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## ARTICLES

# ECG-Gated Three-dimensional Intravascular Ultrasound

## Feasibility and Reproducibility of the Automated Analysis of Coronary Lumen and Atherosclerotic Plaque Dimensions in Humans

Clemens von Birgelen, Evelyn A. de Vrey, Gary S. Mintz, Antonino Nicosia, Nico Bruining, Wenguang Li, Cornelis J. Slager, Jos R. T. C. Roelandt, Patrick W. Serruys and Pim J. de Feyter

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## Abstract

*Background* Automated systems for the quantitative analysis of three-dimensional (3D) sets of intravascular ultrasound (IVUS) images have been developed to reduce the time required to perform volumetric analyses; however, 3D image reconstruction by these nongated systems is frequently hampered by cyclic artifacts.

*Methods and Results* We used an ECG-gated 3D IVUS image acquisition workstation and a dedicated pullback device in atherosclerotic coronary segments of 30 patients to evaluate (1) the feasibility of this approach of image acquisition, (2) the reproducibility of an automated contour detection algorithm in measuring lumen, external elastic membrane, and plaque+media cross-sectional areas (CSAs) and volumes and the cross-sectional and volumetric plaque+media burden, and (3) the agreement between the automated area measurements and the results of manual tracing. The gated image acquisition took  $3.9 \pm 1.5$  minutes. The length of the segments analyzed was 9.6 to 40.0 mm, with  $2.3 \pm 1.5$  side branches per segment. The minimum lumen CSA measured  $6.4 \pm 1.7$  mm<sup>2</sup>, and the maximum and average CSA plaque+media burden measured  $60.5 \pm 10.2\%$  and  $46.5 \pm 9.9\%$ , respectively. The automated contour-detection required  $34.3 \pm 7.3$  minutes per segment. The differences between these measurements and manual tracing did not exceed 1.6% (SD<6.8%). Intraobserver and interobserver differences in area measurements (n=3421; r=.97 to .99) were <1.6% (SD<7.2%); intraobserver and interobserver differences in volumetric measurements (n=30; r=.99) were <0.4% (SD<3.2%).

**Conclusions** ECG-gated acquisition of 3D IVUS image sets is feasible and permits the application of automated contour detection to provide reproducible measurements of the lumen and atherosclerotic plaque CSA and volume in a relatively short analysis time.

ultrasonics coronary disease imaging

Intravascular ultrasound allows transmural, tomographic imaging of coronary arteries in humans in vivo and provides insights into the pathology of coronary artery disease by defining vessel wall geometry and the major components of the atherosclerotic plaque.<sup>1 2 3 4 5 6 7</sup> Although invasive, IVUS is safe<sup>8 9</sup> and allows a more comprehensive assessment of the atherosclerotic plaque than the “luminal silhouette” furnished by coronary angiography.<sup>10 11 12 13 14</sup> Nevertheless, conventional IVUS analysis is a planar technique. Volumetric analysis of conventionally obtained IVUS images using Simpson’s rule and planar analysis of multiple image slices is possible and may yield additional information, although it is time-consuming. To reduce the time for volumetric analysis<sup>15</sup> of IVUS images, automated 3D image reconstruction systems have been developed.<sup>16 17 18 19 20 21 22 23 24 25 26 27</sup> However, these systems have limitations, including (1) an inconsistent ability to detect the external arterial boundary and (2) imaging artifacts produced by cyclic changes in vascular dimensions and by movement of the IVUS catheter relative to the vessel.<sup>20 22 24</sup>

As a consequence, we have developed an analysis system that (1) uses 3D IVUS image sets acquired with an ECG-gated image acquisition workstation and pullback device to limit cyclic artifacts<sup>28</sup> and (2) detects both the luminal and external vascular boundaries of atherosclerotic coronary arteries to permit plaque volume measurement.<sup>10 29 30 31</sup> We report the feasibility of IVUS image acquisition and the reproducibility of analysis with this methodology.

