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Automated versus manual segmentation of atherosclerotic carotid plaque volume and components in CTA: associations with cardiovascular risk factors

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Abstract The purpose of this study was to validate automated atherosclerotic plaque measurements in carotid arteries from CT angiography (CTA). We present an automated method (three initialization points are required) to measure plaque components within the carotid vessel wall in CTA. Plaque components (calcifications, fibrous tissue, lipids) are determined by different ranges of Hounsfield Unit values within the vessel wall. On CTA scans of 40 symptomatic patients with atherosclerotic plaque in the carotid artery automatically segmented plaque volume, calcified, fibrous and lipid percentages were 0.97 ± 0.51 cm^3, $10 \pm 11\%$, $63 \pm 10\%$ and $25 \pm 5\%$; while manual measurements by first observer were 0.95 ± 0.60 cm^3, $14 \pm 16\%$, $63 \pm 13\%$ and $21 \pm 9\%$, respectively and manual measurement by second observer were 1.05 ± 0.75 cm^3, $11 \pm 12\%$, $61 \pm 11\%$ and $27 \pm 10\%$. In 90 datasets, significant associations were found between age, gender, hypercholesterolemia, diabetes, smoking and previous cerebrovascular disease and plaque features. For both automated and manual measurements, significant associations were found between: age and calcium and fibrous tissue percentage; gender and plaque volume and lipid percentage; diabetes and calcium, smoking and plaque volume; previous cerebrovascular disease and plaque volume. Significant associations found only by the automated method were between age and plaque volume, hypercholesterolemia and plaque volume and diabetes and fibrous tissue percentage. Significant association found only by the manual method was between previous cerebrovascular disease and percentage of fibrous tissue. Automated analysis of plaque composition in the carotid arteries is comparable with the manual analysis and has the potential to replace it.

Keywords Carotid artery · Atherosclerotic plaque · Cardiovascular risk factors · Multidetector CT angiography · Automated segmentation

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Introduction

One of the major causes of death in the western world is atherosclerotic disease, which manifests itself as ischemic heart disease and ischemic stroke [1]. The amount of atherosclerotic disease in carotid arteries is

normally expressed by the severity of luminal narrowing. Risk of (recurrent) stroke is related to the severity of stenosis [2]. However, the presence of a large atherosclerotic plaque is not always associated with luminal narrowing [3], which demonstrates that luminal narrowing alone is probably not a reliable marker of atherosclerosis. In addition, studies on carotid atherosclerotic plaque show that plaque morphology and composition are also important in the risk assessment of patients with carotid artery stenosis [4–6].

Atherosclerotic plaque volume and composition can be determined with Magnetic Resonance Imaging (MRI) [7–10] and CT angiography (CTA) [11–14]. CTA has established itself as an accurate modality to assess the presence of atherosclerotic disease and to grade the severity of stenosis [15]. Carotid plaques with a thin fibrous cap and a large lipid core are also considered to increase the risk for stroke [16, 17], while plaques with high calcium content, especially when located superficially, are thought to be associated with a lower risk for stroke [18].

Manual measurement of plaque volume and the contribution of the different plaque components to the plaque volume in MRI or CTA data is a very labor intensive task. Several methods address the segmentation of the outer vessel wall and plaque components in both MRI and CTA data in carotid arteries [19–24] as well as coronary arteries [25, 26]. We previously developed an algorithm to automate the plaque measurements in CTA imaging data of the carotid arteries. In this algorithm we combined outer vessel wall segmentation [27] with lumen segmentation [28]. Once the outer vessel wall and lumen were segmented, the plaque components were segmented using distinctive ranges of Hounsfield Unit (HU) values [11]. However, with this algorithm the outer vessel wall was automatically segmented only in common carotid artery, while atherosclerotic disease is commonly present in both the common and internal carotid artery.

The purpose of this study was to develop and evaluate a method to obtain automated measurements of plaque volume and its components at the carotid bifurcation and to demonstrate that this method has potential to replace the manual measurements in terms of accuracy in plaque volume and plaque component characterization. Furthermore, we investigated whether in group associations studies similar trends can be found with automated processing. Hereto, the method validation consists of (1) evaluation of the accuracy by comparing differences between method and manual tracings with variability of manual measurements of different observers and (2) comparison of the associations between cardiovascular risk factors and plaque features as assessed with manual segmentation and automated segmentations.

