Evaluation of Computer-Assisted Quantification of Carotid Artery Stenosis

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Abstract The purpose of this study was to evaluate the influence of advanced software assistance on the assessment of carotid artery stenosis; particularly, the inter-observer variability of readers with different level of experience is to be investigated. Forty patients with suspected carotid artery stenosis received head and neck dual-energy CT angiography as part of their pre-interventional workup. Four blinded readers with different levels of experience performed standard imaging interpretation. At least 1 day later, they performed quantification using an advanced vessel analysis software including automatic dual-energy bone and hard plaque removal, automatic and semiautomatic vessel segmentation, as well as creation of curved planar reformation. Results were evaluated for the reproducibility of stenosis quantification of different readers by calculating the kappa and correlation values. Consensus reading of the two most experienced readers was used as the standard of reference. For standard imaging interpretation, experienced readers reached very good ($k=0.85$) and good ($k=0.78$) inter-observer variability. Inexperienced readers achieved moderate ($k=0.6$) and fair ($k=0.24$) results. Sensitivity values 80%, 91%, 83%, 77% and specificity values 100%, 84%, 82%, 53% were achieved for significant area stenosis >70%. For grading using advanced vessel analysis software, all readers

achieved good inter-observer variability ($k=0.77$, 0.72, 0.71, and 0.77). Specificity values of 97%, 95%, 95%, 93% and sensitivity values of 84%, 78%, 86%, 92% were achieved. In conclusion, when supported by advanced vessel analysis software, experienced readers are able to achieve good reproducibility. Even inexperienced readers are able to achieve good results in the assessment of carotid artery stenosis when using advanced vessel analysis software.

Keywords Computed tomography · Digital image processing · 3D segmentation · Dual-energy subtraction · Image interpretation · Computerized method · Graphical user interface

Introduction

In recent years, advances in computed tomography (CT) and image post-processing has been made [1]. CT angiography (CTA) has become an established method for the evaluation of head and neck arteries [2–4]. Therefore, the amount of CTA data to be evaluated has grown considerably over the recent years [5–7]. Assessment of vascular studies based on axial images alone is not straightforward; 2D and 3D visualization methods are routinely employed. Advanced visualization tools such as multiplanar reformations (MPRs), maximum intensity projections, volume rendering techniques (VRTs), and curved planar reformations (CPR) allow for advanced reading and presentation of results [1, 8].

Furthermore, new technologies were introduced to overcome pitfalls in case preparation by performing an improved bone removal and vessel segmentation. Dual-energy (DE) technology offers high quality in bone and

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plaque removal in images for a rapid and highly sensitive overview of vascular structures in clinical routines [9, 10]. Machine learning approaches as introduced by Seifert et.al. [11] and Zheng et.al. [12] for the detection of body landmarks in combination with vessel segmentation algorithms [13, 14] allow a fully automatic segmentation of vessels and visualization in preparation for reading.

Benefits for inexperienced readers using advanced post-processing were mentioned by Busch et.al. [15]. Hacklaender et.al. [16] noticed that the post-processing procedure did not improve the result, but might be useful to assist the radiologist in identifying the location of the greatest narrowing.

The aim of this study was to analyze the influence of advanced post-processing software, including state-of-the-art segmentation and visualization technology, on diagnostic results of readers with different levels of experience.

Materials and Methods

Patients

After agreement of the institutional ethics review board, 40 patients with known or suspected carotid artery disease who were scheduled for stent-protected angioplasty or carotid endarterectomy were included in the study. Written informed consent was obtained from all patients. All patients received a standardized DE-CTA of the head and neck arteries as part of their pre-interventional workup.

