Atherosclerosis Risk in Communities
Carotid MRI Study
Manual 4
Magnetic Resonance Imaging Reading Center

Version 1.0

For Copies, Please Contact
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# Table of Contents

Johns Hopkins University

1.0 GOALS AND OBJECTIVES: IMAGING ................................................................. 4

2.0 READING CENTER EQUIPMENT .................................................................. 4

3.0 READING CENTER PERSONNEL .................................................................... 5

   3.1 MRI RC PI: BRUCE WASSERMAN, MD ...................................................... 5
   3.2 MRI RC PROJECT MANAGER: BONNIE COSNER .................................. 5
   3.3 MRI RC PHYSICIAN READERS: SAURABH MALHOTRA, MD, MPH, TBA 6
   3.4 MRI RC AFFILIATE: BRAD ASTOR, PhD, MPH ..................................... 6
   3.5 MRI RC AFFILIATE, SIEMENS: CORY SWINGEN, PhD .......................... 6
   3.6 MRI RC AFFILIATES, GENERAL ELECTRIC: THOMAS FOO, PhD AND GLENN SLAVIN, PhD .............................................. 6
   3.7 MRI RC AFFILIATE, MEYAPPAN SOLAIYAPPAN, B.E. .................... 6
   3.8 MRI RC AFFILIATE (LEIDEN UNIVERSITY): ROB J. VAN DER GEEST ... 6
   3.9 MRI RC ADJUNCT MRI COMMITTEE ...................................................... 6

4.0 MRI EQUIPMENT ............................................................................................ 7

   4.1 SCANNER ..................................................................................................... 7
   4.2 COIL ........................................................................................................... 7
   4.3 EQUIPMENT CHANGES ............................................................................ 7
   4.4 MRI SAFETY ............................................................................................. 7

5.0 MRI MEASUREMENTS .................................................................................... 7

6.0 ARTERIAL SITES, ANATOMIC STRUCTURES, AND ATEROMA COMPOSITION TO BE STUDIED ......................................................... 8

   6.1 NORMAL ANATOMY .................................................................................. 8
   6.2 IMAGING PLAQUE COMPOSITION ......................................................... 9

7.0 MRI PROTOCOL ............................................................................................ 10

   7.1 SEQUENCE OUTLINE ............................................................................ 10
   7.2 SIDE TO IMAGE ........................................................................................ 11
   7.3 OUTLINE OF PROTOCOL WITH CORRESPONDING IMAGES .............. 12

8.0 PILOT STUDIES ............................................................................................ 16

   8.1 COIL PERFORMANCE ............................................................................. 16
   8.2 PROTOCOL DEVELOPMENT .................................................................. 16
   8.3 PROTOCOL IMPLEMENTATION .............................................................. 16

9.0 MRI TECHNOLOGIST TRAINING AND CERTIFICATION .................................................................................................................. 16

   9.1 MRI TECHNOLOGIST TRAINING SCHEDULE ...................................... 16
   9.2 MRI TECHNOLOGIST TRAINING OUTLINE ........................................ 16
   9.3 MRI TECHNOLOGIST CERTIFICATION .................................................. 17

10.0 DATA TRANSMISSION ................................................................................. 17

   10.1 PARTICIPANT IDENTIFYING INFORMATION ...................................... 17
   10.2 REQUIRED FIELDS ................................................................................ 18
   10.3 ARIC MRI READING CENTER ORGANIZATION OF DATA FLOW AND FORMS ................................................................. 19

11.0 READING ASSIGNMENTS ......................................................................... 21

12.0 QUALITY CONTROL .................................................................................... 24

   12.1 MRI IMAGE CALIBRATION .................................................................. 24
12.2 IMAGE GRADING
12.3 INTER-READER AND INTRA-READER RELIABILITY
13.0 MEETINGS AND CONFERENCE CALLS
14.0 ALERT STATUS CATEGORIES AND ALERT FORM HANDLING
15.0 APPENDIX
PART I: OVERVIEW OF ARIC MR READING CENTER

1.0 GOALS AND OBJECTIVES: IMAGING

The purpose of the ARIC MRI Reading Center is to design and implement a standardized protocol to obtain magnetic resonance imaging studies for 2,000 participants enrolled in the fifth clinic visit of the Atherosclerosis Risk In Communities (ARIC) study. The MR studies will be performed at the four ARIC Field Centers. The ARIC MRI Reading Center will prepare for these studies by implementing a pilot study, conducting a training course to certify all MRI technologists in this study and testing the protocol at each site before the imaging begins.

The goals of the ARIC MRI Reading Center are to provide quantitative measurements of early atherosclerotic changes in the carotid artery wall and of morphologic characteristics in more advanced carotid artery disease with enough precision to (1) determine the normal variation of these measurements, (2) characterize MRI features of plaque emphasizing those thought to be predictive of clinical events, and (3) study the predictors of these MRI features. Subsequent studies will relate MRI measure to subsequent risk of coronary heart disease and stroke.

The MRI RC will accomplish these goals via the following objectives:

1. Identify MRI measurements in carotid artery walls that relate to early atherosclerosis formation and measurements in atheromas that relate to its vulnerability to rupture or thrombosis based on clinical and laboratory measures of disease.

