and emonthly.ssd01 (Eva). You must go into this directory each time you process new data and rename these sas datasets. The naming convention is as follows: use the first letter of each techs name plus the date you process the data. For example, if you processed data on 1/22/2001 and it was Birgitta's data, you would rename bmonthly.ssd01 to b012201.ssd01. If it is a remeasured study you do not need to rename it in the directory because it was all ready outputted with the correct name (it should have been changed in the program).
5. In the /home/brachial/michelle/data/output directory, there are also three frequency programs, one for each tech. Every time a sas dataset gets created, run the fq30.sas (Birgitta), fq88.sas (Shuxia), and fq49.sas (Eva) programs. It will give some simple frequencies to look over and see if there are any errors. If any errors are found, then make a program that will make the changes. For example, if Birgitta's dataset, b012201.ssd01, had an error then make a program called b012201m.sas and output a new dataset called b012201m.ssd01.
6. Once each techs dataset is in place then the cleaning process can begin.

Step 3- Cleaning:

1. First create a new directory under /home/brachial/michelle/finaldat. The naming convention that is used is br______ . Insert the date that cleaning is started on; for example, if you start cleaning on 1/22/2001 then make a new directory called br012201.

2. Copy all the .sas program files from the directory with the most current date.

3. Brach1.sas: This program sets all the sas datasets that were created from the text files together. Each time a new cleaning round is started, add in the new names of the datasets. It also checks to make sure there are no duplicates and prints out a list of the new data that was added on to the old data. Printout the .lst file and check it against the sheets that were used to check against the logbook. Also check to make sure the code1 variable is correct- change any "10's" that have re-reads to "9's", etc.

4. Brach2.sas: Make any changes to code1 that are necessary. Create round variable and change to the correct round of cleaning.

5. Brach3.sas: This program takes any id that has interpretation date not equal between the baseline and deflation reading and changes it to be equal by updating it to the later of the two dates. The worksheet data gets hooked up to the data at this point. Note that only the unclean id's get the worksheet hooked on to them at this point because the clean data should not be touched.

6. Brach4.sas: This program includes the first round of checks to be done on the data. There are 34 checks in total and they are mostly looking for discrepancies between the worksheet and data. This program provides a list of all the id's with the problem number- any changes that need to be made must be made on this list.

7. Brach5.sas: This program is almost the same as the one above but this program provides a description of the problem, one page per id. Place the printout of the problem and the brachial worksheet into a maroon folder and give to the techs. If it is a simple problem it may just be corrected by the data cleaner.

8. Brach6.sas: Type in any changes/corrections that need to be made (if-then statements).

9. Brach7.sas: This program includes the second round of checks to be done on the data. There are 9 checks in total and they mostly check for problems with the brachial diameter. There is a section that checks for which id's only have a baseline or deflation reading and these id's need to be deleted before checks 7, 8, and 9 because we cannot calculate an FMD for them.

10. Brach8.sas: This program is very similar to brach7.sas, but produces a description of the problem, one page per id. Place the printout of the problem and the brachial worksheet into a maroon folder and give to the techs. Make any corrections or changes to be made on the printout from brach7.sas.

11. <u>Brach9.sas:</u> Use this program to printout any of the id's that have problems with their diameters. The printout of the whole record should be included in the maroon folder with the description of the problem and the brachial worksheet.

12. <u>Brach10.sas:</u> Type any changes/corrections that need to be made that deal with the study time and the worksheet time (if-then statements).

13. <u>Brach11.sas:</u> Type any changes/corrections that need to be made to specific diameters, for example, if just one frame needs to get deleted.

14. <u>Brach12.sas:</u> Make any changes to code2 that are necessary.

15. <u>Brach13.sas:</u> This program just double-checks that the techs made changes to the brachial floppy number on the worksheet if they remeasured a study.

<u>Description of Coding Variables in Brachial Dataset:</u>

Variable Name	*Variable Value*	*Comment*
Code1 (Status variable)	Code1 = 9	This is an original reading and a re-read coded as '11' should exist for any id coded as a '9'.
	Code1 = 10	This is the original reading but no other readings exist for id's coded as a '10'.
	Code1 = 11	This is a re-read; there should be a matching id in the dataset that has a code1 = '9'.
	Code1 = 50	Reproducibility Reading that should be in final dataset.
	Code1 = 51	Extra Reproducibility reading or extra reading.
Code2 (Cleaning Variable)	Code2 = 0	This means that the id has not been through cleaning yet.
	Code2 = 1	This means an id is cleaned.
	Code2 = 2	This means an id has gone through the cleaning process but will pop up again with cleaning issues.
Reprod (Reproducibility Round)	Reprod = 0	Not a reproducibility study.
	Reprod = 1	Reproducibility Round 1.
	Reprod = 2	Reproducibility Round 2.
	Reprod = 3	Reproducibility Round 3.
	Reprod = 4	Reproducibility Round 4.
	Etc…	
Round (Round of Cleaning)	Round = 1	Round 1 of cleaning.
	Round = 2	Round 2 of cleaning.
	Round = 3	Round 3 of cleaning.
	Etc…	

Brachial Cleaning Instructions

List of checks that are done in Brach4.sas:

Check Number	Check
Check 1	Checking idtype is either a 1 or a 7
Check 2	Checking that the data interpretation date is the same as the worksheet interpretation date (ef45)
Check 3	Checking Sonographer ID in data is the same as the worksheet sonographer id (ef17)
Check 4	Checking Interpreter ID in data is the same as the worksheet interpreter id (ef44)
Check 5	Making sure that the study date is not later than the interpretation date
Check 6	Making sure the Study date on the worksheet (ef01) is the same as the contact date in the Offstatus table
Check 7	Making sure the Study date in the data is the same as the Study date on the worksheet (ef01)
Check 8	Making sure if the Study date on the worksheet is the same as the Study date in the data that the worksheet question, 'Exam date?' (ef02) is coded as 'Yes'
Check 9	If a participant has Raynaud's disease, should not continue with exam. Making sure that this question (ef03) is not coded as 'Yes' and the rest of worksheet is filled out
Check 10	If a participant has had a radical mastectomy, should not continue with exam. Making sure this question (ef04) is not coded as 'Yes' and the rest of worksheet is filled out
Check 11	Checking sex from Roster with a sex variable created from the worksheet
Check 12	Checking the range of discomfort scale for brachial is between 0 and 100
Check 13	Checking the range of discomfort scale for venipuncture is between 0 and 100
Check 14	Making sure that Cuff inflation pressure (ef30) is not less than initial SBP (ef23)
Check 15	Making sure that Radial (ef50) not less than brachial (ef49)
Check 16	Making sure that if tonometry was done, measurements are there. Or if measurements are there and worksheet says tonometry was not done
Check 17	Checking that if person said they had caffeinated beverages (ef05) that subquestion (ef06) is filled in ('if yes, how many cups?') or if they didn't have any caffeinated beverages that the subquestion is coded as missing
Check 18	Checking if person said they smoked in last 6 hours (ef08) that the subquestion (ef09) is filled in ('if yes, how many hours and minutes since your last cigarette') or if they had not smoked in the past 6 hours that the subquestion is coded as missing
Check 19	Checking range of initial SBP (ef23) (80-200 mm Hg)
Check 20	Checking range of initial DBP (ef24) (30-110 mm Hg)
Check 21	Checking range of initial pulse (ef25) (40-140 mm Hg)
Check 22	Checking range of Cuff inflation pressure (ef30) (200-240 mm Hg)
Check 23	Checking range of post-deflation SBP (ef34) (80-200 mm Hg)
Check 24	Checking range of post-deflation DBP (ef35) (30-110 mm Hg)
Check 25	Checking range of post-deflation pulse (ef36) (40-240 mm Hg)
Check 26	Checking for any missing values
Check 27	Checking range of room temperature (ef21) (15-28 degrees Celsius)
Check 28	Making sure that the variable reprod in the data which stands for whether or not a study is a reproducibility is coded correctly
Check 29	Making sure that if a study has a code1=9 or 10 that the variable reading = 1 or that if code1=11 that the variable reading=2
Check 30	Making sure that the round variable is coded correctly
Check 31	Making sure that on the brachial floppy disk number from worksheet (ef48) that the first portion of the variable is one of the technicians id numbers
Check 32	Making sure that the variables baseline measurable (ef53), deflation measurable (ef54), and ok to calculate FMD (ef55) are filled out.
Check 33	Making sure if code1=11 that the techs updated the worksheet interpretation date and brachial floppy number
Check 34	Making sure that if brachial scan protocol was completed (ef38) that subquestion (ef39) not filled in, or if brachial scan protocol was not completed, that the subquestion is filled in with a reason

List of checks that are done in Brach7.sas:

Check Number	Check
Check 1	Checking the range of the brachial diameter (bdia): range goes from 2.2-6.5 mm
Check 2	Checking that the difference between the mean of the baseline brachial diameters and the mean of the first five deflation diameters is not greater than 0.2 mm
Check 3	Checking that any adjacent frames are not greater than 0.2 mm different from each other
Check 4	Checking that the difference between the mean of the baseline diameters is not greater than 0.4 mm different than any one of the baseline diameters
Check 5*	Checking that the tape start time on the worksheet (ef27, ef28, ef29) is not greater than 15 minutes different than the data start time
Check 6*	Checking that the tape stop time on the worksheet (ef31, ef32, ef33) is not greater than 15 minutest different than the data stop time
Check 7	Checking that the FMD raw 60 second is between –2% and 12%
Check 8	Checking that the FMD regressed 60 second is between –2% and 12%
Check 9	Checking that the FMD regressed maximum is between –2% and 12%

*NOTE: We did not do Check 5 or Check 6 on any study done before 8/26/1999. There were many problems with the study times and there was not a way to reconcile them.

Appendix Item 8

FHS Original Specific Aims of RO1 Grant Submission

Study of Endothelial Function at the Framingham Heart Study

Increasingly, researchers have come to understand that loss of the vasodilator, anti-thrombotic, and anti-inflammatory properties of the vascular endothelium may play a dynamic role in the pathogenesis of coronary artery disease and stroke. Invasive and non-invasive studies suggest that impaired endothelial function, particularly loss of endothelium-derived nitric oxide, is associated with cardiovascular disease risk factors including aging, male gender, post-menopausal status, elevated cholesterol, diabetes mellitus, cigarette smoking, hypertension, and elevated homocysteine levels. Further, researchers have observed that endothelial function is compromised in the presence of some, but not all subjects with coronary artery disease, and that endothelial dysfunction can be improved by risk modification.

Prior studies, have not definitively resolved the issues of the cross-sectional correlates of endothelial dysfunction, because they have been limited to small samples of highly selected patients. For example it remains unclear whether hypercholesterolemia, hypertension, or hyperglycemia are independent determinants of endothelial dysfunction. Most importantly, no study has shown a relation between endothelial dysfunction and increased cardiovascular risk in follow up. Prior studies of endothelial function used invasive methodology, but the recent development of a rapid, non-invasive method for assessment of endothelial function using brachial artery ultrasound now makes such a study feasible.

We propose to use brachial ultrasound to examine endothelial function in a population-based sample of about 3800 men and women of the **Framingham Heart Study**. We hypothesize that endothelial dysfunction is a subclinical marker for atherosclerotic cardiovascular disease, and that after adjusting for standard cardiovascular risk factors, endothelial dysfunction will be significantly associated with prevalent and incident cardiovascular disease. Our proposal has the following specific aims:

Aim 1. To examine the cross-sectional correlates of endothelial function.
A multivariable model will be used to examine the relations between brachial artery flow-mediated dilation and cardiovascular risk factors including age, gender, menopausal status, estrogen replacement therapy, cigarette smoking, plasma lipids, blood pressure, hemoglobin A_{1C}, homocysteine, and hemostatic factors. We also propose to examine the relation of endothelial function to other noninvasive assessments of subclinical disease.

Aim 2. To perform cross-sectional analyses on the relation of endothelial function to prevalent cardiovascular disease.
A multivariable model will assess if endothelial dysfunction is related to prevalent myocardial infarction, angina, heart failure and stroke, accounting for standard cardiovascular risk factors.

Aim 3. To investigate the familial and genetic aspects of brachial artery endothelial function.
Capitalizing on a rich family structure with extensive sibling-sibling relationships, we propose to use generalized estimating equations to derive estimates of genetic heritability. Using a genome scan which is being performed on an estimated 1800 subjects we propose to perform genetic linkage analyses to look for sites of linkage with the quantitative phenotype.

Aim 4. To examine the prognostic relation of brachial artery endothelial function to incident and recurrent cardiovascular disease events.
Subjects will be followed prospectively to determine the prognostic relation of endothelial dysfunction to sudden death, myocardial infarction, angina, heart failure, and stroke.

The Framingham Heart Study and the study investigators are uniquely suited to complete this proposal. The Framingham Heart Study provides a large, single site, population-based sample of middle-aged and elderly subjects with a wealth of antecedent and contemporary risk factor data, and the availability of longitudinal follow-up beyond the length of the proposed grant. The principal investigator, Dr. Benjamin, has proven expertise in the conduct of non-invasive imaging studies in the Framingham population and is well experienced with the essential quality control and data management procedures for a large-scale study of this nature. The co-investigator, Dr. Vita, is an established expert in the field of endothelial function and the use of the proposed methodology. This unique combination of investigator expertise and a well characterized population, provides an opportunity to definitively address the relations between endothelial function and other risk factors, and the prognostic value of endothelial dysfunction. These insights will increase our understanding of the pathophysiology of cardiovascular disease, and if endothelial function proves to have prognostic value, the study will lead to improved management and prevention of cardiovascular disease.

Appendix Item 9

FHS Brief Overview of Tonometry &

Brachial Reactivity Data Acquisition

NIHem

Noninvasive Hemodynamics Workstation
Tonometry Applications Note

Note: This workstation is not approved for routine clinical use. It is intended to be used for research purposes only under the supervision of an experienced physician.

Warning: The NIHem Workstation utilizes multiple high resolution and multimedia timers, including those supplied with the Windows NT® operating system. Unauthorized software or hardware may interfere with the proper function of these timers. Therefore:

- **Do NOT install unauthorized hardware or software onto the NIHem Workstation.**
- **Do NOT modify the Windows NT® configuration in any way without prior approval from Cardiovascular Engineering, Inc.**
- **Do NOT activate or load screen savers onto the computer.**

Rev. 2.1
August 3, 2000

1.0. General

1.1. Confirm that all pulses (especially the femoral artery) are accessible prior to initiating the pulse acquisition sequence.

1.2. Ask the patient not to talk unless necessary during the pulse acquisition. Proceed through the sequence of pulses as quickly as possible without feeling rushed. Do not comment to the patient on the quality of the recordings during the acquisition.

1.3. Using your fingers, take the time to establish the course of the artery and to find the point of maximal pulsation at each site prior to attempting tonometry.

1.4. Tonometry uses dry contact.

1.5. Characteristics of an optimal waveform include:

- Steadily falling diastolic tracing
- Clean, smooth transition into the upstroke at the "foot" of the waveform
- Monophasic early systolic upstroke
- Recognizable reflected wave or secondary pressure peak either in systole or diastole
- Crisp dicrotic notch
- Stable baseline.

These features apply to all waveforms, although the shape of the waveform and timing of the reflected wave will vary from site to site. Specifically, in the femoral artery, the dicrotic notch will appear as an abrupt change in slope rather than a true notch and the reflected wave will merge with the primary wave producing a single peak.

1.6. Signs of poor positioning or too much pressure include:

- Flat diastolic phase, producing a "square wave" tracing
- Scooped diastole that reaches an early minimum and is rising prior to the foot of the waveform
- Sudden negative dip just prior to the upstroke, producing a "square root sign" at the foot of the waveform
- Inverted pressure waveform, suggesting that the tonometer is off to one side of the vessel

1.7. Beware of excessive pressure, especially in slender patients with superficial arteries and in all patients at the radial artery. The artery will collapse or will slide out from under the tonometer if too much pressure is used. A common error is to use excessive pressure in an attempt to rectify improper centering. Make certain that you locate the optimal centering before attempting to optimize pressure.

1.8. Mark the site of each waveform acquisition with a lip liner as soon as a suitable pulse waveform has been recorded. The impression of the tonometer should be visible on the skin and the dot should be placed where the center of the sensing button was located.

2.0. Use of the NIHem Low Profile Tonometer

2.1. Using your fingers, carefully establish the optimal location for tonometry before attempting to obtain a recording. Tips for finding the optimal location for each pulse site are described below.

2.2. Place the white sensor of the low profile tonometer at the midpoint of the long axis of the vessel at the point of maximal pulsation and apply approximately as much pressure as was required to optimally palpate the pulse. For brachial arteries, this will elevate the blue pressure tracing to about ¼ to ½ way up the screen on a 200 scale, depending on arm size, artery depth, etc. Radial arteries are superficial with bone immediately behind the artery; thus light pressure (¼ screen) should be used to start. Femoral arteries are deeper and require more pressure (generally ½ screen or more). Carotids generally require light pressure (often ¼ screen or less) if the optimal location is chosen, as detailed below.

2.3. Generally, the index finger is used to hold down the tonometer. It is better to rest the entire finger flat on the patient's skin rather than having only the fingertip in contact with the tonometer. Resting the fingers of the hand flat against the patient stabilizes hand position and minimizes tremor and baseline drift.

