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Basic Science

Fully Automatic Three-Dimensional Quantitative Analysis of Intracoronary Optical Coherence Tomography: Method and Validation

Kenji Sihan,[1,2] BSc, **Charl Botha,**[2] PhD, **Frits Post,**[2] PhD, **Sebastiaan de Winter,**[2] BSc, **Nieves Gonzalo,**[1] MD, **Evelyn Regar,**[1] MD, PhD, **Patrick J.W.C. Serruys,**[1] MD, PhD, **Ronald Hamers,**[1] PhD, and **Nico Bruining,**[1*] PhD

Objectives and background: Quantitative analysis of intracoronary optical coherence tomography (OCT) image data (QOCT) is currently performed by a time-consuming manual contour tracing process in individual OCT images acquired during a pullback procedure (frame-based method). To get an efficient quantitative analysis process, we developed a fully automatic three-dimensional (3D) lumen contour detection method and evaluated the results against those derived by expert human observers. Methods: The method was developed using Matlab (The Mathworks, Natick, MA). It incorporates a graphical user interface for contour display and, in the selected cases where this might be necessary, editing. OCT image data of 20 randomly selected patients, acquired with a commercially available system (Lightlab imaging, Westford, MA), were pulled from our OCT database for validation. Results: A total of 4,137 OCT images were analyzed. There was no statistically significant difference in mean lumen areas between the two methods (5.03 ± 2.16 vs. 5.02 ± 2.21 mm^2; P = 0.6, human vs. automated). Regression analysis showed a good correlation with an r value of 0.99. The method requires an average 2–5 sec calculation time per OCT image. In 3% of the detected contours an observer correction was necessary. Conclusion: Fully automatic lumen contour detection in OCT images is feasible with only a select few contours showing an artifact (3%) that can be easily corrected. This QOCT method may be a valuable tool for future coronary imaging studies incorporating OCT.

Key words: angiography; coronary; diagnostic cardiac catheterization; quantitative vascular angiography

INTRODUCTION

Optical coherence tomography (OCT) has been rapidly accepted as an additional invasive coronary imaging tool [1]. It allows highly detailed imaging of the coronary lumen and vessel wall morphology at resolutions of 10 times higher than what current intracoronary ultrasound (ICUS) can offer. The details shown within OCT images are close to histopathology, allowing accurate evaluation of by example apposition of stent struts and—in longitudinal studies—tissue-coverage of drug-eluting stents (DES) [2]. This advantage has resulted in an increasing use of OCT in studies evaluating new therapeutic treatments, in addition to ICUS, the current de facto reference method for intravascular imaging [3,4].

To apply an imaging method in studies, accurate quantitative analysis tools are required, as has been proven by quantitative angiography (QCA) [5] and quantitative ICUS (QCU) [6,7]. Recently, results of

[1]Thoraxcenter, Delft, The Netherlands
[2]Department of Cardiology, Erasmus MC, Rotterdam, The Netherlands and TU-Delft, Delft, The Netherlands

Conflict of interest: Dr. Hamers is an employee of CURAD BV, Wijk Bij Duurstede, The Netherlands.

*Correspondence to: Nico Bruining, PhD, Erasmus MC, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands. E-mail: n.Bruining@erasmusmc.nl

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computer-assisted quantitative OCT (QOCT) have been reported showing good results for coronary lumen measurements [8]. However, because an OCT examination contains hundreds of individual images, such analysis can, despite the use of computer-assisted tools, be a tedious and time-consuming process [8]. However, because the lumen-intima interface is so clearly visualized in OCT, far better than in ICUS, a fully automatic lumen contour detection approach could be feasible.

This article reports on a novel in-house developed fully automatic three-dimensional (3D) OCT lumen contour detection approach and its validation using expert human observer computer-assisted analysis as a reference.