Data Acquisition and Reconstruction

All examinations were performed with a dual-source CT system (Somatom Definition, Siemens Healthcare, Forchheim, Germany). The examination region was planned from the aortic arch to the cranial end of the skull. After intravenous injection of 60 ml of iodinated contrast medium [Imeron 400 (iomeprol), 400 mg I/ml, Bracco Altana Pharma, Konstanz, Germany] with a flow setting of 5 ml/s and a saline chaser (50 ml; flow, 5 ml/s), bolus tracking was performed in the aortic arch. The DE examination was performed in a caudocranial direction using default acquisition parameters for carotid CTA [tube A, 140 kV, 80 mAsref; tube B, 80 kV, 234 mAsref, automated tube current modulation (CareDose 4D); collimation, 32×0.6 mm for each detector with flying focal spots; rotation time, 0.33 s; pitch, 0.65]. After examination, axial sections (slice thickness, 1.0 mm; increment, 0.6 mm) were reconstructed using a specific non-edge-enhancing reconstruction kernel (D30). Two individual stacks of images for each detector (80- and 140-kV images) and standard image interpretation DE mixed images were reconstructed. The latter contains weighted information

from both detectors with a weighting factor of 0.4 (40% from the 80-kV images and 60% from the 140-kV images) and thus approximating regular 120-kV images.

Image Interpretation

Forty CTA datasets were read by four different readers: two radiologists with more than 3 years of reading experience, a computer scientist experienced in reading head and neck images, and a technician with extensive general experience who is nonetheless inexperienced in the quantification of stenosis. Each reader first performed the standard image interpretation for all 40 datasets, as described in “[Standard image interpretation](#).” With a latency of at least 1 day and up to 1 month, stenosis quantification was performed with the advanced vessel analysis software, as described in “[Advanced vessel analysis software](#).” Finally, a consensus reading of the two experienced radiologists was performed 1 month later to determine the reference values by using standard image interpretation and the advanced vessel analysis software.

Standard Image Interpretation

All mixed images were anonymized and transferred to a workstation, which was equipped with standard imaging interpretation software (syngo 3D, Siemens Healthcare). Carotid arteries of both sides were evaluated by readers blinded to the results of the other readers and the reference values. Grading was performed by eyeballing with means

Fig. 1 Flowchart shows steps performed for the preparation of data for standard image interpretation and image interpretation using advanced vessel analysis software

of freely adjustable MPRs on DE mixed images, as is used regularly in the institute. No measurement tools were used for eyeballing. A scoring system was used (I, 0%; II, 1–49%; III, 50–69%; IV, 70–99%; V, 100%) for stenosis grading.

Advanced Vessel Analysis Software

All reconstructed images from tubes A and B were anonymized and transferred to the imaging server (syngo.via, Siemens Healthcare, premarket version presented on RSNA 2009). On the server, preprocessing of the images was performed. Figure 1 shows the order of the preprocessing calculation steps performed on the server. First, DE mixed images, DE bone, and plaque removed data are calculated. Subsequently, body landmarks are determined [12]; bifurcation analysis is performed to enlarge and improve the amount of landmarks [13]. Finally, automatic vessel tracing is performed between landmarks for common carotid arteries, and tracing starts at single landmarks in a

predetermined direction for internal carotid arteries [14]. Readers then began the evaluation of carotid arteries using the advanced vessel analysis software (syngo.via CT Vascular, Siemens Healthcare, premarket version presented on RSNA 2009). Readers were blinded to the results of the other readers, to the results of the standard image interpretation, and to the reference results.

Directly after loading patient data, segmented carotid arteries are visualized (see Fig. 2). Readers can switch between CPR views of different carotid arteries. In a first step, readers had to identify the internal carotid artery, which can easily be performed on bone removed VRT image. In case automatic segmentation of vessel failed, semiautomatic creation of the centerline has to be initialized by setting the start and end point for performing vessel segmentation. In the second step, the stenotic lesion has to be identified on CPR view. If no stenotic lesion exists, this step should be excluded. Calipers were used to quantify stenotic lesion. One caliper, as a stenosis marker, and one caliper, as a reference marker, were used to evaluate carotid

Fig. 2 Graphical user interface right after loading of case study. Carotid arteries of both sides are segmented and two arteries are visualized in CPR view. Selection of other carotid artery is possible via selection of labels in VRT. Measurement of stenotic lesions can be performed on CPR view