## Methods

### Patient Population

Between August 1, 1995, and February 29, 1996, we examined 28 patients with ECG-gated 3D IVUS, which represented a consecutive series of patients investigated with this approach. There were 23 men and 5 women who ranged in age from 38 to 72 years (mean, 55.3±8.9 years). All but 3 of them, studied at routine follow-up after previous catheter-based interventions, were symptomatic and/or had revealed signs of myocardial ischemia during noninvasive functional testing. Reasons for cardiac catheterization were either for diagnostic evaluation (n=20) or for follow-up study after a previous angioplasty procedure (n=8). Of the 20 patients examined during diagnostic catheterizations, 6 had one-vessel, 8 had two-vessel, and 1 had three-vessel disease. All patients with one- and two-vessel disease subsequently underwent successful catheter-based interventions (balloon angioplasty, n=3; directional atherectomy, n=2; stenting, n=9). Bypass surgery was performed in the patient with three-vessel disease. Of the 8 patients investigated at follow-up after previous interventions (after balloon angioplasty, n=5; directional atherectomy, n=3), 3 patients showed a significant restenosis and were successfully treated by repeat balloon angioplasty.

Thirty atherosclerotic coronary segments located in the left anterior descending coronary artery (n=15), right coronary artery (n=12), and left circumflex coronary artery (n=3) were analyzed; 13 segments were proximal, 15 mid, and 2 distal. As a condition for inclusion, segments had to be angiographically relatively straight (in at least two angiographic views from opposite projections). An exclusion criterion was calcification encompassing  $>180^\circ$  of the arterial circumference over a  $\geq 5$ -mm-long axial segment. This study was approved by the Local Council on Human Research. All patients signed a written informed consent form approved by the Medical Ethical Committee of the University Hospital Rotterdam-Dijkzigt.

## IVUS Imaging

All patients received 250 mg aspirin and 10 000 U heparin IV. If the duration of the entire catheterization procedure exceeded 1 hour, the activated clotting time was measured, and intravenous heparin was administered to maintain an activated clotting time of  $>300$  seconds. After intracoronary injection of 0.2 mg nitroglycerin, the atherosclerotic coronary segment to be reconstructed was examined with a mechanical IVUS system (ClearView, CardioVascular Imaging Systems Inc) and a sheath-based IVUS catheter incorporating a 30-MHz beveled, single-element transducer rotating at 1800 rpm (MicroView, CardioVascular Imaging Systems Inc). This catheter is equipped with a 2.9F 15-cm-long sonolucent distal sheath with a common lumen that alternatively houses the guidewire (during catheter introduction) or the transducer (during imaging after the guidewire has been pulled back), but not both. This design avoids direct contact of the IVUS imaging core with the vessel wall. The IVUS transducer was withdrawn through the stationary imaging sheath by an ECG-triggered pullback device with a stepping motor developed at the Thoraxcenter Rotterdam.<sup>28</sup>

## ECG-Gated 3D IVUS Image Acquisition

The ECG-gated image acquisition and image digitization was performed by a workstation initially designed for the 3D reconstruction of echocardiographic images<sup>28</sup> (Echoscan, TomTec). This workstation received input from the IVUS machine (video) and the patient (ECG signal) and on the other hand, controlled the motorized transducer pullback device.

The steering logic of the workstation considered the heart rate variability and checked for the presence of extrasystoles during image acquisition and digitization (Fig 1↓). First, the RR intervals were measured over a 2-minute period to define the upper and lower limits of the range of acceptable RR intervals (mean value $\pm$ 50 ms). IVUS images were acquired 40 ms after the peak of the R wave. When the length of the RR interval met the preset range, the IVUS image was stored in the computer memory. Consecutively, the IVUS transducer was withdrawn 200  $\mu$ m to acquire the next image. Although the longitudinal resolution available with this technical setup is 100  $\mu$ m,<sup>28</sup> in the present study only one IVUS image per 200  $\mu$ m axial arterial length was acquired. Thus, an average of 114 images per segment were digitized and analyzed (range, 48 to 200 images per segment; corresponding segment length, 9.6 to 40.0 mm).



