Semiautomated Quantitation of Carotid Artery Stenosis in Gadolinium-Bolus Magnetic Resonance Angiography

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Magnetic resonance angiography (MRA) has become the standard method for evaluation of carotid occlusive disease. Fast imaging methods combined with bolus intravenous injection of gadolinium contrast have improved the quality of these images. Nevertheless, the gold standard for evaluation was based on projection arterial angiography. The properties of these images are rather different. Whereas most previous evaluations of MRA have used visual assessment of images, we evaluate an algorithm in which a computer algorithm plays the primary role in defining arterial lumen margins, hence, disease. The accuracy of this semiautomated algorithm is shown to compare favorably with gold-standard arteriography in a series of 50 patients.

KEY WORDS: magnetic resonance angiography, carotid atherosclerosis, North American Symptomatic Carotid Endarterectomy Trial, quantitation

MMAGNETIC RESONANCE ANGIOGRAPHY (MRA) has become a popular method for noninvasively diagnosing vascular disease. The addition of bolus injection of gadolinium, although invasive, appears to significantly improve the quality of MRA images for some anatomies.¹⁻³ However, the majority of MRA images are reviewed by creating maximum intensity projection (MIP) images that appear like intra-arterial angiography (IAA), ignoring the ability to compute values, because of the digital nature of the acquisition device. In this study, we compared a semiautomated algorithm (SAA) for measuring carotid stenosis versus observer ratings of the IAAs and MRA source data in a cohort of 50 patients.

METHODS

Patient Recruitment

After informed consent and Institutional Review Board approval, 50 patients undergoing IAA for suspected carotid occlusive disease were recruited to have bolus gadolinium MRA studies of their necks performed within 3 days of the IAA. Three neuroradiologists reviewed the conventional angiograms and MRA source images and assigned a percent stenosis using North American Symptomatic Carotid Endarterectomy Trial (NASCET) methods.⁴ The values for the left carotid arteries on IAA then were provided to one of us who used an internally developed application to determine a method of operation that provided good agreement with IAA values. The method then was applied to all vessels in a blinded fashion. Measurements were repeated 3 times for one of us to provide intraobserver variability estimates and one time by 2 other observers. Of the 100 vessels, 15 were totally occluded by conventional angiography.

Gadolinium Bolus MRA Technique

The details of the gadolinium bolus technique have been described elsewhere² and has been quite robust and successful in clinical practice. Briefly, a phase-contrast MRA of the entire neck is obtained to provide location information to position the gadolinium bolus sequence. Then a "timing sequence" is run at the level of the carotid bifurcation to

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Fig. 1. Upon selecting the study, a coronal MIP is displayed. The user draws an ROI on it, which includes the vessel segment of interest.

Fig. 2. This ROI defines a volume of interest (VOI), which is displayed as a MIP. The user may view this VOI at any angle and interactively refine the VOI. Refining the VOI improves the appearance and does not affect the measurement.

Fig. 3. The user then places a line with a “tick” mark at the point of stenosis, with the line perpendicular to the lumen at the stenosis.

allow estimation of the time when the bolus of gadolinium would arrive. Finally, a bolus of gadolinium is injected followed by saline, and the MRA sequence is acquired beginning at the time the bolus arrives as seen on the timing sequence. This sequence is an elliptical K-space acquisition in the coronal plane (22 × 16 cm Field of View (FOV) with 1.4-mm slice thickness).

Algorithm Description

The overlying concept of this algorithm is to have the user select the location of abnormal and normal vessel, as per the NASCET method. The computer then takes these locations and computes the minimal diameter using 50% of the peak intensity as the threshold for defining vessel boundaries. The user may override this threshold, but this was not permitted for this study. The algorithm also computes the cross-sectional area, which probably better reflects flow, but because the NASCET gold standard is based on projection angiography, this was not considered in this study.

The algorithm uses the AVW(C) library developed by the Biomedical Imaging Resource at the Mayo Clinic⁵. Its algorithms are used for rendering the MIP and oblique sections. A low-pass anisotropic diffusion filter⁶ also was

applied to the source image data. This filter has the properties of reducing noise while preserving edges. The steps used for the semiautomated method were:

1. Select the study.
2. Draw a Volume of Interest (VOI) over the vessel of interest from the whole volume MIP (Fig. 1).
3. Refine this VOI to remove any structures that might confuse the operator or that degrade rendered image quality (Fig. 2).
4. Place a line perpendicular to the vessel, centered at the point of maximum stenosis on the MIP (Fig. 3).
5. Place a line perpendicular to the narrowest channel on the oblique section (Fig. 4). At this point, the computer will adjust the angle of the line to minimize the diameter, and compute the threshold that defines the vessel diameter, using half the peak intensity as the threshold (with user option to override).
6. Repeat steps 3 and 4 for a normal segment of the ICA.
7. The results (diameters, areas, and % stenosis based on lumen and area) are displayed, and saved to a file (Fig. 5). Note that for this study, only the diameter measurements were used, because the gold standard IAA could only provide diameter measurements.