2.4. Use the tonometer and the following steps to find the midline of the vessel:

- Position the tonometer at the presumed (palpated) midline of the vessel and apply moderate pressure as appropriate for the site.
- Then use skin traction to purposefully displace the sensor medial to the long axis of the vessel.
- Next, slowly and systematically move laterally, using skin traction (i.e., do not attempt to actually slide the tonometer across the skin), until a pulsation is seen (Figure 1). Continue to move laterally until the pulsation becomes maximal and then declines. In this manner, the center of the vessel and optimal point for tonometry is clearly established since the tonometer has moved across the entire spectrum from too medial to optimal to too lateral.
- Move back medially until at the optimal central point (maximal amplitude for the current amount of hold-down pressure and sharpest waveform features).

- With experience, you will notice that it is possible to feel the pulsations of the vessel through the tonometer. This tactile feedback will help with optimal positioning of the sensor.
- Note that it is important to maintain a constant amount of hold-down pressure during this maneuver and to move slowly. If hold-down pressure is varied during the sweep, the baseline will wander, making it difficult to see pulsations as the tonometer passes over the center of the vessel. If the sweep is performed too rapidly, it is possible to move across the vessel in a single diastole and never see a pulsation. Recall that the entire sweep from too medial to too lateral is only a few millimeters.

2.5. Optimize the hold-down pressure (see attached Figures 2-3). This is accomplished by gently and gradually applying increased amounts of pressure. Assuming that minimal pressure is applied initially, as more pressure is applied the pressure waveform amplitude (i.e., the pulse height from waveform foot to peak) will become larger and the features (especially the dicrotic notch) will become clearer. The waveform tracing will also move higher on the screen in proportion to the amount of pressure applied—this is not what we are referring to as "amplitude." As even more pressure is applied, the waveform amplitude will become smaller, the dicrotic notch will fall, and diastole will become flat, approximating a square wave, because the vessel is actually collapsing in diastole. This indicates that the optimal pressure point has been passed. Reduce hold-down pressure until the maximal waveform amplitude is obtained, hold this position for 10 seconds and save.

3.0. Site Specific Notes: Brachial

3.1. Start with the patient's arm fully extended on the bed at their side with the hand in a neutral position (palm toward their thigh) or palm up.

3.2. Place the index and middle fingers of your right hand along the antecubital crease with your index finger lateral to the biceps tendon and your middle finger medial to the tendon. The pulse should be palpable under one of the two fingers, indicating whether to approach the artery from the medial or lateral side of the tendon. In most cases, medial to the tendon and just above the antecubital crease is the optimal location. Avoid palpating the artery through the tendon, as this will produce a damped tracing.

3.3. The initial location to look for the pulse should be at or just above the antecubital crease, realizing that the maximal pulsation may be 1-2 cm above or (less often) below this reference point, depending on the relationship between the artery and biceps tendon. If the pulse is weak or not apparent, try turning the patient's hand palm down. If you still cannot find the artery, palpate along the medial edge of the biceps muscle to find the artery as it emerges between the biceps and the triceps.

3.4. Once the pulse is located, use the index, middle and ring fingers of the left hand to identify the course of the artery along the long axis of the arm.

3.5. When all three fingers are on the artery, use small amounts of medial/lateral traction to roll the artery under your fingers to determine its size, course and mobility.

3.6. Move your index finger aside and place the tonometer at the point of maximal pulsation. Use only enough pressure to elevate the blue pressure tracing to about ¼ the height of the screen (200 scale).

3.7. Optimize location and hold-down pressure as detailed above.

3.8. Once an optimal waveform is obtained, stabilize your position, hold for 10 seconds and save.

4.0. Site Specific Notes: Radial

4.1. The radial artery is superficial and reasonably constrained just proximal to the first of the wrist creases, at approximately the location of the styloid process of the radius.

4.2. The radial artery is generally very superficial and is surrounded by bone. Therefore, use only enough pressure to elevate the blue pressure tracing to about ¼ the height of the screen (200 scale).

4.3. If the artery is recessed below the level of the flexor tendons of the wrist, it may be necessary to place the tonometer body and cable in-line with (rather than perpendicular to) the long axis of the vessel in order to avoid a bridging effect of surrounding tendons and bone.

4.4. Optimize location and hold-down pressure as detailed above.

4.5. Once an optimal waveform is obtained, stabilize your position, hold for 10 seconds and save.

5.0. Site Specific Notes: Femoral

5.1. The femoral artery is the most deeply located of the vessels. Therefore, finding the optimal pulse location prior to attempting tonometry is important.

5.2. In general, "high and inside" is a good starting place. Thus, start at or above the inguinal crease, and stay well medial to the insertion of the quadriceps tendons.

5.3. Locate the pulse with the right hand by placing all four fingers along the inguinal ligament (essentially perpendicular to the long axis of the vessel). One of the fingertips should fall on the artery.

5.4. Place the index, middle and ring fingers of the left hand along the long axis of the artery, realizing that the proximal vessel is angling toward the midline. Once the fingers are aligned with the artery, move the hand along the vessel as needed to position the index finger at the point of maximal pulsation. Then move the index finger aside and, using your right hand, place the tonometer at the point of maximal pulsation while maintaining patient contact with the middle and ring fingers of the left hand. This will help establish localization of the vessel as the tonometer is properly positioned.

5.5. The femoral artery will require more pressure than the brachial or radial. Apply enough pressure with the tonometer to elevate the blue pressure tracing to mid-screen on 200 scale. Find the vessel midline as detailed above in the section on use of the tonometer. Once the waveform is visible, if you have kept the fingers of your left hand on the pulse, gradually reduce the pressure being applied by the fingertips of the left hand, if possible. Occasionally, especially with obese patients, it will be necessary to maintain some pressure with the left hand in order to compress or displace overlying adipose tissue. However, do not press hard enough with the left hand to compress the artery.

5.6. If it is difficult to apply and maintain sufficient hold-down pressure with the index finger of your right hand alone, use your left hand to apply additional pressure to your right index finger.

5.7. Waveform morphology will be somewhat less well defined with the femoral artery. The dicrotic notch will be evident more as an abrupt change in slope rather than an actual notch in most patients. Furthermore, the reflected wave will generally merge with the forward wave to form a single peak. However, pulse amplitude should be comparable to that of the brachial and radial.

5.8. Once an optimal waveform is obtained, stabilize your position, hold for 10 seconds and save.

6.0. Site Specific Notes: Carotid

6.1. Position the patient's head so that the chin is slightly up and the patient is looking slightly away from you. Exaggeration of either of these adjustments will make tonometry more difficult as it will place excessive tension on the sternocleidomastoid (SCM) muscle and skin.

6.2. The optimal location for carotid tonometry is just lateral to the larynx, in the angle between the SCM muscle and the larynx, i.e., cranial and medial to the SCM. It is possible to compress the carotid against the pre-vertebral muscles in this region. Do not palpate the carotid from the side of the neck through the SCM. This will require excessive hold-down pressure and will produce a damped tracing.

6.3. Locate the carotid pulse and determine the mobility of the vessel. Then use the very tip of your fully extended right index finger (as though pointing at the pulse) to imitate a tonometer and determine the optimum approach, i.e., one which allows you to palpate a suitable pulse without causing the vessel to move. The initial approach should be approximately 45 degrees lateral to the midline and perpendicular to the long axis of the vessel. Once the vessel is located, decreasing the angle with respect to the midline may help to stabilize the vessel against the pre-vertebral muscles. If your finger is properly located in the angle between the SCM and larynx, you will find that very light pressure will be needed to palpate the pulse even in patients with fairly large necks.

6.4. Attempt tonometry using the optimum approach that was established using your finger. Note that once the vessel is located, a more stable tracing is often obtained by adjusting the hold-down angle of the tonometer to be more parallel with a plane through the midline, i.e., in an anterior-posterior direction.

6.5. It is important to stabilize your arm and hand during carotid tonometry. Your arm should lie across the patient's deltopectoral groove or chest; thus, you must be seated just across from the patient's shoulder. This position is facilitated by setting up the room with the head of the bed pulled away from the wall by 18-24" so that when the NIHem cart is pushed against the wall it is out of the way. The arm can also rest on the patient's chest, although respiratory artifact may be a problem. Additionally, the fingers of the hand holding the tonometer should be flat against the skin of the neck if possible.

6.6. Tell the patient that it is OK to swallow as needed. If the patient swallows during a suitable recording period, it will create an artifact that will require a few seconds of additional recording; however, the patient will be more relaxed.

6.7. In the average patient, very little pressure will be required to obtain a waveform. Therefore, use only enough pressure to elevate the blue pressure tracing to about ¼ the height of the screen (200 scale). In heavier patients, it may be necessary to apply more pressure, though rarely to beyond the mid-screen level.

6.8. Once an optimal waveform is obtained, stabilize your position, hold for 10 seconds and save.

Figure 1a. Performing a sweep across the long axis of the brachial artery.

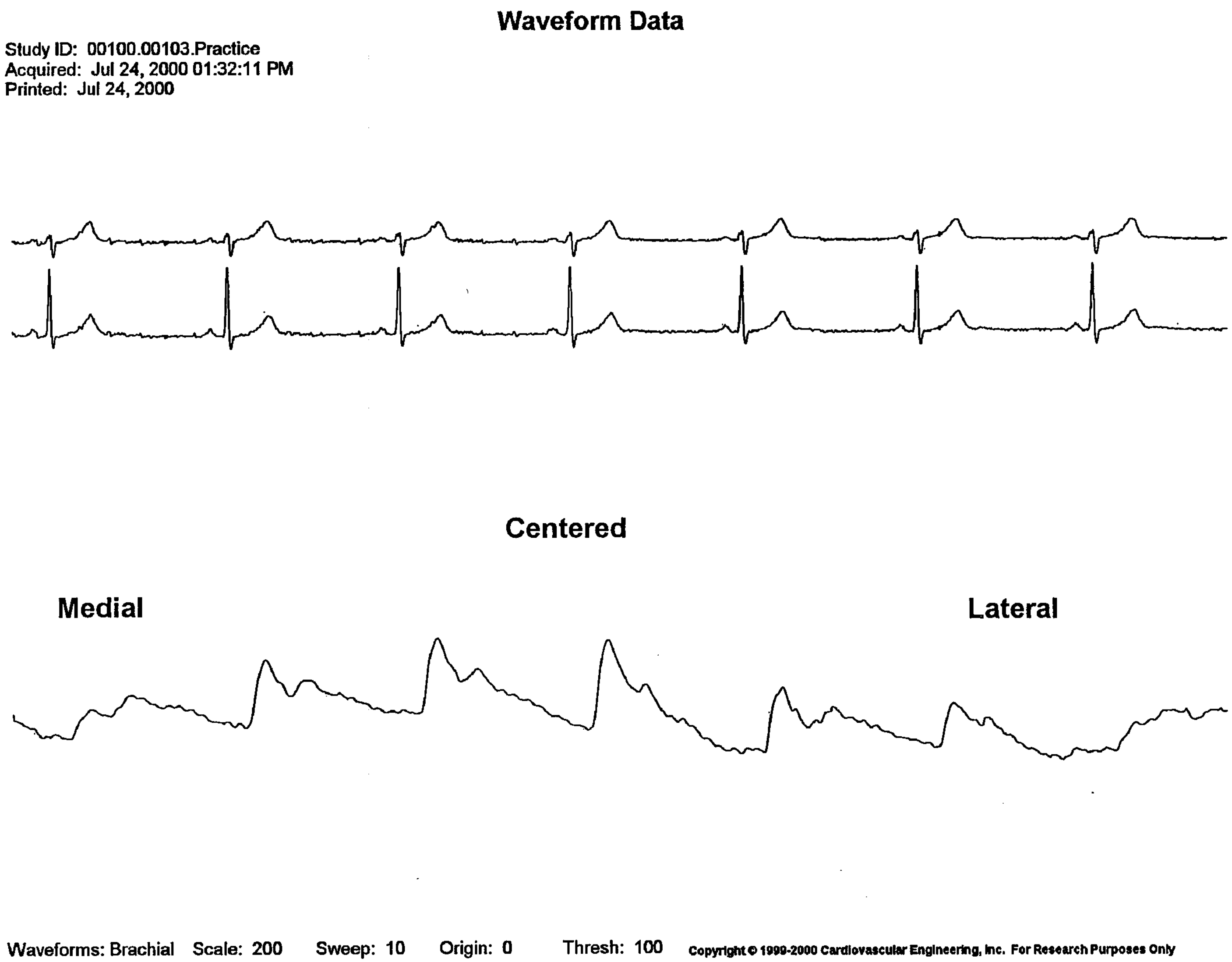
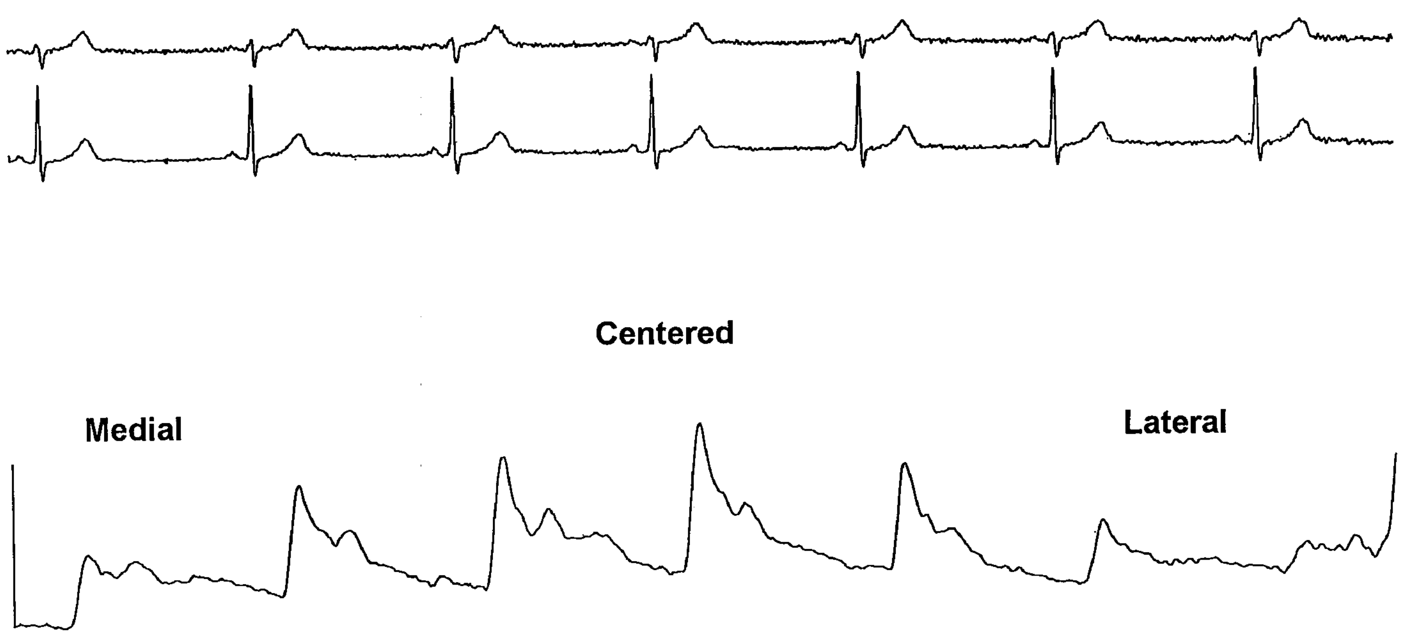


Figure 1b. Performing a sweep across the long axis of the radial artery.

Waveform Data

Study ID: 00100.00103.Practice
Acquired: Jul 24, 2000 01:33:59 PM
Printed: Jul 24, 2000

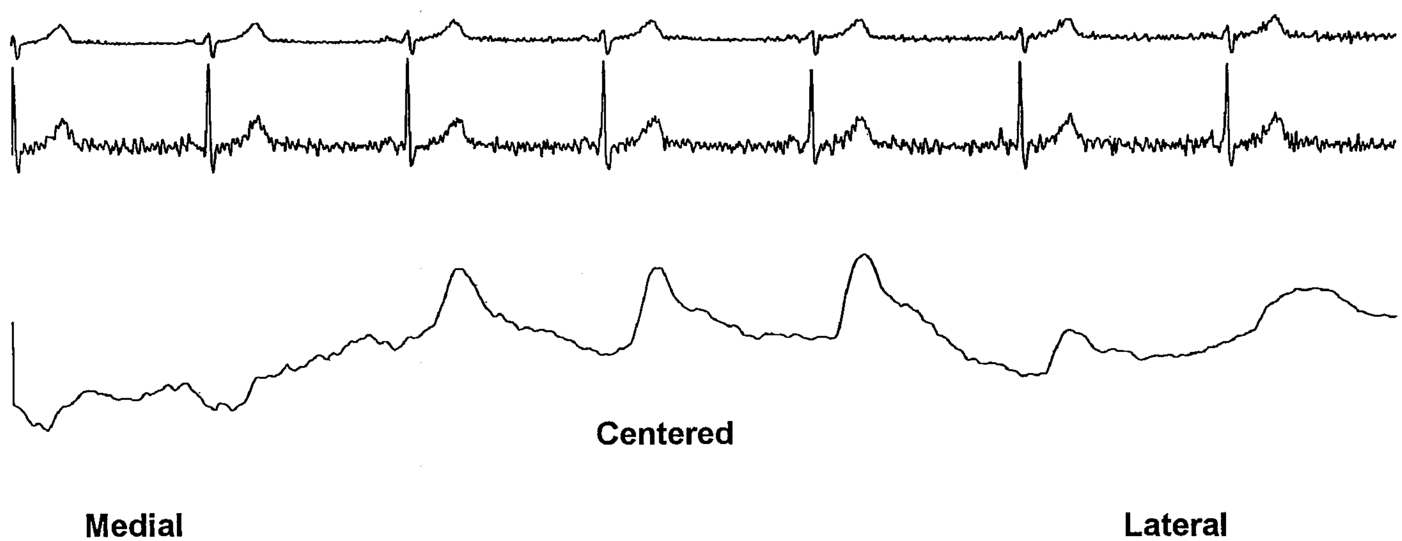


Waveforms: Radial Scale: 200 Sweep: 10 Origin: 0 Thresh: 100

Figure 1c. Performing a sweep across the long axis of the femoral artery.