2. Design a protocol that can be implemented at all MRI centers to acquire the measurements identified in (1).

3. Oversee equipment needs to enable protocol implementation and data uniformity across sites.

4. Ensure the successful implementation of the MRI protocol at each site.

5. Ensure protocol adherence and adequate image quality for ongoing MRI studies.

6. Provide the MRI measurements listed in (1) to the Coordinating Center to be used for analysis and participate in manuscript preparation providing insight into the use of these measures to assess cardiovascular disease and atheromas.

2.0 READING CENTER EQUIPMENT

The preferred image data transmission and archiving format will be DICOM. Immediate and long-term storage will be provided through the utilization of a RAID unit. The hardware includes network connections and a tape based storage medium and a workstation for initiating file transfers.

Field Centers will transmit studies, in DICOM format, via the Internet, directly to the RAID unit. For the duration of the imaging phase of the study, the Field Centers will be required to maintain on a back-up tape or disk, a copy of all studies performed at their sites, in case of network failure. If network failures occur, the Field Centers may mail studies to the RC in DICOM format on either a tape or CD. The tapes/CDs can be restored from the disk drive on the GE Signa scanner or Siemens scanner, using the Magic View workstation, to the RAID for permanent storage as well as quick and reliable access.
The images will then be transmitted from the RAID to the Linux desktop workstation that houses the interactive software package VesselMass (Leiden University Medical Center, The Netherlands) for reader interpretation. After completion of the image analysis, the image contours and reports will be archived on CD, using the CD-creation capabilities of the Linux workstation. This data will be archived using a tape backup. Images received from FCs will be archived to CD daily, and one AIT jukebox tape drive will be used as a back-up archive for long term storage and disaster recovery of all material stored on the RAID. Images will be archived to the AIT jukebox weekly. All measurements and post-processed images with ROIs drawn on the arterial wall will be archived to a central backup, for permanent storage and disaster recovery.

A MRI RC spreadsheet will be created for all Field Centers, using the data on the Carotid MRI Data Adherence and Tracking Form, the Alert Form and the Carotid MRI Completion Form. This will be used to track the status of studies received, reader assignments for interpretation, and the progress of the interpretation, sorted by Field Centers.

3.0 READING CENTER PERSONNEL

MRI RC PI
MRI RC PROJECT MANAGER
MRI RC PHYSICIAN READER
MRI RC PHYSICIAN READER
MRI RC AFFILIATE (JHSPH)
MRI RC AFFILIATE (SIEMENS)
MRI RC AFFILIATE (GE)
MRI RC AFFILIATE (GE)
MRI RC AFFILIATE
MRI RC AFFILIATE (Leiden University)
MRI RC ADJUNCT MRI COMMITTEE

Bruce Wasserman
Bonnie Cosner
Saurab Malhotra
TBA
Brad Astor
Cory Swingen
Thomas Foo
Glenn Slavin
Meiyappan Solaiyappan
Rob J. van der Geest
Brad Astor, Jeff Carr, Gerardo Heiss, Robert Mazzei, Richey Sharrett, Cory Swingen

3.1 MRI RC PI: Bruce Wasserman, MD
Oversee the design and implementation of the final MRI protocol, oversee establishing the necessary MRI equipment, supervise the pilot study, oversee the design and implementation of the data base management system and the computer image analysis software. Will oversee the quality control of the database, evaluate and monitor intra- and inter-reader reliability of MRI interpretation including delineation of clinically meaningful differences in MRI scan interpretation. Will oversee the design and interpretation of data analyses performed to identify clinically and statistically significant predictors of clinically important cardiovascular events. Will design and implement any change in the methodology used for the MR RC for the final study. Participate in the analysis and publication of the ARIC MR data. Will review urgent clinical alerts and respond to participant queries regarding alerts.

3.2 MRI RC Project Manager: Bonnie Cosner
Responsibilities include assisting in implementation and maintenance of the ARIC MR RC data management system. Will act as a liaison between the MR RC and the ARIC FC and Coordinating Center on issues relating to the MRI RC. The Project Manager will report to the MRI RC PI results of the FC quality control monitoring, MRI RC turnaround and results of interpretation analyses. Will communicate to the Coordinating Center and FC any changes in protocol or MR data management as directed by the MRI RC PI. The project manager will assist in the planning, implementation, and

Revised 8/3/2005. MOP 4 ARIC Carotid MRI Magnetic Resonance Imaging Reading Center Version 1.0 Page 5
control modifications regarding the MRI RC resulting from the pilot project. Responsibilities include coordination and communication of the MRI RC data entry inputs and outputs. Will also maintain schedules for readers, report problems or concerns relating to the MRI RC operations at the monthly QC meetings. Communicates to FC’s any protocol changes and issues regarding operations. The project manager will communicate to the appropriate personnel status of alerts and data transfer.

3.3 MRI RC Physician Readers: Saurabh Malhotra, MD, MPH, TBA
Will perform all quantitative analysis using Vesselmass MR Analytical Software System. If an alert is identified, they will report the findings to the PI.

3.4 MRI RC Affiliate: Brad Astor, PhD, MPH
Will assist in the analysis design and supervision of the database programmer, and he will oversee data collection and analysis issues including those related to quality control and reliability of measurements.

