ARIC Manuscript Proposal # 1572

PC Reviewed: 11/10/09	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Reproducibility of Vascular Lumen Geometry Factors from Routine Carotid MRA

b. Abbreviated Title (Length 26 characters): Reliability of Geometry

2. Writing Group:

Writing group members: Payam B. Bijari, Luca Antiga, Bruce A. Wasserman, David A. Steinman; others welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _PBB_ **[please confirm with your initials electronically or in writing]**

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3. Timeline:

Apr-Jun 2009: Development of streamlined analysis protocol
Jul-Sep 2009: Data analysis
Oct-mid-Nov2009: Manuscript preparation

4. Rationale:

Recent work from Steinman's group has demonstrated that the amount of disturbed flow at the carotid bifurcation, believed to be a local risk factor for carotid atherosclerosis, can be predicted from luminal geometric factors [Lee et al., Stroke

2008;39(8):2341-7]. As part of an approved ARIC Ancillary Study (2006.14C: Geometric Risk Factors for Atherosclerosis, GenAth), we will eventually carry out a retrospective analysis of ARIC Carotid MRI data (N~2000) to discern the influence of lumen geometry vs. systemic risk factors on early wall thickening at the carotid bifurcation. Our intent is to use CARMRI contrast-enhanced MR angiograms (CEMRA) to quantify geometry; however, these were acquired at relatively low spatial resolution (0.8x0.8x2mm) mainly for the purpose of grading stenosis severity and arbitrating possible flow artifacts in black blood MRI images of the vessel wall. As a result, it is important to first demonstrate how reliably the three-dimensional lumen geometry can be extracted from these "routine" CEMRA images. To do this, we make use of data acquired from the CARMRI repeatability cohort (N=61).

5. Main Hypothesis/Study Questions:

The specific aim of this study is to quantify the scan-scan repeatability of geometric factors extracted from "routine" CEMRA of the carotid bifurcation. Because the techniques are largely automated, we assume that operator variability is negligible, something we will also test.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

***Inclusion criteria*:** N=61 participants for whom replicate MRI studies (median interval 55 days) were acquired as part of the CARMRI substudy.

***Study design*:** An operator (author Bijari), blinded to the identity of the N=61x2 replicate scans, uses a fast (<5 min) protocol for digitally segmenting the lumen geometry from the CEMRA images, based on authors Antiga and Steinman's Vascular Modeling ToolKit (VMTK). The operator also rates the surface quality on a three-point scale in order to identify possible effects of image quality on repeatability. VMTK is then used to automatically quantify various geometric factors including bifurcation angle, planarity, tortuosity and area ratios as defined by the Lee et al. paper cited above. Of the N=122 cases, five from each quality rating, for a total of 15, are randomly selected for segmentation by another operator, blinded to the rating, in order to confirm operator independence.

***Data Analysis*:** Primary outcome variable is the intraclass correlation coefficient (i.e., ICC(2,1)) for the geometric factors noted above. Baseline and repeat lumen surfaces will be automatically registered using the Iterative Closest Point (ICP) method in order to quantify the root-mean-squared error (RMSE) between the paired surfaces, as a measure of the absolute precision of the digitized lumen surfaces. One-way ANOVA will be used to test for any significant influence of image quality rating on the baseline vs. repeat differences. Author Steinman is in sole possession of the identity of the replicate scans, and will carry out all statistical analyses using the open-source R statistical package.

***Limitations*:** N/A

7.a. Will the data be used for non-CVD analysis in this manuscript? ____ Yes __X__ No

b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used? ____ Yes ____ No
(This file ICTDER03 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? ____ Yes __X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = "No use/storage DNA"?
____ Yes ____ No

9.The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/ARIC/search.php

___X__ Yes _____ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? __X_ Yes ____ No

11.b. If yes, is the proposal
_X_ A. primarily the result of an ancillary study (list number: *2006.14C)
___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

12. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

All data analysis has been completed, and the manuscript is currently being drafted for **anticipated submission by mid-November 2009**.