Fig. 3 Measurement of a stenotic lesion. Positioning of markers is initialized via a single user click. Position of the narrowest lumen and the reference position are determined based on the area profile curve. To set

the stenosis marker, the local minimum is defined around click point. Reference position is set on start of closest distal plateau

stenosis, similar to NASCET measurements [17]. To increase the reproducibility of the results, calipers can be set performing a single click on the position closest to the narrowest lumen. Using a contouring algorithm [18], the narrowest lumen position is identified as stenosis position and

the closest distal plateau as a reference position (see Fig. 3). The percentage of area stenosis is given instantaneously. Contouring algorithm is based on active contour models. By default, algorithm excludes calcification and considers bifurcation as well as bypassing vessels (see Fig. 4) [18]. For this

Fig. 4 Examples for results of contouring algorithm in presence of calcified plaque, stent material, and in the absence of plaque. Windowing were set for screenshots according to the rule of Saba et.al. [29]. Window settings have no influence on the contouring algorithm

study, the possibility of adaption of vessel contours was not used to facilitate ease of use for inexperienced readers and due to the initially satisfactory algorithm results. Afterwards, the calculated results of vessel analysis software were scored using the previous scoring system (I–IV) in order to compare them with the results of standard image interpretation.

Analysis

The results achieved by all readers using the standard imaging interpretation method and the advanced vessel analysis software with reference to consensus reading of the most experienced readers, 1 and 2, were evaluated with a correlation analysis (Pearson correlation coefficient). The inter-observer variability was calculated to determine the agreement between the different readers for both reading methods. Kappa values were interpreted as follows: <0.20—poor agreement; 0.21–0.40—fair agreement; 0.41–0.60—moderate agreement; 0.61–0.80—good agreement; and 0.81–1.00—very good agreement. The specificity and sensitivity were calculated to analyze the validity of the results. Therefore, true positive resp. true negative values of the reference results and false positive resp. false negative results for each reader were counted. Values of categories I, II, and III were rated as true negative, whereas categories IV and V were rated true positive. If the reference value was category I, II, or III and the reader's result was IV or V, it was counted as a false positive. If the reference value was category IV or V and the reader's result was I, II, or III, it was counted as a false negative.

Results

All 80 carotids could be evaluated. Only one reader was unable to evaluate one carotid artery due to dental artifacts. Despite the high percentage of severe stenosis (see Table 1), advanced vessel analysis software automatically detected 56% of carotid arteries. Semi-automatic centerline creation algorithm was used for the remaining carotids.

Standard Image Interpretation

Results for standard image interpretation are presented in Table 2.

Table 1 Distribution of stenosis grades among study collection based on consensus reading of reader 1 and reader 2 (used as reference values)

I (0%)	II (1–49%)	III (50–69%)	IV (70–99%)	V (100%)
9	17	11	41	2

Table 2 Statistical results of evaluation with standard image interpretation

Statistical parameter	Reader 1	Reader 2	Reader 3	Reader 4
Correlation coefficient	0.93	0.86	0.68	0.15
<i>p</i> value	<0.0001	<0.0001	<0.0001	0.3
Kappa value	0.85	0.78	0.6	0.24
Sensitivity (%)	80	91	83	77
Specificity (%)	100	84	82	53

Experienced readers (readers 1 and 2) reached good results. Reader 3 (inexperienced reader) reached unexpectedly good results, but significantly poorer than experienced readers. Reader 4 reached poor results, with a *p* value above 0.05.

Advanced Vessel Analysis Software

The results for image interpretation using advanced vessel analysis software are presented in Table 3.

All readers achieved good results regardless of their level of experience. High reproducibility was reached. All readers achieved good kappa values, high specificity values, and high sensitivity values. There were no significant differences between readers. In comparison to standard image interpretation, no significant differences were observed for experienced readers (readers 1 and 2). For inexperienced readers (readers 3 and 4), statistical analysis has shown significant improvements of reading quality in comparison to standard image interpretation. Reproducibility as well as the validity of inexperienced reader results were as good as the results of experienced readers.