3.5 MRI RC Affiliate, Siemens: Cory Swingen, PhD
Will work with Dr. Wasserman on protocol development and will help to ensure compatibility of the protocol between sites.

3.6 MRI RC Affiliates, General Electric: Thomas Foo, PhD and Glenn Slavin, PhD
Will work with Dr. Wasserman on protocol development and will help to ensure compatibility of the protocol between sites.

3.7 MRI RC Affiliate, Meiyappan Solaiyappan, B.E.
Will develop an efficient and robust approach to extract and visualize geometric features from MRI images of carotid atherosclerosis using both 3D visualization and geometric computing, for quantification and analysis.

3.8 MRI RC Affiliate (Leiden University): Rob J. van der Geest
Will support the analysis software and modify existing software applications to accommodate specific needs for ARIC MRI measurements.

3.9 MRI RC ADJUNCT MRI COMMITTEE
Will work with PI to design and implement MRI protocol to acquire measurements listed in section 5.0, and help to establish the necessary equipment to successfully run the protocol. Will provide QC for FC MRI exams including ongoing study oversight and MRI technologist supervision. Will help with design of MRI calibration phantom. Will offer recommendations to SC and EC regarding MRI exclusion criteria and MRI measurements attainable within the allotted scan time. A radiologist from each field center will be available to respond to participant or field center staff questions about clinical alerts.
4.0 MRI EQUIPMENT

4.1 Scanner

**GE sites**
Requirements: (1) Black blood FSE option, (2) Cardiac gating option, (3) FSEUNO

*Requires a research key

University of Mississippi Medical Center: EXCITE platform, 8 channel *(Not finalized)*
Wake Forest University Health Sciences: EXCITE platform, 8 channel
Washington Field Center: EXCITE platform, 8 channel

Siemens site:
University of Minnesota: Symphony with Maestro upgrade

4.2 Coil

**GE and Siemens sites**
Machnet bilateral four channel receive-only phased array (PA) carotid coil (Figure 1).
Dimensions: Effective length, 105 mm PA mode; width, 60mm

![Figure 1](image)

4.3 Equipment Changes
Any changes in equipment during the imaging phase of the ARIC Carotid MRI study must be approved by the MRI Reading Center.

4.4 MRI Safety
Prior to imaging, the MRI Committee will recommend a set of exclusions that will be universally accepted, ensure participant safety and avoid needless processing and scheduling if a particular MRI center uses more stringent limitations and refuses to perform the scan.

5.0 MRI MEASUREMENTS

*Non-atheromatous wall measurements:*
  - Wall thickness (mean, max, min)
  - Percent Gd-enhancement (mean, max)
  - T2 relaxation (mean, max, min)

*Atheroma measurements:*
  - Plaque volume; Plaque thickness (median, max); Outer wall area; Lumen area
  - Fibrous cap: Percent Gd-enhancement (in radial segments), thickness (median, min, max), T2 relaxation (median, max)
  - Lipid core: Presence/absence, Volume, T2 relaxation, % Gd-enhancement
  - Presence and Volumes/Areas of other components: Calcification, hemorrhage, ulceration
6.0 ARTERIAL SITES, ANATOMIC STRUCTURES, AND AThEROMA COMPOSITION TO BE STUDIED

6.1 Normal Anatomy

Internal carotid artery: Has no branches; Usually posterior and lateral to external carotid artery

External carotid artery: Has branches (may have variations in branching patterns)

Example: Normal anatomy
Time-of-flight MRA just above the level of the bifurcation.

3 Superior saturation pulse applied so jugular vein is dark.
4 Flow artifact is hazy, not discrete, starts along outer wall (where plaque forms) and extends into center of lumen more distally.
6.2 Imaging Plaque Composition

Example: Plaques
Time-of-flight MRA

Plaque formation in typical location – Along outer wall of carotid bulb opposite the flow divider.

The right vertebral artery is absent in 10% of the population [unrelated to plaque].

Example: Plaque
Contrast-enhanced black blood image of plaque seen in Figure 4.

Contrast-enhanced black blood MRI

Goal of plaque imaging:

Schematic

Calcium
Lumen
Fibrocellular tissue
Lipid core

Figure 4
Figure 5
Figure 6a
Figure 6b
7.0 MRI PROTOCOL
7.1 Sequence Outline
The MRI exams for all 2000 participants will include the image sequences outlined in this table. The sequences are used to localize the carotids (#1), identify the most stenotic plaques (#2), acquire a long-axis view of each carotid to serve as a scout for slice positioning, acquire measurements at standardized locations for both carotids (#4-7 and 13) and provide detailed information on one selected carotid artery (#8-10 and 13).

1If plaque: 8 precontrast slices are placed through plaque centered at most stenotic point.
2If no plaque: 8 precontrast slices are centered through the bifurcation with 4th slice from bottom centered through flow-divider.

