Evaluation of Semiautomated Internal Carotid Artery Stenosis Quantification from 3-Dimensional Contrast-Enhanced Magnetic Resonance Angiograms

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Rationale and Objectives: The performance of a semiautomatic technique for internal carotid artery (ICA) stenosis quantification of the internal carotid artery in contrast-enhanced magnetic resonance angiography was evaluated.

Materials and Methods: The degree of stenosis of 52 ICAs was quantified by measuring the cross-sectional area along the center lumen line. This was performed both by 3 independent observers and the semiautomated method. The degree of stenosis was defined as the amount of cross-sectional lumen reduction.

Results: Agreement between the method and observers was good (weighted-kappa, $\kappa_w = 0.89$). Reproducibility of measurements of the semiautomated technique was better ($\kappa_w = 0.97$) than that of the observers ($\kappa_w = 0.76$), and the evaluated technique was considerably less time-consuming.

Conclusions: Because the user interaction is limited, this technique can be used to replace an expert observer in 3-dimensional stenosis quantification of the ICA at CE-MRA in clinical practice.

Key Words: internal carotid arteries, stenosis quantification, contrast-enhanced MR

(*Invest Radiol* 2004;39: 418–426)

Two large randomized trials have proven that carotid endarterectomy is beneficial for patients with severe symptomatic carotid artery stenosis (70–99%).[1–3] The degree of stenosis was determined using intra-arterial digital subtraction angiography (DSA), which depicts the carotid arterial bifurcation in a limited number of projections, usually 2 or 3. Consequently, the maximum internal carotid artery (ICA) stenosis will often not be assessed using DSA because of the small number of projections.[4] Clinical studies have demonstrated that less- and noninvasive techniques, such as 3-dimensional time-of-flight (TOF) magnetic resonance angiography (MRA) and contrast-enhanced (CE) MRA, are useful alternatives for selecting patients for carotid endarterectomy.[5]

Vessel analysis can be performed most accurately using the original slices of 3-dimensional imaging modalities, but this is a tedious procedure. Maximum-intensity projection (MIP) images provide angiogram-like images and are useful to get a 3-dimensional impression of the anatomy. However, it is well recognized that lower-intensity features of the vessels may be lost in MIP images.[6] In this article, we evaluate the method for segmentation and stenosis quantification of the ICA in 3-dimensional CE-MRA introduced previously.[7] Quantification was performed by measuring the cross-sectional area in planes perpendicular to the center lumen line of the ICA. The performance of the algorithm was assessed by comparing the results with the measurements of 3 independent observers as reference.

SUBJECTS AND METHODS

Patients and Equipment

Data that were used in this retrospective diagnostic study were derived from a prospective trial held from January 1997 to November 2000 that evaluated different visualization techniques for carotid artery stenosis.[8,9] From this database, we used the 3-dimensional CE-MR angiograms of 35 consecutive patients (mean age, 64 years, range 45–72 years) with symptoms of carotid disease (transient ischemic attack, stroke, or amaurosis fugax) in the preceding 6 months. Thirty-one patients were male.

In our hospital, all symptomatic patients are first screened with carotid duplex ultrasonography. If peak systolic velocity values in the ICA are 150 cm/s or higher, patients are suspected of having carotid disease.[10] Patients

Received December 5, 2003 and accepted for publication, after revision, February 16, 2004.

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Supported by Medical IT-Advanced Development (Philips Medical Systems, Best, Netherlands).

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ISSN: 0020-9996/04/3907-0418
DOI: 10.1097/01.rli.0000129469.56134.3a

with this finding were subsequently referred for DSA, 3-dimensional TOF-MR, and CE-MR angiographic examinations within a period of 2 weeks.

Contrast-enhanced MR angiography was performed with a 1.5-T MR system (Gyroscan ACS-NT; Philips Medical Systems, Best, Netherlands). Bolus-track technology (Philips Medical Systems) was used to determine the arrival of the bolus of contrast agent in the carotid artery. This protocol included an optimized centric profile order and a variable matrix. The acquisition parameters were 4.5/1.5 (TR/TE both in milliseconds), 40° flip angle. Thirty-five slices were acquired at a 1.2-mm slice thickness, which were reconstructed to 70 slices of 0.6-mm slice thickness. The acquisition matrix was 140 × 256, with 1.0 × 1.0 mm^2 in-plane resolution. Images were reconstructed using a 280 × 512-reconstruction matrix resulting in a 0.5 × 0.5 × 0.6-mm^3 voxel volume. Two dynamic scans were acquired of 22 seconds each. The contrast agent used is a 500-mM solution of gadopentate dimeglumine (Magnevist, Schering, Berlin, Germany). Figure 1 shows an example of a 3-dimensional contrast-enhanced MR angiogram.