Fig. 4. The previous step defines a plane, and that plane is displayed at the lower left. The user now drags this second line and tick mark to the center of the vessel lumen. If the tick mark is near the center of the lumen, clicking the “Minimize Diameter” button causes the computer to find the lumen

center and then the angle that minimizes the diameter. It calculates the threshold defining the lumen using the FWHM. A profile of intensities along the line is shown on the right. The user may override the computed values if desired. For this study, this was not allowed.

Initial results were disappointing, particularly for extreme values. But we found that if we imposed 4 rules, results improved significantly. Those rules (which were applied for the results presented here) are listed below.

1. Negative stenosis values are converted to 0% stenosis. (There were 17 vessels in which the bifurcation segment was wider than the more distal normal segment).
2. A diameter of less than 3 mm for the normal segment is defined as a “string sign” or 99% stenosis. This value was arrived at by reviewing the cases of severe stenosis, and noting that the “normal” vessels distal to a 99% stenosis were all well less than 3 mm (typically around 2 mm), whereas “normal” vessels distal to less than 99% stenosis were much larger (typically 4 to 5 mm).
3. We also excluded total occlusions because no meaningful measure of the vessel exists.
4. If the maximum intensity of the vessel is less than 50% of the 95th percentile intensity in the total volume histogram, adjust the threshold for defining the vessel from half the peak height to 75% of peak height. This is to compensate for the low intensity of very stenotic vessels.

After these rules were implemented, the measurements were performed on all vessels, and the results were recorded for this study with no further “tuning.”

Conventional Imaging Measurement

Conventional angiograms were obtained using conventional film methods. An intra-arterial (common carotid artery) injection of iodinated contrast material was performed and serial films obtained at an angle that produced minimum superposition of internal and external carotid arteries, and at 90° (biplane filming). Subtraction images were produced and presented to board-certified neuroradiologists trained in the NASCET method. Three blinded readers provided a percent stenosis for each vessel. MRA images also were provided to 3 blinded readers, with at least 6 months’ time passing between interpretation of the IAA and MRA data sets. These readers independently measured the percent stenosis on MIP images of each vessel, and based on the source images. The source images were magnified, but only straight axial images were provided.

Fig. 5. Steps 3 and 4 are repeated for the normal segment. Then the measurements and calculated values are displayed, as shown here. A film can be printed with the MIP and MPR images at this time.

Fig. 6. Graph of semiautomated algorithm values for stenosis versus average of 3 rater values based on IAA. The correlation coefficient was 0.93, slope was 0.93, and the intercept was -6.46.

Fig. 7. Graph of semiautomated algorithm values for stenosis versus average of 3 rater values based on MRA source images. The correlation coefficient was 0.95, slope was 0.9, and intercept was -7.9.

Magnetic Resonance Image Measurement

Three experienced neuroradiologists, blinded to both conventional angiography and the semiautomated results, were trained on how to use high-resolution eyepieces and image reformatting. They then provided measurements of the percent stenosis for all vessels using MIP renderings of each vessel and measurements based on the MRA source images.

RESULTS

Of the 100 vessels included in the study, 85 were not occluded. We found that the SAA agreed reasonably well with IAA (Fig. 6), MRA source images (Fig. 7), and MIP images (Fig. 8). The

correlation coefficient for all 85 nonoccluded vessels was 0.93 versus conventional angiography, 0.95 versus the MRA sources images, and 0.94 versus the MIP images. The maximum absolute errors were 41%, 45%, and 47%, respectively. This compares well with the accuracy of interpretation of the MIP and source images at .93 for MIP images and .94 for source images versus the conventional angiogram.

Inter-observer variability (based on intraclass coefficient) for the SAA was 0.760 with a 95% confidence interval, whereas the intraobserver variability was lower with a coefficient of 0.881.

Fig. 8. Graph of semiautomated algorithm values for stenosis versus average of 3 rater values based on MRA MIP images. The correlation coefficient was 0.94, slope was 0.86, and intercept was -15.5.

Fig. 9. Two examples of good agreement between conventional angiography and the semiautomated algorithm applied to MRA. (A) The conventional angiogram on the left where a 47% stenosis was found; the semiautomated algorithm measured 47%. (B) The conventional angiogram on the left where a 55% stenosis was found; the semiautomated algorithm measured 56%.

According to Cohen,⁷ this agreement is considered “very good.”

The time to perform the SAA measurement averaged 3.4 minutes per examination (2 vessels, except when a vessel was occluded), and ranged from 1.7 minutes to 5.6 minutes.