<table>
<thead>
<tr>
<th>Number</th>
<th>Sequence</th>
<th>Explanation</th>
<th>Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Scout (Ax/Cor)</td>
<td>Localize carotids</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>3D TOF MRA</td>
<td>Bright blood sequence</td>
<td>3</td>
</tr>
<tr>
<td>3 (R)</td>
<td>1st Oblique BB PD (3 slices) R carotid</td>
<td>Long axis view through bifurcation for slice placement</td>
<td>4</td>
</tr>
<tr>
<td>4 (L)</td>
<td>1st Oblique BB PD (3 slices) L carotid</td>
<td>Long axis view through bifurcation for slice placement</td>
<td>4</td>
</tr>
<tr>
<td>4 (R)</td>
<td>2nd Obl BB T1 thru R CCA</td>
<td>Baseline for comparison with Gd-enhanced image</td>
<td>0.5</td>
</tr>
<tr>
<td>5 (R)</td>
<td>2nd Obl Multiecho R CCA</td>
<td>To calculate T2</td>
<td>2</td>
</tr>
<tr>
<td>6 (L)</td>
<td>2nd Obl BB T1 thru L CCA</td>
<td>Baseline for comparison with Gd-enhanced image</td>
<td>0.5</td>
</tr>
<tr>
<td>7 (L)</td>
<td>2nd Obl Multiecho L CCA</td>
<td>To calculate T2</td>
<td>2</td>
</tr>
<tr>
<td>8 (S-Bif)</td>
<td>2nd Obl PCMRA (L or R) CCA</td>
<td>Measure stiffness</td>
<td>2</td>
</tr>
<tr>
<td>9 (S-Bif)</td>
<td>2nd Obl BB T1 thru Bif (8 slices)</td>
<td>Baseline for comparison with Gd-enhanced images</td>
<td>4</td>
</tr>
<tr>
<td>10 (S-Bif)</td>
<td>2nd Obl Multiecho - 2 thickest contiguous slices</td>
<td>To calculate T2</td>
<td>4</td>
</tr>
<tr>
<td>11</td>
<td>Coronal 3D MRA mask - Gd injection</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>Coronal Gd-enhanced 3D MRA</td>
<td>Begin 10sec after injection starts</td>
<td>-</td>
</tr>
<tr>
<td>13 (R)</td>
<td>2nd Obl BB T1 thru R CCA</td>
<td>To measure contrast enhancement</td>
<td>0.5</td>
</tr>
<tr>
<td>13 (L)</td>
<td>2nd Obl BB T1 thru L CCA</td>
<td>To measure contrast enhancement</td>
<td>0.5</td>
</tr>
<tr>
<td>13 (S-Bif)</td>
<td>2nd Obl BB T1 thru Bif (16 slices)</td>
<td>To measure contrast enhancement</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2 groups of 8 slices with 1 min break)</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>43</td>
</tr>
</tbody>
</table>

2Postcontrast images: 8 precontrast slices are copied and 5 added above and 3 below.

All slices are 2mm thick with no gap if multiple.

Legend:
BB = Black blood (Uses a double inversion recovery sequence.)
S-CCA = Selected side through distal CCA (same as either R CCA or L CCA slice)
S-Bif = Selected side for detailed imaging of carotid bifurcation
CCA = Common carotid artery
PCMRA = Phase contrast MRA (to quantify flow)
CEMRA = Contrast-enhanced MRA
Gd = Gadolinium
L = Left
MRA = MR Angiography
Obl = Oblique
R = Right
TOF = Time-of-Flight (A noncontrast technique for MR angiography)

Times are conservative estimates.

### 7.2 Side to Image

The same side-selection criteria apply both to the 1200 participants selected based on having an increased max carotid IMT measurement by ultrasound and to the remaining 800 randomly selected from the ARIC cohort.

The multi-slice acquisitions (Sequences # 9 and 13 in Table 7.1) and sequence numbers 8 and 10 will be acquired only on one selected side. This is indicated by “S-Bif” in Table 7.1.

Initial side selection: The side with the higher maximum carotid IMT measurement or the side with plaque if present will be determined by the Coordinating Center based on the most recent available carotid ultrasound study. This side will be provided by the Coordinating Center to the MRI technologist at the time the participant arrives for imaging.

Final side selection: The MRI technologist will use the side specified by the Coordinating Center unless a lesion is seen on the opposite side that causes greater stenosis. The technologist will look for and compare the presence of such stenotic lesions on both sides on the MR angiogram (sequence #2) and the long-axis black blood image (sequence #3). This condition is possible since the ultrasound studies cover only 1 cm distal to the flow divider and more distal lesions will be missed, and the presence of a plaque may not be recorded as a high IMT value.
7.3 Outline of Protocol with Corresponding Images

(Detailed protocol outlines with sequence parameters for GE and Siemens will be provided in the MRI Training Protocol)

1) Localize the carotid bifurcation(s) (2 min)

*Localization is done by reviewing GRE images and recording the location of the bifurcation on each side.*

2) 3D TOF MRA (3 min)

*Center of 3D imaging volume should be just above location of lower bifurcation. This is used to look for carotid stenosis. This sequence is used to confirm if the side selected by the coordinating center indeed has the greatest stenosis. The side with greatest stenosis will be selected for detailed imaging.*

3) Oblique BBMRI through long-axis of the carotid bifurcation using MRA as a scout (4 min x 2 sides, Left and Right carotid bifurcations)

*Middle slice*
4) 2nd oblique T1 through CCA – Baseline for comparison with Gd-enhanced image (30 sec – Right side)
5) 2nd oblique MultiEcho through CCA – T2 measurement (2 min – Right side)

Contralateral carotid:
6) 2nd oblique T1 through CCA – Baseline for comparison with Gd-enhanced image (30 sec – Left Side)
7) 2nd oblique MultiEcho through CCA – T2 measurement (2 min – Left Side)
8) 2nd Obl PCMRA of CCA to measure arterial stiffness (on the selected side) (2 min)

9) 2nd oblique T1 BBMRI through bif/plaque - Baseline for comparison with Gd-enhanced image (4 min for 8 slices of one selected side only).
   For plaque cases: Slices are placed through the plaque and centered at (a) most stenotic point or (b) where plaque appears thickest if location of (a) is difficult to determine.
   If no plaque present: Slices are centered through the bifurcation with the fourth slice from bottom centered through the flow divider.