FIGURE 1. MIP image of origin and intracranial part of the carotids on CE-MRA.

Manual and Semiautomated Quantification

ICA stenoses were quantified by measuring the cross-sectional area along the center lumen line of the carotid arteries both manually by 3 independent observers and semiautomatically. Manual quantification of the 3-dimensional CE-MRA data was performed using a clinical workstation (EasyVision, Philips Medical Systems). For each ICA the observers manually defined the center lumen line. Subsequently, multiplanar reformatted (MPR) images are created, showing the cross-sectional images along the center lumen line and perpendicular to it. In the stenosis the MPR image shows maximal lumen reduction in the ICA. Here the cross-sectional area is measured. To determine the degree of stenosis, the cross-sectional area is also determined at a reference location the bulb.[1] In the MPR images the cross-sectional area of the ICA was defined using a full-width-half-maximum (FWHM) criterion.[11] Figure 2 shows how cross-sectional areas were measured using the FWHM criterion.

Finally, the degree of ICA stenosis was calculated using a criterion derived from the NASCET criterion:[1] stenosis = [1 − (minimal residual luminal area/distal ICA luminal area)] × 100%. Because cross-sectional area reduction is considered here, this is a different criterion than the NASCET criterion, which is based on diameters.

Semiautomatic stenosis quantification of the ICA has been described in more detail in.[7] A brief description follows next. After resampling the 3-dimensional CE-MRA dataset to obtain isotropic voxels (resolution 0.5 × 0.5 × 0.5 mm^3), the dataset is filtered to enhance vessel-like structures.[12] Subsequently, 2 user-defined points are indicated that are used to initialize the automatic center lumen line detection. The center lumen line is determined as a minimum-cost path between these 2 points, at which costs are given by the reciprocal value of the vessel-enhanced image. The automatically determined center lumen line is inspected by the observer. Hereto, the semiautomatically determined center lumen line is displayed both in a MIP image and in the source data.

If it is decided that the estimated center lumen line does not represents the true center lumen line, a new center lumen line can automatically be determined using more initialization

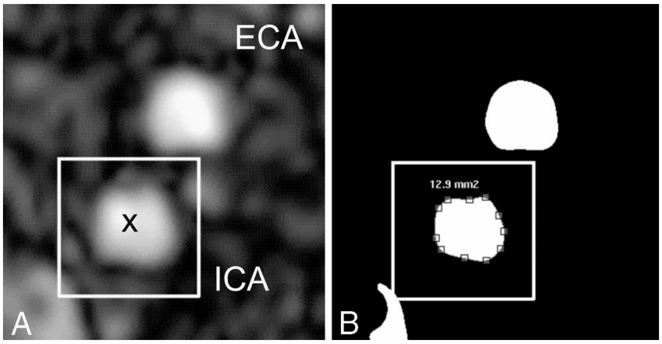

FIGURE 2. In panel **A**, cross-sectional view along the center lumen line (marked with a cross) of the ICA. The external carotid artery (ECA) is also visualized. The ICA boundaries are estimated using the FWHM criterion. Hereto, the maximum intensity within the square is determined, which is here 1090. In this image, the window width/window level is 1504/752. In **B**, the window levels are adjusted to obtain a binary image in which the ICA boundaries can be determined. Hereto, half of the maximum gray value within the square is calculated, ie, 545. Subsequently, the window width/window level is set 0/376, so that a binary image is obtained from which the cross-sectional area of the ICA can be measured unambiguously.

points. If the observer decides that the automatically determined center lumen line correctly represent the true center lumen line, the carotid artery is segmented with subvoxel precision using this center lumen line as an initialization of an expanding surface. The ICA boundaries are determined by controlling the growth of the surface using the FWHM criterion.[11]

Subsequently, the cross-sectional area along the center lumen line of the segmented ICA is quantified. Finally, the ICA stenosis is calculated using the criterion as stated above. The minimal residual luminal area in the nominator is the cross-sectional area in the stenosis and is depicted automatically. The distal ICA luminal area in the denominator is determined as the median ICA cross-sectional area along a reference segment that is indicated by the observer, in contrast to the manual stenosis grading that uses the cross-sectional area at a single reference position. Since the cross-sectional area along the center lumen line of the normal artery beyond the bulb can show large variation, the degree of stenosis can vary accordingly (Fig. 3). The use of the median cross-sectional area in a segment as reference for stenosis grading rather than a measurement at a single location should ensure better reproducibility. For the present study, all algorithm parameters were set to the values as determined in.[7]

Method of Evaluation

Three expert observers (O.E.H.E, M.F., and E.P.A.V.) participated in this evaluation study. Manual examination of the 3-dimensional CE-MR angiograms was performed with at least a 2-week interval. The observers manually defined the ICA center lumen line and manually measured the ICA cross-sectional area in the stenosis and at a reference location. From these measurements the degree of stenosis was derived accordingly.