Waveform Data

Study ID: 00100.00103.Practice
Acquired: Jul 24, 2000 06:32:40 PM
Printed: Jul 25, 2000

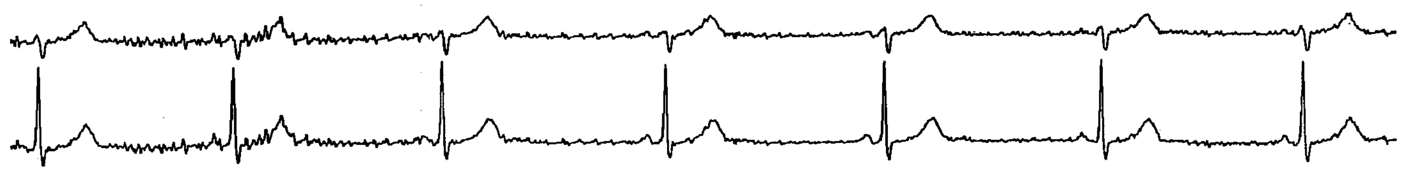


Waveforms: Femoral Scale: 200 Sweep: 10 Origin: 0 Thresh: 75

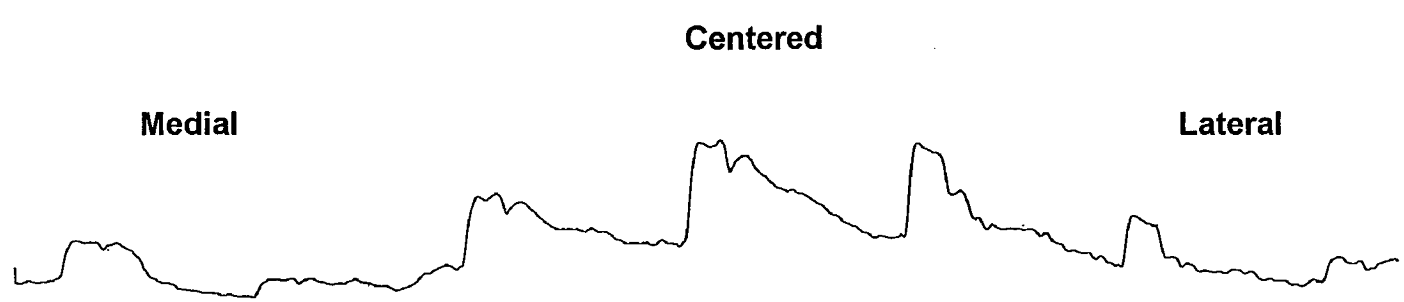
Figure 1d. Performing a sweep across the long axis of the carotid artery.

Waveform Data

Study ID: 00100.00103.Practice
Acquired: Jul 24, 2000 01:39:47 PM
Printed: Jul 24, 2000



Note the loss of features and merging of the dicrotic notch with a flattened diastolic baseline as the tonometer moves off center, giving a low amplitude, square-wave appearance to the pressure waveform

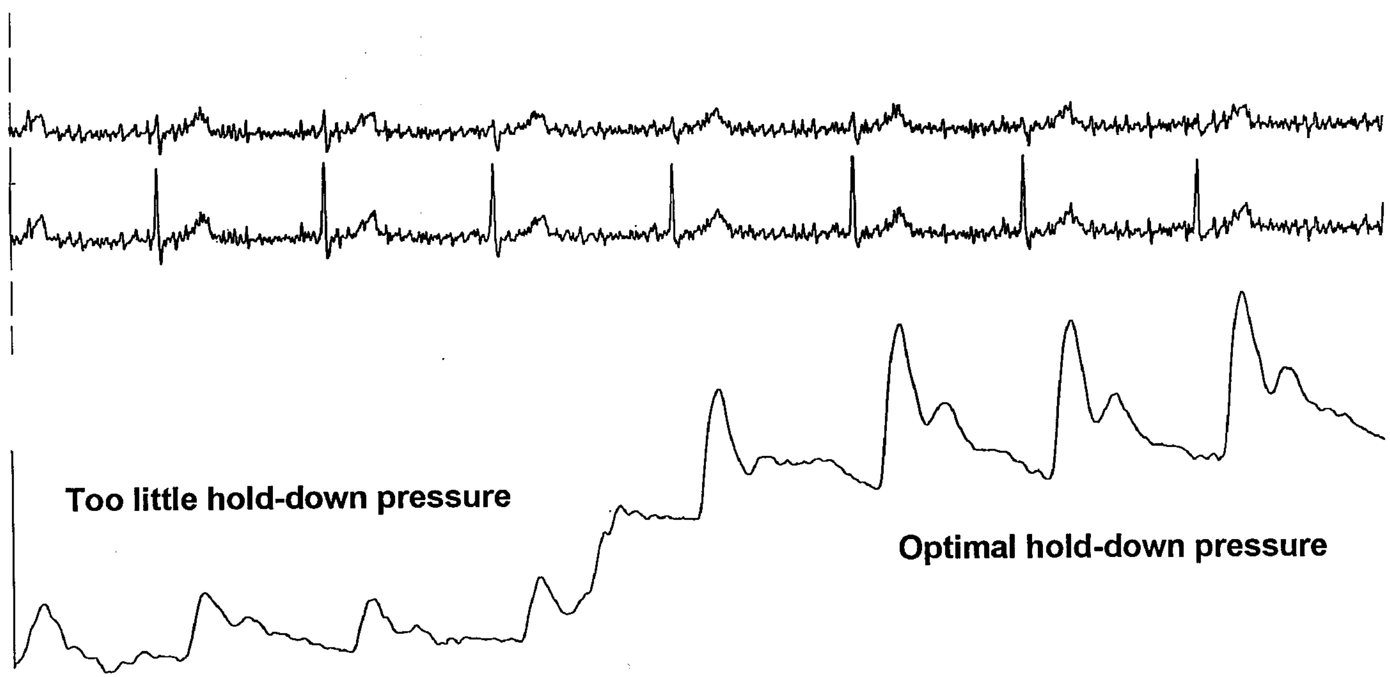


Waveforms: Carotid Scale: 200 Sweep: 10 Origin: 0 Thresh: 100

Figure 2a. Changing brachial hold-down pressure from too little to optimal.

Waveform Data

Study ID: 00100.00101.Practice
Acquired: Jul 24, 2000 01:01:03 PM
Printed: Jul 24, 2000



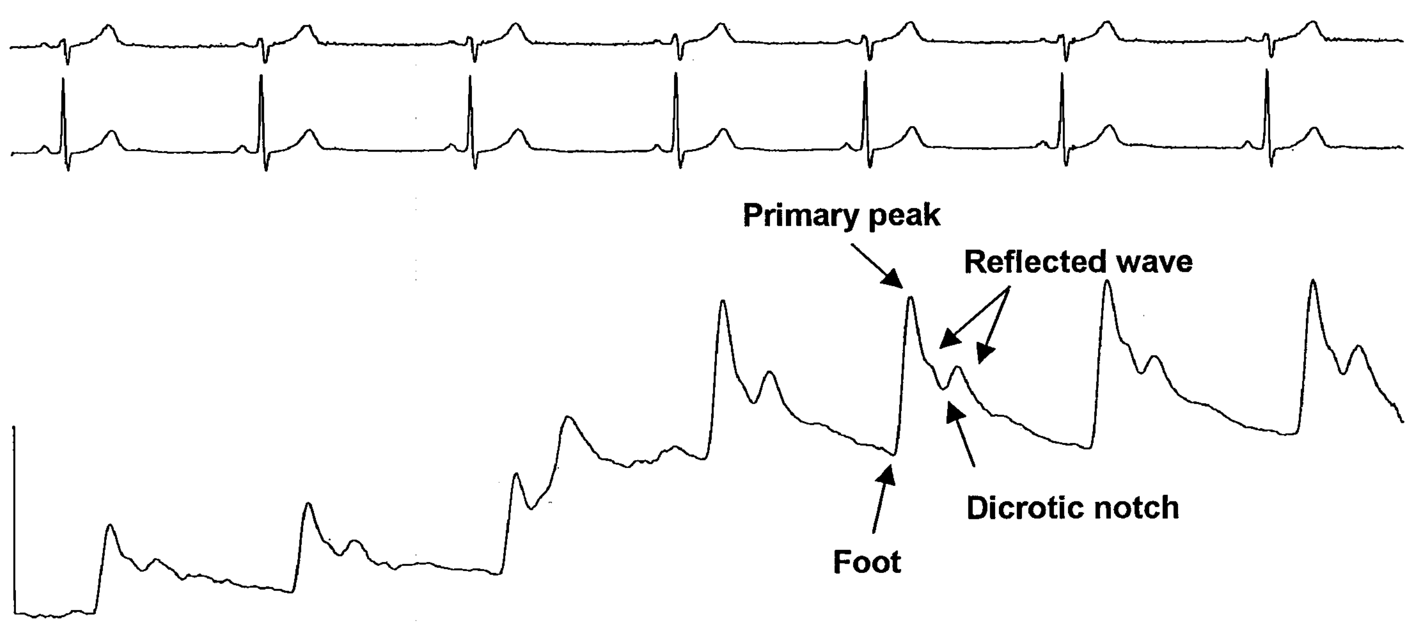
The pulse is located using enough pressure to elevate the waveform to about mid-screen. Once a waveform is located, additional hold-down pressure is applied, resulting in higher amplitude and sharper waveform features (dicrotic notch and reflected wave).

Waveforms: Brachial Scale: 200 Sweep: 10 Origin: 0 Thresh: 100

Figure 2b. Changing radial hold-down pressure from too little to optimal.

Waveform Data

Study ID: 00100.00101.Practice
Acquired: Jul 24, 2000 01:02:04 PM
Printed: Jul 24, 2000

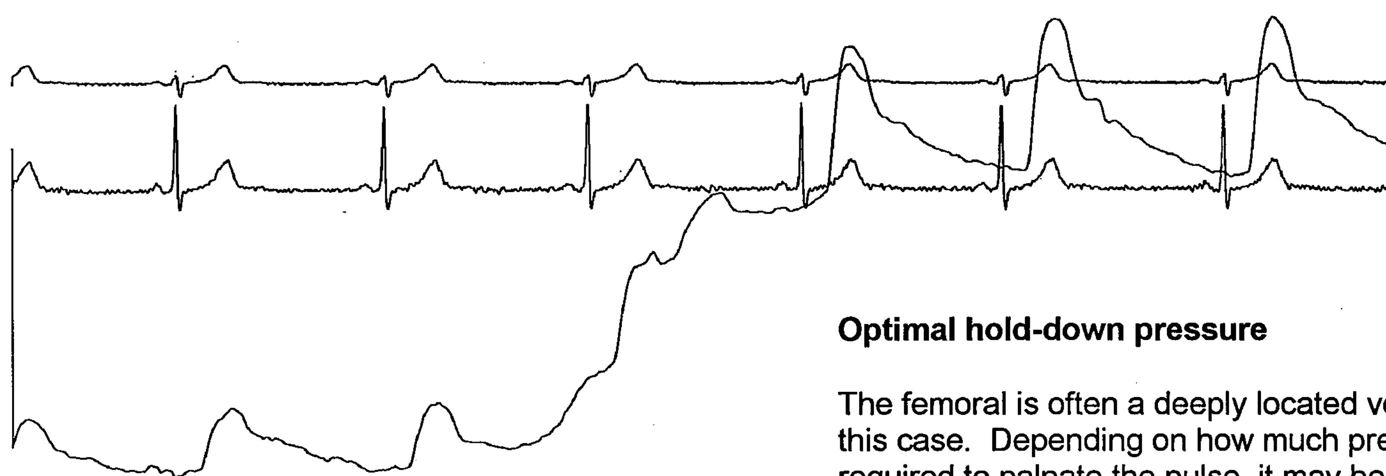


Waveforms: Radial Scale: 200 Sweep: 10 Origin: 0 Thresh: 100

Figure 2c. Changing femoral hold-down pressure from too little to optimal.

Waveform Data

Study ID: 00100.00101.Practice
Acquired: Jul 24, 2000 06:27:48 PM
Printed: Jul 25, 2000



Too little hold-down pressure

Optimal hold-down pressure

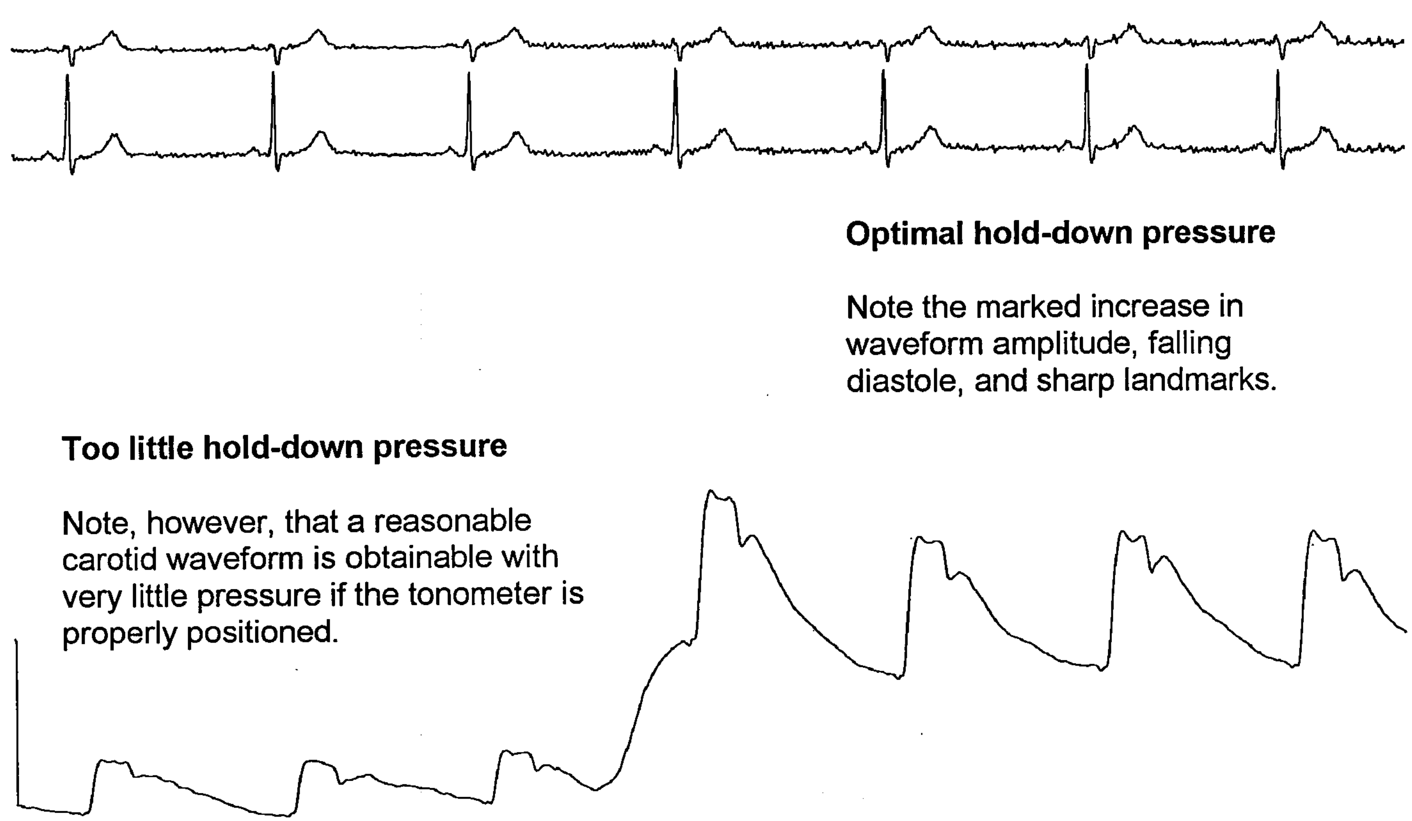
The femoral is often a deeply located vessel as in this case. Depending on how much pressure is required to palpate the pulse, it may be necessary to use moderate pressure (1/2 screen) to find the pulse and full screen (into the ECG region as shown here) to find an optimal waveform. It is fine to overlap the ECG, but if more range is needed, change the scale from 200 (shown here) to 400.

Waveforms: Femoral Scale: 200 Sweep: 10 Origin: 0 Thresh: 75

Figure 2d. Changing carotid hold-down pressure from too little to optimal.

