ORIGINAL ARTICLE

Reproducibility of Semi-Automated Measurement of Carotid Stenosis on CTA

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ABSTRACT: ***Purpose:*** To compare the reproducibility of semi-automated vessel analysis software to manual measurement of carotid artery stenosis on computed tomography angiography (CTA). ***Methods:*** Two observers separately analyzed 81 carotid artery CTAs using semi-automated vessel analysis software according to a blinded protocol. The software measured the narrowest stenosis in millimeters (mm), distal internal carotid artery (ICA) in mm, and calculated percent stenosis based on NASCET criteria. One observer performed this task twice on each carotid, the second analysis delayed two months in order to mitigate recall bias. Two other observers manually measured the narrowest stenosis in mm, distal ICA in mm, and calculated NASCET percent stenosis in a blinded fashion. Correlation coefficients were calculated for each group comparing the narrowest stenosis in mm, distal ICA in mm, and NASCET percent stenosis. ***Results:*** The semi-automated vessel analysis software provided excellent intraobserver correlation for narrowest stenosis in mm, distal ICA in mm, and NACSET percent stenosis (Pearson correlation coefficients of 0.985, 0.954, and 0.977 respectively). The semi-automated vessel analysis software provided excellent interobserver correlation (0.925, 0.881, and 0.892 respectively). The interobserver correlation for manual measurement was good (0.595, 0.625, and 0.555 respectively). There was a statistically significant difference in the interobserver correlation between the semi-automated vessel analysis software observers and the manual measurement observers ($P < 0.001$). ***Conclusion:*** Semi-automated vessel analysis software is a highly reproducible method of quantifying carotid artery stenosis on CTA. In this study, semi-automated vessel analysis software determination of carotid stenosis was shown to be more reproducible than manual measurement.

RÉSUMÉ: Reproducibilité de la mesure semi-automatique à l'angiographie par tomodensitométrie dans la sténose carotidienne. ***Objectif :*** Le but de cette étude était de comparer la reproductibilité de la mesure effectuée au moyen d'un logiciel d'analyse semi-automatique à la mesure manuelle de la sténose carotidienne à l'angiographie par tomodensitométrie (AT). ***Méthodes :*** Deux observateurs indépendants ont analysé 81 AT de la carotide au moyen d'un logiciel d'analyse de vaisseaux semi-automatique selon un protocole à l'insu. Le logiciel mesurait la sténose la plus serrée en millimètres (mm), la portion distale de la carotide interne (CI) en mm et calculait le pourcentage de sténose basé sur les critères de NASCET. Un observateur faisait cette évaluation deux fois au niveau de chaque carotide et la deuxième évaluation avait lieu 2 mois après la première afin de minimiser le biais de rappel. Deux autres observateurs mesuraient manuellement la sténose la plus serrée en mm et la partie distale de la CI en mm, et calculaient à l'insu le pourcentage de sténose selon NASCET. Les coefficients de corrélation ont été calculés pour chaque groupe afin de comparer la sténose la plus serrée en mm, la partie distale de la CI en mm et le pourcentage de sténose selon NASCET. ***Résultats :*** La meilleure corrélation intra-observateurs pour la sténose la plus serrée en mm, la CI en mm et le pourcentage de sténose selon NACSET était celle obtenue avec le logiciel d'analyse de vaisseaux semi-automatique (coefficients de corrélation de Pearson 0,985, 0,954 et 0,977 respectivement). Le logiciel d'analyse de vaisseaux semi-automatique a fourni une excellente corrélation interobservateurs (0,925, 0,881 et 0,892 respectivement). La corrélation interobservateurs pour la mesure manuelle était bonne (0,595, 0,625 et 0,555 respectivement). Nous avons observé une différence significative au point de vue statistique dans la corrélation interobservateurs entre les observateurs du logiciel d'analyse de vaisseaux semi-automatique et les observateurs de la mesure manuelle ($P < 0,001$). ***Conclusion :*** Le logiciel d'analyse de vaisseaux semi-automatique est une méthode de quantification de la sténose carotidienne à l'AT dont la reproductibilité est excellente. Dans cette étude, la détermination de la sténose carotidienne au moyen du logiciel d'analyse de vaisseaux semi-automatique s'est avérée plus reproductible que la mesure manuelle.