10) 2nd oblique MultiEcho through 2 thickest contiguous slices of ICA/plaque – T2 measurement (2 min x 2 slices of the selected side)
11) Coronal 3D MRA Mask

- Administer Gadolinium
  Use right arm
  Single dose (0.1 mmol/kg) at 2 cc/sec
  RECORD EXACT TIME

12) Coronal contrast-enhanced 3D MRA
    Use timing bolus or image after 10 seconds from time of injection.

------------------------- WAIT 5 MINUTES FROM TIME OF INJECTION -------------------------------

13) Repeat steps 4 (Right side), 6 (Left side) and 9 (16 slices of selected side - 8 precontrast slices are copied and 5 added above and 3 below) beginning 5 minutes after injection.
8.0 PILOT STUDIES  
*November 1 through December 22, 2004*

8.1 Coil performance  
A pilot will be performed to test the Machnet coils. This will be used to calibrate the coils and test their performance on the EXCITE platform. New GE coils may be tested as well for their performance.

8.2 Protocol development  
A pilot of 10 studies will be performed at JHH to develop the protocol. The pilot will investigate the limitations of wall thickness overestimation at varying slice obliquities and thicknesses while considering signal limitations for wall visualization. It will also test the feasibility of acquiring the designated MRI measurements within the given time constraints. This will be used to finalize the protocol on the GE system.

A pilot of 5 studies will be performed at University of Minnesota to develop the protocol for the Siemens scanner.

*December 22, 2004 through January 5, 2005*

8.3 Protocol implementation  
A pilot of 2 studies will be performed at each FC. These studies will be supervised by the MRI Committee member for that site and will test the basic sequences to be used in the protocol. It will also ensure adequate performance of the coil. Images will be transmitted to the MRI RC for assessment of image quality and protocol parameters.

9.0 MRI TECHNOLOGIST TRAINING AND CERTIFICATION

9.1 MRI Technologist Training Schedule  
One day training session. Two sessions are planned for each vendor (GE, Siemens) to facilitate sending techs in groups rather than all at once.

Siemens: Central training at U MN; January 10.  
GE: Central training at JHH; January 11, 12,

9.2 MRI Technologist Training Outline

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>9am – 11:30am</td>
<td>Refreshments &amp; introductions</td>
</tr>
<tr>
<td></td>
<td>Lecture</td>
</tr>
<tr>
<td></td>
<td>Welcome</td>
</tr>
<tr>
<td></td>
<td><em>Introduction to study</em></td>
</tr>
<tr>
<td></td>
<td><em>Overview of the objectives of MRI Protocol</em></td>
</tr>
<tr>
<td>11:30am – 12:30pm</td>
<td>Lunch</td>
</tr>
<tr>
<td>MRI Center</td>
<td></td>
</tr>
<tr>
<td>12:30 – 5pm</td>
<td>Scan, Review cases</td>
</tr>
<tr>
<td>5pm-6pm</td>
<td></td>
</tr>
<tr>
<td>6 - 7</td>
<td>Questions; Farewell</td>
</tr>
</tbody>
</table>

A test will be administered during the lunch break.

Revised 8/3/2005.  MOP 4 ARIC Carotid MRI Magnetic Resonance Imaging Reading Center  Version 1.0  Page 16
Scoring will be processed by 6pm and feedback will be given at that time.

9.3 MRI Technologist Certification
A test will be administered as described in section 9.1.

MRI Technologists will be required to scan volunteers and the images will be graded by the RC for image quality and protocol adherence. Two exams must be approved as acceptable by the RC for the MRI Technologist to be certified.

No re-certification will be required since the imaging period is under a year and a half. However, technologists will be provided with reports summarizing the quality of their images after the first 5 scans and then quarterly.

New MRI Technologists who start the study after the initial training period will have to have tailored training and certification. The goal is to minimize the need for such tailored training.

10.0 DATA TRANSMISSION

Field Centers will transmit studies to the central site, in DICOM format, via a VPN, directly to a RAID unit. Data encryption is mandated by HIPAA rules if there is a remote possibility that patient identity could be established. All patient identifying information should be removed from any data being transmitted before transmission. We are proposing to utilize data encrypting systems and a security service provider that will manage the flow of secured data between Johns Hopkins and the Field Centers. The Field Centers will enter relevant patient information on the Carotid MRI Completion Form, including the ARIC identification number and acrostic, and transmit these forms to the Reading Center with each study. Instructions for completing the Completion Form are listed in section 10.2.