Waveform Data

Study ID: 00100.00101.Practice
Acquired: Jul 24, 2000 01:07:23 PM
Printed: Jul 24, 2000

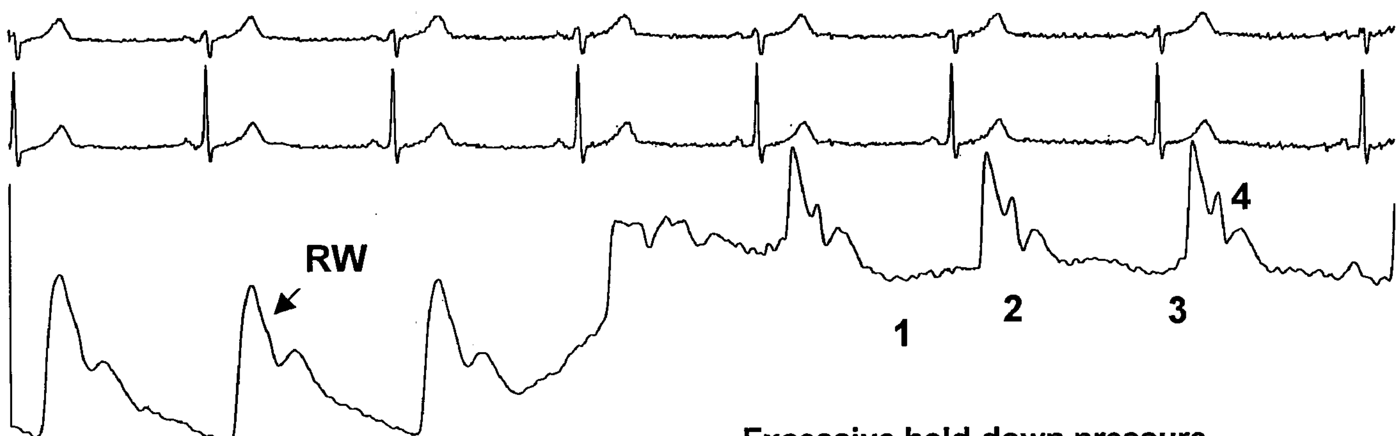


Waveforms: Carotid   Scale: 200   Sweep: 10   Origin: 0   Thresh: 100

Figure 3a. Changing brachial hold-down pressure from optimal to excessive.

Waveform Data

Study ID: 00100.00102.Practice
Acquired: Jul 24, 2000 01:10:48 PM
Printed: Jul 24, 2000



Optimal hold-down pressure

Optimal waveform has falling diastole, sharp foot, monophasic upstroke, reflected wave (RW), which begins in systole with remainder in diastole and obvious dicrotic notch.

Excessive hold-down pressure

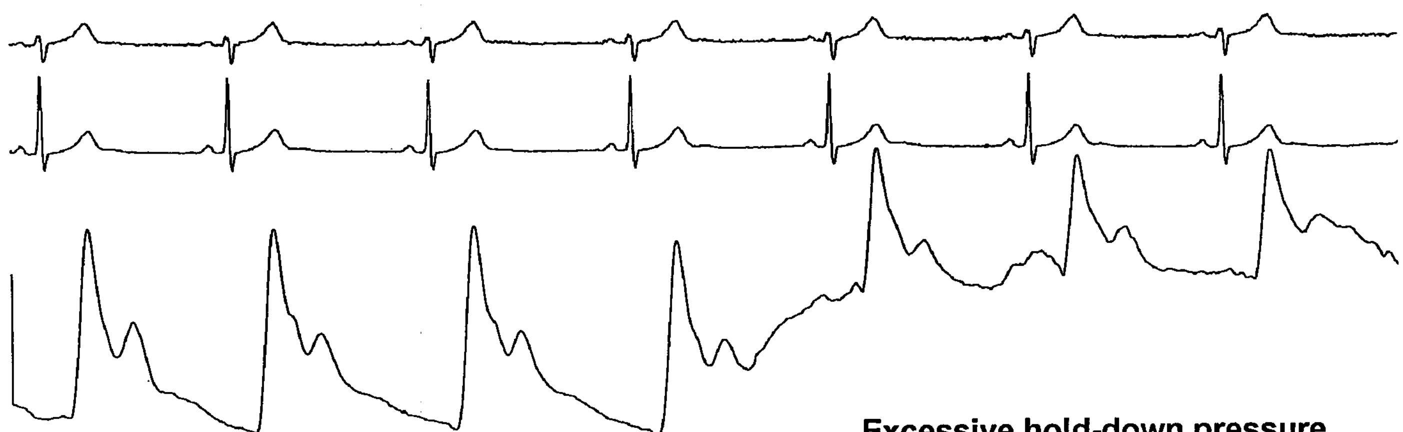
When excessive pressure is applied diastole flattens (1), waveform amplitude is reduced (2), waveform foot is slurred (3) and reflected wave and dicrotic notch become excessively peaky (4).

Waveforms: Brachial Scale: 200 Sweep: 10 Origin: 0 Thresh: 100

Figure 3b. Changing radial hold-down pressure from optimal to excessive.

Waveform Data

Study ID: 00100.00102.Practice
Acquired: Jul 24, 2000 01:13:55 PM
Printed: Jul 24, 2000



Excessive hold-down pressure

Note: Flat-to-scooped diastole and reduced waveform amplitude when excessive hold-down pressure is applied.

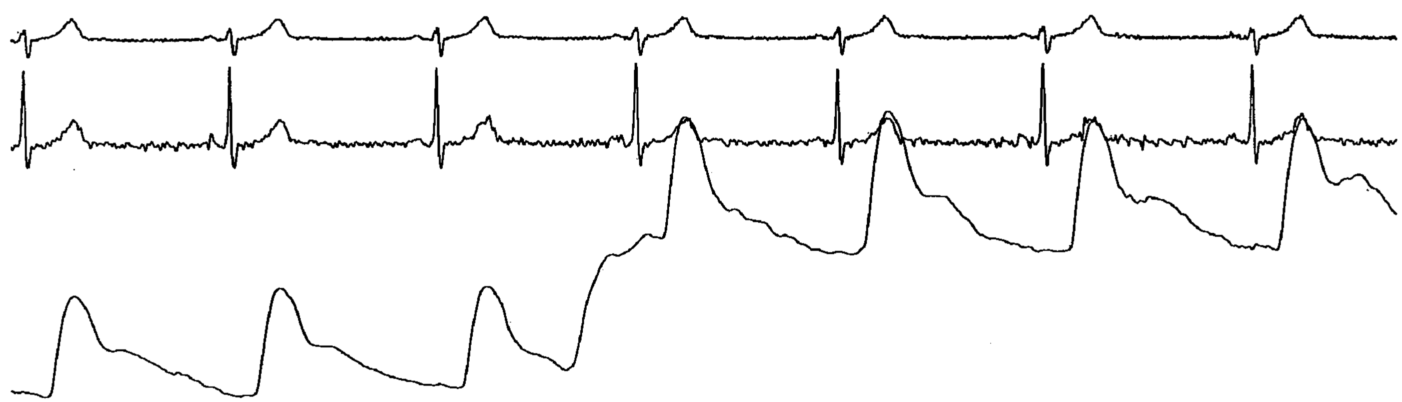
Optimal hold-down pressure

Waveforms: Radial Scale: 200 Sweep: 10 Origin: 0 Thresh: 100

Figure 3c. Changing femoral hold-down pressure from optimal to "excessive."

Waveform Data

Study ID: 00100.00102.Practice
Acquired: Jul 24, 2000 06:13:28 PM
Printed: Jul 25, 2000



"Excessive" hold-down pressure

Optimal hold-down pressure

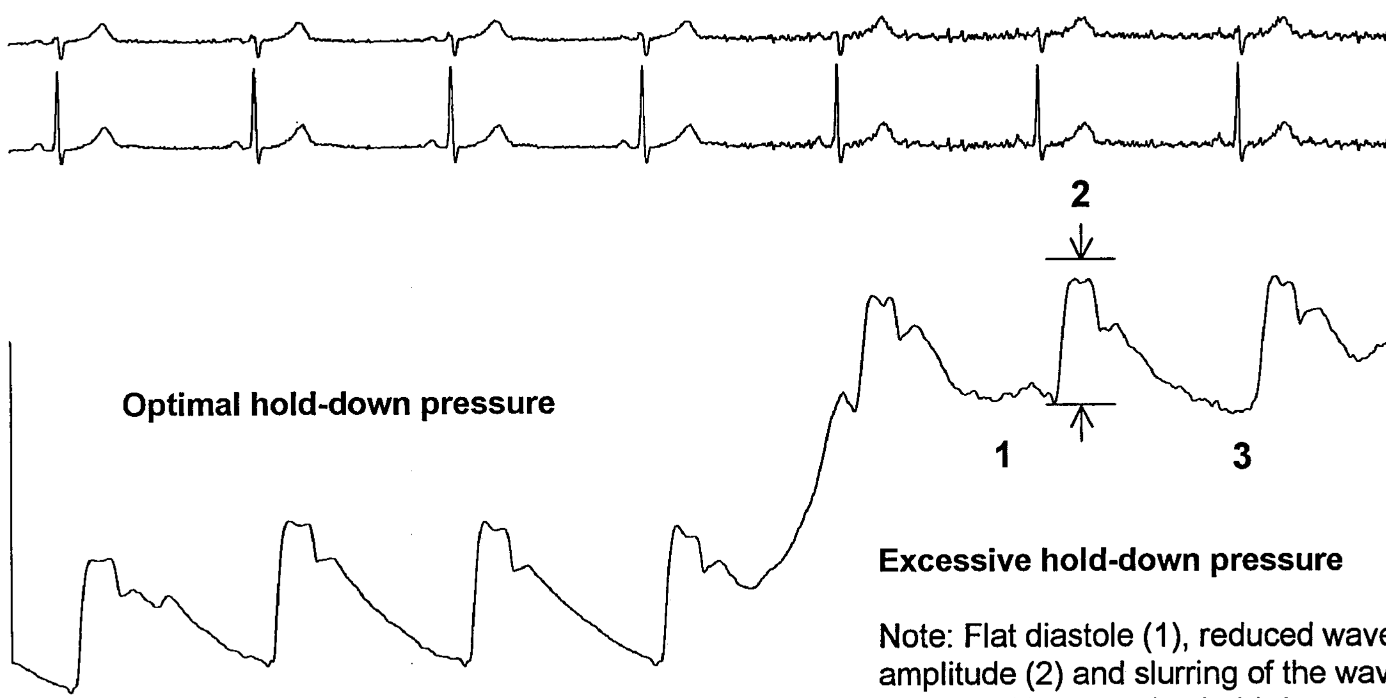
Note that the pressure scale is 400. Despite the considerable hold-down pressure, the waveform still looks reasonable, with the possible exception of mild scooping of diastole. Waveform amplitude continues to increase due to improved coupling with increased pressure in this deeply located vessel.

Waveforms: Femoral Scale: 400 Sweep: 10 Origin: 0 Thresh: 75

Figure 3d. Changing carotid hold-down pressure from optimal to excessive.

Waveform Data

Study ID: 00100.00102.Practice
Acquired: Jul 24, 2000 01:27:39 PM
Printed: Jul 24, 2000



Note: Flat diastole (1), reduced waveform amplitude (2) and slurring of the waveform foot (3) with excessive hold-down pressure.

Waveforms: Carotid Scale: 200 Sweep: 10 Origin: 0 Thresh: 100

NIHem

Noninvasive Hemodynamics Workstation Transit Distance Measurement Notes

Note: This workstation is not approved for routine clinical use. It is intended to be used for research purposes only under the supervision of an experienced physician.

Warning: The NIHem Workstation utilizes multiple high resolution and multimedia timers, including those supplied with the Windows NT® operating system. Unauthorized software or hardware may interfere with the proper function of these timers. Therefore:

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Rev. 1.0
February 9, 2001

1.0. Overview

1.1. This document provides an outline of the steps that must be taken in order to obtain an acceptable assessment of transit distances using the NIHem system.

2.0. Patient Preparation

2.1 Transit distances are measured at the end of the hemodynamic evaluation. To avoid ambiguity at the time of the measurements, use an eyebrow pencil or lip liner to mark the location of each tonometry acquisition site as soon as each successful measurement is obtained.

2.2 All measurements are made from the supra-sternal notch (SSN) to the various pulse acquisition sites.

2.3 The patient should remain supine exactly as they were positioned during the tonometry acquisition sequence.

2.4 Use the tape measure supplied with the NIHem system. This fiberglass tape measure will not stretch. It also has an extension at the zero end, which is used as a handle. This allows the operator to place their thumbnail exactly on the zero mark and to then keep the zero mark firmly seated in the SSN without the need to look at both ends of the tape measure.

3.0. Measure the SSN-Brachial and SSN-Radial transit distances.

3.1 Abduct the patient's arm to 90° to form a straight line from supra-sternal notch to brachial site to radial site.

3.2 The arm must be kept in the plane of the body to avoid under- or over-estimating the distance.

3.3 Place your right thumbnail on the zero mark, and then place the zero mark in the "V" at the base of the SSN.

3.4 Pull the tape measure across to the dot at the brachial acquisition site and note the distance in mm to the nearest 5 mm.

3.5 Use your left hand to anchor the tape measure at the brachial location. Release the zero point with your right hand, transfer your right hand to the brachial location and anchor the tape measure at the brachial site so that the brachial distance is still aligned with the brachial dot. Then use your left hand to further extend the tape measure to the radial site. This approach provides a surface measurement of the full distance from SSN to radial site and avoids a bridging effect that is possible if the tape measure is pulled directly between SSN and radial.

4.0. Measure the SSN-Femoral transit distance.

4.1 Place your left thumbnail on the zero mark, and then place the zero mark in the "V" at the base of the SSN.

4.2 Extend the tape measure down to the dot at the femoral site and pull it moderately tight.

4.3 Record the distance in mm to the nearest 5 mm.

5.0. Measure the SSN-Carotid transit distance.

5.1 Place your right thumbnail on the zero mark, and then place the zero mark in the "V" at the base of the SSN.

5.2 Position the patient's head just as it was during the tonometry acquisition.

5.3 Extend the tape measure up to the dot at the carotid site and pull it moderately tight.

5.4 Record the distance in mm to the nearest 5 mm.

Table. Typical transit distances (mm).

Site	Mean	SD	Minimum	Maximum
SSN-Brachial	415	30	345	500
SSN-Radial	650	40	550	765
SSN-Femoral	520	40	400	600
SSN-Carotid	87	10	60	110

NIHem

Noninvasive Hemodynamics Workstation
Blood Pressure Acquisition Notes

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Rev. 1.1
August 3, 2000

1.0. Overview

1.1. This document provides an outline of the steps that must be taken in order to obtain an acceptable assessment of blood pressure using the NIHem system.

2.0. Patient Preparation

2.1 The patient should be supine and otherwise prepared for the NIHem evaluation. The PPG probes and ECG leads should be attached prior to placing the blood pressure cuff on the patient.

2.2 Apply the cuff to the patient's right arm. The cuff should be snug but not tight, with the microphone wire and hose exiting the cuff along the medial aspect of the arm, with the microphone wire overlying the patient's brachial artery. If you consider a cross-section through the patient's right upper arm viewed from below, the brachial artery will be at about 2 o'clock (just medial to the biceps tendon), which is where the microphone cable should be placed. This will place the pressure hose at about 5 o'clock, which is along side the medial edge of the triceps muscle. This requires that the hose and cable assembly pass between the patient's arm and chest.

2.3 The patient's arm should rest comfortably at their side on the bed during acquisitions. The arm should not be against the chest wall as this will produce respiratory artifacts in the pressure and microphone waveforms.

2.4 Allow the patient to rest supine for at least 5 minutes before starting blood pressure acquisitions. This is a good time to register the patient, who will acclimate to the surroundings and to the presence of the operator.

3.0. Recording the Blood Pressures

3.1. After registering the patient, select [Waveforms] from the main menu toolbar at the top of the screen.

3.2. Select [BP] from the Waveforms toolbar at the bottom of the screen.

3.3. Turn the headphone volume down (fully counterclockwise) and put on the headphones.

3.4. Set the maximum cuff pressure to approximately 40 mmHg higher than the expected systolic pressure.

3.5. Click [BP1] and wait for the cuff to inflate.

3.6. Adjust the volume knob to the nominal listening level, which should sound comparable to a stethoscope. Avoid excessively high volume levels.

3.7. Click [Systole] when the first beat with a Korotkoff sound is heard. If the first Korotkoff sound is too soon (less than 10 seconds) after the motor stops inflating, the maximum cuff pressure is too low. Hit [Abort], increase maximum cuff pressure, wait a minute, and redo that blood pressure.

3.8. Click [Diastole] when the first beat with no Korotkoff sound is seen.

3.9. If either landmark is clicked prematurely, it is fine to click again and update the landmark to a later event. However, it is not possible to update landmarks to an earlier event unless the BP acquisition is repeated. Therefore, the user should maintain a low threshold for clicking.

3.10. When the cuff reaches 40 mmHg, the deflate valve will close for 20 seconds so that pressure waveforms can be acquired. It is important that the patient remain still during this period. Therefore, the user should remain focused on the computer monitor during this "hold period" so that the patient does not think that the blood pressure acquisition is complete.

3.11. If an error is made during a given blood pressure acquisition, the user should click the [Abort] button and redo that blood pressure prior to proceeding to the next blood pressure. This will minimize the need for redoing multiple blood pressures later. Examples of errors that require aborting and restarting include:

- The first few Korotkoff sounds are missed
- The end of the Korotkoff sounds is missed
- The patient moves or the cuff is against the chest creating substantial artifacts on the pressure waveforms

3.12. When a blood pressure acquisition is complete, the data is saved automatically.

3.13. Repeat for BP2 and BP3 in that order.

4.0. Reviewing and Repeating Blood Pressures

4.1. After performing all three blood pressures, click the [Review] button to load the "Blood Pressure Summary" dialog box. This dialog box tabulates all three individual blood pressure values along with the mean and range for systole and diastole.