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### **Figure 1.**

IVUS images were acquired 40 ms after peak of R wave and stored (accepted) in computer memory only if RR intervals met predefined range (top). Consecutively, transducer was withdrawn 200  $\mu\text{m}$  to adjacent acquisition site (step) to acquire next image. If an RR interval did not meet range, image was not stored (rejected), and transducer was kept at that site until an image was acquired. Image acquisition and motorized pullback were controlled by steering logic of image acquisition workstation. Automated detection of intimal and medial boundaries was first performed on two perpendicular longitudinal sections (X, Y) reconstructed from image data of entire 3D stack of images (bottom); edge information of these longitudinal contours was represented as points on planar images, defining there the center and range of final automated contour detection process.

## **IVUS Analysis Protocol**

Each set of digitized IVUS images was analyzed off-line by two independent observers using an automated, computerized contour detection algorithm.<sup>29 30 31</sup> These measurements (Ia and II) were compared to study the interobserver variability. Blinded analyses were repeated by the first observer after an interval of at least 6 weeks. These measurements (Ia and Ib) were compared to study the intraobserver variability.

Two hundred planar images were randomly selected for “manual” analysis by a third investigator (MA-III) who was experienced in IVUS image analysis but blinded to the (above) automated contour detection results. This analyst could review the videotape to ensure a maximum accuracy of contour tracing, performed within an average of 4.1 minutes per image. Validation of manual CSA measurements by IVUS has been reported previously.<sup>32 33 34</sup> These measurements were compared with the automated contour detection analysis made by observer I.

## Data Analysis

The CSA measurements included the lumen and EEM CSA. Plaque+media CSA was calculated as EEM minus lumen CSA, and the CSA plaque+media burden was calculated as plaque+media CSA divided by EEM CSA. The EEM CSA (which represents the area within the border between the hypoechoic media and the echoreflexive adventitia) has been shown to be a reproducible measure of the total arterial CSA. As in many previous studies using IVUS, plaque+media CSA was used as a measure of atherosclerotic plaque, because ultrasound cannot measure media thickness accurately.<sup>35</sup> Lumen,

EEM, and plaque+media volumes were calculated as

where  $H$  is the thickness of a coronary artery slice, represented by a single tomographic IVUS image, and  $n$  is the number of IVUS images in the 3D data set. The volumetric plaque+media burden was calculated as plaque+media volume divided by EEM volume.

Plaque composition was assessed visually to identify lesion calcium. Calcium produced bright echoes (brighter than the reference adventitia), with acoustic shadowing of deeper arterial structures. The largest arc(s) of target lesion calcium was identified and measured in degrees with a protractor centered on the lumen. The overall length (in mm) of lesion calcium was measured by use of the length measurements provided by the 3D reconstruction.

## Computerized Contour Detection in ECG-Gated 3D IVUS

### Steps Involved in Image Analysis

Two longitudinal sections were constructed, and contours corresponding to the lumen-tissue and media-adventitia interfaces were automatically identified (Fig 1↑). The necessity to manually edit these contours was significantly reduced, because cyclic “saw-shaped” image artifacts that can hamper the automated detection in nongated image sets were virtually abolished (Fig 2↓). The sufficiency of the contour detection was visually checked, requiring an average of 5 minutes. If necessary, these longitudinal contours were edited with computer assistance (see below) within <1 minute. The longitudinal contours were transformed to individual edge points on the planar images, defining center and range of the automated boundary search on the planar images.



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## **Figure 2.**

Example of automated 3D contour detection analysis in diseased left anterior descending coronary artery. Range of 14.6-mm-long IVUS reconstruction and analysis is indicated by arrowheads in angiograms (top) taken from opposite angiographic projections. Cut planes of two reconstructed longitudinal sections (X, Y; lower left) are indicated on planar IVUS image (lower right), depicting calcification (Ca) of atherosclerotic plaque. Horizontal cursor on longitudinal sections can be used to scroll from distal (dist.) to proximal (prox.) through planar images. Thickness of that cursor is artificially increased to improve visibility (true thickness=half a scan line). 3D approach permitted interpretation in longitudinal dimension and facilitated tracing of estimated external vascular contour in acoustic shadowing behind calcium. Angiograms (top) and radiographic image of ultrasound catheter during image acquisition (insert, top left) illustrate that analyzed arterial segment was relatively straight and showed no more than mild vessel curvatures. As linear 3D analysis systems do not account for vascular curvatures, this premise was important because it limits curve distortion–induced deviation of volumetric measurements.