We will use the Internet to transport data and will require the encryption services throughout the data acquisition period. Secure devices will be installed at each of the Field Centers to receive data, which will then be transmitted, via a VPN, to a secure server controlled by the security service provider. This would be accomplished in a transparent manner, and no special precautions would need to be taken by the operator at the Field Center. The encrypted data will then be forwarded, again via VPN to the RAID unit installed at the Central Site. Data can be transmitted to the Field Centers from the Central Site, through the VPN, if necessary.

For the duration of the imaging phase of the study, the Field Centers will be required to maintain on a back-up tape or disk, a copy of all studies performed at their sites, in case of network failure. If network failures occur, studies may be mailed to the RC in DICOM format on either a tape or CD. These tapes/disks can be restored, using a workstation connected to a scanner, to the RAID for permanent storage as well as quick and reliable access. One AIT jukebox tape drive will be used as a back-up archive for long term storage and disaster recovery of all material stored on the RAID.

10.1 Participant identifying information

All participants in addition to having a 7-digit ARIC identification number, will also have a 10 character acrostic ID assigned by the Coordinating Center. These IDs will be entered onto the Alert Form and the Carotid MRI Completion Form by the Field Center.

The acrostic will be also used to help match the forms and image data to the participant if the ARIC identification number is corrupted. This acrostic will be entered into the name field and will be
generated by the Coordinating Center using the following algorithm: Acrostic = CLLLMFFGBB, where
C = Field Center identifier (F, M, J, W), LLL = first three letters of last name, M = first letter of middle
name, FF = first two letters of first name, G = gender (M or F), and BB is the day component of the
birthdate.

Example of acrostic: Ludwig van Beethoven, who was born on the 16th of the month, was scanned at
Hagerstown - WBEEVLUM16

10.2 Required Fields

ARIC Carotid MRI Completion Form data will be entered into the database by the FC

ARIC ID number
• must be within the specified range
• required value

ACROSTIC -
• must be within the specified range
• entered into the name field as detailed in section 10.1

Most Recent Weight of Participant
• required value

Side of Body Being Imaged
• required - L or R

MRI Completed
• required - Y or N
• If Y - skip 3a - Reason MRI Not Completed
• If N - enter Reason MRI Not Completed
  Value A-G listed on form
  If G “Other” specify “other” in space provided

Report Date of MRI
• required - mm/dd/yyyy

Contrast Completed
• required - Y or N

• If Y - skip 4a - Reason Contrast Not Completed
• If N - enter Reason Contrast Not Completed
  Value A-G listed on form
  If G “Other” specify “other” in space provided

Contrast Volume Given
• enter volume in milliliters
Contrast lot number
• required

If MRI was not completed, and participant was not given contrast agent, skip to Exam # (number 8 on form)

Series Description
• For each sequence, enter Series Number, and Number of Images in each series.

Screen saves
Specify Series Number and Image Number

Repeated Images
Specify series and number of original images to be repeated, and series and image number of rescanned images. Form shows spaces for three instances of re-scanned series.

Exam #
required

Primary MRI Technician Code Number
required

Comments for Reading Center
optional - for use by data manager

Contrast Side Effects

Abnormality noted by MRI technician

Date of Data Collection
for use by data manager - mm/dd/yyyy

10.3 ARIC MRI Reading Center Organization of Data Flow and Forms

A Virtual Private Network (VPN) communication will be established between the Reading Center and each Field Center. Approximately 28 MRI examinations will be performed per month at each Field Center. The DICOM header for each study will contain the participant identification number, date, and Field Center identification. The designated Field Center representative will transmit the MRI data to the Reading Center, at the completion of the exam. Studies will be auto-routed to the RAID unit at the RC upon receipt, for permanent storage and access. At the completion of the MRI exam, the ARIC MRI technician will enter the MRI completion form information into the coordinating center database.

Overview of Data Flow:
• The information from the completion form will be entered at the Field Center and transmitted to the Reading Center within 24 hours of the time the exams are performed.
• The Completion Form received from the Field Center will be entered into the Reading Center Completion Form database. Daily, the Reading Center project manager will query the database for examinations received.

• Each week, the Project Manager will query the RAID unit for total exams received during that week and match this against the number of completion forms for the corresponding time interval. Any mismatch will be reported to the FC by the Project Manager. The ACROSTIC will be used in conjunction with the Study I.D. information to help identify missing cases.

• A copy of the completion form will be printed and used to reference the data transmitted by the Field Center to determine if all images from each series were received. If all images were received, a box will be checked on a web-based form indicating all sequences were received for that participant.

• The completion forms will then be placed in the queue for reader assignment.

• The project manager will transmit the assigned studies from the RAID unit to the Linux workstation that houses the VesselMass analysis software. This directory will be: /home/aric/Images/

• Image analyst assignments will be made on a weekly basis by the Study Coordinator or PI.

• Analyst ID's will be entered into the MRI RC Spreadsheet and a list for each reader will be generated and placed near the analysis workstation.

• If the image analyst is unable to process the data because of difficulty loading images into the VesselMass program, he/she will contact the project manager.

• The Image Analyst (reader) will complete the Carotid MRI Alert Form for the assigned study within two weeks of receipt of the MRI Completion form and the complete set of images. A critical stenosis (>90%) or another urgent finding (mass) (item 4 on Alert Form) will require notification of Dr. Wasserman by the Analyst. See section 14.0 ALERT STATUS CATEGORIES AND ALERT FORM HANDLING.