MATERIALS AND METHODS

OCT Imaging System

OCT imaging was performed with a commercially available system (Lightlab imaging, Westford, MA). This system uses a 1,310-nm broadband light-source generated by a super luminescent diode with an output power in the range of 8.0 mW. The average tissue penetration depth is approximately 1.5 mm with an axial and lateral resolution of 15 and 25 μm, respectively. The imaging probe has the size of a guide-wire with a maximum outer diameter of 0.019 inch (Imagewire™, LightLab Imaging). The wire contains a single-mode fiber optic core within a translucent sheath. The imaging-wire is connected to an imaging console, similar as ICUS, which performs the real-time image data processing, visualization, and image storage. Systematic imaging of a coronary segment is also analogue to ICUS by an automatic continuous speed pullback (between 1 and 3 mm/sec) of the imaging wire [6]. OCT images are generated at a rate of 10–20/sec (cf. ICUS 30 frames/sec). The accuracy of OCT for dimensional measurements—determined using a phantom—has been recently reported to be excellent (mean difference in measured length of −0.03 mm with 0.02 mm precision) [8].

Patients and OCT Image Acquisition

For validation of the automated method, we made a random selection of 20 OCT cases from our database of patients participating in different studies. In all cases a standard femoral approach with 7F guiding catheters was used. Before imaging, all patients received weight-adjusted heparin intravenously to maintain an activated clotting time of >300 sec as well as intravenous analgesics. To be able to see the coronary vessel wall, the coronary artery must be cleared of blood by replacing it with lactated Ringer's solution. This procedure is performed by occlusion of the artery with a dedicated occlusion catheter (Helios, Goodman, Japan) including a short balloon (6.0 mm length) that can be inflated by a low pressure (0.3 atm). The Ringer's is infused distally from the balloon at a rate of 0.5 ml/sec at a temperature of 37°C). Sufficient occlusion of the coronary is checked by contrast injection via the guiding catheter and the balloon pressure is increased (at 0.5 atm increments) when necessary. The images were digitally stored in the AVI file format on DVD's and were translated later into the DICOM medical imaging standard by in-house developed software.

Automated Quantitative OCT Method

The automated OCT lumen contour detection method was developed in the Matlab environment (The Mathworks, Natick, MA). The method has five stages:

Preprocessing. Each individual OCT frame is preprocessed to remove speckle noise and gaps and to adapt the contrast for proper image normalization. Prepocessing consists of the application of a Gaussian filter and using different relative thresholds (Fig. 1B). The relative thresholds are applied on the pixel values to remove extreme values and to improve image normalization.

Edge detection. A Canny [9] filter is applied to detect edges in the OCT image. The final lumen contour is the result of appropriately selected edges, which are positioned on the lumen-intima border only. Straightforward application of the standard Canny filter to the OCT images leads to many false and/or missed contours. Therefore, we iteratively apply the Canny filter to match the constraints necessary for OCT images (percentage of image pixels classified as true edges). This percentage is based on a test-set where it is set in such a way that the lumen contour is detected while detecting as little noise as possible. Within this procedure, the threshold of the Canny filter is optimized using a binary search algorithm.

Lumen edge selection. The result of the Canny edge detection stage includes some edges that do not belong to the lumen-intima interface, for example radially behind bright areas (Fig. 1C). These false edges are mostly due to noise caused by the catheter and by speckle noise which was not be removed by the preprocessing step without significantly impairing image details. The majority of these false edges are identified by two constraints:

1. The angle between the gradient orthogonal to the line segment and the line connecting it to the catheter center should be smaller than a certain threshold.
2. The length of the edge should be longer than a certain threshold (Fig. 1).

Lumen edge linking. The final lumen contour is the optimal combination of the resulting true edges. This is