Subsequently, contour detection of the planar images was performed. The axial location of an individual planar image was indicated by a cursor, which was used to scroll through the entire set of planar images while the detected contours were visually checked. Correct detection of the longitudinal contours

minimized the need for computer-assisted editing of the cross-sectional contours. Careful checking and editing of the contours of the planar images was performed within an average of 25 minutes. Finally, the contour data of the planar images were used for the computation of the results.

## Minimum-Cost Algorithm and Computer-Assisted Contour Editing

A minimum-cost algorithm was used to detect the luminal and external vessel boundaries.<sup>29</sup> Each digitized IVUS image was resampled in a radial format (64 radii per image); a cost matrix representing the edge strength was calculated from the image data. For the boundary between lumen and plaque, the cost value was defined by the spatial first derivative.<sup>36</sup> For the external vessel boundary, a cross-correlation pattern matching process was used for the cost calculations. The path with the smallest accumulated value was determined by dynamic programming techniques.<sup>29</sup> The computer-assisted editing differed considerably from conventional manual contour tracing. The computer mouse was pointed on the correct boundary to give that site a very low value in the cost matrix, and subsequently the automated detection of the minimum cost path was updated within <1 second. Editing the contour of a single slice caused the entire data set to be updated (dynamic programming).

## Handling of Side Branches and Calcification

Side branches with a relatively small ostium were generally ignored by the algorithm as a result of its robustness, which means that the automated contour detection did not follow every abrupt change in the cost path. However, in branches with a large ostium, the contour did follow the lumen and vessel boundaries of the side branch. This was corrected by displaying the side branch in one of the longitudinal sections and interpolating the longitudinal vessel contours as straight lines. As a result, the side branch was outside the region of interest on the planar images. Similarly, small calcific portions of the plaque did not affect the detection of the external vessel boundary because of the robustness of the algorithm. In case of marked vessel wall calcification, the automated approach fails to detect the external vessel boundary. However, the 3D approach of the analysis system allowed interpretation of the external vessel boundary in the longitudinal dimension and facilitated tracing of a straight contour line behind the calcium.

## Previous Validation In Vitro and In Vivo

In vitro, the algorithm has been validated in a tubular phantom consisting of several segments. The automated measurements revealed a high correlation with the true phantom areas and volumes ( $r=.99$ ); mean differences were  $-0.7\%$  to  $3.9\%$  ( $SD<2.6\%$ ) for the areas and  $0.3\%$  to  $1.7\%$  ( $SD<3.8\%$ ) for the volumes of the various segments.<sup>30</sup> A comparison between automated 3D IVUS measurements in 13 atherosclerotic coronary specimen (area plaque+media burden  $<40\%$ ) in vitro and morphometric measurements on the corresponding histological sections revealed good correlations for measurements of lumen, EEM, plaque+media, and plaque+media burden ( $r=.94, .88, .80$ , and  $.88$  for areas and  $.98, .91, .83$ , and  $.91$  for volumes).<sup>31</sup> In vitro, both area and volume measurements by the automated system agreed well with results obtained by manual tracing of IVUS images, showing low ( $-3.7\%$  to  $0.3\%$ ) mean between-method differences with  $SD <6\%$  and high correlation coefficients ( $r\geq .97$  for areas and  $r=.99$  for volumes).<sup>31</sup> In vivo, using 3D IVUS image sets acquired during nongated continuous pullbacks through 20 diseased coronary segments, intraobserver and interobserver comparisons revealed high correlations ( $r=.95$  to  $.98$  for area and  $r=.99$  for volume)<sup>30</sup> and small mean differences ( $-0.9\%$  to  $1.1\%$ ), with  $SD$  of lumen, EEM, and plaque+media not exceeding  $7.3\%$ ,  $4.5\%$ , and  $10.9\%$  for

areas and 2.7%, 0.7%, and 2.8% for volumes. The time of (automated) analysis in that study was  $69\pm 19$  minutes. Importantly, that study did not include segments with more than focal calcification, more than one side branch, or extensive systolic-diastolic movement artifacts in the longitudinally constructed images.