• The technical adequacy will be indicated on the Carotid MRI QC Spreadsheet, which will be completed by the Image Analyst (reader) at the time the contours are drawn. Only protocol violations that pertain to series or images essential for MRI measurements (see Section 5.0) will be recorded on the MRI QC Spreadsheet. This spreadsheet will be used later for the interpretation of MRI measurements (MRI Interpretation Database) to determine data integrity. This Spreadsheet will indicate: Protocol Adherence - 0=Failure, 1=Adequate; and Image Quality - 0=Failure, 1=Poor quality, 2=Good.

• Problems with data received will be reported to the Project Manager, who will notify the Field Centers and/or Coordinating Center via email.

• The Image Analyst will analyze the images by drawing contours around regions of interest as outlined in Section 11 (Reader Assignments).

• The Image Analyst will complete the Carotid MRI Data Adherence and Tracking Form and forward the form to the Project Manager to be finalized and signed off. Unlike the MRI QC
Spreadsheet, all protocol violations will be recorded on the Carotid MRI Data Adherence and Tracking Form.

All protocol violations recorded on this form will result in notification of the MRI committee representative and technologist via email by the Project Manager.

• The Project Manager or P.I. will sign the Carotid Data Adherence and Tracking Form, indicating the completion of this stage of analysis for each study.

• The P.I. will review a select number of cases for quality control, and will sign the Adherence and Tracking Form to indicate completion of an exam. Tracking forms for those cases not reviewed by the P.I. will be signed by the Project Manager.

• The MR RC PI will periodically review interpretations completed by the ARIC MR readers. This will provide a check on the accuracy of data entry and demonstrate whether any reader needs re-training regarding interpretation of MR scans.

• At the completion of the image processing, the project manager will export the quantitative data (i.e., contour and report files) to the ARIC Interpretation database. This database is under the supervision of the MR RC with affiliates at Johns Hopkins Bloomberg School of Health. The Project Manager will also transmit the data electronically (i.e., via email or FTP) to the Coordinating Center each month in the format specified by the Coordinating Center.

• Weekly, a designated image analyst will archive the VesselMass-generated contours and reports on to a CD, using the CD burning software and capabilities installed on the Linux workstation. The image analyst will enter MRI measurements into the MRI Interpretation Database.

  The file name of the back-up will be the name of the project and the date the CD was burned (i.e. ARIC20050105 for Jan 5, 2005). Back-up CDs will be stored securely in a remote location, away from the workstation being used to create the contours and reports. All post-processed data will also be backed up to a central site for long term storage and disaster recovery.

• The MRI QC Spreadsheet will be stored with the MRI Interpretation Database to determine integrity of this data.

• Weekly, the project manager will archive all MRI studies received that week to DVD. These will be labeled and numbered for easy access and retrieval of studies. All MRI studies will also be automatically archived to tape.

11.0 READING ASSIGNMENTS

Reader assignments are as follows:

Two image analysts will be assigned by the PI or Study Coordinator to read a total of 28 cases per week (26 original studies from the queue and 2 repeat studies). The repeat studies will be exams already analyzed by the other analyst or by the same analyst earlier in the study. The adjudicator will be assigned to review 5 cases per week for quality control.

Thus, each ARIC participant may have 1-3 different records corresponding to different readings:

• original
• intra-reader
• inter-reader

Technical adequacy
The image analyst assesses initial image quality and completes an Image Quality/Protocol Adherence Excel spreadsheet, and completes the appropriate sections of the Data Adherence and Tracking Form:
• Adherence to Protocol
  • 1 = Adequate: protocol was followed
  • 0 = Failure: protocol violation

For the Image Quality/Protocol Adherence spreadsheet:

Only series or images essential for MRI measurements (see Section 5.0) are recorded:
• Adherence to Protocol
  • 1 = Adequate: protocol was followed
  • 0 = Failure: protocol violation

• Image Quality
  (If examination is considered a failure, there is no quantitative analysis.)
  • 2 = Good: no problems, or minor technical problems
  • 1 = Poor Quality: images are suboptimal, but are minimally adequate for interpretation
  • 0 = Failure: major problems; examination is not of diagnostic quality.

Some criteria for a minimally adequate exam include:
• mild or moderate motion artifact
• missing series or missing images which are not essential for data entry

The Image Analyst (Reader) will be responsible for drawing contours around the vessel wall (i.e., lumen and outer wall) for vessels without atheromas, and around plaque components (e.g., lipid core, calcification, ulcer, hemorrhage) as well as around the lumen and outer wall if plaque is present. Regions of interest will also be drawn around the calibration phantoms and around air outside the subject’s neck to measure noise. The MRI measurements will then be processed by the Analyst using Vesselmass software.

The RC will not make any effort to stratify scan reading assignments based on the particular field center at which the scan was performed. The RC will examine the distribution of scans performed at each of the FC’s across MRI readers on a monthly basis. If the observed distribution of scans by FC is markedly distorted, we will revise our MRI reading assignment strategy in order to achieve a better balance.