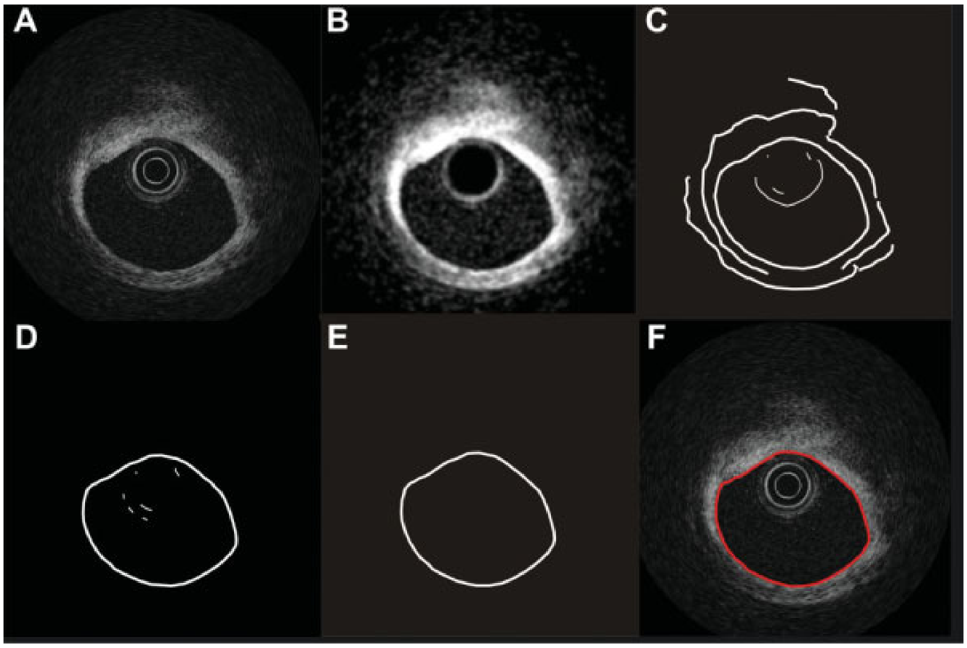

Fig. 1. This figure shows the results of the different processing steps. (A) An original OCT image is presented. (B) The image after the application of a Gaussian filter. (C) The detected edges as a result of the iteratively applied Canny filter. (D) The remaining edges after application of the angle constraint. Short edges are removed after application of a length threshold (E). The postprocessed and smoothed final contour is presented in (F). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

performed using a quality score determined by the resultant lumen area, length (relative to the area), and gaps in the contour (relative to the length). For all possible combinations of edge selections, the quality score is calculated and the combination with the highest score results in the final lumen contour.

Postprocessing. Postprocessing is applied to overcome possible errors introduced by the pre-processing and those inherent to the nature of OCT imaging itself (such as large side-branches, gaps caused by guide-wire artifacts, etc.). The postprocessing is divided into several subprocesses:

Contour correction and smoothing. The iterative application of the Canny filter does not select the edges with local maximum gradient. In a postprocessing step, the maximum gradient search is automatically performed within a 5 pixel radius from the initially found contour. Subsequently, the contour is smoothed, weighing neighbor coordinates with the gradient magnitude in a normal distribution.

Side-branch gaps and out-of-range borders. The resulting luminal contours may still have gaps, which are mostly caused by side-branches and/or guide-wire artifacts. Furthermore, often in OCT images the lumen border is out of range, in large vessels, or is not pronounced enough to produce an edge (Fig. 2). To close these gaps and omissions, a mathematical circular correction model is applied (Fig. 2).

Replacement of falsely detected contours (3D analysis). In the case of large side-branches, heavy noise or large parts of missing visible lumen data within the OCT images (Fig. 3), it is still possible that the automated contour detection does not result in the desired contour. For each consecutive image, the enclosed area of the lumen contour is calculated. Frames showing a relatively large deviation in areas compared to their neighbors are labeled as incorrect. A search and substitute algorithm replaces these contours by the closest available correct contour in the longitudinal direction.

Final approval and correction. It is very difficult, or even impossible, to develop a 100% accurate fully automatic detection method in medical image processing. The large differences found in coronary morphology will always result in unexpected images that could not have been foreseen during development. Therefore, the results must be validated by an expert. To facilitate this, a user interface was developed, similar to that used for QCU [10].