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Carotid artery stenosis can be accurately and reliably quantified using computed tomography angiography (CTA)[1-4]. The measurement of carotid artery stenosis has traditionally been performed using NASCET-style ratios and more recently direct millimeter measurements[1-5]. There are pitfalls with this method, mainly in deriving the denominator or distal normal internal carotid artery (ICA) diameter, in placement of the distal ICA measurement along the tapering distal bulb rather than where the walls of the ICA are parallel, and in not recognizing near occlusion. The development of semi-automated vessel analysis software allows quantification of carotid artery stenosis without manual measurements or calculations.

The quantification of extracranial ICA stenosis is an established method of determining which patients may benefit from carotid revascularization, thus reducing the risk of

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ipsilateral stroke[5-7]. It has been demonstrated that symptomatic patients with severe carotid artery stenosis (70-99%) benefit most from revascularization, while some risk reduction of ipsilateral stroke has been conferred to symptomatic patients with moderate grade lesions (50-69%)[5-7].

Traditionally, carotid artery stenosis measurements were made from catheter film/screen or digital subtraction angiography using NASCET-style calculations[5]. The evolution of high-speed, high-resolution CTA techniques currently enables accurate, non-invasive, and reliable measurement of carotid artery stenosis using NASCET-style percent stenosis, direct millimeter and luminal cross-sectional area measurements[1-4,8-10].

The evolution of semi-automated vessel analysis software allows quantification of carotid artery stenosis without manual measurements or calculations but with some limitations[9,10]. The purpose of this paper is to examine the intraobserver and interobserver reproducibility of semi-automated software on the measurement of carotid artery stenosis on CTA. This was compared to the interobserver reproducibility of manual measurements.

Methods

Inclusion criteria

Examinations were retrospectively collected from a single institution from over a six month period. All consecutive patients examined by CTA during this time period for known or suspected carotid artery disease were entered into the study. Exams were not included for cases of trauma, dissection, or vascular anomalies. Examinations where severe motion artifact prohibited accurate manual or semi-automated measurements were excluded. One case was excluded for this reason. Cases of observed complete occlusion were omitted. There were five cases of occlusion that were excluded. Suspected ICA near-occlusions (small or collapsed distal ICAs) were identified by comparing the distal ICA axial lumen measurement to the axial lumen measurements of the contralateral distal ICA and the ipsilateral distal ECA. Distal ICAs with a diameter 80% or less than the contralateral distal ICA were excluded. If the contralateral ICA was also narrowed or occluded, an ICA was excluded if both reviewers' measurement averages met all our arbitrary "near-occlusion" criteria: notable bulb stenosis, distal ICA diameter of 3 mm or less, and distal ICA/distal external carotid artery ratio of 1.25 or less. These criteria were adapted from criteria to recognize subtle near-occlusions recognized from standard conventional angiography[11-14]. Twenty cases of near occlusion were excluded. A total of 81 carotid arteries were included in the study. Institutional research board approval was obtained.

Materials / Image Acquisition

All CTA examinations were performed using a GE Medical Systems (Waukesha, Wisconsin, USA) Lightspeed Plus 4-slice helical CT with a 6.3 MHU Performix tube. Images were obtained from C6 to vertex using the helical HS mode with 7.5 mm/rotation and 1.25 x 1.25 mm collimation (120 kVp, 350 mA). Intravenous access was via an antecubital vein using an 18 or 20 gauge angiocatheter. A total of 100 to 125 ml iohexol 300 mg/ml (Omnipaque 300, GE Healthcare, Princeton, New Jersey, USA) were injected at a rate of 4.0 to 4.5 ml/second, with a 17 second delay or the use of Smart Prep at the pulmonary artery. CT technologists performed multiplanar reformats (MPRs) at the CT operator's console. Coronal and sagittal thick and thin MPR images were created; the thick MPRs were 10 mm thick spaced ever 3 mm. Bilateral rotational MPRs were created at the carotid bifurcations with a thickness of 7 mm and spacing by 3 mm. Three dimensional (3D) volume rendered images were created on a GE Medical Systems (Waukesha, Wisconsin, USA) Advantage workstation, Version 4.2.