Semiautomatic segmentation of the carotid artery was performed by indicating 2 user-defined points to initialize the center lumen line determination (C.M.v.B.) The resulting center lumen line was inspected by the observer. If the automatically determined center lumen line was judged to be correct, ICA segmentation and quantification of the cross-sectional area along the center lumen line of the ICA was performed without any user interaction. As a result, a plot was generated showing the cross-sectional area as a function of the position along the center lumen line. Using this graph and the segmentation, the observer pointed out what part of the segmented ICA was to be used as a reference segment. From this reference segment the median cross-sectional area was determined, which was used to determine of the degree of stenosis. The observer was blinded for results by the expert observers. Measurements were repeated with a two-months interval to assess the method's reproducibility.

Statistical Analysis

Agreement was assessed by using a kappa (κ) test for classification.[13] To account for the degree of disagreement, we used the weighted-kappa (κ_w) test. To perform a κ_w test, stenoses were categorized into 5 categories: 0–29%, 30–49%, 50–69%, 70–99%, or 100% (occlusion). The weights for discrepancies of 0, 1, 2, and 3 categories in the ratings were 1, 2/3, 1/3, and 0, respectively.[14] A κ_w value of 1.0 indicates that the agreement is perfect, and a value of 0 indicates that it is not different from chance agreement. For the interpretation of κ_w values in between these extremes, we used the Landis–Koch guidelines:[15] 0.00–0.20 indicates slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 good agreement, and 0.80–1.00 almost perfect agreement. Occlusions were excluded from the analyses because no measurements could be performed. Agreement was determined for 2 situations, viz. (1) all ICAs included in this study and (2) symptomatic ICAs separately.

Intraobserver agreement was assessed for all 3 observers using a κ_w test. Also, we determined the mean of differences ($\pm$ 95% confidence interval [CI]) in degree of stenosis between the first and second measurement.

Interobserver agreement was determined by comparing an observer's average degree of stenosis of 2 readings with the average degree of stenosis of 2 readings of another observer. This analysis yields 3 values of κ_w and 3 means of differences ($\pm$ 95% CI), viz. the agreement between observer 1 and observer 2 (O_1 versus O_2), observer 2 and observer 3 (O_2 versus O_3), and observer 3 and observer 1 (O_3 versus O_1), respectively. The interobserver agreement for all ICAs in-