Validation

For validation of the automated method, the quantitative results were compared against those derived by application of a computer-assisted lumen detection

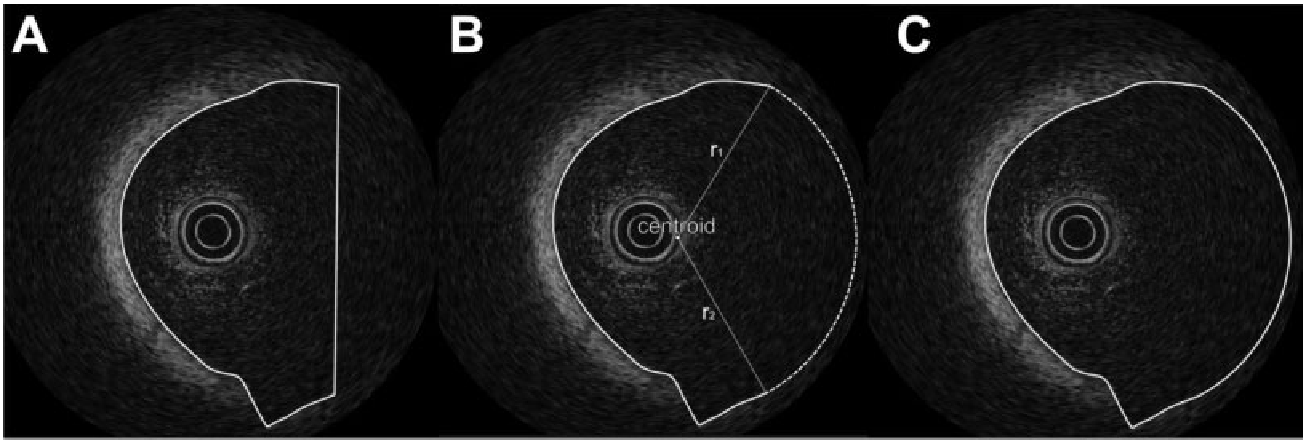

Fig. 2. To close the remaining gaps, the straight line at the right-hand side (A), a circular arc interpolation is performed automatically using the center of gravity of the contour as the center of the circle (B). For the radius, linear interpolation is used from r1 to r2. The repaired contour is presented in (C).