4.2. To be acceptable, the range for both systole and diastole must be 5 mmHg or less. If either range is greater than 5 mmHg, additional blood pressures should be performed.

4.3. If the range is 5 mmHg or less for both systole and diastole, BP acquisition is complete. Click [Close] on the "Blood Pressure Summary" dialog box, click [Close] on the BP toolbar and proceed with waveform acquisition.

4.4. If either blood pressure range is greater than 5, close the summary dialog and repeat the first blood pressure (BP1), regardless of which blood pressure appears to be "out of range." This circular pattern is employed to avoid bias since it is not possible to know which blood pressure is actually incorrect.

4.5. After repeating BP1, click [Review] and reassess the range. If still greater than 5 mmHg, close the summary dialog box and repeat BP2. If the range remains greater than 5 mmHg after repeating BP2, do not take additional blood pressures. Close the summary dialog box and the blood pressure toolbar and proceed with the examination.

4.6. Please note that this "circular" pattern of blood pressure acquisitions will result in three possible acquisition sequences:

- BP1, BP2, BP3
- BP1, BP2, BP3, BP1
- BP1, BP2, BP3, BP1, BP2

NIHem

Noninvasive Hemodynamics Workstation
Sonographer Notes

Note: This workstation is not approved for routine clinical use. It is intended to be used for research purposes only under the supervision of an experienced physician.

Warning: The NIHem Workstation utilizes multiple high resolution and multimedia timers, including those supplied with the Windows NT® operating system. Unauthorized software or hardware may interfere with the proper function of these timers. Therefore:

- **Do NOT install unauthorized hardware or software onto the NIHem Workstation.**
- **Do NOT modify the Windows NT® configuration in any way without prior approval from Cardiovascular Engineering, Inc.**
- **Do NOT activate or load screen savers onto the computer.**

Rev. 1.0
July 20, 2000

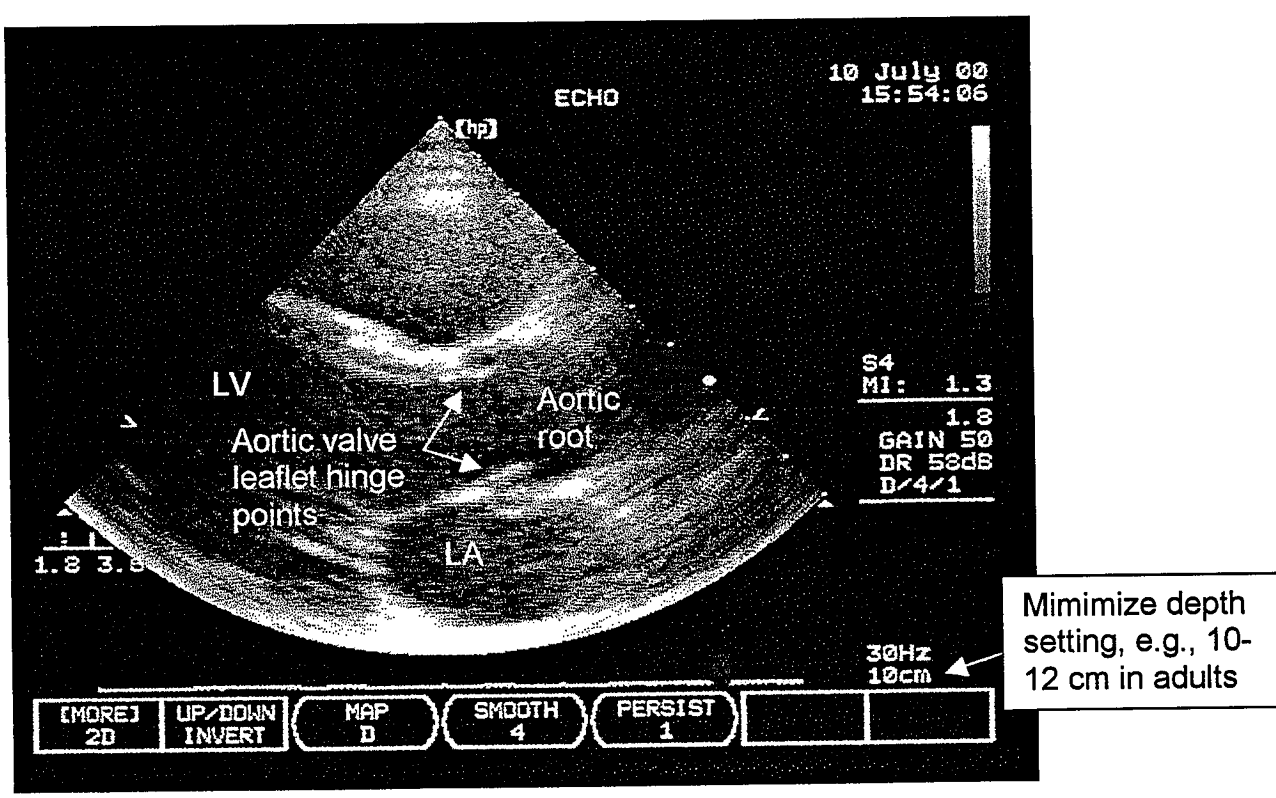
Overview

- This document provides an outline of the essential steps that must be taken by the ultrasonographer in order to ensure high quality images and Doppler recordings.

Aortic root and left ventricular outflow tract (LVOT) imaging (Aortic US from main menu bar)

- Images are obtained using a parasternal long axis view with the aortic valve plane at the horizontal center of the image.
- Depth setting is minimized (10-12 cm in most adults) in order to maximize the size of the valve.
- Aortic leaflets should be visible throughout the cardiac cycle so that the hinge points of the leaflets can be established (Figure 1).
- Measurements are taken in systole, so it is important to ensure that the LVOT does not rock out of plane during systole.

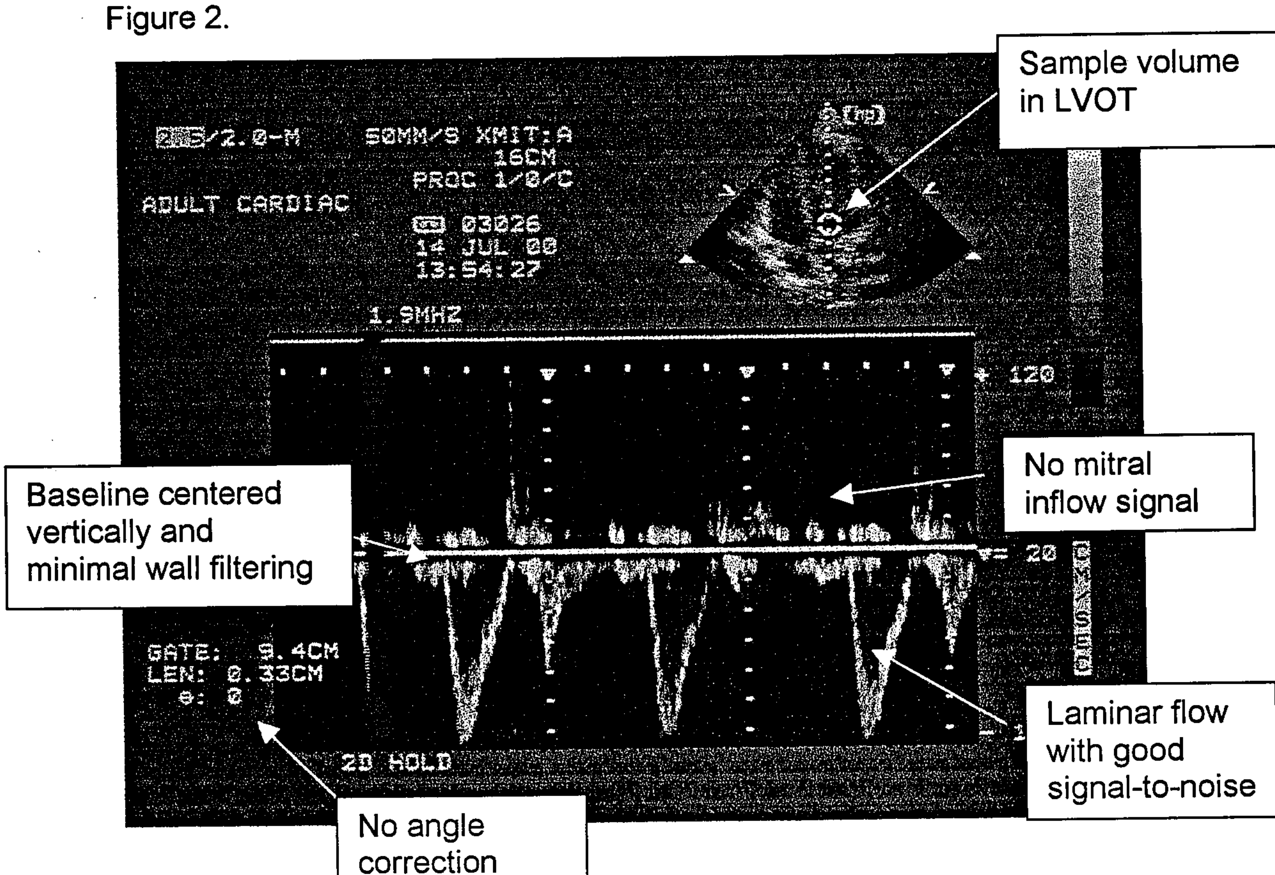
Figure 1.



Left ventricular outflow tract (LVOT) Doppler (Aortic PQ from main menu bar)

- Obtain pulsed Doppler from the left ventricular outflow tract just proximal to the aortic valve in an apical five-chamber view (Figure 2).
- Find maximal peak flows, which should correspond to the LVOT.
- Keep the zero baseline at the center of the spectral display so that the scale is symmetrical, e.g. –80 to +80, -120 to +120, etc. If aliasing is seen, change the scale in order to eliminate the aliasing. Do <u>not</u> shift the zero baseline, as this only obscures the aliasing (but does not eliminate it from the audio signal that is recorded by the computer).
- Use minimal wall filter settings in order to avoid a loss of information on either side of the zero baseline. Excessive filtering creates a wide gap, which makes it difficult to assess the onset and end of flow.
- There should be no mitral inflow contamination if the Doppler cursor is in the LVOT, as opposed to when the cursor is too low in the left ventricular chamber. Flows should be laminar in these patients with no aortic valve disease. Flow envelopes should be bright (on screen) and clearly audible, indicating a good signal-to-noise ratio.

Figure 2.



NIHem Noninvasive Hemodynamics Protocol Flowsheet

Phase	Time (min) Total	Time (min) Phase	Cuff Inflator / PPG	Patient Junction Box	Computer	Verbal	Misc.
Setup	0-5	5	• Use adhesive rings to attach PPG to back, just to the left of midline, red at T4, blue at L2 • Place BP cuff on RA, microphone over brachial artery, pressure hose behind arm	• Apply 4 ECG leads to chest (arm leads under L & R collarbones, leg leads on lower L & R ribcage) • Attach tonometer to PJB	• Machine on, [Register] • Enter Pt initials • Enter Center ID & Pt ID • Enter date of birth • Study date (default) • Select Study Type • Select Operator • Click [OK]	• 'I am going to place electrodes on your back' • 'Please lie down and make yourself comfortable' • 'I am going to place ECG electrodes on your chest and a BP cuff on your right arm'	• Change into hospital gown (open in front), undershorts OK, remove bra or T-shirt • If gown is tight on arm, remove RA from sleeve before applying BP cuff
Acquire BP	5-14	9	• Cuff will automatically inflate/deflate • Remove BP cuff and headphones and store after BP complete	• Adjust headphone volume • Check volume setting, put on headphones • May want to decrease volume during cuff inflation then turn up during deflation	• Click [Waveforms] on toolbar • Click [BP] • Set Max Cuff Pressure • Click [BP1] • Click [Systole] on first beat with K-sound and [Diastole] on first beat without K-sound; repeat clicks OK • Program automatically saves data • Wait 2 min, then BP2, BP3. • Click [Review], range should be ≤ 5/5 mmHg • Click [Close]	• 'Now I'm going to check your blood pressure several times' • 'The cuff will inflate and deflate automatically' • 'Lie and breathe quietly and try not to talk even between measurements'	• Make sure there is space between cuff and chest to avoid respiratory artifact • Watch for motion artifact on red and orange traces. • If major motion artifact or clicked [Systole] or [Diastole] too late, [Abort] and redo.
Acquire Tonometry	14-22	8		• Find maximal pulsation with fingertips first • Place tonometer over artery • Sweep across artery to find center, adjust pressure, maximize waveform amplitude and features	• Click [Bra] • Optimize brachial waveform • Step on footswitch to freeze tracing • Repeat for radial [Rad], femoral [Fem] & carotid [Car] • Click site again to replace data as needed, but complete each site before moving to next	• 'Now I'm going to check your pulses with the tonometer' • Before Femoral: 'I'm going to check the pulse at the top of your leg'	• Put on gloves • Place a small dot at each pulse site just after tonometry is acquired • Remove gloves
Acquire PPG	22-23	1			• Click [PPG] • Obtain stable segment. Red and blue tracings should both resemble pressure waveforms • Step on footswitch to freeze tracing • Click [Close]	• 'Now I'm taking measurements of blood flow from the probes on your back' • 'Breathe quietly, try not to move'	• If red or blue trace does not resemble pressure waveform, place patient in the left lateral decubitus position and reposition bad probe

NIHem Noninvasive Hemodynamics Protocol Flowsheet

Phase	Time (min) Total	Time (min) Phase	Cuff Inflator / PPG	Patient Junction Box	Computer	Verbal	Misc.
Aortic Imaging	23-27	4			• Click [Aortic US] • Click [LVOT] to initiate acquisition into a 5 sec circular buffer • Step on the footswitch as soon as a continuous 5 sec loop of satisfactory images is obtained • Click [Close]	• Ask echo tech to obtain parasternal long axis view through LVOT during systole, hinge points of aortic valve leaflets visible • Use minimal depth setting (10-12 cm) • Echo tech: 'I'm placing cold gel on your chest'	• Place patient in the left lateral decubitus position • Use pillows as props to ensure patient comfort • Confirm that ECG tracing is intact after moving patient
Aortic Pressure-Flow	27-29	2		• Prepare to use tonometer	• Click [Aortic PQ] • Click [PQ1] • Obtain 10 sec of good pressure and flow waveforms • Click [PQ2] and repeat • Click [Close]	• Verify 'Are you comfortable?' • 'I am going to record the pulse in your neck while (echo tech) takes pictures of your heart'	• Pulsed Doppler from apical 5-chamber • Maximize peak velocity in LVOT • Minimize wall filters • Adjust scale (not zero) if aliasing
Transit Distances	29-31	2			• Click [Distances] • Enter values in mm, e.g., SSN-B = 380-500, SSN-R = 600-800, SSN-F = 450-700, SSN-C = 70-120 • Click [OK]	• 'I'm going to take a few measurements'	• Measure Bra and Rad with arm out at 90° • Each distance from SSN to site; hold down tape at Bra when measuring Rad • Measure PPG from top of T4 probe to top of L2 probe
Wrap Up	31-33	2	• Remove PPG probes from patient, remove adhesive rings from probe holders.	• Disconnect ECG from patient • Disconnect tonometer and store	• Close NIHem program	• Thank patient	
Write CD	ASAP	10			• See CD recording instructions • Shutdown computer from the NT [Start] menu • Power off and unplug main power cord after shutdown complete		• Make 2 copies (Data CD and Archive CD) • Append to the Archive CD until full.

