Accuracy of Coronary Plaque Detection and Assessment of Interobserver Agreement for Plaque Quantification Using Automatic Coronary Plaque Analysis Software on Coronary CT Angiography

Genauigkeit der Koronarplaque-Detektion und Beurteilung der Interobserver-Übereinstimmung von Plaquequantifizierung unter Verwendung einer automatischen Koronarplaqueueanalyse-Software in der Koronar-CT-Angiografie

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Abstract
Purpose: To evaluate the accuracy of automatic plaque detection and the interobserver agreement of automatic versus manually adjusted quantification of coronary plaques on coronary CT angiography (cCTA) using commercially available software.

Materials and Methods: 10 cCTA datasets were evaluated using plaque software. First, the automatically detected plaques were verified. Second, two observers independently performed plaque quantification without revising the automatically constructed plaque contours (automatic approach). Then, each observer adjusted the plaque contours according to plaque delineation (adjusted approach). The interobserver agreement of both approaches was analyzed.

Results: 32 of 114 automatically identified findings were true-positive plaques, while 82 (72%) were false-positive. 20 of 52 plaques (38%) were missed by the software (false-negative). The automatic approach provided good interobserver agreement with relative differences of 0.9 ± 16.0% for plaque area and -3.3 ± 33.8% for plaque volume. Both observers independently adjusted all contours because they did not represent the plaque delineation. Interobserver agreement decreased for the adjusted approach with relative differences of 25.0 ± 24.8% for plaque area and 20.0 ± 40.4% for plaque volume.

Conclusion: The automatic plaque analysis software is of limited value due to high numbers of false-positive and false-negative plaque findings. The automatic approach was reproducible but it necessitated adjustment of all constructed plaque contours resulting in deterioration of the interobserver agreement.

Key points:
- Automatic plaque detection is limited due to high false-positive and false-negative findings.
- Automatic plaque quantification was reproducible in the few accurately detected plaques.

Key words
atherosclerotic plaque coronary computed tomography angiography coronary artery disease software tools automatic quantification
Coronary CT angiography (cCTA) has become a valuable diagnostic tool for the noninvasive detection of coronary artery disease. This technique has been widely implemented in clinical practice during the last decade [1, 2]. Besides the detection of coronary stenosis, cCTA also allows the assessment of morphologic and geometric characteristics of coronary artery plaques [3–6]. Reproducible quantification of plaque dimensions by cCTA has great importance for individual risk stratification and therapeutic monitoring [7, 8]. Recent developments of dedicated post-processing tools enable automatic segmentation of the coronary artery tree with automatic plaque detection and quantification of the plaques [9–12]. Current studies suggest that these tools provide reproducible, observer-independent plaque detection and quantification [9–13]. However, these studies only evaluated the automatic approach for analyzing plaque dimensions. The accuracy of automatic plaque detection has not been evaluated so far. Furthermore, the effect of a potentially necessary adjustment of the automatically generated incorrect plaque contours on the interobserver agreement was not assessed. Assessment of both approaches is of importance because the automatic approach does not always represent the true plaque dimension, thus requiring manual adjustment of the plaque contours.

The aim of this study was to evaluate the accuracy of automatic plaque detection and the interobserver agreement of automatic versus manually adjusted quantification of coronary plaque dimensions on cCTA using commercially available software.

Materials and Methods

Patient population
Written informed consent was waived for this retrospective study by the institutional review board. In 10 patients (6 men, 4 women, mean age: 63 ± 10 years, range: 46 – 75 years), clinically indicated cCTA was performed for the diagnostic workup of suspected coronary artery disease. The inclusion criterion was high image quality of the coronary arteries in all segments. The exclusion criteria were cCTA scans with artifacts related to motion, heart rhythm disturbances, a metallic foreign material such as pacemakers, and patients with stents or with aortocoronary bypass.

Patient preparation
Patients with heart rates greater than 65 bpm and no contraindications received up to 100 mg of atenolol (Atenolol-ratiopharm®, ratiopharm GmbH, Ulm, Germany) per os 30 min. before the scan. Immediately prior to the scan, all patients received a single dose of 0.8 mg glycerol nitrate (Nitrolingual® N-Spray, Pohl-Boskamp, Hohenlockstedt, Germany) sublingually.