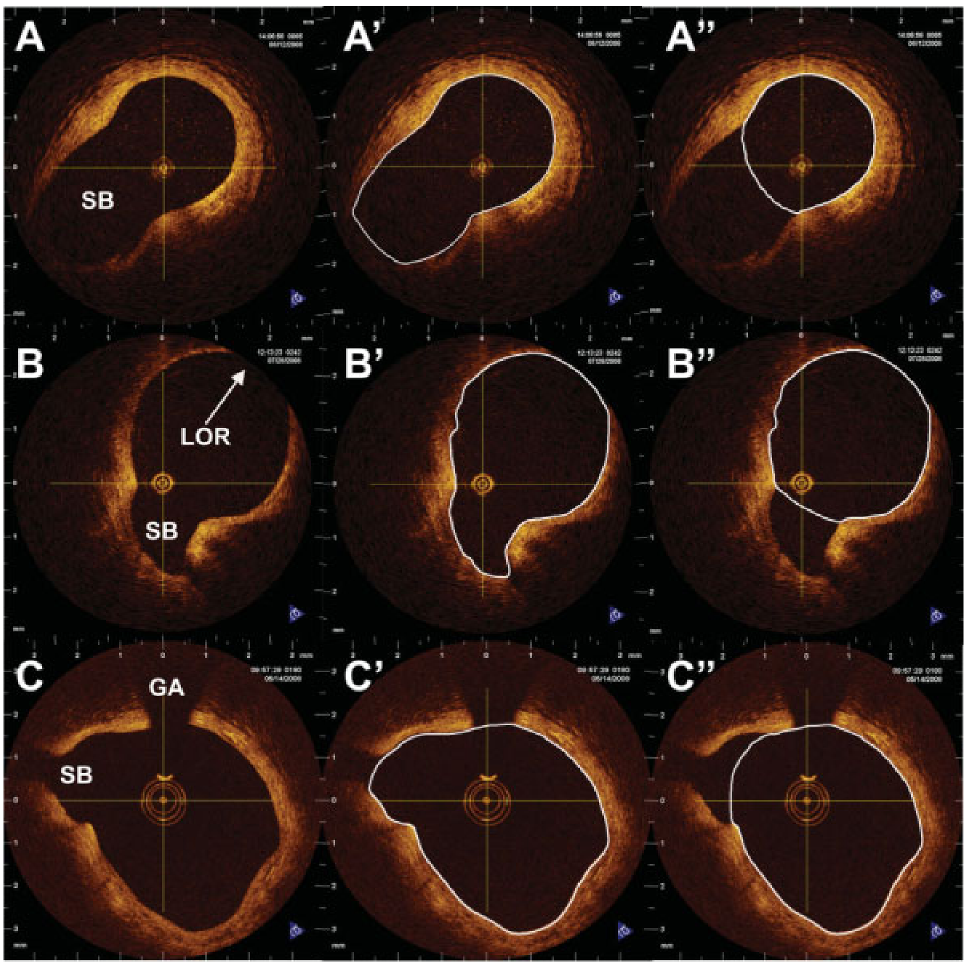

Fig. 3. This figure presents a few different lumen morphologies which are difficult to detect correctly fully-automated. (A) A large side-branch can be appreciated (indicated by SB). (A') The detected automated contour, which has been corrected by the human observer (A″). (B) In addition to a side-branch also a case were part of the lumen is out of range for the OCT catheter. The automated contour detection applied the automated circular correction (B') and the human observer corrected for the large side-branch artifact (B″). Finally, in (C) a guide-wire artifact is presented (C, GA). This relatively small gap is automatically repaired by the correction algorithms (C'). Again, also in this example the observer corrected for the large side-branch (C″). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