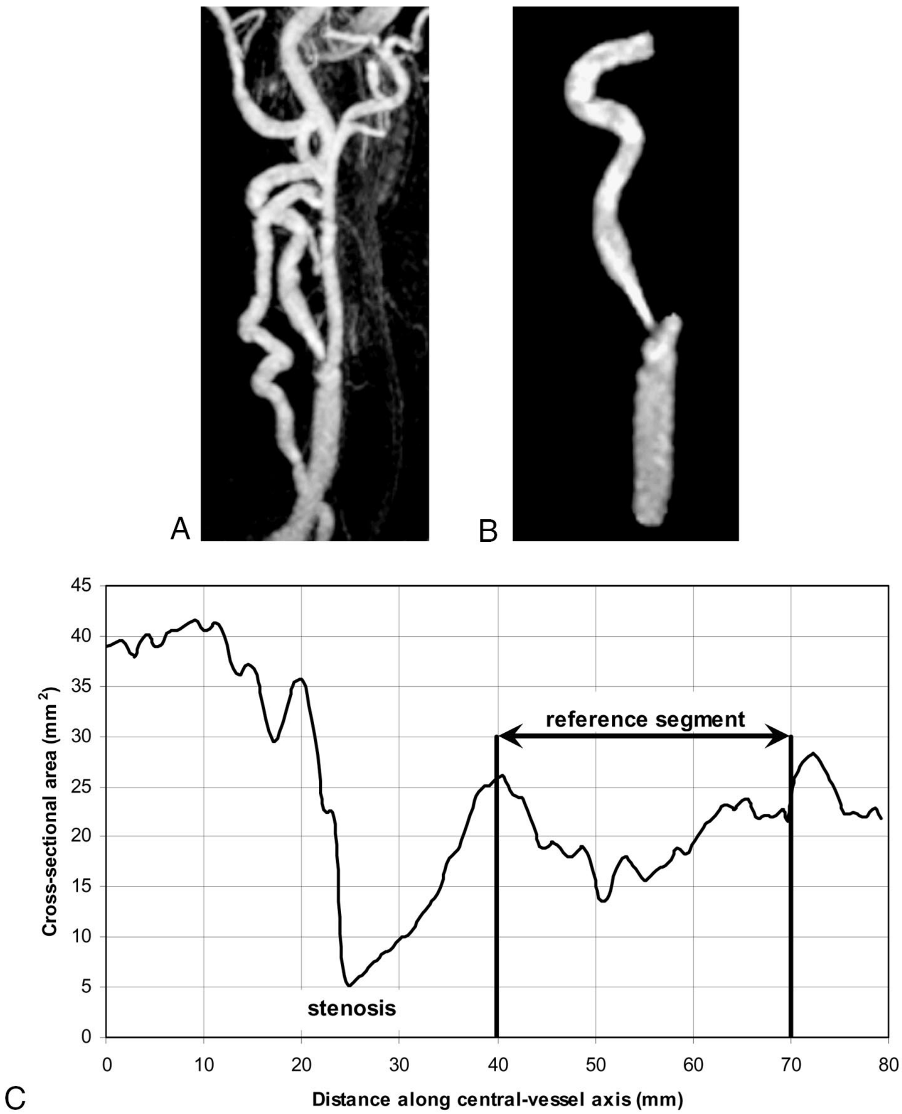

FIGURE 3. In panel **A**, MIP images of a stenosed internal carotid artery and in **B**, the corresponding segmentation. In **C**, the cross-sectional area is plotted as a function of the distance along the center lumen line. The median cross-sectional area of the reference segment was used to calculate the degree of stenosis. In this example the cross-sectional area in the stenosis is 5.0 mm^2, and the median cross-sectional area of the reference segment was 19.3 mm^2, yielding a 72.6%-degree of stenosis. It can be seen that a single reference position would yield large variability in the degree of ICA stenosis.

cluded in this study was visualized using a Bland & Altman plot.[16]

To assess the reproducibility of the algorithm, the degree of ICA stenosis was determined twice, both using a κ_w test and by determining the means of differences (± 95% CI) in degree of stenosis between the first and second measurement. For all ICAs included in this study, the reproducibility of the algorithm was visualized by means of a Bland & Altman plot, showing the differences between the first and second measurement obtained by this semi-automated technique versus their average value.

To evaluate the performance of the algorithm, the average degree of stenosis of 2 measurements obtained by the technique was compared with the average degree of stenosis of 2 readings of each observer. This analysis yields 3 values of κ_w and 3 means of differences (± 95% CI), viz. the agreement between the semi-automated method (M) and observer 1 (M versus O_1), M and observer 2 (M versus O_2), and M and observer 3 (M versus O_3), respectively. Furthermore, the average degree of stenosis of 2 measurements obtained by the technique was compared with the average degree of stenosis of 6 measurements performed by all 3 observers (M versus O_{mean}). Finally, the agreement between the proposed technique and the observers was visualized for all ICAs included in this study using a Bland & Altman plot.

RESULTS

Seventy carotid arteries in 35 patients were identified and evaluated by using 3-dimensional CE-MRA. Contrast-enhanced MR angiograms were of nondiagnostic quality in 5 cases. Reasons for nondiagnostic quality were failure in the timing of contrast-material arrival and the start of imaging, which caused too much enhancement of the jugular vein. This occurred in one patient (two carotid arteries). One ICA could not be assessed due to disturbance by blood clot in plaque that severely obscured the vessel signal. Another ICA was excluded because it was too tortuous, so that the center lumen line could not be determined accurately. A near-occluded ICA was excluded from analysis, because neither the center lumen line could not be determined nor segmentation could be obtained. Furthermore, thirteen ICAs were occluded and therefore excluded from this evaluation study. Therefore, 52 carotid arteries (21 symptomatic, 25 asymptomatic, and 6 with aspecific symptoms) remained for comparison.