Materials and methods

Study population

From November 2002 to December 2005, patients with amaurosis fugax, TIA or minor ischemic stroke (Rankin score ≤3) were consecutively enrolled in the study cohort and clinical and research data were derived in a standardized way. Multi-detector CT angiography (MDCTA) of the carotid arteries was performed as part of a research protocol, approved by the Institutional Review Board. All patients gave written informed consent. All patients underwent neurological examination on admission and symptoms and risk factors were reported. Subsequently, all carotid arteries of those patients with symptoms in the anterior circulation were evaluated for the presence of atherosclerotic plaque. This validation study of the automated plaque segmentation has a retrospective study design. The main test set contained the symptomatic carotid artery from 90 randomly selected patients (63% male, mean age 67 ± 11 years) from the group of patients with atherosclerotic plaque in the symptomatic carotid artery. The symptomatic carotid artery was the artery ipsilateral to the ischemic hemisphere, which was based on clinical symptoms and findings on MDCT of the brain. A subset of 40 datasets, which has a similar distibution of stenosis degrees as the full set, was used for the interobserver study.

Training set for automated method

The parameter settings for the automated method were previously trained on 40 manually annotated datasets, which are not part of the 90 datasets for which the method is evaluated. Furthermore this training was manually annotated by a different observer than the two observers who annotated the

imaging data reported on this study. Hence, a possible bias of the method to one of the observers is prevented.

Scan protocol and image reconstruction

CTA of the carotid arteries was performed on a 16-slice MDCT system (Siemens, Sensation 16, Erlangen, Germany) with a standardized optimized contrast-enhanced protocol (120 kVp, 180 mAs, collimation 16 × 0.75 mm, table feed 12 mm/rotation, pitch 1) [29]. All patients received 80 ml contrast material (Iodixanol 320 mg/ml, Visipaque, Amersham Health, Little Chalfont, UK), followed by 40 ml saline bolus chaser, each at an injection rate of 4 ml/s. Synchronization between the passage of contrast material and data acquisition was achieved by real-time bolus tracking at the level of the ascending aorta. Image reconstructions were made with a 120-mm field of view, a matrix size of 512 × 512, a slice thickness of 1.0 mm, an increment of 0.6 mm, and an intermediate reconstruction filter (B46f).

Plaque volume and composition measurements

To define different plaque components by using different HU ranges, it is sufficient to have a segmentation of the carotid artery outer vessel wall and the lumen [11].

Automated Segmentation of the outer vessel wall and lumen

An automatic method using a three-point initialization was used to segment the outer vessel wall of the carotid artery in CTA [27, 30]. First, the vessel lumen was segmented using a level set approach [28], using an initialization point in the common, internal and external carotid artery. Subsequently, using a set of image features, calcium objects which are part of the vessel wall were detected using a GentleBoost framework [27]. Calcium object classification is used as a preprocessing step for the outer vessel wall segmentation since it is a much easier task than outer vessel segmentation and it can improve the accuracy of outer vessel wall segmentation. In the third step probability images were created that indicate the

likeliness of a voxel lying within or outside the vessel, using the same GentleBoost framework. Each voxel is represented by a set of descriptive features: distance of the pixel to the lumen center and a set of contextual features. Contextual features in this case are radial image intensity profiles emanating from the lumen center. These profiles are extracted from the original image, the image smoothed with 2D Gaussian filters at different scales and directional 2D, Gaussian derivatives also at different scales. Based on this set of features, a GentleBoost classifier is trained to classify each pixel as being inside or outside vessel wall. The classifier provides a confidence measure which reflects the likelihood that a pixel lies inside or outside the vessel.

Finally, ellipsoids are fitted using both the calcium and vessel classification results.

Manual Segmentation of the outer vessel wall and lumen

Images of carotid arteries that contained plaque were analyzed using custom-made quantitative image analysis software, developed using MeVisLab (MeVis Research, Bremen, Germany). Using this software, regions of interest (ROI) were manually drawn over the outer vessel wall contour in consecutive axial MDCTA images (Fig. 1). Since the observers placed the ROI over the outer vessel wall contour, the ROI consisted of both plaque and lumen. The window/level setting was fixed at 1200/800 HU for all measurements.