If a reader is sick during all or part of a week during which they have been assigned to read, the scans to be read on a particular day during that week or during the entire week will be read by a substitute reader. The program manager will revise the reading assignment reader id into the database.
12.0 QUALITY CONTROL

12.1 MRI Image Calibration

a. Calibration schedule:

Baseline calibration
Scheduled for February, 2005.
9 tubes with 3 sets of T1 values and 3 sets of T2 values (Table 12.1).

Drift
The scanner will be calibrated every 50-75 cases at each FC. An e-mail from the CC will notify Field Center MRI technicians after 45 scans are completed that a calibration needs to be done the following week. A chicken heart will be used to facilitate cardiac gating.

Participant studies
Three small tubes will be attached to each carotid coil. Each tube will have a different T2 value but the same T1 value for calibration during each study.

Regions of interest will be drawn on the MRI images of the tubes to standardize the signal measurements made in the ipsilateral vessel wall. The tube diameters will be measured on the MRI image for geometric calibration.

b. Calibration design:

The calibration test will include the following:

1) T2 relaxation based on the multi-echo sequence
2) Signal intensity measurements based on double inversion recovery images with T1-, proton density-, and T2-weighting.
3) Geometric measurements based on thickness of test tubes.

<table>
<thead>
<tr>
<th>Phantom</th>
<th>T2 ms</th>
<th>T1 ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24.9</td>
<td>249.8</td>
</tr>
<tr>
<td>2</td>
<td>79.4</td>
<td>268.1</td>
</tr>
<tr>
<td>3</td>
<td>178.7</td>
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<td>1230.0</td>
</tr>
<tr>
<td>9</td>
<td>407.7</td>
<td>1240.0</td>
</tr>
</tbody>
</table>

Table 12.1

T1 and T2 values for 9 test tubes in calibration phantom based on mixtures of NiCl2 and Agarose.
12.2 Image Grading
As outlined in section 10, the image analyst will grade each exam for image quality and protocol adherence. Only images relevant to the designated MRI measurements will be graded. For example, if the scout images that localize the bifurcation are of poor quality but the T2 measurements are adequate, the T2 measurements will receive an adequate score.

Violations of protocol adherence will result in notification of the MRI committee representative and technologist by email. Repeated violations may result in retraining at the RC or training a different technologist.

Image quality grading will be used for the MRI Measurements database to be managed at the JHSPH.

12.3 Inter-reader and intra-reader reliability
Selection of Scans
Once a month the Coordinating Center will send a list of QC assignments to the Data Manager. The list will specify the reader and the reading assignment (intra- or inter) for those cases that have been randomized to QC reading by the coordinating center. The Data Manager will display 2-3 cases per week with the new cases that are to be interpreted. Statistical variation of more than 10% will require retraining by the RC PI.

Statistical analysis
The Reading Center and the Coordinating Center will monitor the analysis for both intra-rater and inter-rater reliability. Agreement will be considered within acceptable ranges if they are within 10% +/- of the recommended indexed value range.

13.0 MEETINGS AND CONFERENCE CALLS
Conference calls or in person meetings will be held on a weekly basis throughout the pilot study and monthly during the main trial. All ARIC MR RC personnel will be required to attend. The meetings will serve to address any problems with MR RC data management, data transmission, and MR interpretations.

Results obtained from the analysis of the inter- and intra-reader reliability will be reviewed. Variations that are found statistically significant will be discussed and, if needed, the reference manual will be modified or readers will be retrained.

The MRI Committee will conduct monthly conference calls, or more frequent calls if needed. This will serve to discuss protocol implementation and address difficulties with image quality or protocol adherence, equipment maintenance or upgrades, or data transfer issues.

14.0 ALERT STATUS CATEGORIES AND ALERT FORM HANDLING
The MR Reading Center image analyst will record the participant’s alert status on the MRI Alert form. During the qualitative analysis, the image analyst will record the percent stenosis for each carotid artery based on the TOF MRA and categorize the carotid artery into one of three groups:

a. Normal - No evidence of significant disease
b. Abnormal – Narrowing by greater than 50%*  
c. Cannot be evaluated

• *E-mail to Field Center (patient ID only, without name) with computer generated letter to be mailed to participant and, if the participant gave permission, to his/her physician as well.
• Follow-up will be documented at the Field Center on the Alert and Referral Form and the
Coordinating Center computer will monitor for any undue delays in sending alert letters.

- For participants who have both carotid stenosis of greater than 50% and a positive report of neurological symptoms (on the medical history questionnaire – i.e., history of stroke or TIA) a telephone call will be made by Field Center staff to confirm that the participant received the letter and facilitate follow-up with a physician.

- If a nonvascular abnormality is incidentally noticed, an email to the Field Center will be performed similar to that for vascular alerts. **However, the MRI RC will read images for carotid vascular abnormalities only and is not responsible for detecting nonvascular abnormalities.** This policy follows from the tailored nature of the scans which does not allow a full clinical evaluation.

Alerts identified during a quality control reading will be handled in the following manner:

- The Reading Center will first determine if an alert was reported on the original reading. If the alert is identical to the one previously reported, no alert letter for the QC interpretation will be sent. If the alert was not reported on the original interpretation, the Reading Center Principal Investigator will review the case. The Field Center and Coordinating Center will be contacted by telephone and an alert letter will be generated.

All participants will be notified of their results, normal or abnormal, in writing. For abnormal alerts, letters will be sent within on week of the reading.