Time Aspect

Manual determination of the center lumen line was performed in approximately 7 minutes. Subsequent manual measurement of the cross-sectional area at 2 locations was performed in approximately 4 minutes. Semiautomated center lumen line determination was performed in less than 3 seconds. The average number of initializations for the automated center lumen line determination was 2.2 (median 2, range 2–5). More than 2 initialization points were needed in 7 situations, where the carotid artery was very tortuous and/or there was a severe signal loss in the stenosis (see also Table 1). Automated segmentation by a computer was performed in approximately 7 minutes. The cross-sectional area along the center lumen line of segmented ICA was automatically quantified in less than 20 seconds. Both the automatic segmentation and automatic quantification were performed off line. As a result of the quantification, a plot was generated showing the cross-sectional area versus distance along the center lumen line (Fig. 3). Hereafter, a final user interaction was needed, viz. indicating the position and length of the reference segment that was needed from which the median cross-sectional area was determined, to determine the degree of stenosis. Altogether, the actual operator time for semi-automated stenosis grading was limited to a few seconds.

Observer Agreement

Intra-Observer Agreement

For all ICAs included in this study (n = 52), the intraobserver agreement (expressed in terms of κ_w) was 0.82, 0.71, and 0.83 for observer 1, 2, and 3, respectively. The mean of differences (± 95% CI) was 0.9% ± 23.0%, 1.4% ± 23.1%, and 1.0% ± 22.3%, respectively. Results for the symptomatic ICAs separately are listed in Table 2.

Interobserver Agreement

For all ICAs included in this study, the interobserver agreement (in terms of κ_w) for all ICAs included in this study was 0.75, 0.74, and 0.80, for O_1 versus O_2, O_2 versus O_3, and O_3 versus O_1, respectively. Means of differences are listed in Table 3. Figure 4 visualizes the interobserver agreement. Hereto, we plotted the results of O_1 versus O_2, O_2 versus O_3, and O_3 versus O_1, respectively, into one Bland & Altman plot. Results for the symptomatic ICAs separately are listed in Table 2.

Reproducibility and Performance of the Method

Reproducibility

For all ICAs included in this study, reproducibility of the method (expressed in terms of κ_w) was 0.97. The mean difference (± 95% CI) in degree of stenosis was 0.1% ± 7.2% (Fig. 4). Results for the symptomatic ICAs separately are listed in Table 2. Furthermore, we observed that in the region of interest the plot showing the cross-sectional area along the center lumen line was identical; only at the user-indicated points determining the length of the reference segment varied.

Performance

For all ICAs included in this study, the method's performance (in terms of κ_w) was 0.81, 0.84, 0.81, 0.89, for M versus O_1, M versus O_2, M versus O_3, and M versus O_{mean}, respectively. Means of differences are listed in Table 3. The cross-sectional area lumen reduction measurements of ICA

TABLE 1. Number of Initialization Points That Were Needed to Initialize the Automated Center Lumen Line Determination

Number of Initialization Points	2	3	4	5
Number of ICAs	45	3	3	1

Evaluation of Semi-Automated Internal Carotid Artery Stenosis Quantification from 3-D Contrast-Enhanced MR Angiograms

TABLE 2. Categorized Cross-sectional Area Lumen Reduction Measurements of ICA Stenosis at 3D CE-MRA for All ICAs Included in this Study and the Symptomatic (Between Brackets) ICAs Separately

	Manual				
	0–29%	**30–49%**	**50–69%**	**70–99%**	**Total**
Semiautomated method					
0–29%	**19 (1)**	1 (0)	0 (0)	0 (0)	20 (1)
30–49%	3 (0)	**7 (5)**	1 (0)	0 (0)	11 (5)
50–69%	0 (0)	0 (0)	**11 (9)**	1 (1)	12 (10)
70–99%	0 (0)	0 (0)	1 (0)	**8 (5)**	9 (5)
Total	22 (1)	8 (5)	13 (9)	9 (6)	**52 (21)**

Manual represents the average results of 6 manual ICA assessments by three expert observers. Method represents the average results of 2 semiautomated ICA assessments.

TABLE 3. Intraobserver Agreement, Method's Reproducibility, Interobserver Agreement, and Agreement Between the Semiautomated Method and the Observers in 3D ICA Stenosis Grading in CE-MR Angiograms for all ICAs Included in This Study

All ICAs Included in This Study (n = 52)	Mean*	± 95% CI*	K_W
Intraobserver†			
O_1	0.9	23.0	0.82
O_2	1.4	23.1	0.71
O_3	1.0	22.3	0.83
Method's reproducibility†			
	0.1	7.2	0.97
Interobserver†			
O_1 vs O_2	3.2	24.3	0.75
O_2 vs O_3	−2.1	25.8	0.74
O_3 vs O_1	−1.2	24.3	0.80
Method's performance†			
$M - O_1$	1.3	22.9	0.81
$M - O_2$	−2.0	23.1	0.84
$M - O_3$	−0.8	20.2	0.81
$M - O_{mean}$	0.5	16.9	0.89

*In % stenosis.