To assess the border between lumen and atherosclerotic plaque it was necessary to draw a second ROI close to the lumen in each image. Normally, the lumen area was then automatically differentiated from atherosclerotic plaque based on the adjusted cut-off value. But in those plaques in which calcifications bordered the lumen and the two dense structures merged with each other, lumen area and calcifications had to be separated by manual drawing. One observer (S.R.) who was blinded to other clinical information, manually drew lumen and outer vessel wall contours. A second observer (M.G.) performed the manual segmentations in the interobserver dataset. A third observer (T.W.) performed manual annotation of the training set on which our automated method was trained.
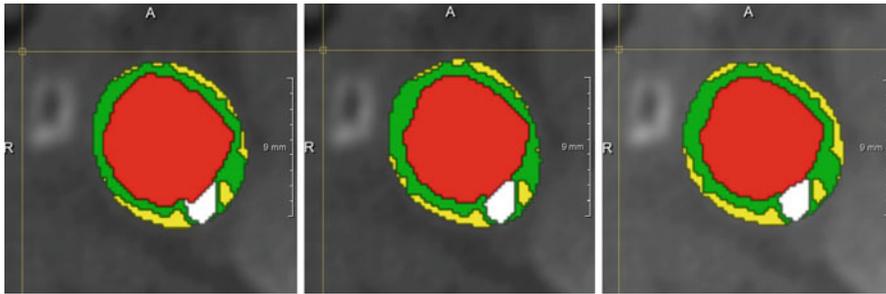
Fig. 1 Different plaque components on one cross sectional slice segmented by the automated method (*left*), observer S.R. (*center*) and observer M.G. (*right*). *Red square* lumen, *Green square* fibrous, *yellow square* lipids, *white square* calcium

Calculation of the volume of plaque and the components

Having the carotid artery vessel wall and lumen segmented, different HU ranges were used to define—different plaque components. The cut-off point for the distinction between calcifications and fibrous tissue was set at 130 HU, the value currently used for calcium scoring. The cut-off point for the distinction between fibrous tissue and lipid was set at 60 HU as determined in previous studies [11]. We adjusted the cut-off point for the distinction between atherosclerotic plaque and vessel lumen for each patient on the basis of the full-width-half-maximum principle (mean lumen attenuation plus mean fibrous tissue attenuation (≈ 88 HU) divided by two). The pixels surrounding the vessel lumen, with a density between 130 HU and the adjusted cut-off value, were considered to be fibrous tissue.

The plaque volume and the volume of the plaque components were calculated by multiplying the number of pixels of the total atherosclerotic plaque or its components, with the pixel size and the slice increment. The proportion of plaque components was calculated as the ratio of volume of the component to the total plaque volume multiplied by 100. As an example, in Fig. 1 a cross-sectional slice with outer vessel wall and all three plaque components in different colors automatically segmented and manually segmented by two observers is shown.

Cardiovascular risk factors

We obtained clinical measures and information on risk factors and medication during the patient's visit at the outpatient clinic. Subjects were categorized as currently, ever, or never smoking. Hypertension was defined as systolic blood pressure over 140 mmHG and/or diastolic blood pressure over 90 mmHg during two episodes of at least 15 min of continuous noninvasive blood-pressure measurement and/or treatment with antihypertensive medication. Blood pressure-lowering drugs comprised ACE inhibitors, calcium-antagonists, beta-blockers, and diuretics. Hypercholesterolemia was defined as fasting cholesterol over 5.0 mmol/l and/or use of cholesterol-lowering drugs. Diabetes was defined as fasting serum glucose levels over 7.9 mmol/l, nonfasting serum glucose levels over 11.0 mmol/l, or use of antidiabetic medication. Information was collected on previous cardiovascular events and conditions (myocardial infarction, atrial fibrillation, angina pectoris, chronic heart failure, coronary artery bypass grafting) and previous cerebrovascular events.