Semi-automated carotid artery stenosis evaluation

Two observers independently analyzed the carotid arteries using semi-automated vessel analysis software (GE Advantage Workstation, Advanced Vessel Analysis,Version 4.2) with a blinded protocol. One observer repeated the semi-automated carotid artery analysis at a separate sitting. The first and second measurement sessions were separated by two months in order to prevent any recall bias. For each ICA, the software determined the narrowest luminal diameter in mm, the distal ICA luminal diameter in mm, and calculated the percent stenosis based on NASCET criteria.

For each carotid artery, the software users selected multiple points in the lumen of the distal common and internal carotid artery using the axial source images. The selected vessel lumen was subsequently mapped by the software and displayed to the user as MPRs and curved reformats. In the event of poor tracking of the vessel by the software program, reference points were reset and more reference points were selected. Reference points were also made on the MPRs in cases of poor vessel tracking. Improper vessel tracking most commonly occurred at the bulb stenosis. With densely calcified plaques, more reference points were selected through the region of the plaque. A reference point in the distal ICA was selected beyond the tapering of the carotid bulb. The software then determined the narrowest luminal diameter in mm, luminal diameter of the reference point in the distal ICA in mm, and calculated percent carotid artery stenosis. Stenosis measurement tables and the post-processed images were saved on PACS (AGFA Impax, Version 4.5, Mortsel, Belgium) (Figure 1,2,3,4).

Manual carotid stenosis evaluation

Two separate observers independently measured the same carotid arteries in a blinded fashion[1]. Millimeter measurements were obtained by using the submillimeter measurement and magnification tools on the PACS workstation. As in the semi-automated group, special attention was directed to some of the more densely calcified plaques to ensure accurate measurement. Windowing was used to best visualize the contrast filled lumen. Measurement of carotid stenosis was performed at the narrowest portion of the carotid bulb on the axial source data. Multiplanar reformats were used to ensure true cross-sectional measurements. Internal carotid arteries identified as passing oblique to the axial plane were measured perpendicular to their own oblique carotid axis as seen on MPRs. These measurements were verified with measurements from the reformats to ensure accuracy in obtaining the narrowest diameter in a true cross-sectional plane. The distal ICA was measured beyond the bulb where the walls of