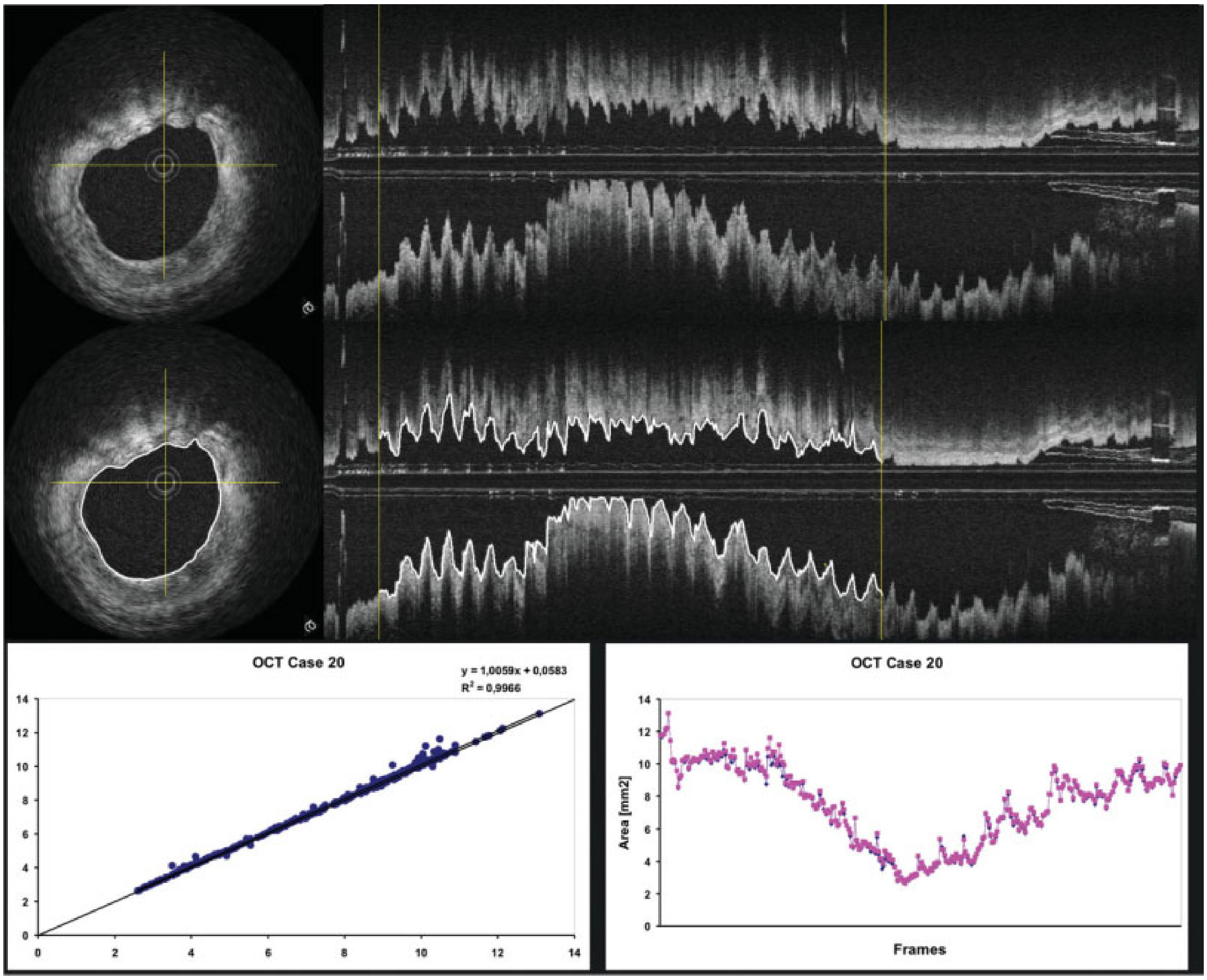

Fig. 4. A typical analysis example is presented. In (A) an individual cross-sectional image is shown and in (A') the longitudinal reconstruction of the pullback examination. In (B and B'), the same images are presented with the automated contour detected result superimposed. It can be appreciated that the cross-sectional OCT images present a lot of details of the lumen-intima morphology. (C) The regression analyses of the area measurements of all frames with the manual results on the *x*-axis and the automated results on the *y*-axis. Finally in (D), all the area measurements are presented of both methods. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

method (CURAD vessel analysis, CURAD BV, Wijk bij Duurstede, The Netherlands) [8]. The expert (N.G.) was blinded for the automated results.

Statistical Analysis

Quantitative data are presented as mean ± standard deviation (SD). Comparison between the methods was performed by the two-tailed paired Student's *t*-test. A P value < 0.05 was considered statistically significant. In addition, regression analysis and the method as proposed by Bland and Altman [11] was performed.

RESULTS

In the 20 OCT cases a total of 4,167 frames were analyzed (208 ± 92 frames on average per patient). In each case, the OCT images were analyzed consecutively, without intervals (Fig. 4). Although the human analysis time was not measured, it is well known that this is usually a lengthy process. The automated method required on average approximately 2–5 sec of calculation time per frame. In 125 OCT frames (3%), the automatic results had to be corrected.

The computer-assisted manual analysis showed a mean lumen area of 5.0 ± 2.2 mm^2 versus 5.1 ±