Appendix Item 10

Overview of Training & Quality Assurance[a]

FHS Quality Control Protocol

[a] Note: Developed by Drs. Corretti and Benjamin for International Brachial Reactivity Task Force

Training and Quality Assurance
Framingham Heart Study

<table>
<tr><th colspan="3">Table. Training and Quality Improvement Protocol</th></tr>
<tr><th>Elements</th><th>Scanning</th><th>Measurement</th></tr>
<tr><td>Manuals</td><td>
Written description of procedure for participants
Succinct protocol flow sheet @ station
Longer protocol documentation manual to train sonographers

Acquisition protocol outlines

Equipment presets
Study sequence
Sonographer script to convey to subjects

Specification of optimal 2-D images

Near & far artery wall interface with continuous & distinct intima-media layers over > 50% of vessel length, sonolucent lumen

Specification of inadequate 2-D images

Near & far artery wall interface with discontinuity, lack of ability to recognize intima-media interface, oblique artery view

</td><td>
Explicit written documentation to enhance consistency
Manual & automated measurements

Frame selection techniques
Segment selection
Criteria for unmeasurable studies
Criteria to reevaluate measurements

Automatic analysis packages

Technique for selecting image & segment for 'training'
Criteria for rejecting frames
Criteria delineating when to make manual measurements

</td></tr>
<tr><td>Worksheets</td><td>
Record subject factors

If ineligible, why

Refused, mastectomy, Raynaud's

Potential modifiers of FMD

Time of day, last cigarette, caffeine, medications, food, menses

Systolic blood pressure & cuff inflation pressure

Record scan factors

Equipment issues, any deviations from protocol

</td><td>
Log book to track status of studies

Dates performed, saved, measured
SVHS and/or disk numbers

Worksheet to record technical quality of study
</td></tr>
<tr><td rowspan="2">Training</td><td colspan="2">Scientific rationale and physiology of flow-mediated dilation</td></tr>
<tr><td>
Basic knowledge of ultrasound equipment, 2-D & Doppler analysis
Demonstration, review of technical tips & pitfalls, hands-on experience
Ergonomic issues

Essential to train in techniques to minimize stress related injuries

Qualification criteria

Training period with close supervision & feedback on protocol adherence & image quality
Periodic review of scan performance
Minimum number of studies

At least 20 supervised scans prior to scanning independently
At least 50 per year to maintain competency

</td><td>
Demonstration, technical tips & pitfalls of segment selection, hands-on experience
Develop & adhere to written protocol
Qualification criteria

Training period with close supervision & feedback
Formal observer-specific reproducibility assessment prior to independent reading
Minimum number of studies

All observers from a given study measure 20 studies together prior to reading independently
At least 50 per year to maintain competency

</td></tr>
</table>

Training and Quality Assurance
Framingham Heart Study

<table>
<tr><td rowspan="2">Descriptive Statistics</td><td>• Assess for systematic differences by sonographer & site</td><td>• Assess for systematic differences by observer & site</td></tr>
<tr><td colspan="2">• Mean baseline and peak deflation diameters, and FMD. Doppler data if reported.
• Per time period & over time to assess for secular drifts in measurements</td></tr>
<tr><td>Data Cleaning</td><td colspan="2">• Missing worksheet or measurement data
• Criteria to reevaluate study
  • Range checks
    • FMD out of range (-2 to 12%)
    • Diameter out of range (2.5 to 5.5 mm)
    • Any image > 0.2 mm different than adjacent images in acquisition sequence
  • Consistency checks
    • For continuous analysis data are baseline & immediately post-deflation diameters within 0.1 mm?
    • Do subject visit date and time and scan date and time match?</td></tr>
<tr><td>Lab Meetings</td><td colspan="2">• Periodic lab meetings
  • Review work flow
  • Review compliance with scan & measurement protocols
  • Measure random and difficult studies together
  • Review results of data cleaning and reproducibility analyses</td></tr>
<tr><td rowspan="3">Reproducibility</td><td>• Image variability
  • In single site study each sonographer scan the same participants under similar conditions to assess systematic differences in scanning technique</td><td>• Multi-site studies should have core reading laboratory
• Intra- & interobserver variability: Interpreters measure a minimum of 20 scans twice to assess for systematic differences within and between observers
• Temporal variability Interpreters measure a calibration set over the duration of a longitudinal study to assess for secular drifts in measurement technique</td></tr>
<tr><td colspan="2">Potential sources of variability
• Subject
  • Day to day, time of day, exercise, smoking, food, caffeine, medications, menstrual cycle
• Sonographer
• Protocol
  • Cuff: duration of occlusion, occlusion above vs. below elbow, mm Hg of occlusion, automatic vs. manual cuff inflation
  • Transducer held manually vs. with stereotactic device
• Observer
  • Intraobserver, interobserver, temporal measurement differences
• Equipment
  • Ultrasound
    • Transducer frequency, proprietary differences in ultrasound equipment, settings
  • Digital analysis
    • Image storage on SVHS vs. digital media, ECG gating & point in cardiac cycle, manual vs. automated measurements, different analysis algorithms, upgrades</td></tr>
<tr><td colspan="2">Statistics
• Correlations, mean and absolute differences, components of variability [systematic vs. random differences]
• Assess on baseline and peak deflation diameter and FMD. Doppler, if assessed.</td></tr>
</table>

Training and Quality Assurance
Framingham Heart Study

Education	• For those beginning to adopt technique, currently, education is most efficiently gained by visiting experienced labs • The field would benefit from the availability of more formal course opportunities
Certification	• While noninvasive measurement of endothelial function is a research tool, certification will remain study-specific • Prior to becoming a clinical tool, formal certification requirements, courses, & ongoing continuing medical education will be necessary

Quality improvement (QI) protocol for Vascular Station

Element	Frequency	Procedure	Statistics
Reproducibility	Annual	• Intra- Inter-observer measurement variability Interpreters measure 20 scans twice	• Mean ± sd • Correlation coefficients
	Annual	• Temporal variability • Interpreters measure calibration scan set	• Mean ± sd $\vert y - y \vert$ • Range $\vert y - y \vert$ • Components of variability
	Once	• Sonographer variability • Sonographers scan 18 FHS personnel	• Subject • Within sonographer • Between sonographer
Descriptive statistics	Quarterly	• Generated by data management staff • Assessment of differences across sonographers and observers for routine scans	• Measurement variability • Mean ± sd
Data cleaning	Monthly	• Generated by data management staff	• Out of range data • Missing data
QI reports	Quarterly	• Generated by data management staff • Reproducibility statistics included in reports	• Descriptive statistics • Data cleaning
Lab meetings	Bi-weekly	• FHS sonographers measure random or difficult studies together	
	Monthly	• FHS review QC reports • FHS Review lab flow, issues	
	Quarterly	• Review Cardiovascular Engineering & FHS reports with key personnel	

QI = quality improvement; sd = standard deviation

Appendix Item 11

Illustrations

Illustration Item 1

Room Set-up
for Brachial Artery Ultrasound Examination

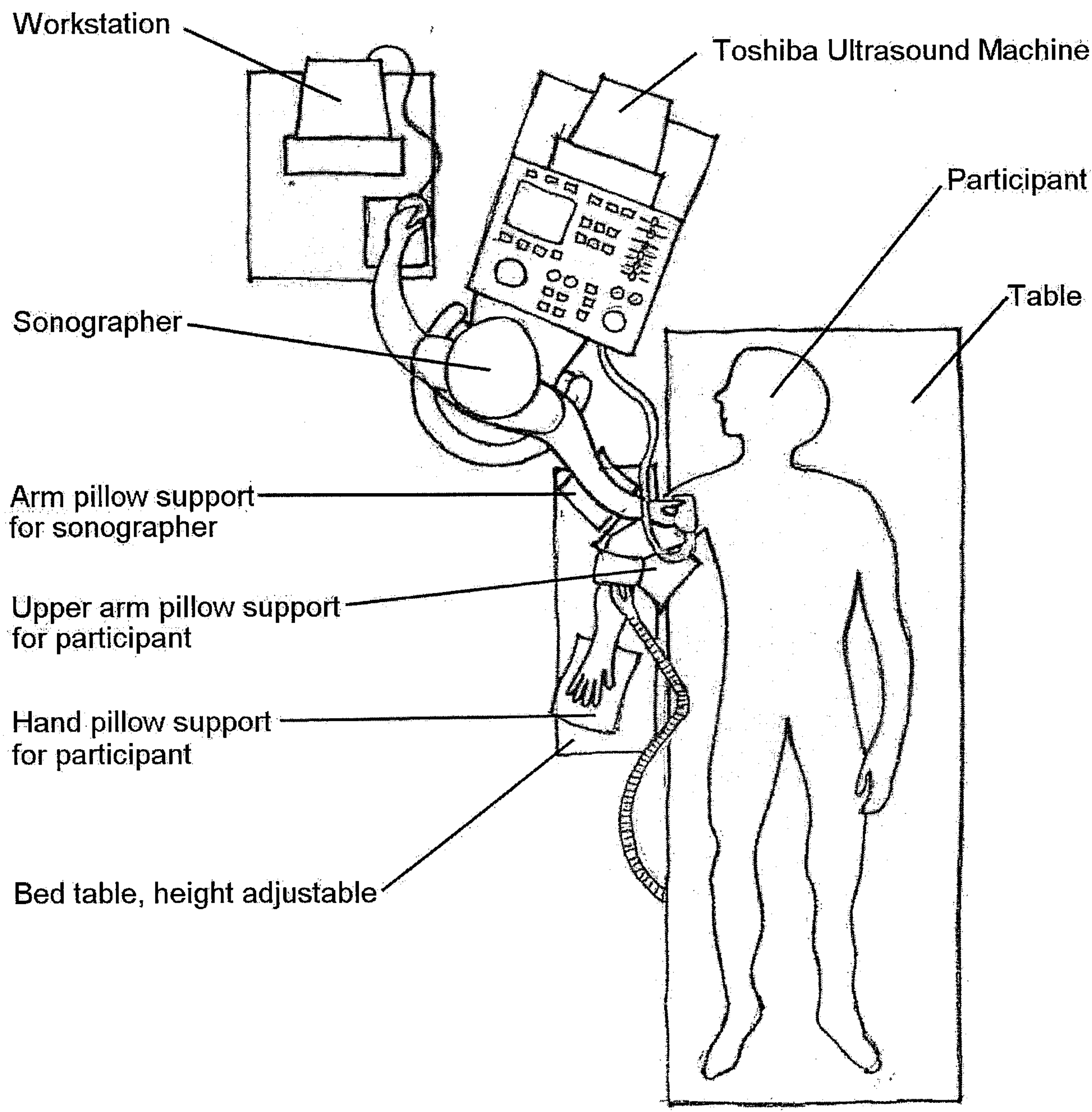


Illustration by Marty Lehman

Illustration Item 2

Sonographic and Participant Set-up for Brachial Artery Ultrasound Examination

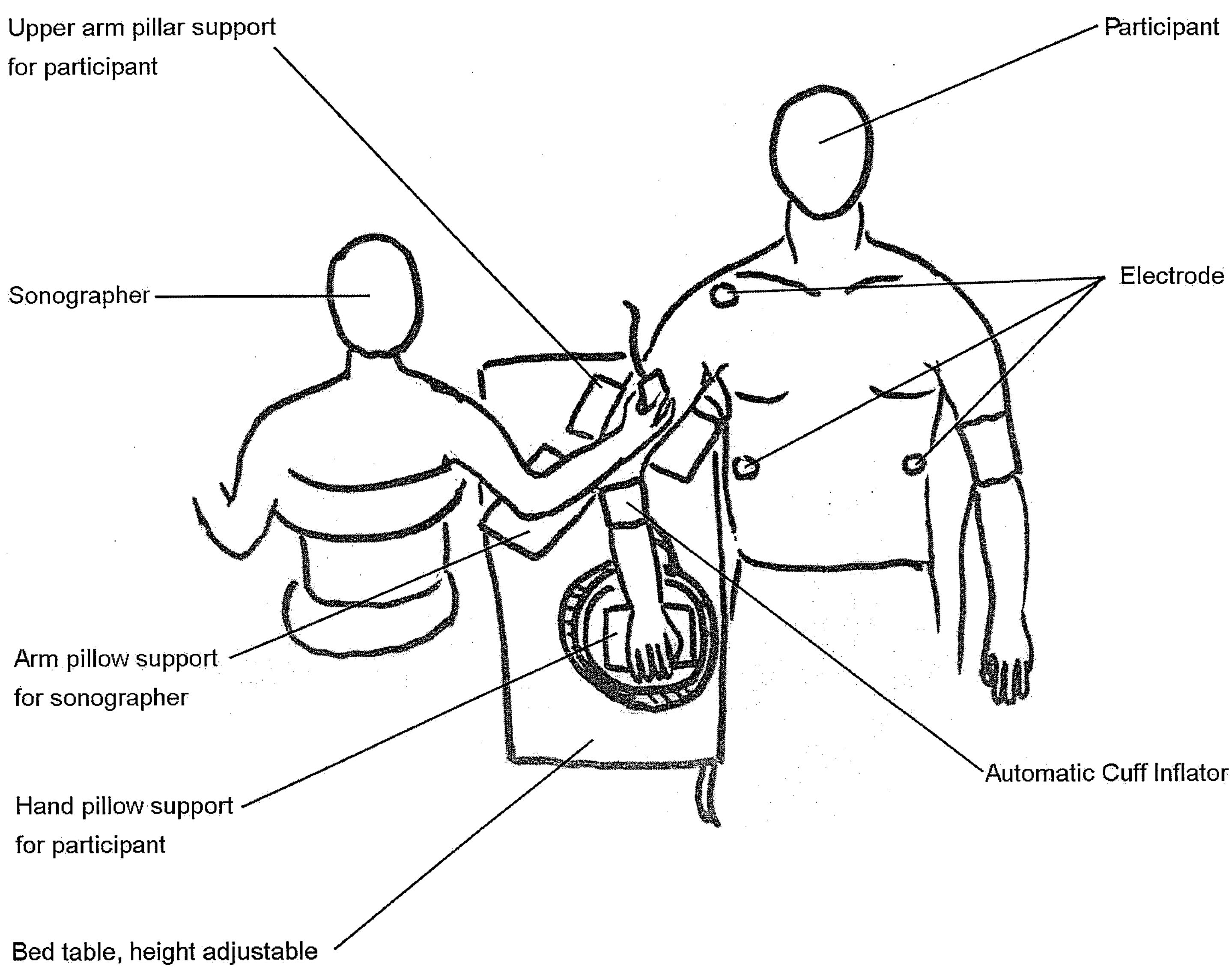


Illustration by Eva Osypiuk

Illustration Item 3

Tonometry Pulse Aquisition Sites

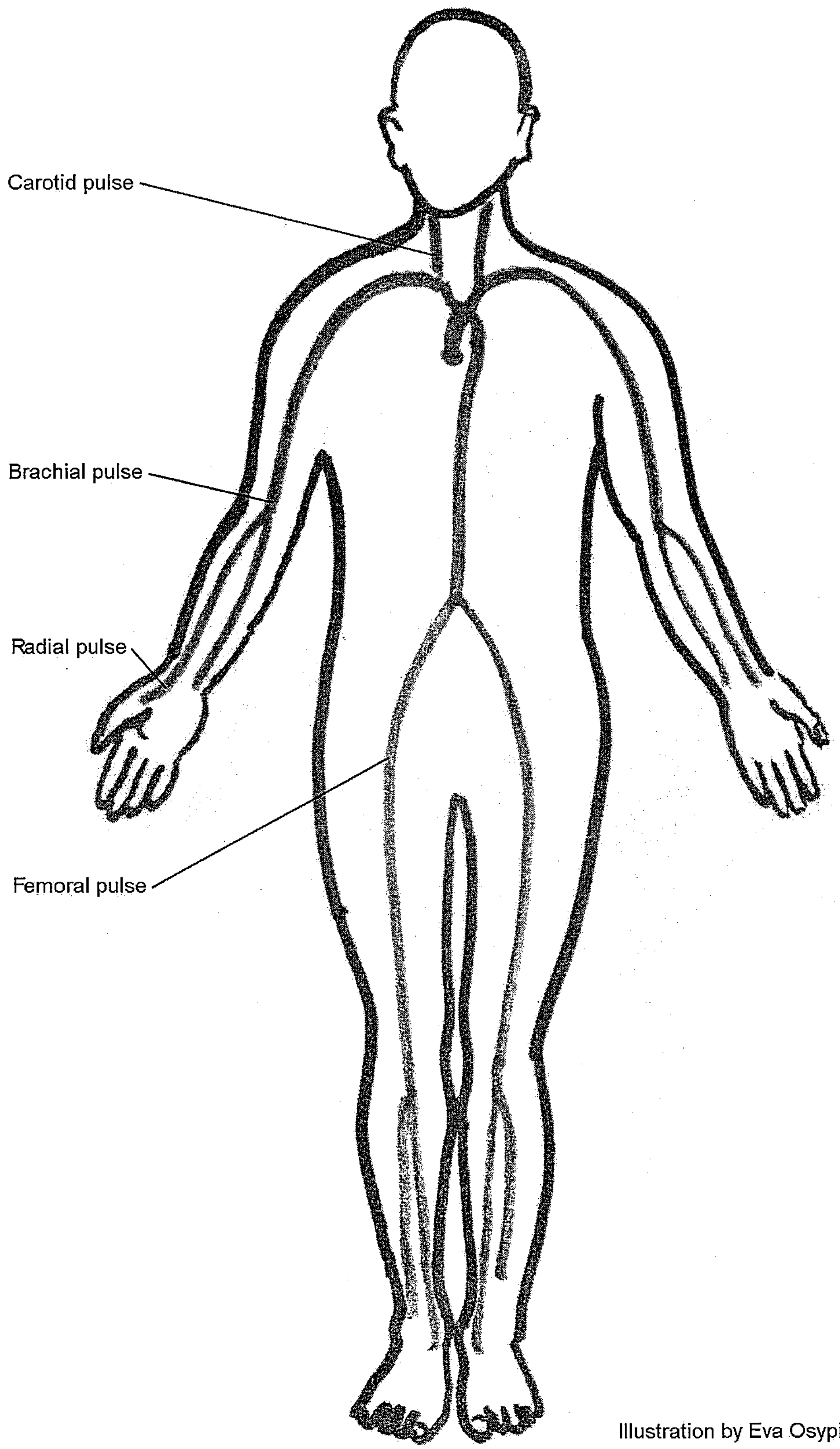
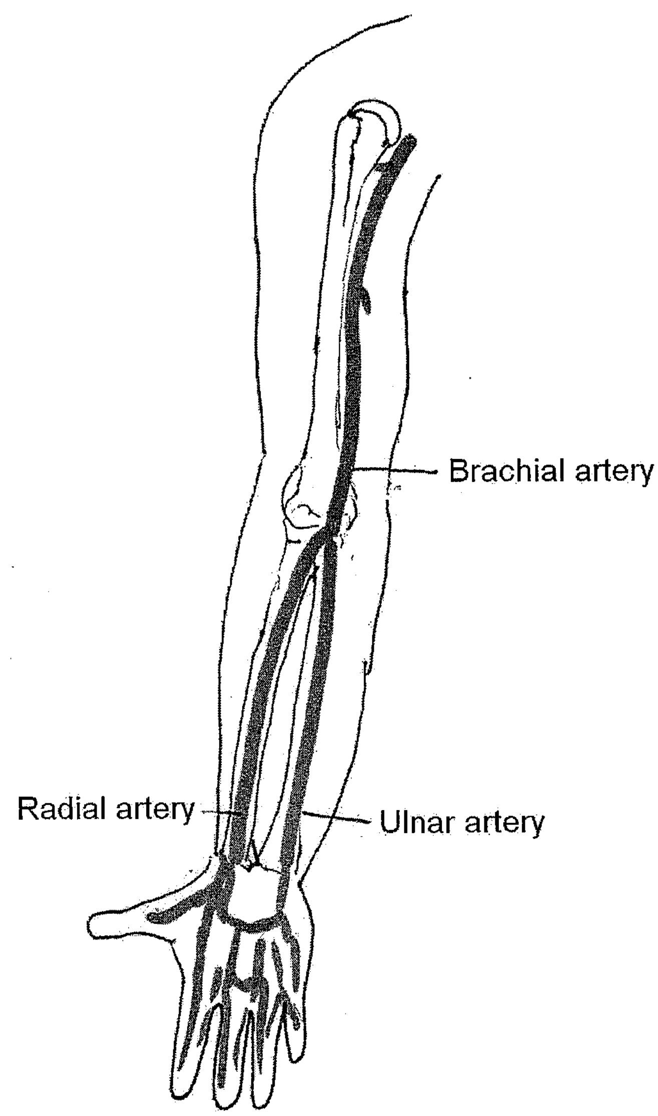