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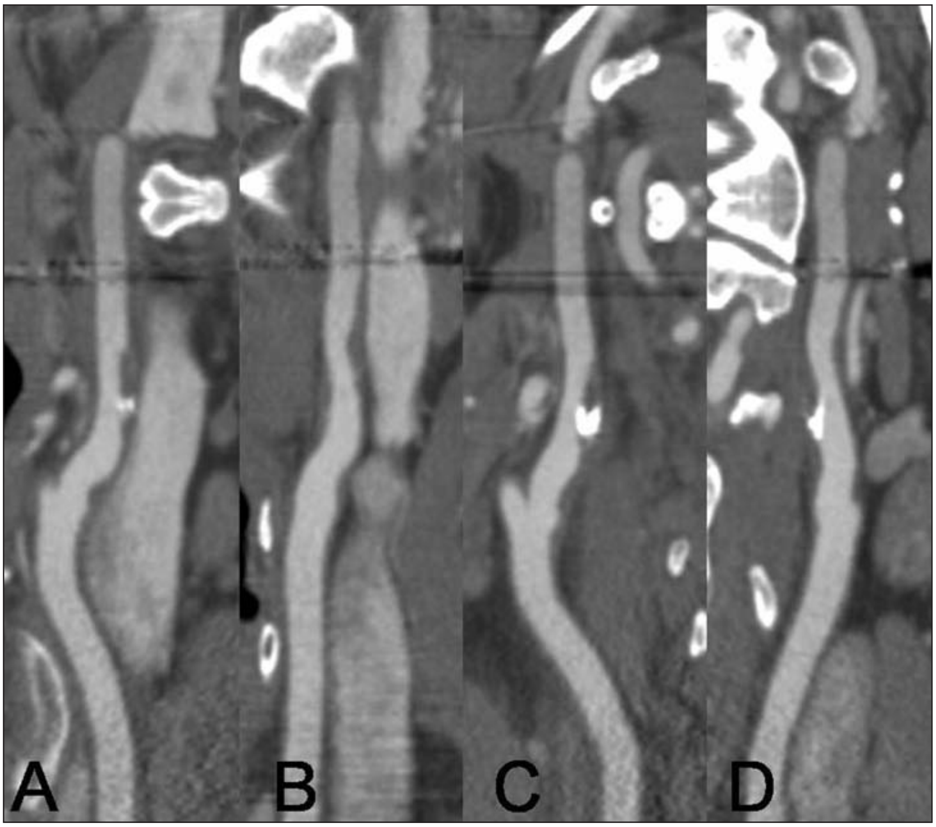

Figure 1: Advanced vessel analysis curved reformations of a left internal carotid artery.