Image analysis
Images were analyzed by commercially available plaque analysis software (Comprehensive Cardiac Analysis, Extended Brilliance Workspace, V4.0; Philips Healthcare, Best, The Netherlands) supplied by the vendor of our CT system. This software automatically performed model-based whole heart segmentation, coronary artery segmentation including luminal and vessel wall contouring, and detection of coronary plaques without any user interference. Two board-certified radiologists with 12 and 6 years of experience in cCTA, who were blinded to the cCTA results, evaluated the accuracy of the automatic plaque detection in consensus reading. The software finding was classified as a true positive result when both observers considered the detected lesion to be plaque. In the event of a false-positive finding, the supposed reason for the software misinterpretation was noted. Plaques that were not detected by the software were classified as false-negative plaques that were correctly detected by the software were included in the automatic quantitative analysis. Subsequently, the two observers separately and independently performed automatic plaque segmentation and quantification (automatic approach). Both observers analyzed the plaque area (mm²), plaque volume (mm³), and plaque burden (%). In the case of inaccurate plaque delineation by the software, the observers were requested to manually correct the contour positioning.

Citation Format:
in a further step to adjust the plaque contours according to their personal assessment of the plaque delineation.

Statistical analysis
Continuous data are expressed as mean ± standard deviation (SD). Interobserver agreement was determined for the automatic and the manually adjusted approach. Absolute and relative differences between observers were calculated as described by Bland and Altman [14]. Relative differences were calculated as difference of two measurements divided by the mean of both measurements multiplied by 100 to give percentages. Variance was calculated as the square of the standard deviation of the relative differences. Unpaired t-tests were used to compare the relative differences, and F-tests were used to compare the variances of the results of the automatic and the manually adjusted approach. Differences between mean plaque dimensions of the automatic and the manual approach were compared using paired t-tests. P < 0.05 was considered statistically significant.

Results

Automatic plaque detection
The software identified 114 findings along the coronary arteries as plaques. Consensus reading revealed that 32 (28 %) of these lesions were true-positive, while 82 (72 %) were false-positive findings. The software did not detect 20 (38 %) plaques of 52 true coronary artery plaques. There were classified as false-negative findings. The majority of false-positive findings (n = 48, 59 %) were related to an intermediate signal in the pericoronary epicardial fat. 20 false-positive findings (24 %) were related to vessel branching. 6 false-positive findings (7 %) were due to false vessel contouring with placement of the outer border and inner lumen border significantly off the course of the coronary artery. Contrast in the adjacent vein resulted in 5 false-positive findings (6 %). The software marked a kinking of the coronary artery in 3 lesions (4 %) as plaque.

Reasons for false-positive findings
With 80 %, a small plaque size was the most common reason for a plaque not being detected with the automatic approach. The mean plaque area of the undetected plaques (3.7 ± 1.1 mm²) was significantly smaller than that of the detected plaques (5.7 ± 2.1 mm²) (P<0.05). 4 false-negative findings (20 %) were related to two adjacent plaques, which were identified as one plaque by the software.

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**Fig. 1** Representative examples for false-positive findings (red arrows). The blue lines represent the vessel wall and the red lines represent the border of the vessel lumen generated by the software. The software identified findings between these two lines as plaques. False-positive findings were related to an intermediate signal in the pericoronary epicardial fat a, vessel branching b, false contouring of the coronary artery c, contrast in an adjacent vein d, and kinking of the coronary artery e.


**Fig. 2** Representative examples for false-negative findings (red arrows). a shows a small plaque, which was missed by the software. b shows two adjacent plaques, which were identified by the software as one plaque.

**Abb. 2** Repräsentative Beispiele für falsch-negative Befunde (rote Pfeilmarkierungen). a zeigt einen kleinen Plaque, welcher von der Software nicht detektiert wurde. b zeigt zwei benachbart lokalisierte Plaques, welche von der Software als eine Plaque identifiziert wurde.

**Fig. 3** Example of the automatic and manually adjusted approach. a displays the automatic vessel delineation with the vessel wall in blue and the vessel lumen in red. b displays the plaque area marked by the software in yellow. c displays the vessel contour and the resulting plaque area after adjustment of the contours by observer 1.

**Abb. 3** Beispiel für die automatische und manuell adjustierte Vorgehensweise. a zeigt die automatisch erstellte Gefäßkontur mit der Gefäßwand in blau und dem Gefäßlumen in rot. b zeigt die Plaquefläche, welche durch die Software gelb markiert wurde. c bildet die Gefäßkontur und die resultierende Plaquefläche nach Adjusitierung der Konturen durch Untersucher 1 ab.
that an intermediate signal in the pericoronary epicardial fat was with 59% the main reason for false-positive findings. This finding indicates that the software has a low signal threshold to detect plaques. Despite this low threshold, the software failed to detect 38% of plaques, with small plaque sizes being the main reason for false-negative findings with 80%. Our data show that the low threshold does not guarantee a high sensitivity for detecting plaques. Other false-positive findings are related to wrong segmentation of the coronary artery. With 24%, vessel branching represented the second most common reason for false-positive plaque findings.