Illustration by Eva Osypiuk

Illustration Item 4

Brachial Artery and Radial Artery



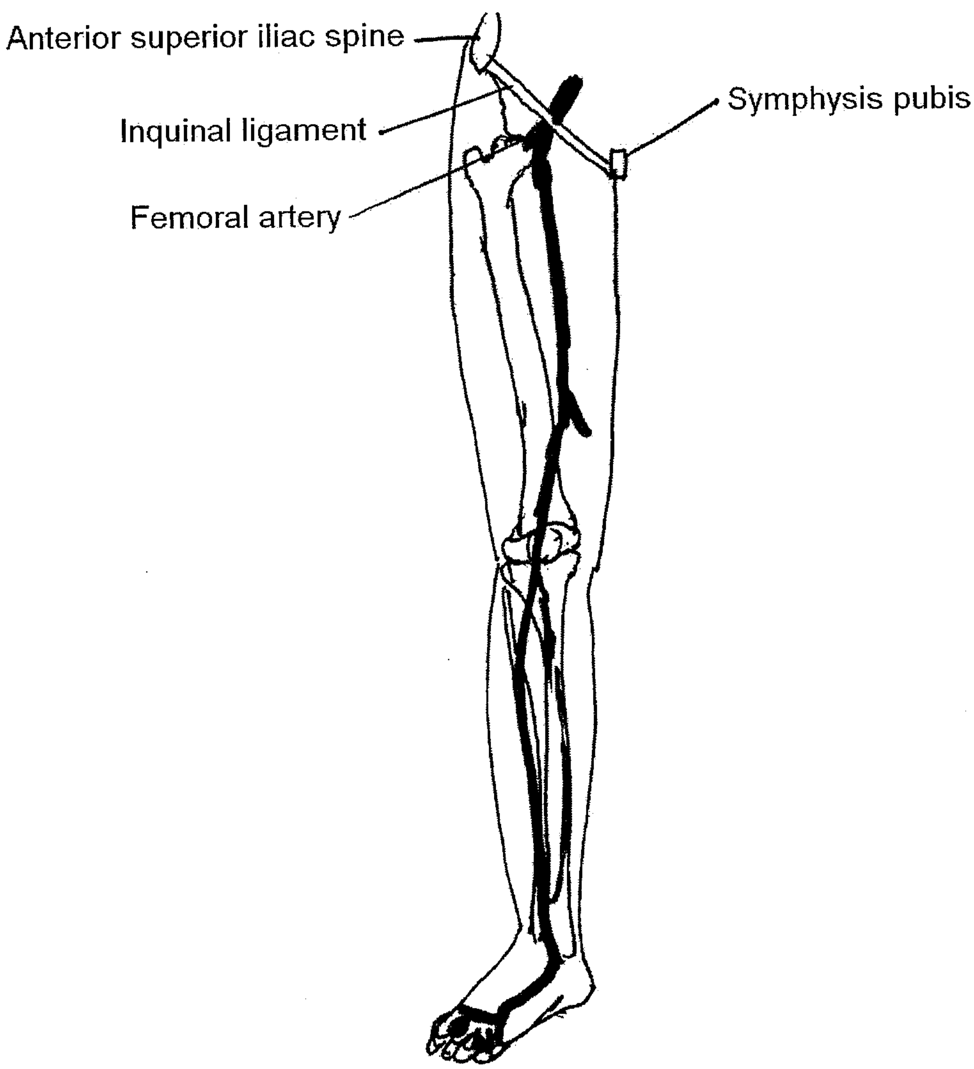
Brachial artery can be felt in and above the bend of the elbow, just medial to the biceps tendon and muscle.

Radial artery can be felt on the flexor surface of the wrist laterally.

Illustration by Eva Osypiuk

Illustration Item 5

Femoral Artery



Femoral artery is palpable below the inquinal ligament, midway between the anterior superior iliac spine and the symphysys pubis.

Illustration by Eva Osypiuk

Illustration Item 6

Carotid Artery

Optimal location for carotid tonometry is just lateral to the larynx, in the angle between the SCM muscle and the larynx.

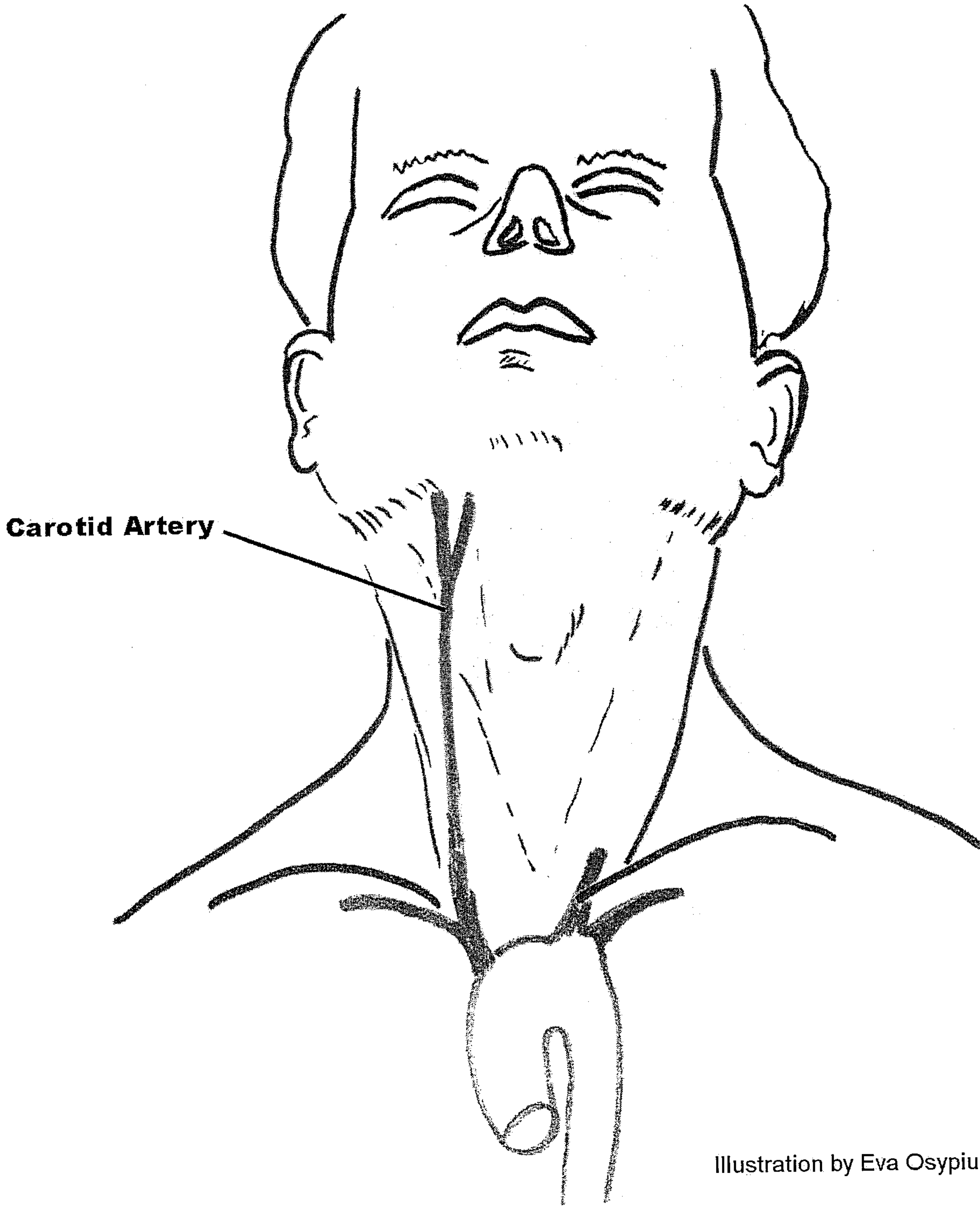


Illustration by Eva Osypiuk

Brachial Analyzer

Figure 1:

Measuring lines are correctly placed on the M-Line on near wall as well as far wall.

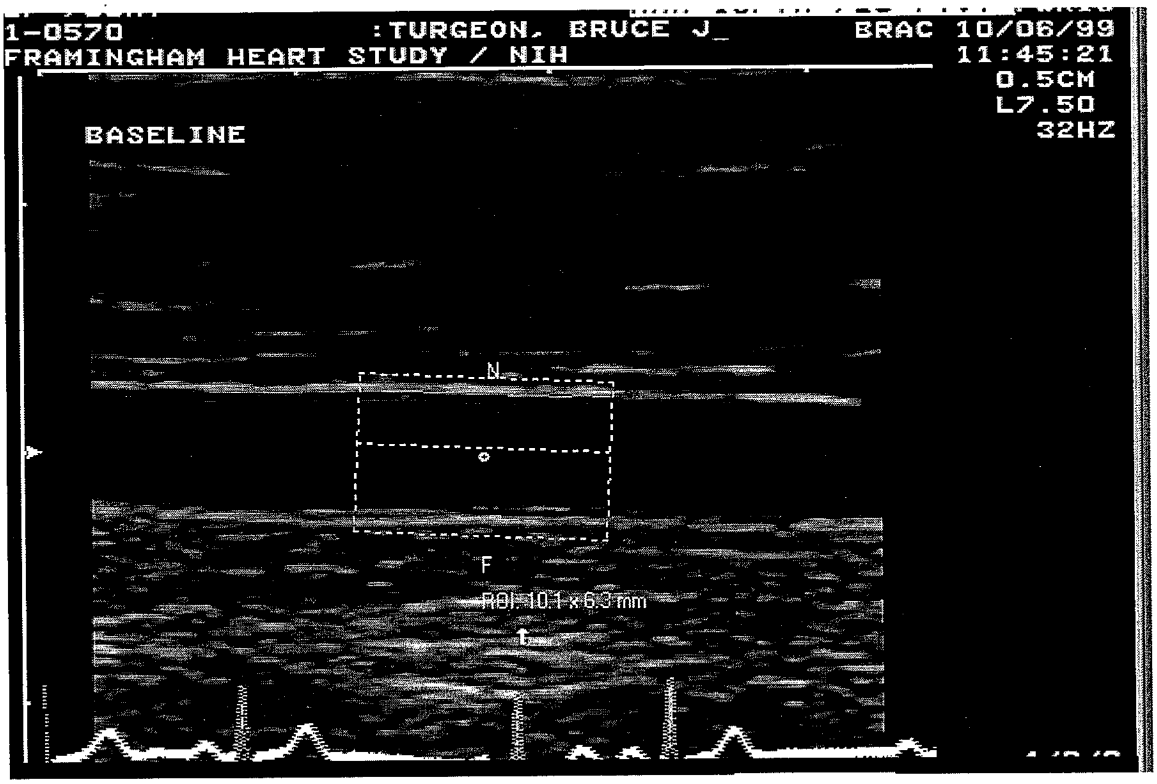
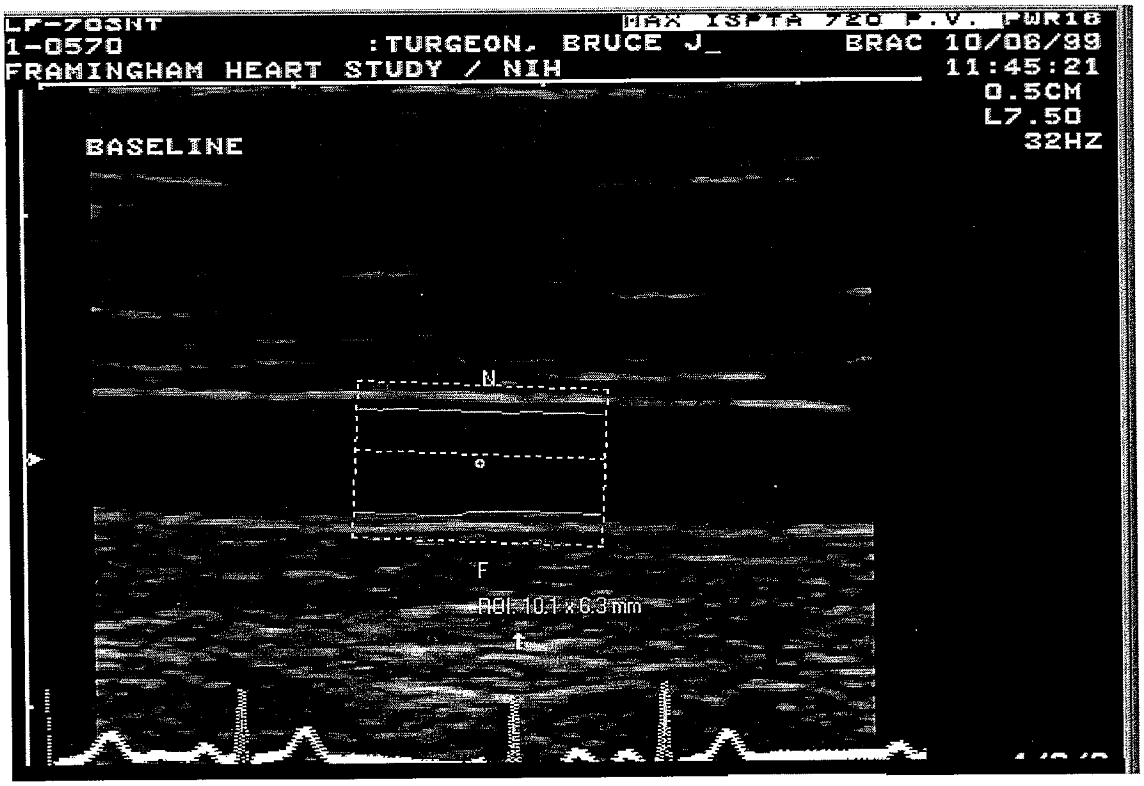


Figure 2:

Measuring lines are incorrectly placed inside the intima on near wall as well as far wall.



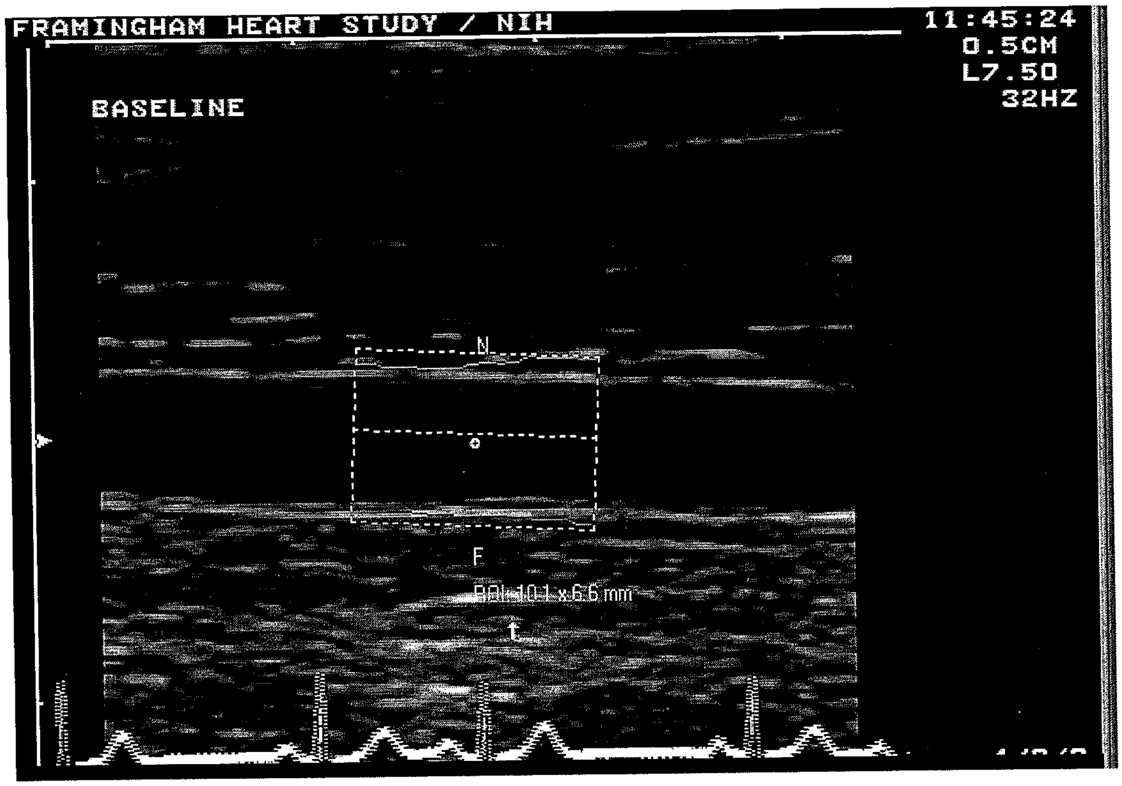


Figure 3:
Measuring lines have incorrectly jumped to outside adventia on near wall as well as far wall.