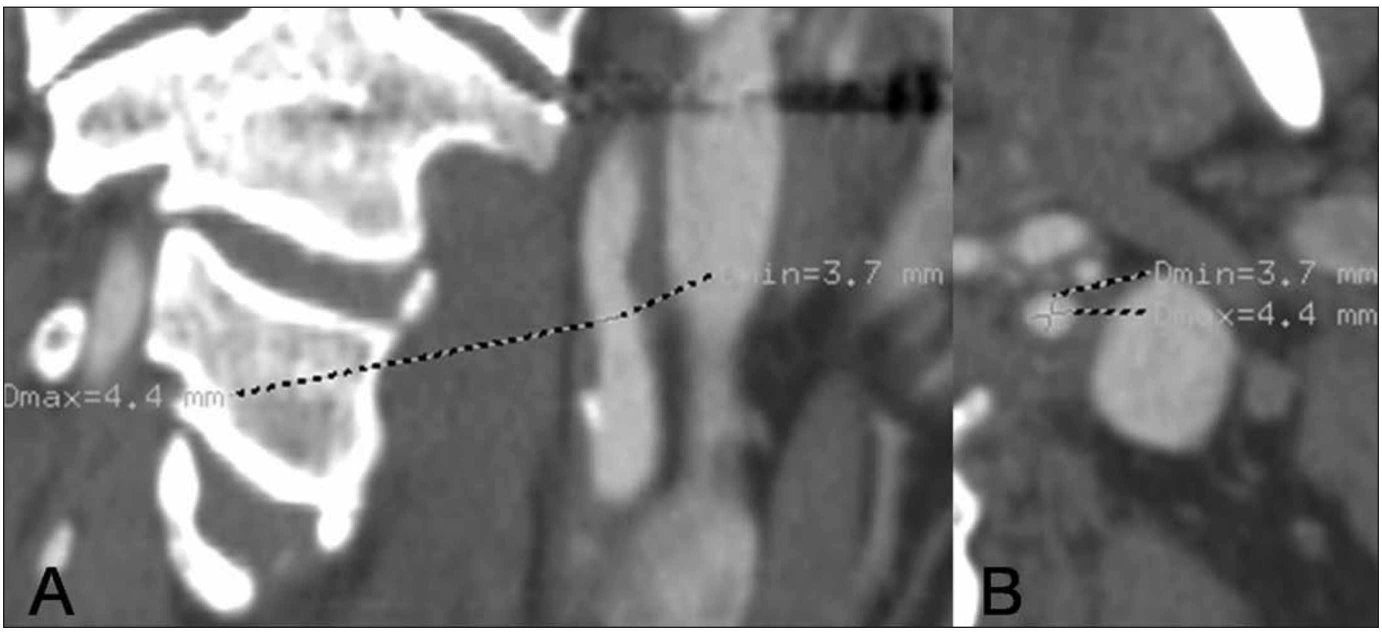

Figure 2: Advanced vessel analysis measurement of most severe stenosis on a curved reformat (A) and a reformatted axial image (B). The software determines the level of most severe stenosis. At that level, it provides the narrowest stenosis measurement (Dmin) used for NASCET stenosis calculation. The largest diameter at that level (Dmax) is also determined but this is not used in stenosis calculation.

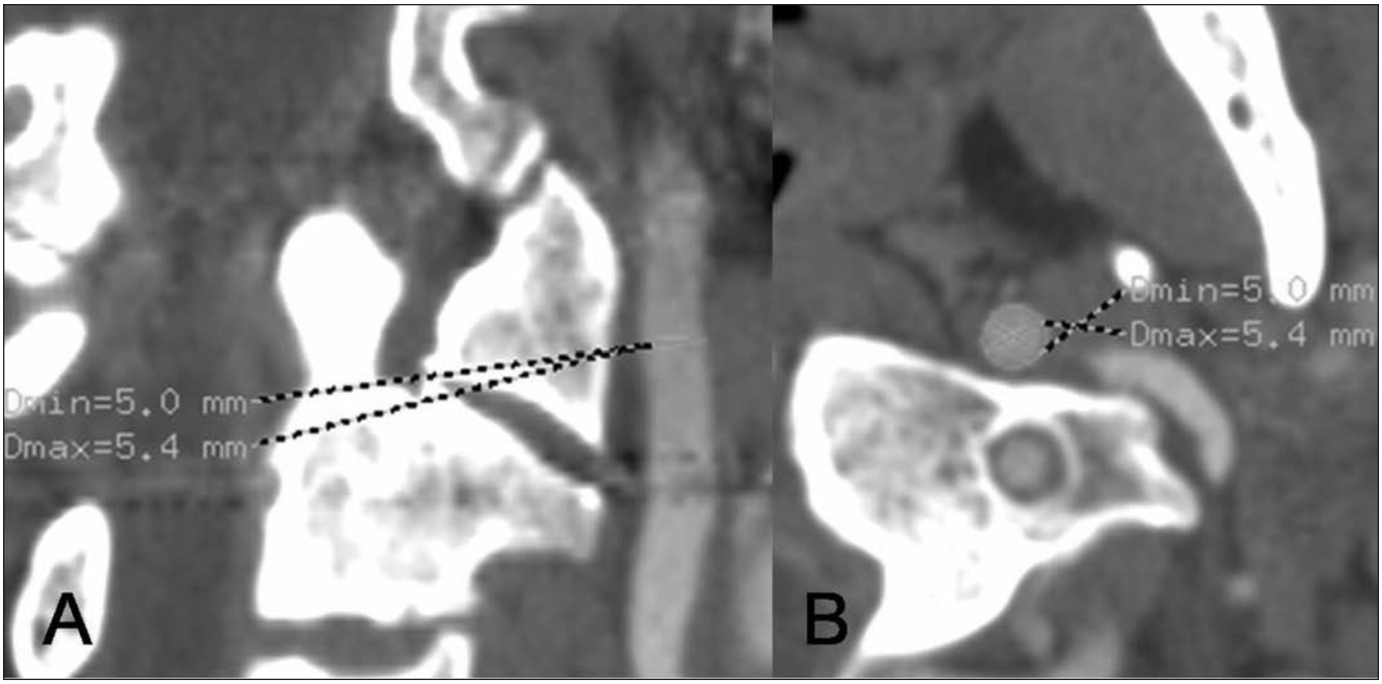

Figure 3: *Advanced vessel analysis measurement of distal ICA reference on curved reformat (A) and reformatted axial image (B). The software determines the narrowest diameter at the reference level (Dmin) and this is used for NASCET stenosis calculation. The widest diameter at the reference level (Dmax) is also determined but this value is not used in stenosis calculation.*

the vessel are parallel and no longer tapering from the carotid bulb as per NASCET.