Statistical analysis

Both for automated and manual measurements (2 observers), plaque and plaque component volumes and proportions were presented on 40 datasets with mean $\pm$ (SD). The differences between automated and manual measurements and those between the measurements of two observers are presented with mean values and standard deviations. The differences between the automated and manual measurements (2 observers) on 40 datasets were plotted against the mean value of the measurements (Bland–Altman plot), they were evaluated with paired Student t test and the correlation between the measurements by the two methods was evaluated by Pearson's correlation

coefficient (R_P). Bland–Altman plots are plotted in Excel. Limits of agreement are calculated as average difference $\pm$ 1.96 * standard deviation of the difference.

The differences between automated and manual measurements on 90 datasets (1 observer) are presented with mean values and standard deviations and the correlation was evaluated by R_P.

Both for automated and manual measurements (1 observer) we determined the associations between cardiovascular risk factors and PV and plaque composition on 90 datasets using univariable linear regression. Multivariable analysis was not performed for two reasons. Firstly, the focus of the study was to show that automated method can replicate the associations between manually measured plaque components and cardiovascular risk factors. Second, we did not focus on the assessment of independent associations between risk factors and plaque

characteristics as this was not possible due to limited sample size. Because the distribution of plaque volume was skewed, we used a log10 transformation prior to statistical analysis. Similarly, for proportion of plaque components we used square root (sqrt) transformation.

P values < 0.05 were considered statistically significant. Statistical analyses were performed using SPSS software (version 15.0, Inc., Chicago, Illinois).

Results

Baseline clinical characteristics

The baseline characteristics are presented in Table 1.

Plaque measurements: comparison to interobserver variability

Table 2 shows lumen, plaque volume, plaque component volumes and plaque component proportions assessed by the automated method and by the manual methods (two observers) in 40 datasets. The differences between the automated and the manual method and between the manual measurements of two observers are also shown. The differences between automated method and both observers were in the same range as the differences between observers:

The difference between the automated method and first observer manual measurements of PV, calcified, fibrous and lipid percentages were 0.02 ± 0.24 cm^3, $-4 \pm 6\%$, $-0 \pm 8\%$ and $4 \pm 7\%$, respectively. The

Table 1 Demographic and clinical characteristics of 90 patients

Characteristics	N = 90
Age (years; mean ± SD)	67 ± 11
Male sex (%)	63
Hypertension (%)	84
Hypercholesterolemia (%)	85
Diabetes mellitus (%)	24
Smoking: current or past (%)	44
Previous cardiac disease (%)	35
Previous cerebrovascular disease (%)	31

Table 2 Plaque features measured by automated method and by two observers in 40 datasets with the differences and coefficients of variation

40 Datasets	μ (A) ± SD	μ (Obs 1) ± SD	μ (Obs 2) ± SD	μ (Diff (A, Obs1)) ± SD	μ (Diff (A, Obs2)) ± SD	μ (Diff (Obs1, obs2)) ± SD
Plaque volume (mm^3)	965 ± 511	946 ± 595	1052 ± 754	19 ± 235	−87 ± 432	−106 ± 288*
Lumen volume (mm^3)	1030 ± 577	1040 ± 562	1052 ± 567	−10 ± 84	−22 ± 73	−12 ± 27*
Calcium volume (mm^3)	129 ± 178	155 ± 197	136 ± 174	−26 ± 50*	−6 ± 45	19 ± 31*
Fibrous volume (mm^3)	591 ± 271	564 ± 302	602 ± 336	26 ± 101	−10 ± 165	−37 ± 112*
Lipid volume (mm^3)	244 ± 144	225 ± 215	314 ± 348	18 ± 133	−69 ± 272	−88 ± 190*
Calcium proportion (%)	10 ± 11	14 ± 16	11 ± 12	−4 ± 6*	−1 ± 4	3 ± 5*
Fibrous proportion (%)	63 ± 10	63 ± 13	61 ± 11	−0 ± 8	2 ± 8	2 ± 6*
Lipid proportion (%)	25 ± 5	21 ± 9	27 ± 10	4 ± 7*	−1 ± 9	−5 ± 7*

μ mean, A automated method, Obs1 first observer, Obs2 s observer, SD standard deviation, Diff difference, CoV coefficient of variation, * t test, P value < 0.05

differences between automated method and second observer manual measurements of PV, calcified, fibrous and lipid percentages were -0.09 ± 0.43 cm^3, $-1 \pm 4\%$, $2 \pm 8\%$ and $-1 \pm 9\%$. respectively. The differences between two observers manual measurements of PV, calcified, fibrous and lipid percentages were 0.11 ± 0.29 cm^3, $3 \pm 5\%$, $2 \pm 6\%$ and $-5 \pm 7\%$, respectively. Similar differences were found between automated plaque measurements and manual measurements performed on 90 datasets by observer S.R.