†O_1, O_2, and O_3 represent observer 1, 2, and 3, respectively. M is the semiautomated method. O_{mean} represents the average observation, ie, the average of all 6 measurements obtained by the 3 observers.

stenosis obtained by the method versus those obtained by the observers are listed in Table 4. Figure 4 visualizes the method's performance. Hereto, we plotted the results of the 3 comparisons (M versus O_1, M versus O_2, and M versus O_3, respectively) into one Bland & Altman plot. Results for the symptomatic ICAs separately, are listed in Table 2.

DISCUSSION

The degree of stenosis of the ICA is an important measure for selecting patients for carotid endarterectomy.[1,2] Intra-arterial DSA is the gold standard for visualization of the ICA, but there are several disadvantages: it is an invasive procedure that requires the use of an iodinated contrast medium and radiation, and is associated with a 4% risk of transient ischemic attack, or minor stroke, a 1% risk of major stroke, and even a small (<1%) risk of death.[17,18] Also, DSA is limited in depicting the maximum degree of stenosis of the ICA, since mostly 2 or 3 projections are used. In case of a noncircular stenosis, DSA may actually cause underestimation of the stenosis, whereas volumetric imaging modalities do not suffer from this limitation.[4,19]

Well-known volumetric imaging modalities for visualizing the carotid arteries are 3-dimensional TOF-MRA and 3-dimensional CE-MRA. 3-dimensional TOF-MRA is a noninvasive method of evaluating patients with suspected vascular disease. It is particularly well suited for the evaluation of low-resistance vessels with continuous laminar flow. However, in patients with vascular disease that disturbs laminar flow, TOF images are degraded. Furthermore, the image acquisition time for 3-dimensional TOF-MRA is relatively long.[20] Substantial improvements in image quality have been achieved with the introduction of minimally invasive 3-dimensional CE-MRA.[21] In 3-dimensional CE-MRA, the vasculature is visualized by using a T1-shortening contrast agent, reducing flow artifacts. Therefore, this technique is less sensitive to flow conditions than nonenhanced MRA techniques.[22] Furthermore, the technique is fast; the current protocol for 3D CE-MRA that is used in our hospital visualizes the complete tract of the carotid artery from origin to siphon in approximately 22 seconds. Lenhart et al have demonstrated that 3D CE-MRA allows for a selective visualization of the internal carotid arteries without degradation from venous enhancement. Furthermore, it was demonstrated that 3D CE-MRA is a reliable method with a good interobserver agreement.[23] Vessel analysis in 3-dimensional CE-MRA is performed most accurately using the original slices, since it better agrees with the true topology than projection images (like MIP images) do. MIP images are useful to obtain a 3-dimensional impression of the anatomy (tortuous vessels can be traced more readily than by using the source data) and they can be used for assessing the degree of stenosis. However, lower-intensity features of vessels may be lost in MIP images in contrast to source images.[6] Furthermore, in MIP images vessels may be obscured by superimposition of other vessels, limiting the number of angles that can be used for vessel assessment.

Reproducibility and Agreement

In this work, the evaluation of a method for ICA stenosis quantification in 3-dimensional CE-MR angiograms has been described. Hereto, the cross-sectional area along the center lumen line is determined. This procedure was assessed manually by 3 independent observers and by using a semiautomated method. Manual evaluation of the original slices of 3-dimensional CE-MR angiograms is a tedious procedure: both manually finding the center lumen line and manually determining the cross-sectional areas at 2 locations (one in the stenosis and one at a reference location) is laborious and prone to intra- and interobserver variability. According to the Landis-Koch guidelines, the intraobserver agreement was good for all ICAs. However, the intraobserver agreement for the symptomatic ICAs separately was moderate. Similar, the interobserver agreement was good for all ICAs, but only moderate for the symptomatic ICAs separately.