DISCUSSION

MRA has become a popular method for non-invasively diagnosing vascular disease and carotid atherosclerotic disease in particular. Early MRA techniques used either changes in phase related to flow (phase contrast MRA) or the lack of saturation of in-flowing protons (time of flight MRA) to produce high signal in areas of flow. The addition of bolus injection of gadolinium is a recent development that significantly improves the quality of MRA¹⁻³ by increasing the signal within flowing tissues.

MRA images typically are then reconstructed using MIP to produce DSA-like images. Although this quickly and easily created familiar “DSA-like” images, it probably is suboptimal for 2 reasons. First, by projecting 3-dimensional data onto 2 dimensions, information can be lost because of superposition. Second, blood flow is more closely related to the cross-sectional area

rather than the minimum lumen diameter. The reason lumen diameter is measured in this and other studies is because the major studies validating therapy for carotid atherosclerotic disease were based on lumen diameter (not cross-section area) measurement.⁴ Of course, features like irregularity and ulceration can affect patient symptoms and outcome. These factors were not considered in this study.

There have been prior reports of semiautomated measurement of MRA data. The majority have focused on reformatting data with manual measurement of lumen geometry.⁸⁻⁹ There also are reports of semiautomated measurement but based on MIP images, not source images¹⁰ for peripheral vessels. There also has been good work on phantoms and theoretical models in which phantom vessels are imaged, and computers then reconstruct the geometry of the phantom using source images.¹¹

The SAA described here has a fairly high correlation with both IAA and MRA source images. However, there were a few notable exceptions (Fig. 10). In some cases, the SAA failed because of markedly reduced signal intensity in regions of stenosis (likely caused by turbulence). This reduced lumen intensity caused a lower threshold to be used, resulting in

Fig. 10. Two examples of divergence between conventional angiography and semiautomated measurements. (A) The conventional angiogram showed a 78% stenosis, whereas the semiautomated method measured a 45% ste-

nosis. (B) The conventional angiogram showed a 70% stenosis, (as did visual review of the MIP), but MRA source analysis and semiautomated method measured 39% and 31%, respectively.

an incorrectly high lumen size. However, initial attempts to “correct” this low threshold using information about the normal segment intensity have not been successful to date. We did add a rule to improve performance for these situations, and we allow users to override the incorrectly low threshold. These changes did improve accuracy. The disadvantage of allowing user intervention is greater variability in measurements, although this is outweighed by the greater accuracy in the cases of marked disease.

Once the vessel geometry has been defined, one can produce attractive 3-dimensional renderings, including MIP images with less background noise, 3-dimensional surface displays, as well as curved multiplanar reformats along the center of the lumen of the vessel. These may be helpful in confirming the SAA output in clinical practice.

Semiautomated methods for quantitating MRA data may improve patient care by providing more objective and reproducible measures for clinical trials as well as routine care.

CONCLUSIONS

Computer quantitation of carotid disease based on MRA imaging is feasible and competitive with visual assessment of projection images. Future improvements may permit more accurate diagnosis because of the 3-dimensional nature of the data sets (see Fig. 9).

REFERENCES

1. Matthews V, Ulmer J, White M, et al: Depiction of intracranial vessels with MRA: Utility of magnetization transfer saturation and gadolinium. *J Comput Assist Tomogr* 23:597-602, 1999
2. Phan T, Huston Jr, Bernstein M, et al: Contrast-enhanced magnetic resonance angiography of the cervical vessels: Experience with 422 patients. *Stroke* 23:2282-2286, 2001
3. Debatin J, Hany T: MR-based assessment of vascular morphology and function. *Eur Radiol* 8:528-539, 1998
4. NASCET: Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 325:445-453, 1991
5. Robb RA, Hanson DP: The ANALYZE software system for visualization and analysis in surgery simulation,

In: Lavalée S, Taylor R and Burdea G (eds): Computer Integrated Surgery. Cambridge, MA, MIT Press, 1995, pp 175-190

6. Gerig G, Kubler O, Kikinis R, et al: Nonlinear anisotropic filtering of MRI data. *IEEE Trans Med Imag* 11:221-232, 1992

7. Cohen J: A coefficient of agreement for nominal scales. *Educational and Psychological Measurement* 20:37-46, 1960

8. Vanninen RL, Manninen HI, Partanen PK, et al: How should we estimate carotid stenosis using magnetic resonance angiography? *Neuroradiology* 38:299-305, 1996

9. Morasch M, Gurjala A, Washington E, et al: Cross-sectional magnetic resonance angiography is accurate in predicting degree of carotid stenosis. *Ann Vasc Surg* 16: 266-272, 2002

10. Westenberg J, van der Geest R, Wasser M, et al: Vessel diameter measurements in gadolinium contrast-enhanced three-dimensional MRA of peripheral arteries. *Magn Reson Imaging* 18:13-22, 2000

11. Flasque N, Desvignes M, Constans J, et al: Acquisition, segmentation and tracking of the cerebral vascular tree on 3D magnetic resonance angiography images. *Med Image Anal* 5:173-183, 2001