Figure 2 shows regression plots and Pearson's correlation coefficient (R$_P$) between automated and manual measurements by both observers of plaque features on 40 datasets. For PV, calcium, fibrous and lipid contribution correlation coefficients between automated and manual measurements of observer S.R. and M.G. were: 0.92 and 0.83; 0.94 and 0.94; 0.79 and 0.73 and 0.57 and 0.52, respectively. Correlation coefficients between automated and manual measurements by observer S.R. on 90 datasets of PV, calcium, fibrous and lipid contributions were 0.89, 0.86, 0.77 and 0.55, respectively.

From the Bland–Altman plots, in Fig. 3, it can be observed that the difference between automated and manual measurements of plaque volume increases when the volume increases. Similarly, the difference between automated and manual measurements of plaque components proportions increase with the components proportions.

Risk factors associations with plaque features: comparison between manual and automated measurements

Table 3 shows the associations between cardiovascular risk factors and automatically assessed and manually assessed plaque volume and plaque component percentages on 90 datasets. Mostly, similar associations were found with automatically and manually assessed plaque features and cardiovascular risk factors.

Older patients had significantly larger PV measured by the automated method, whereas the association with manually assessed PV was not significant ($P = 0.065$). Male patients had significantly higher plaque volume for both automated and manual plaque measurements. Patients with hypercholesterolemia had significantly lower plaque volume when

measured with the automated method, and not when measured manually. Patients who were smokers and patients who had a history of cerebrovascular disease had significantly higher plaque volume for both automated and manual plaque measurements.

For both automated and manual plaque measurements older patients had a significantly higher calcium contribution and a significantly lower fibrous contribution. Male patients had a significantly higher lipid contribution for both automated and manual plaque measurements. Patients with diabetes had a significantly higher calcium contribution for both automated and manual plaque measurements and a significantly lower fibrous contribution when measured with the automated method and not when measured manually.

Patients with a history of cerebrovascular disease had a significantly lower fibrous contribution when measured manually and not when measured automatically.

Discussion

In this study we presented a method for automated plaque volume and plaque composition assessment. Furthermore, we evaluated its accuracy (i) with respect to manual tracings, and (ii) its ability to replicate associations between plaque characteristics and cardiovascular risk factors.