Semiautomatic ICA evaluation requires only 3 user interactions: initialization and inspection of an automatically

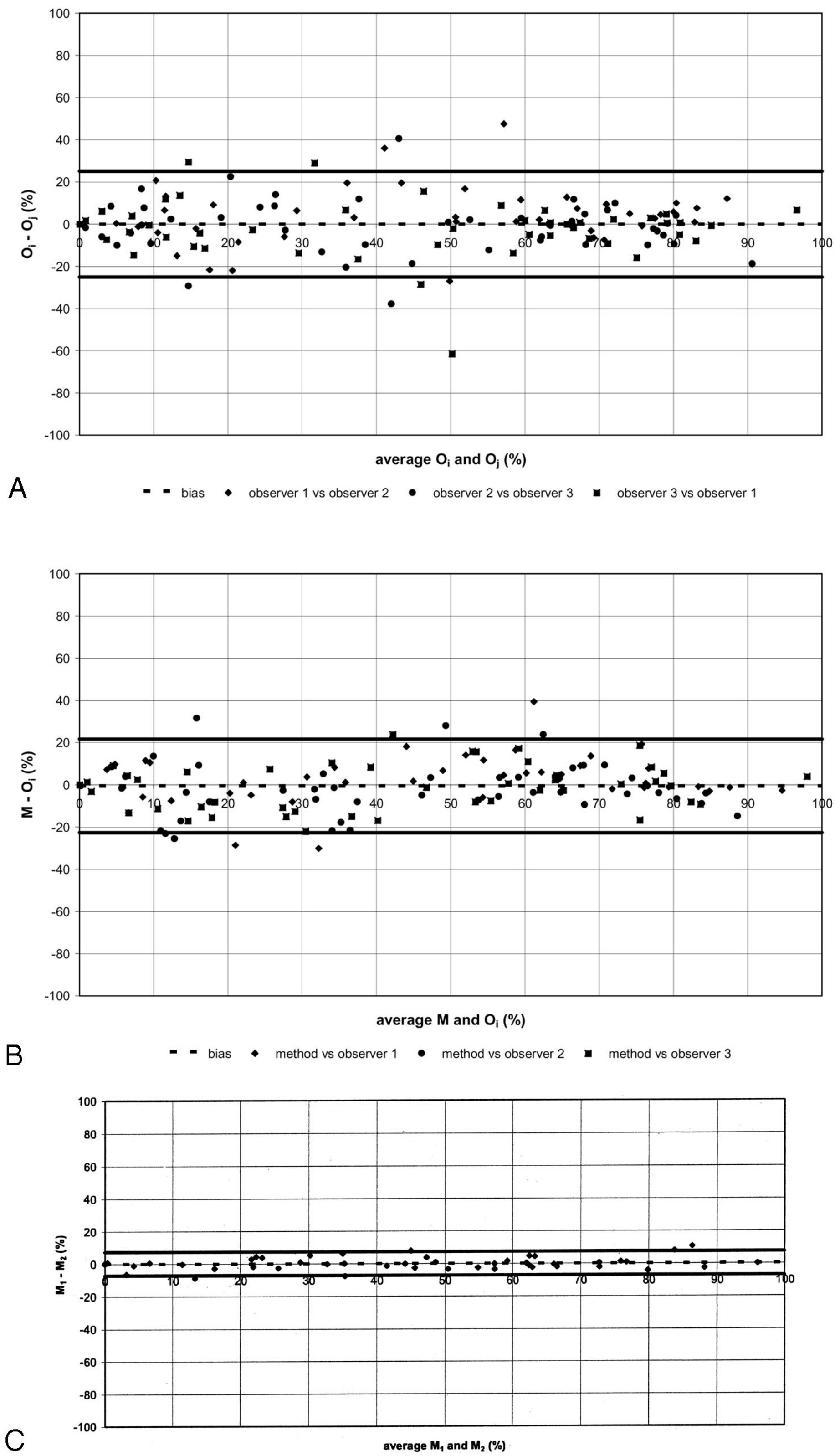

FIGURE 4. Bland & Altman plots showing the difference between measurements as a function of the average measurements. O_i is the i-th observer, M is the semi-automated method. In **A**, the interobserver agreement ((i,j) ϵ {(1,2), (2,3), (3,1)}). In **B**, agreement between the algorithm and the observers (i ϵ {1,2,3}). Compared with the observers, the algorithm shows no bias. Furthermore, the 95% limits of algorithm-observer agreement are narrower than for the interobserver agreement. In **C**, reproducibility of the algorithm (M_1 and M_2 are the first and second measurement using the semiautomated technique, respectively). The bias is negligible (0.4%). The 95% CI is very small (−7.8% to 8.7%), indicating a good reproducibility of the algorithm.