Statistical analysis

Each carotid artery was considered unique for statistical purposes. Pearson correlation coefficients were calculated to evaluate interobserver and intraobserver correlation. Data was analyzed using the SPSS statistical software (version 14.0, Chicago, Illinois, USA). A P-value of less than 0.05 was considered to represent statistical significance. All correlation values were calculated with 2-tail significance.

Results

A total of 81 carotid arteries from 58 patients were included in the analysis. There were 41 males and 17 females. Mean age was 71-years-old.

The semi-automated vessel analysis software provided excellent intraobserver correlation for narrowest stenosis in mm, distal ICA reference point in mm, and NACSET percent stenosis (Pearson correlation coefficients of 0.985, 0954, and 0.977 respectively). The semi-automated vessel analysis software provided excellent interobserver correlation for narrowest stenosis in mm, distal ICA reference point in mm, and NASCET percent stenosis (0.925, 0.881, and 0.892 respectively). The interobserver correlation for manual measurement was good for narrowest stenosis in mm, distal ICA reference point in mm, and NASCET percent stenosis (0.595, 0.625, and 0.555 respectively). There was a statistically significant difference in the interobserver correlation between the semi-automated vessel analysis software measurements and those performed manually ($P < 0.001$), for each of the three measured values: narrowest stenosis in mm, distal ICA reference point in mm, and NASCET percent stenosis.

The time to perform the semi-automated measurements was about five minutes for each carotid artery.

Discussion

The development of semi-automated vessel analysis software has the potential to improve accuracy, reproducibility, and speed of quantifying carotid stenosis without manual measurements or calculations. The purpose of this study was to examine the reproducibility of semi-automated vessel analysis software in the evaluation of carotid artery stenosis. Our study achieved excellent interobserver and intraobserver reproducibility in carotid artery stenosis measurements using semi-automated vessel analysis software.

Other reports in the literature have assessed a semi-automated vessel analysis program in the determination of carotid artery stenosis on CT angiography[9,10]. These studies used a slightly smaller sample size but also demonstrated good interobserver correlation when using automated vessel analysis software[11]. Furthermore, we were unable to find a previous study that compared the intraobserver variability between semi-automated and manual carotid artery stenosis measurements. In our study, the semi-automated software was found to be more reproducible than manual calculations in the evaluation of carotid artery stenosis.

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Point Name	Mean (mm)	Min (mm)	Max (mm)	Area (mm2)
Ref.	5.2 ± 0.5	5.0 ± 0.5	5.4 ± 0.5	21.3 ± 3.9
Stenosis	4.0 ± 0.6	3.7 ± 0.6	4.4 ± 0.6	12.3 ± 3.9

Point Name	Mean	Min	Max	Area
Stenosis / Ref.	+23.9 %	+27.6 %	+18.6 %	+42.1 %

Figure 4: *Advanced vessel analysis stenosis calculation. Column 2 (Min) lists the narrowest stenosis measurement in mm (in this case 3.7 ± 0.6), the reference distal ICA measurement in mm (in this case 5.0 ± 0.5 mm), and the NASCET percent stenosis (in this case 27.6%). The software also provides stenosis measurements based on mean diameter at the stenosis and reference levels, widest measurement at the stenosis and reference levels, and area at the stenosis and reference levels, although these types of measurements are not clinically used as a routine.*