With respect to segmentation accuracy, we showed that the differences in estimating plaque volume and plaque components between our automated method and expert observers are in the same range as interobserver variability. The results show some bias between the observers and between observers and the method. All automated volume measurements values are larger than volumes measured by observer S.R. and smaller than the volumes measured by observer M.G. with the exception of calcium volume and fibrous contribution. All the volumes and proportion differences between two observers were statistically significant, although these differences were small. The statistically significant difference is a consequence of a persistent, albeit small, oversegmentation of most plaque components by observer M.G. compared to observer S.R. The differences between automated method and observer S.R. were significant for calcium volume and proportion and lipid
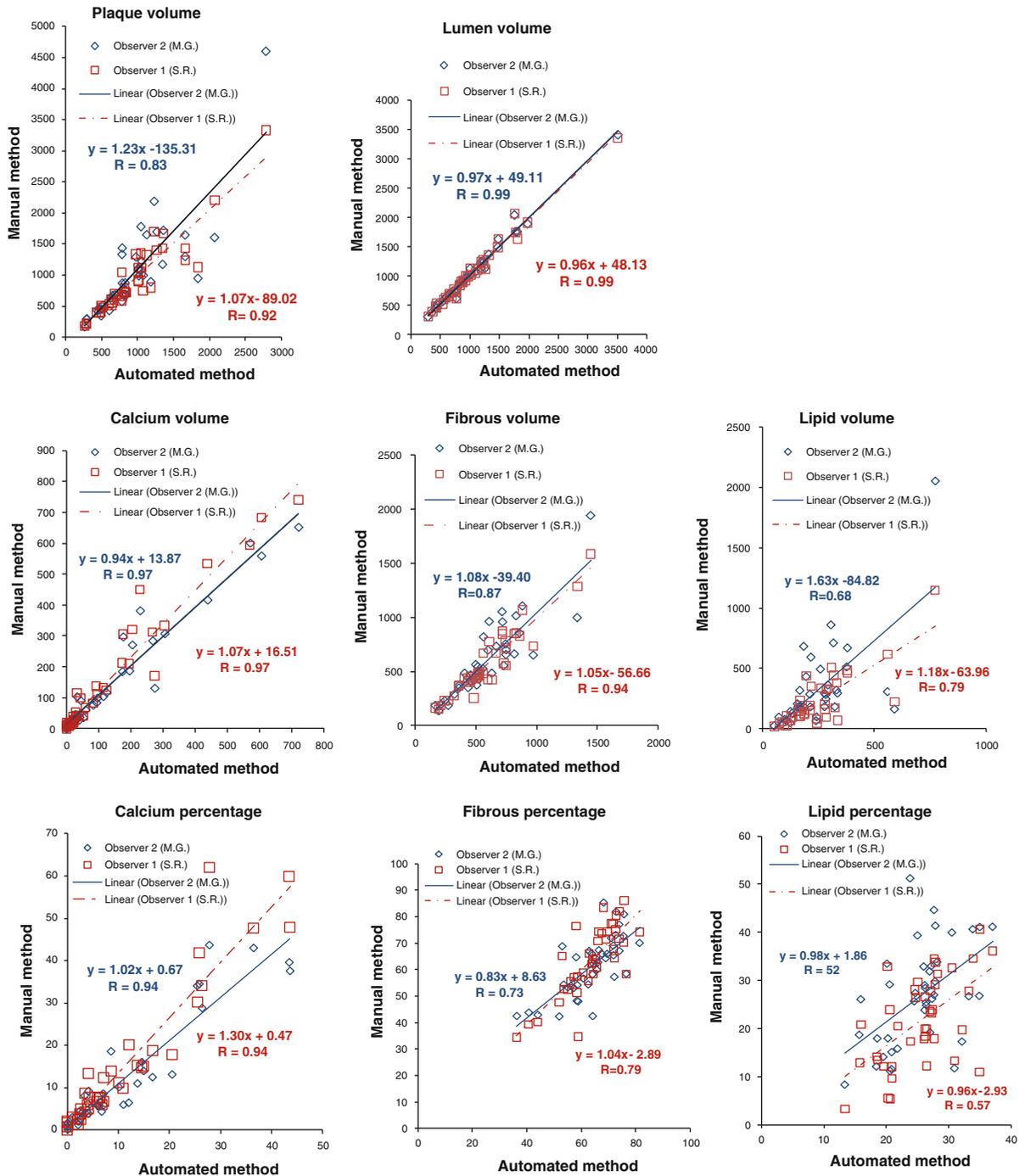
Fig. 2 Regression plots showing the comparison between automated and manual measurements in 40 datasets

proportion. None of the differences between automated method and observer M.G. were significant. The differences between automated method and observer S.R. were larger than the differences