Discussion

Our results show that with standard image interpretation method and by using tested advanced vessel analysis software, very good reproducibility, specificity, and good sensitivity can be reached by an experienced reader. Therefore, we confirm the results of former studies [16,

Table 3 Statistical results of evaluation with advanced vessel analysis software

Statistical parameter	Reader 1	Reader 2	Reader 3	Reader 4
Correlation coefficient	0.88	0.82	0.87	0.89
<i>p</i> value	<0.0001	<0.0001	<0.0001	<0.0001
Kappa value	0.77	0.72	0.71	0.77
Sensitivity (%)	84	78	86	92
Specificity (%)	97	95	95	93

19, 20] for experienced readers. CTA with manual as well as semiautomatic post-processing is a feasible method for diagnosis of vascular lesion for experienced readers.

Furthermore, we have shown that by using tested advanced vessel analysis software for stenosis quantification, inexperienced readers are able to achieve as good results as an experienced reader. We are of the opinion that these good results could be achieved because of a high grade of automation. The readers' main task during the software-supported evaluation was the identification of correct vessel and location of stenotic lesion. The former can be easily identified on VRT view or on familiar MPR view by an experienced reader. The latter is quite easy to perform on CPR view even for inexperienced readers. The accurate positioning of the calipers is proposed by the software to induce a high reproducibility.

The results of inexperienced readers for standard image interpretation method are not sufficient. The results of reader 3 were still astonishingly good, which can be explained by her having some experience in the reading of head and neck images. The results of reader 4, particularly the *p* value, were so poor that they were considered completely insignificant, which means that in the case of reader 4, eyeballing of stenosis grades is no more accurate than guessing.

These results substantiate that longer training is needed to ensure feasible results for eyeballing evaluation of vascular lesions. A second reader is therefore required to assist beginners or to check their results, as is the case with residents at teaching hospitals [21]. This is in accordance with the protocol currently implemented in daily routine at many institutes.

Our results show that with the aid of tested post-processing software, inexperienced readers are able to obtain results of a suitable quality. One possible solution for coping with high workloads [5] would be the use of post-processing software. This could support the inexperienced reader during training the eyeballing capabilities.

To the best of the authors' knowledge, no study exists investigating the reproducibility of stenosis quantification considering readers' varying levels of experience. For computer-aided diagnosis (CAD) in the case of lung nodule detection and evaluation [22–24], and colon polyps [25], it has been shown that CAD software has the potential to assist radiologists of different experience levels by increasing their accuracy and sensitivity. Vascular studies performed in the past focused on proving the feasibility of using CTA in comparison to the gold standard, digital subtraction angiography (DSA), and only examined the feasibility of post-processing as a secondary objective. Different levels of automation were used for these studies. An overview on the studies, used technology, and the achieved results is given in Table 4 and discussed in detail below.

Gerhards et al. [26] performed an initial study with 12 patients and discovered that it is possible to analyze carotid artery stenosis using contour extraction and curved MPR within justifiable time limits.

Zhang et al. [27] used software which not only provides algorithms for the semiautomatic creation of centerline and contour calculation but also an algorithm supporting detection of maximal lumen narrowing. Therefore, the user had to set reference positions above and below stenosis. In comparison to our study, intra-observer agreement was also investigated, and a good intra-observer agreement was measured. However, only a satisfactory inter-observer agreement for automated CTA evaluation was achieved. Additionally, manual correction of evaluation was also investigated. It showed an increased correlation coefficient. This result is not astonishing when the author comments that the segmented contour sometimes, contrary to our contouring algorithm results, poorly matched the actual contour. It implies an unreliable algorithm, sometimes leading to incorrect contour extraction as well as incorrect calculation for the degree of stenosis.