TABLE 4. Intraobserver Agreement, Method's Reproducibility, Interobserver Agreement, and Agreement Between the Semiautomated Method and the Observers in 3D ICA Stenosis Grading in CE-MR Angiograms for the Symptomatic ICAs Only

Symptomatic ICAs included in this study (n = 21)			
	Mean*	**± 95% CI***	K_W
Intraobserver†			
O_1	0.4	24.0	0.51
O_2	2.0	28.3	0.57
O_3	1.2	25.9	0.66
Method's reproducibility†			
	−0.2	6.0	0.95
Interobserver†			
O_1 vs O_2	6.5	29.6	0.45
O_2 vs O_3	−7.4	29.8	0.56
O_3 vs O_1	−0.9	27.3	0.57
Method's performance†			
M–O_1	4.9	20.9	0.73
M–O_2	−1.6	23.3	0.71
M-O_3	−2.5	22.0	0.72
M–O_{mean}	−0.3	14.5	0.95

*In % stenosis

†O_1, O_2, and O_3 represent observer 1, 2, and 3, respectively. M is the semi-automated method. O_{mean} represents the average observation, ie, the average of all 6 measurements obtained by the three observers.

determined center lumen line and indication of the length and position of the reference segment in an automatically determined plot showing the cross-sectional lumen area to determine the degree of stenosis. There was almost full agreement between the algorithm's 2 measurements. For the symptomatic ICAs, the 95% CI was larger than for all ICAs. Reproducibility of the semiautomated method was better than for the observers. Also for the symptomatic carotids separately the algorithm's reproducibility was better than the intraobserver agreement. Repeated experiments with the method yielded the same cross-sectional area versus distance plots in the region of interest. Therefore, it can be concluded that variance in stenosis grading of the semiautomated method was generated by differences in length and position of the reference segment to determine the reference cross-sectional area as indicated by the observer. Inspection of the results of the 2 sessions obtained by the method showed only one outlier. In this case the difference between the first and second semi-automated measurement was 10.6%, which is still considerably within the 95% CI of the intraobserver agreement.

To evaluate the algorithm's performance with respect to manual measurements of the expert observers, we used the average degree of stenosis of 2 measurements obtained by using the algorithm. For all ICAs, the agreement between the semi-automated method and the observers was good. Compared with the average degree of stenosis of 6 measurements performed by all 3 observers, agreement between the semiautomated method and the observers was even better. Regardless of the test that was used (comparison with each observer separately or comparison with the average results of all observers), according to the Landis-Koch guidelines the results show a almost full agreement with the expert observers.

Limitations

In this article it is shown that, by applying an objective criterion for boundary determination in 3-dimensional CE-MRA data, 3 independent observers and the presented semi-automated method for stenosis-grading are in agreement. By the lack of a gold standard, accuracy of the semiautomated method could only be assessed by comparison with the observers. DSA is still considered the gold standard in ICA stenosis grading, although several researchers have demonstrated that the results by DSA depend on the projection angle, eg,.[4]

To be able to determine the cross-sectional area in planes perpendicular to the center lumen line, the center lumen line should be smooth (both manually and semiautomatically determined). This implies that sharp corners must be avoided, because cross-sectional planes cannot be determined correctly at these locations. In one instance the carotid artery was too tortuous to find a suitable center lumen line both manually by the observers and by the method.

Forty-five center lumen lines could be determined with only 2 user interactions as initialization. For the remaining 7 ICAs more user interaction was needed to initialize the center lumen line (maximum 5 points). In all these cases the carotid artery was very tortuous and there was a severe signal loss in the stenosis.

In the evaluated technique the automated center lumen line determination is performed very fast (less than 3 seconds). Therefore, if the observer decides that the resulting center lumen line does not represent the true center lumen line, a new center lumen line can be determined almost instantaneously. Both segmentation and quantification of the cross-sectional area along the ICA center lumen line are fully automatic and performed o. line. Automatic segmentation takes approximately 7 minutes on a UNIX workstation (UltraSPARC-III, 900 MHz processor), but this can be shortened considerably, by optimizing the algorithm. Finally, cross-sectional area quantification is performed in less than 20 seconds. Therefore, the actual operator time is limited to less than half a minute. In contrast, the manual method takes about 11 minutes of operator time.

In conclusion, a semi-automated method for the 3-dimensional quantification of the internal carotid artery at

CE-MRA was evaluated. Quantification was performed by measuring the cross-sectional area along the center lumen line of the ICA. In[7] we showed that the method is fast, robust, reproducible, and accurate. We applied the method to 52 ICAs and showed that the method highly agrees with 3 expert observers. It was shown that the intra- and interobserver variabilities for manual ICA stenosis quantification are large, indicating the need for a more reproducible alternative. We showed that the results obtained by the method are more reproducible than the intraobserver agreement. Since the user interaction is limited, this technique can be used to replace an expert observer in 3-dimensional quantification of the internal carotid artery at CE-MRA in clinical practice.

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