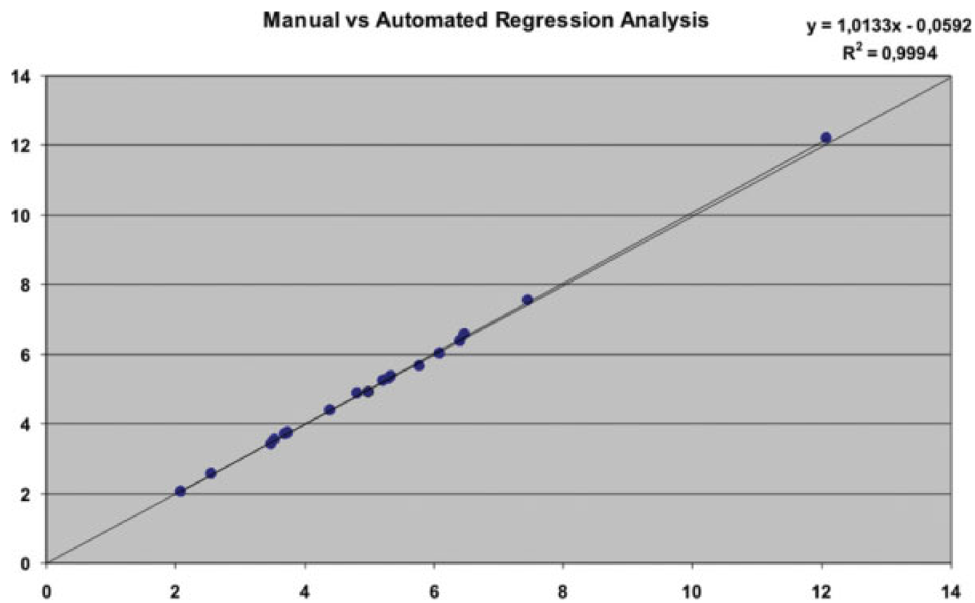

Fig. 5. **The linear regression analysis for the 20 OCT cases analysed computer-assisted (e.g., manual) versus fully automatic. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]**

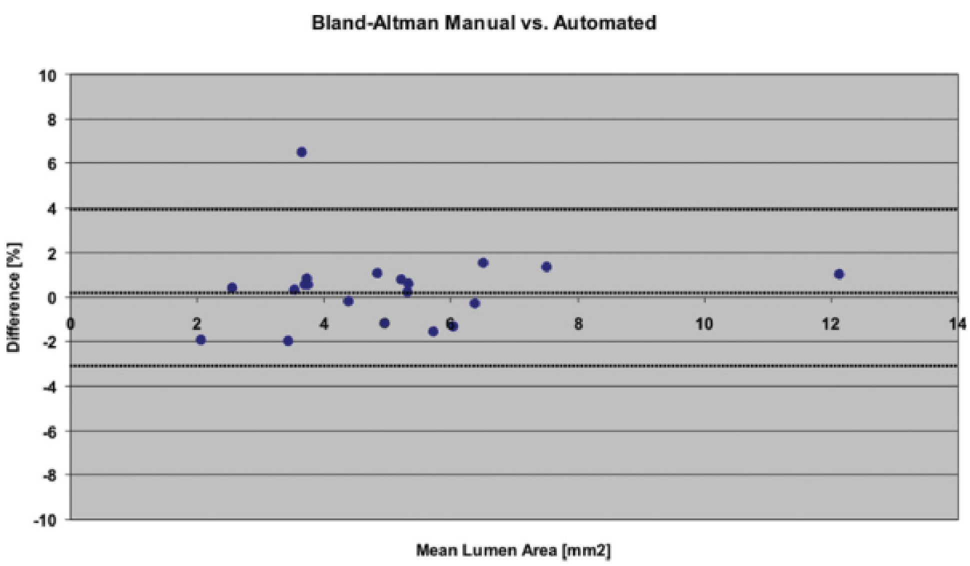

Fig. 6. **The relative differences according to the method as proposed by Bland and Altman [11]. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]**

2.2 mm^2 for the fully automatic method, with no statistical significant difference ($P = 0.26$). The relative difference was 0.4% ± 1.8%. Regression analysis yielded $r = 0.999$ (Fig. 5).

Bland and Altman analysis revealed a single outlier (Fig. 6). All other cases were within an interval of ±2%. Inspection of the outlier showed a deviated contour detection by the expert observer, which resulted in a relative difference of 6%. If this outlier is disregarded, the results are 5.1 ± 2.2 mm^2 (expert) versus 5.1 ± 2.2 mm^2 (automated), $P = 0.52$; relative difference 0.02% ± 1.1%.

DISCUSSION

This study shows that fully automatic 3D lumen contour detection for quantitative OCT analysis is feasible. The quantitative results are similar to those derived manually by an expert.