between automated method and observer M.G. for more measurements: calcium volume, fibrous volume, calcium proportion and lipid proportion. In a previous interobserver study of plaque and plaque
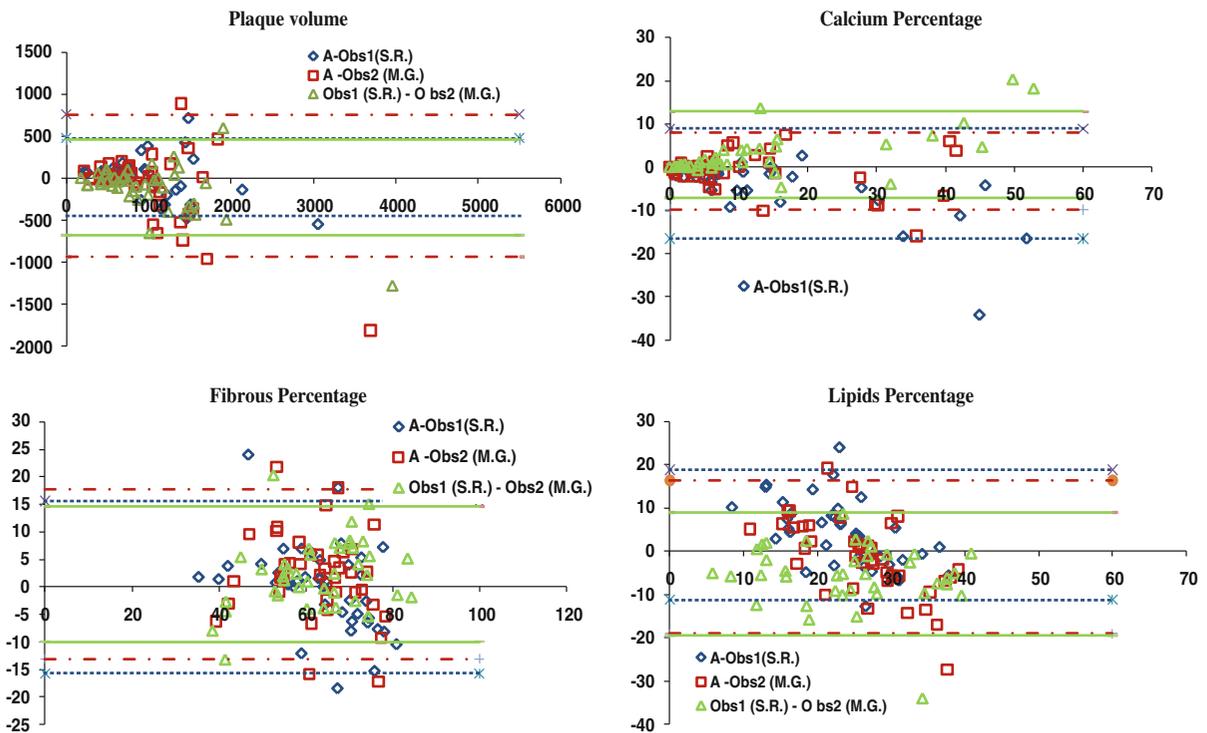
Fig. 3 Bland—Altman plots of plaque volume and plaque components percentages assessed by automated method and manual method by two observers in 40 datasets

components assessment with CTA, in which three observers manually annotated 46 CTA datasets [14], the differences of plaque volume and all plaque components were significant between at least one pair of observers [14]. Pearson's correlation coefficients between automated and manual measurements of both observers for PV and plaque contributions were mostly similar as shown in Fig. 2.

In a second evaluation, we showed that associations between cardiovascular risk factors and automated plaque measurements were mostly similar to the associations found with manual plaque measurements. Seven associations were significant for both the automated and manual plaque measurements; one was significant for the automated method and almost significant for manual method and three were significant for only one of the methods. The associations that were found to be significant for both manual and automated measurements have also similar correlation coefficient values.

To our knowledge, this is the first study that compares cardiovascular risk factors associations with manually and automatically assessed plaque

volume and plaque components. When comparing our results with results of a previous study in which the association between cardiovascular risk factors and manually assessed plaque volume and plaque components was evaluated in 57 symptomatic carotid arteries [31], we found more associations. This can possible be explained by the larger number of datasets that is used in our study. In the previous study age and smoking were related to plaque volume, which is confirmed in our current study. In the previous study, patients with hypercholesterolemia had significantly less lipid and more calcium; these associations were not confirmed. A reason for this could be that automated results are the least similar to manual ones in case of lipids contribution ($R_p = 0.55$). Calcium proportion is shown to be underestimated by the automated method.

In previous studies from our institute on CT based plaque assessment [11], [29] and [14], different datasets were used than in this paper. The 57 datasets used to relate manually derived plaque measurements to cardiovascular risk factors in [31] are a subset of the 90 datasets used in this paper. Compared to this

Table 3 The associations between risk factors and PV and plaque components percentages assessed by automatic method (A) and manual method (M) in 90 datasets