Table 4 Overview about automation level of former studies for vessel evaluation

Study	No. of vessels	Used technologies	Conclusion/reproducibility/validity
Gerhards, 2004	22	Contour extraction, semiautomatic centerline, curved MPR	Detection and analysis possible in justifiable time
Zhang, 2004	72	Semiautomatic centerline, contour extraction, support for stenosis detection, stretched MPR	Sometimes segmented contours matched poorly with actual contour; good resp. satisfactory reproducibility; sensitivity, 52%; specificity, 94%
Diehm, 2005	60	Semiautomatic centerline, semiautomatic measurements based on contour extraction	Significant interobserver variations
Hacklaender, 2006	100	Contour extraction, semiautomatic centerline	33 out of 100 not evaluable; correlation coefficient 0.81
Bucek, 2007	87	Semiautomatic centerline, contour extraction considering calcified plaques	Correlation coefficient, 0.53; sensitivity, 35%; specificity, >90%
Silvennoinen, 2007	73	Semiautomatic centerline, contour extraction, stretched MPR	Accuracy is not improved by vessel analysis method; sensitivity, 47%, specificity, 96%

Diehm et al. [19] also used semiautomatic creation of centerline and *solely* threshold-based contour calculation for measurement of aorto-iliac diameter. The best reproducibility was achieved by performing manual measurements on planes perpendicular to the centerline. The semiautomatic method also showed highly significant inter-observer variation. Contrary to our results, this means that better results were achieved by an increased manual interaction. These results show that the quality of the tracing algorithm used was good enough to achieve sufficient reproducibility, but that the quality of segmentation of contouring algorithm was insufficient.

Hacklaender et al. [16] compared CTA and MRA including dependency of the chosen post-processing procedure. The software tested included semiautomatic vessel centerline extraction and threshold-based contour segmentation. However, the software, unlike our results, did not improve the results achieved by manual post-processing methods. In addition, the problem of many invaluable cases arisen. During standard imaging, 11 of 100 carotids could not be evaluated due to poor image quality. With automatic software, 33 of 100 carotids could not be evaluated. In particular, carotids with stenosis above 20% represented a problem. In the study presented in this paper, no differences regarding the number of evaluable cases were observed between standard imaging and advanced analysis software.

Bucek et al. [8] evaluated software which included a semiautomatic creation of CPR by setting the start and end point for vessel segmentation, which is similar to our method used when the automatic algorithm failed. Contour and diameter calculations were based *solely* on thresholds considering calcium plaques. The location of stenosis and the reference position were manually set. No algorithm was used to support locating of the stenosis as in the software tested in this study. Bucek achieved good correlation between DSA, axial/reformatted images, and automated CTA analysis as well as manually corrected automated CTA analysis, which meant that contour diameters were corrected. However, the sensitivity, in contrast to our results, achieved was still not sufficient for clinical application. Even manual correction failed to significantly improve sensitivity and specificity for relevant stenosis. Bucek gives no comments or explanations which would allow us to draw a direct conclusion, but incorrect centerline or windowing could be considered as a possible reason for the insufficient results.

Silvennoinen et al. [20] was consistent with the results of Zhang [27] and could not improve the accuracy of stenosis assessment in CTA in comparison to standard image interpretation using semiautomatic vessel analysis, including semiautomatic vessel centerline segmentation, automatic contour extraction, and stretched MPRs for visualization.

All these studies have concentrated on experienced readers and have shown that the results of experienced readers using advanced vessel analysis software are the same or even worse than those achieved using standard imaging interpretation tools. Worse results seem to be caused by unreliable and inaccurate algorithms.

The fact that a consensus reading of CTA images was performed instead of the gold standard (DSA) being used as reference values could be viewed as a possible limitation of our study. This was done in order to investigate the differences in various post-processing methods and excluded differences between DSA and CTA imaging. Differences of results in the evaluation of stenotic lesions using CTA imaging versus DSA imaging have already been investigated in numerous studies [3, 20, 27, 28].

Another limitation is that our study only considers the evaluation of stenotic lesions. An overall assessment would be needed in daily routine. However, assuming, that non-physician readers without special training cannot perform an overall assessment, an extension of the study is not of interest. Advanced vessel analysis software only gives additional support for the quantification of stenosis and not for the investigation of other pathologies compared with standard image interpretation tools. Therefore, in the case of other pathologies, no benefits are expected for clinical result in comparison to standard imaging.

Conclusion

Standard imaging interpretation is a feasible method for experienced readers, but is not feasible for the inexperienced reader. The high grade of automation of the advanced vessel analysis software tested allows both experienced and inexperienced readers to achieve very good results in the quantification of stenotic lesions in carotid arteries.

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