Suboptimal Images

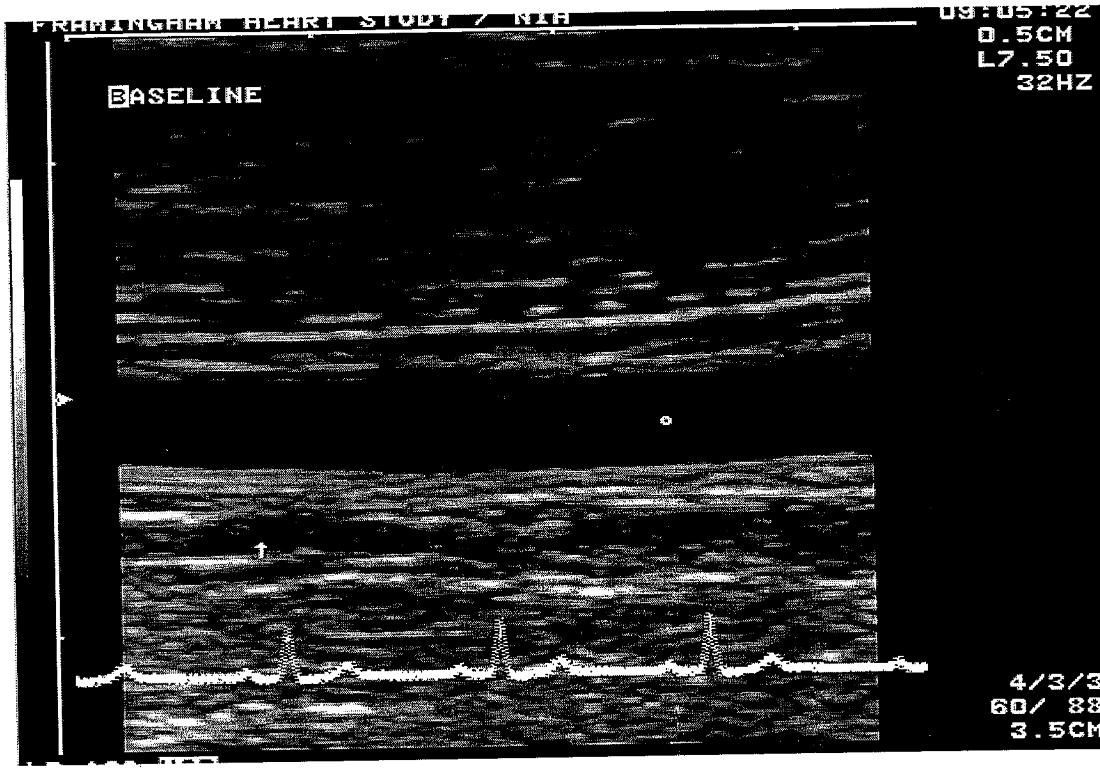


Figure 1:

Chosen segment of artery for area of interest is not in center of screen.

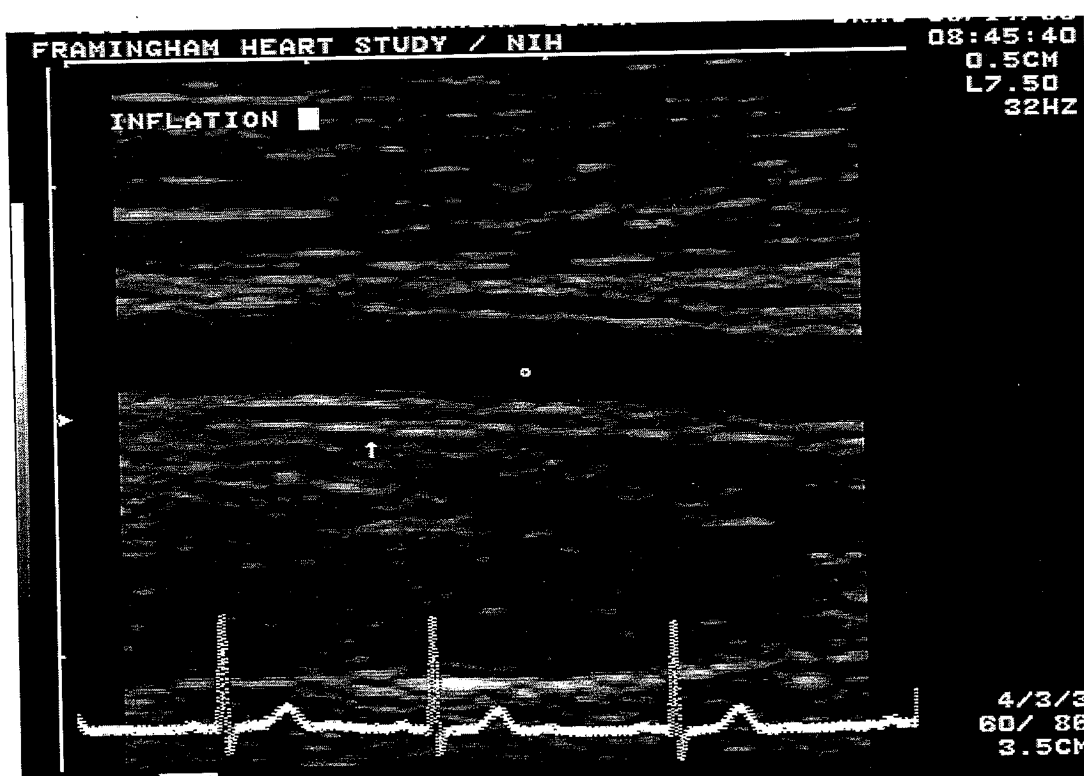


Figure 2:

Poorly imaged M-line.

Figure 3:

Tortuous segment of vessel should be avoided, if possible.

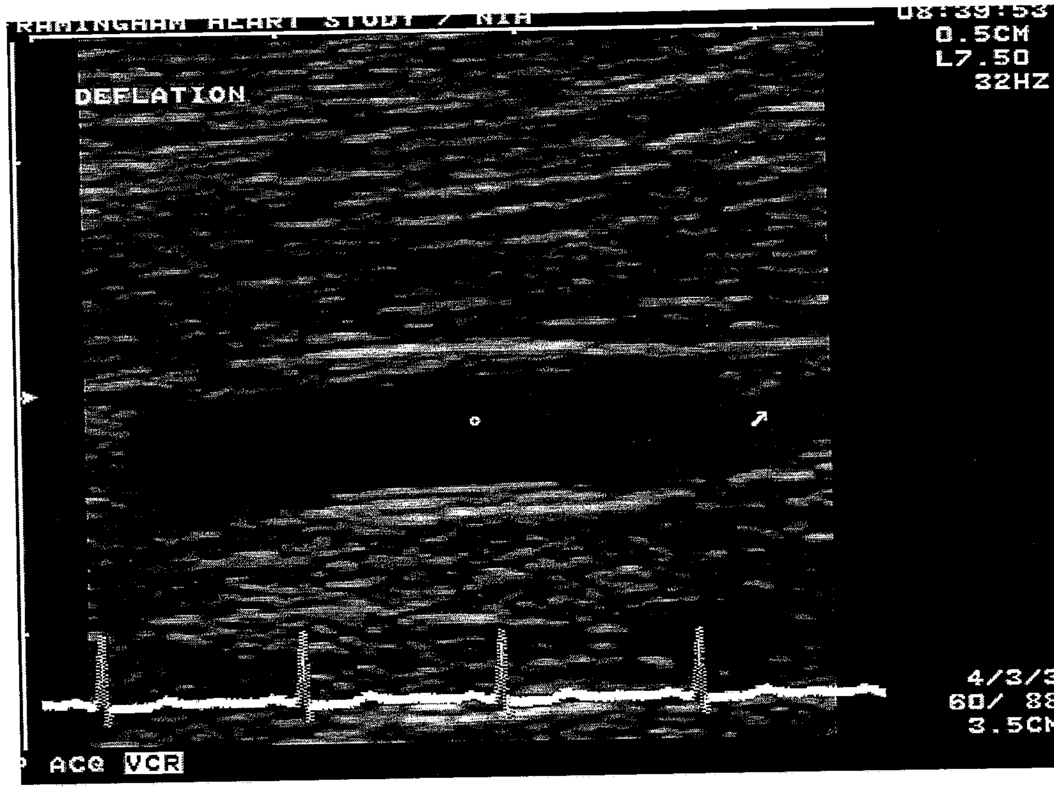


Figure 4:

Another example of a curved vessel.

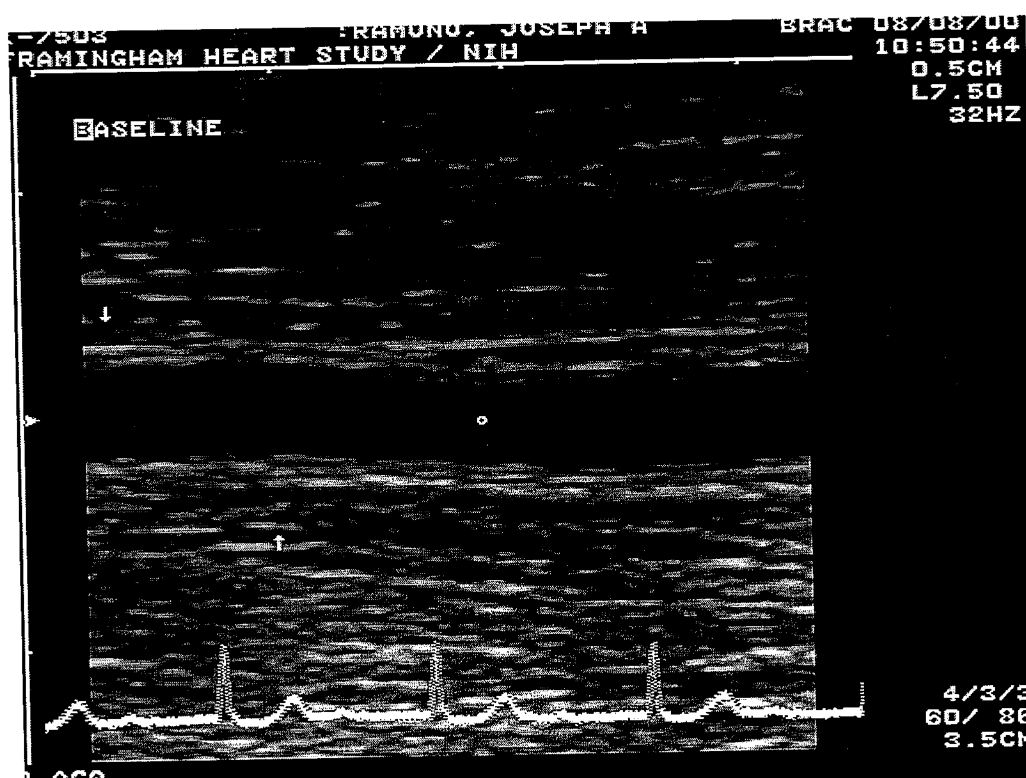


Figure 5:

Try to avoid imaging the vessel diagonally.

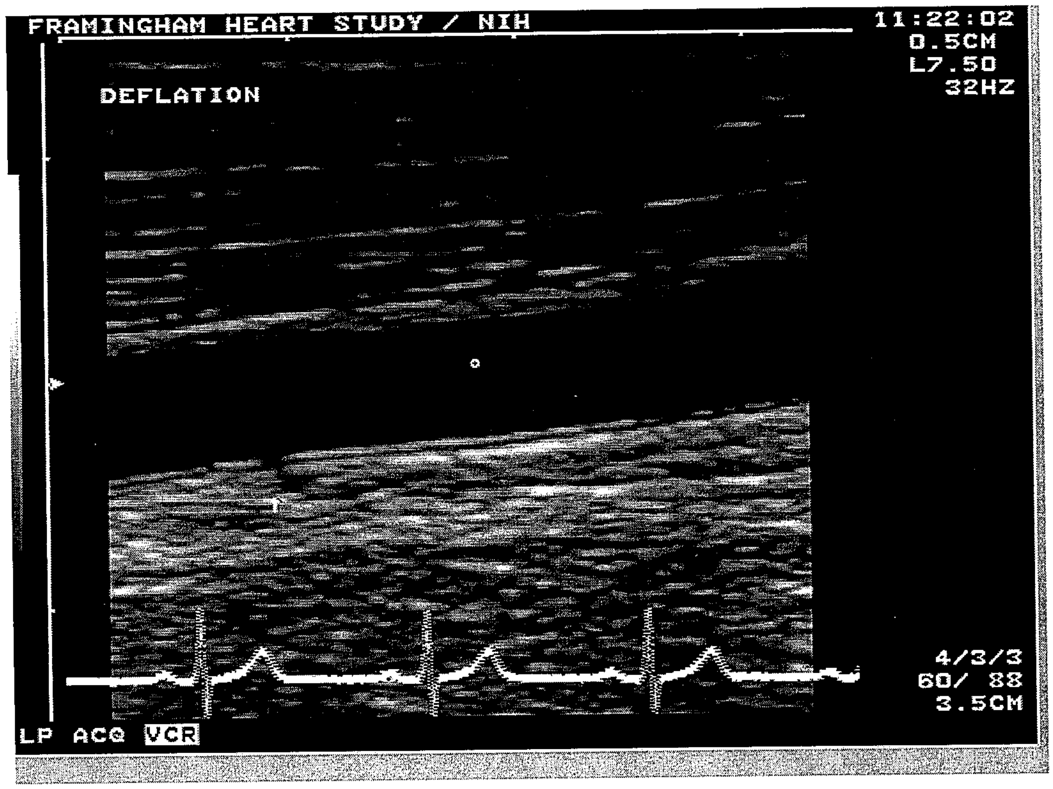


Figure 6:

Try to avoid imaging the vessel too superficially. The vessel is also diagonal rather than horizontal. Note the focus is not directed to the vessel.

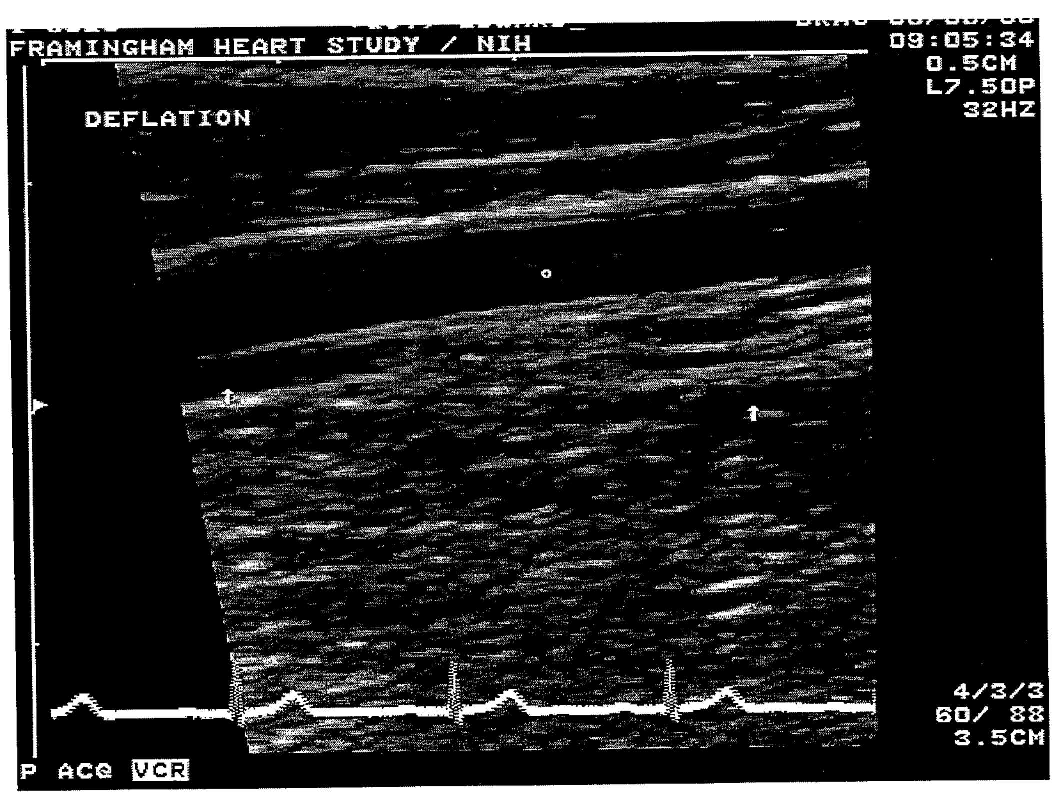


Figure 7:

Try to avoid hypoechoic shadowing in the vessel.