The good interobserver agreement with low limits of agreement of the automatic approach was decreased by the necessity for contour adjustment in all detected plaques. Both observers independently rated that the software contours did not correspond with the true plaque delineation. The necessary adjustment of the plaque contours resulted in significant worsening of the interobserver agreement. This observed deterioration of the interobserver agreement is most likely related to the fact that no precise rules for adjusting the contours were predefined and that the observers were not specially trained in the tracing of plaque contours. Previous work has shown that training and adherence to predefined rules substantially improves the interobserver agreement. This observed deterioration of the interobserver agreement for the investigated plaque dimensions. This low interobserver variability was related to a primary automatic approach with only little human interaction.

### Study limitations

At the first glance the small number of patients may represent a limitation of our study. However, it has to be emphasized that the software detected a high number of 114 plaques, of which 82 (72%) were false-positive findings. Additionally, the software missed 20 of 52 plaques resulting in 38% false-negative findings. In the 32 correctly identified plaques, both observers independently adjusted the automatically generated plaque contours, because the contours were not accurate. Both findings represent a limitation of the software and not of the study design. The inclusion of more patients only would have resulted in a duplication of the reported results with identical conclusions, since none of patients had reduced image quality as a potential explanation for the low performance of the software. Inclusion of cCTA examinations with reduced image quality most likely would have further decreased the performance of the software.

Finally, it has to be underlined that our results only relate to the investigated software version and cannot be applied to software versions that have since been released or to software tools from other vendors.

### Conclusion

Use of the investigated plaque analysis software is of limited value because the software identified a high number of false-positive and false-negative plaques, thus requiring careful revision of the automatically detected plaques. Uncritical clinical use of the software would result in an erroneous plaque detection, consequently resulting in potential over- or underdiagnosis of the presence or absence of coronary artery disease. Therefore, we recommend users of this automatic plaque analysis software to critically review their software results before applying them in a routine clinical setting. The fact that both observers independently adjusted the automatically generated plaques contours represents another software limitation, resulting in a significantly reduced interobserver agreement for the investigated plaque dimensions. This low inter-

<table>
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<tr>
<th>automatic approach</th>
<th>plaque area (mm²)</th>
<th>plaque volume (mm³)</th>
<th>plaque burden (%)</th>
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<tr>
<td>mean ± SD</td>
<td>5.7 ± 2.1</td>
<td>24.8 ± 13.4</td>
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<td>absolute difference ± SD</td>
<td>0.07 ± 0.8</td>
<td>-0.9 ± 6.8</td>
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<td>relative difference ± SD (%)</td>
<td>0.9 ± 16.0</td>
<td>-3.3 ± 33.8</td>
<td>5.0 ± 16.1</td>
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<td>relative limits of agreement (%)</td>
<td>-30 and 32</td>
<td>-69 and 63</td>
<td>-27 and 37</td>
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<td>variance (%)</td>
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<th>plaque volume (mm³)</th>
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<tr>
<td>mean ± SD</td>
<td>6.2 ± 2.4</td>
<td>27.9 ± 16.8</td>
<td>45.2 ± 14.2</td>
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<tr>
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<td>1.5 ± 1.8</td>
<td>3.2 ± 8.4</td>
<td>6.4 ± 13.3</td>
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<td>relative difference ± SD (%)</td>
<td>25.0 ± 24.8</td>
<td>20.0 ± 40.4</td>
<td>13.9 ± 27.8</td>
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<td>relative limits of agreement (%)</td>
<td>-24 and 74</td>
<td>-59 and 99</td>
<td>-41 and 68</td>
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<td>variance (%)</td>
<td>615</td>
<td>1632.2</td>
<td>772.8</td>
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<td>&lt;0.001</td>
<td>&lt;0.08</td>
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<td>p-value (F-test, (automatic vs. manually adjusted)</td>
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<td>= 0.32</td>
<td>&lt;0.001</td>
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</tbody>
</table>

Table 3 Interobserver agreement of plaque dimensions using the automatic and the manually adjusted approach.

Tab. 3 Interobserver Übereinstimmung der Plaquedimensionen für die automatische und die manuell justierte Vorgehensweise.
observer agreement highlights the difficulty regarding serial measurement of coronary plaque development, e.g. under lipid lowering therapy, using the studied software.

**Clinical relevance of the study**

- Uncritical clinical use of the software would provide erroneous plaque detection and quantification, resulting in potential over- or underdiagnosis of the presence, absence

and dimensions of coronary artery disease. Therefore, careful revision of the automatic results is necessary.

- The automatic plaque quantification approach rendered reproducible plaque dimensions.

- The necessary manual adjustment of plaque contours resulted in a reduced interobserver agreement for the investigated plaque dimensions.
References