90 Datasets	PV(A) B (P value)	PV (M.) B (P value)	Calc % (A) B (P value)	Calc % (M) B (P value)	Fib % (A) B (P value)	Fib % (M.) B (P value)	Lip % (A) B (P value)	Lip % (M) B (P value)
Age	0.004 (0.029)*	0.005 (0.065)	0.048 (0.004)*	0.056 (0.001)*	−0.013 (0.033)*	−0.021 (0.005)*	−0.006 (0.25)	−0.006 (0.56)
Gender	0.113 (0.010)*	0.168 (0.003)*	0.182 (0.64)	0.192 (0.64)	−0.196 (0.16)	−0.323 (0.062)	0.234 (0.048)*	0.560 (0.024)*
Hypercholesterolemia	−0.120 (0.049)*	−0.054 (0.49)	−0.728 (0.17)	−1.056 (0.60)	0.268 (0.16)	0.152 (0.53)	−0.064 (0.71)	0.505 (0.14)
Hypertension	0.052 (0.39)	0.048 (0.52)	0.315 (0.54)	0.224 (0.68)	−0.005 (0.98)	−0.044 (0.85)	−0.106 (0.52)	−0.138 (0.68)
Diabetes mellitus	0.025 (0.62)	0.018 (0.78)	1.163 (0.006)*	1.231 (0.007)*	−0.396 (0.010)*	−0.317 (0.10)	−0.103 (0.46)	−0.403 (0.15)
Smoking (ever)	0.093 (0.031)*	0.113 (0.038)*	0.137 (0.72)	0.094 (0.82)	−0.048 (0.72)	−0.093 (0.58)	0.015 (0.90)	0.221 (0.36)
Previous cardiac disease	0.053 (0.24)	0.075 (0.19)	0.593 (0.12)	0.634 (0.13)	−0.095 (0.50)	−0.264 (0.13)	−0.199 (0.11)	−0.058 (0.82)
Previous cerebrovascular disease	0.122 (0.008)*	0.138 (0.019)*	0.489 (0.22)	0.812 (0.056)	−0.234 (0.11)	−0.465 (0.009)*	0.047 (0.71)	0.076 (0.77)

The associations were assessed by linear regression and represented by coefficient of regression (B) and P value

* Significant P values (< 0.05) and P value

A automated method, M manual method, B regression coefficients, Calc calcium, Fib fibrous, Lip lipids

work, we thus both extended the dataset, and we investigated the influence of automated plaque assessment, in order to try to replace laborious manual plaque segmentation.

Manual quantification takes on average around 30 min per carotid artery. This time period depends on the lesion length. The automated method takes on average around 6 min on a single CPU 2GHZ, RAM 24 GB computers. Manual plaque segmentation is not applicable in clinical setting, because it is too time-consuming. Automated plaque assessment already is considerably faster and improved implementation and hardware could reduce processing time such that it would become acceptable in clinical workflow. Also, this automated tool can be used in larger datasets for the investigation of associations between plaque volume/composition and risk factors or recurrent ischemic events and for longitudinal studies on plaque imaging.

Study limitations

A limitation of our study is that we do not have a definite gold standard. The scarcity of histological carotid plaque specimens hampers the validation of automated plaque volume and composition assessment on a sizeable dataset. We therefore compared results from automated plaque segmentation with those from manual plaque segmentation—a method previously validated against histology—thus indirectly evaluating the performance of our automated method.

A second limitation of our study is that we used CT data from a single vendor, collected at a single site. Our automated method might perform less on data from different CT-scanners, different sites or using different image protocols. However, the underlying method is generic and if required can be tuned to different systems by using new training on data. A third limitation concerns the plaque segmentation method that uses distinctive ranges of Hounsfield Unit (HU) values [11]. There is some overlap between the HU of lipid and fibrous tissue and no distinction can made between lipid and intraplaque heamorrhage, which is thought to be an important feature in plaque vulnerability assessment as well [9].

As a final limitation, the comparison of cardiovascular risk factors associations with manually and

automatically segmented plaque components does only indicate that the automated method can be used to find similar associations in a group study. It does not provide information on the method applicability on a single subject.

Conclusion

We presented an approach to automatically segment outer vessel wall and plaque of carotid artery in CTA and to automatically assess plaque volume and plaque components. The results were validated with respect to manual tracings and interobserver variability. Furthermore, the associations between cardiovascular risk factors and plaque volume and plaque component contributions assessed by our automated method and a manual method were compared. We have shown that the difference between our automated method and the observers is in the range of the variability of the observers, and hence can be applied for automated analysis in large studies.

Conflict of interest None.

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