Appropriate training in the operation of the software is essential. Accurate vessel mapping is of paramount importance in the subsequent calculations. If the software improperly tracks the vessel, the calculations will be inaccurate and unreliable. In our experience, inaccurate tracking of the vessel lumen was seen in a minority of cases. The rate of poor tracking increased with the severity of vessel stenosis and plaque burden. This was thought to be secondary to a smaller density difference for the software to track the true lumen and hence the vessel itself. Other interfering factors included calcification, bifurcating vessels and tortuous vessels. These problems were compensated for by placing more region of interest points along the vessel, particularly at the region of poor tracking. This was usually sufficient to allow accurate vessel mapping. Adding extra reference points on the reformats, in addition to the axial images, further increased the accuracy of vessel mapping. At regions of high-grade stenosis, magnification of the axial images before placing regions of interest was quite beneficial.

Such potential pitfalls in semi-automated carotid analysis require that the workstation operator have a detailed knowledge of carotid anatomy. We feel that a radiologist who can intervene to correct vessel tracking problems when they occur is necessary to accurately monitor semi-automated vessel analysis. In our study, the semi-automated software reviewers verified the region of maximal stenosis calculated by the software on visual inspection. This ensured that the true maximal stenosis was quantified.

The highly reproducible semi-automated carotid artery stenosis measurements are promising. Recently, semi-automated stenosis quantification has also been described in magnetic resonance angiography[15-17]. The appeal of semi-automated quantification extends to the ease with which stenosis data tables and post-processed images are stored on PACS for future viewing by radiologists and clinicians. In doing so, stenosis measurements and 3D volume rendered images are available together at each PACS workstation.

There may be numerous reasons why the semi-automated measurements were more reliable. On CTA, the exact margin of the vessel lumen can be blurry and not always certain. There is always some quantum mottle around the perimeter of the contrast lumagram giving the appearance of a halo with diminishing intensity[18]. There will be variations between radiologists as to where within this halo the actual edge of the lumen is. Some will measure from the outside of the halo, others from the inside, and others somewhere in between (our manual observers measured at the centre of the halo in this study). Even for the same radiologist, there will not always be consistency in how the vessel is measured at the stenosis and at the distal ICA reference. That is, an individual radiologist may measure the stenosis at the outside of the halo, and then the distal ICA reference at the inside of the halo, resulting in inconsistent measurements. The semi-automated software eliminates this problem. It determines the lumen edge based on intensity differences and therefore will consistently measure both the stenosis and the distal ICA reference at the same point in the halo. Another problem with manual measurement is the oblique stenosis. The stenosis of a vessel is not always in the exact axial plane. Manual measurements must take this into account with the help of the MPRs but there is potential for small errors. The semi-automated software straightens the vessel alignment so that errors of obliquity do not occur (Figure 2).

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Although reproducible and relatively user-friendly, the accuracy of semi-automated software to manual carotid artery stenosis measurements using CTA remains to be completely evaluated. This study looked only at reproducibility. We did not compare the manual or semi-automated measurements to the gold standard of angiography so the accuracy of these was not determined. The semi-automated analysis technique still requires operators to be knowledgeable of carotid anatomy and vigilant to avoid the pitfalls of percentage stenosis ratios, mainly to not recognize and exclude from measurement near occlusions, and to place the distal caliper well beyond the bulb where the walls are parallel. It is also important to note that although the manual measurements had weaker correlation between observers when compared to the semi-automated measurements, the manual measurement correlation coefficients were still all statistically significant ($p < 0.001$). We do not know whether the incremental increased correlation of the semi-automated measurements over the already well correlated manual measurements makes a clinical difference in carotid stenosis determination.

Conclusion

Our study demonstrates that semi-automated vessel analysis software demonstrates excellent intraobserver and interobserver reproducibility in the measurement of carotid artery stenosis on CTA. We found that careful tracking of the lumen improves the reliability when high-grade stenoses are measured. In addition, the reproducibility of carotid stenosis measurements by the semi-automated vessel analysis software was better than seen with manual measurement.

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