To evaluate new interventional therapies, quantitative imaging tools are mandatory, such as QCA [5] and QCU [6,10]. Although a computer-assisted method for QOCT has been presented showing excellent results [8], the advantages of fully automatic contour detection are obvious. It does not consume the valuable time of an expert neither does it suffer from possible interobserver- and intraobserver-related deviations. Furthermore, as the outlier case in this report shows, contours which are not precisely positioned on the lumen border can result in a relatively large deviation (in this case 6%). The human expert will most likely be more motivated to analyze all images in a pullback (and not a limited subset of images selected at by example 1 mm intervals, e.g. every 15th frame) if the majority of the contours are already correctly detected and the human effort required is purely for inspection and a limited number of corrections (Fig. 3).

OCT is a relatively new coronary imaging technique, but it has gained considerable enthusiasm in a very short period. It can reveal much more information of the region around the lumen border than is achievable with the current available ICUS technology. However, on the down-side, the penetration depth into the coronary vessel wall and present plaques is still limited (1–2 mm). Therefore, at this moment an automated outer vessel contour detector cannot be developed. Furthermore, because OCT cannot be used to perform coronary plaque measurements, the advantages and disadvantages of OCT in several different clinical scenarios have been described recently [8].

At present, several different commercial OCT systems are available. For this study the system of Lightlab was used [12,13]. This system has an integrated quantitative analysis tool that is limited to single frames. Furthermore, to our knowledge the method has not been published. This single frame approach requires a time consuming and operator dependent manual frame selection at 1 mm intervals. It has been reported that depending on the length of the analyzed region it can take up 2–4 hr to complete an analysis [8].

Independent third party quantitative software tools are, to our knowledge, not yet reported, except for one study presented by Tanimoto et al. [8]. In this article, a computer-assisted dedicated OCT analysis tool was reported, showing good inter and intraobserver quantitative results (1.57% ± 0.05% for lumen areas). However, only well-visualized OCT images were included. Images suffering from motion-induced artifacts, dissections, and side-branches—hampering analysis—were excluded (9%). In this study, all available imaging data (real world data) was analyzed and no exclusions were made. To our knowledge, to date, no other reports have been published concerning fully automatic QOCT methods.

Limitations

Unfortunately, because of the nature of OCT, the penetration depth is currently to low to be able to visualize the coronary vessel wall in diseased segments and therefore only the coronary lumen could be quantified in this study. Developments of newer OCT methods, such as OFDI, and application of other light sources, could possibly enhance the penetration depth making it hopefully possible to visualize advanced coronary plaques in the near future.

The number of cases included in this study is limited, a larger number of cases must reveal if the excellent score of fully automatic detection in 97% of the images can be maintained for larger populations. However, we evaluated almost 4,200 individual OCT images of very different lumen morphology, because of the high spatial resolution.

Future Developments

This full-automated approach to quantify the coronary lumen by OCT is the first step towards further developments of highly anticipated additional quantification tools. On the requirements list are currently: detection of stent struts, protrusion of plaque contents through stent struts, in-stent thrombi, fibrous caps (detection and thickness measurements), and plaque composition. If these requirements could be detected automatically remains topic for further research and developments. However, measurements of in-stent intima hyperplasia, lumen-eccentricity and -remodeling (if base-line and follow-up OCT measurements are available) are already possible using the automated approach (for lumen) in combination by computer-assisted tools (for stent contouring) [8].

The described method has been developed in a generic mathematical research environment on a normal desktop personal computer running Microsoft Windows. The processing time of 2–5 sec could most likely be reduced in the near future if the software were to be ported to a dedicated QOCT environment.

Many of the OCT images suffer from motion artifacts, which are caused by the low temporal resolution of current OCT systems as compared to the relatively rapid motion of the heart. The heart motion also causes the saw-tooth shaped appearance of the coronary vessel wall in the longitudinal reconstructions (Fig. 4). These motion-related artifacts could probably be overcome by the application of optical frequency domain imaging (OFDI) to coronary vessel imaging. However, these systems are still in the research phase and not commercially available yet.

CONCLUSION

This study shows that fully automatic lumen contour detection in OCT images is feasible with only a few contours showing an artifact (3%) that can be easily corrected. This QOCT method may be a valuable tool for future coronary imaging studies incorporating OCT.

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