## Statistical Analysis

Quantitative data were given as mean $\pm$ SD; qualitative data were presented as frequencies. According to Bland and Altman,<sup>37</sup> the intraobserver and interobserver agreement (reproducibility) of the contour detection method was assessed by determining the mean and SD of the between-observation and between-observer differences, respectively. The results of the repeated contour analyses (Ia versus Ib), the independent contour detection analyses (Ia versus II), and the manual versus the contour analyses (III-MA versus Ia) were compared by the two-tailed Student's *t* test for paired data analysis and linear regression analysis; values of  $P<.05$  were considered statistically significant.

## Results

### Feasibility and Acquisition and Processing Time

The gated IVUS image acquisition required  $3.9\pm 1.5$  minutes (1.5 to 6.9 minutes) per coronary segment, which corresponds to  $2.0\pm 0.1$  seconds (1.7 to 2.3 seconds) per image (Table 1 $\downarrow$ ). All segments could be analyzed by the computerized contour detection system during an analysis time of  $34.3\pm 7.3$  minutes per segment (21.3 to 48.4 minutes), corresponding to  $0.3\pm 0.1$  minutes (0.2 to 0.5 minutes) per computerized IVUS image analysis.

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**Table 1.**

Feasibility and Processing Time

Seg	ECG Gating	Image Quality	Images/ Seg, n	Acquisition Time/Seg, min	Acquisition Time/Image, s	Analysis Time/Seg, min	A T n
1	+++	++	123	4.2	2.0	34.6	0
2	+++	++	66	2.1	1.9	22.4	0
3	+++	+++	146	4.7	1.9	36.9	0
4	+++	+++	200	6.9	2.1	42.3	0
5	+++	+	71	2.7	2.3	38.2	0
6	+++	++	194	6.8	2.1	47.8	0
7	+++	+++	84	2.9	2.0	28.6	0



	...	...	...	...	...	...	...
8	+++	++	74	2.7	2.2	29.7	0
9	+++	+++	150	4.7	1.9	37.3	0
10	+++	++	94	3.1	2.0	31.7	0
11	+++	++	48	1.5	1.9	21.3	0
12	++	+	129	4.9	2.3	48.4	0
13	+++	++	127	4.3	2.0	35.0	0
14	+++	+	147	5.7	2.3	46.4	0
15	+++	++	194	6.6	2.0	39.4	0
16	+++	++	106	3.5	2.0	36.9	0
17	+++	++	129	4.6	2.2	44.8	0
18	+++	++	150	5.4	2.2	37.3	0
19	+++	+++	148	4.5	1.8	37.1	0
20	+++	+++	152	5.2	2.0	37.5	0
21	+++	++	88	2.9	2.0	31.1	0
22	+++	++	110	3.1	1.7	33.3	0
23	+++	++	94	3.4	2.2	31.7	0
24	+++	++	100	3.5	2.1	33.1	0
25	+++	++	75	2.6	2.0	29.8	0
26	+++	+++	126	4.2	2.0	34.9	0
27	+++	+++	79	2.7	2.0	27.1	0
28	+++	+++	69	2.4	2.1	23.8	0
29	+++	+++	75	2.4	1.9	25.8	0
30	+++	+++	72	2.5	2.0	24.4	0

	III	III	III	III	III	III	III
Mean	...	...	114.0	3.9	2.0	34.3	0
SD	...	...	41.1	1.5	0.1	7.3	0
n	...	...	30	30	30	30	3

Seg indicates segment. ECG gating: +++, easy performance without image artifacts; ++, easy performance with a few cyclic image artifacts. Image quality: +++, excellent; ++, good; +, mediocre.

## IVUS Segment Characteristics

All but two of the segments (93%) contained at least one side branch (Table 2). The average number of side branches per segment was  $2.3 \pm 1.5$  (range, 0 to 6). Calcification was present in 17 segments (57%), 11 (37%) showed a single calcium deposit, and 6 (20%) contained multiple calcium deposits. The maximum arc of calcium was  $114 \pm 49^\circ$  ( $50^\circ$  to  $190^\circ$ ); in 6 segments, the length of the calcified portion exceeded 1 mm.

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**Table 2.**

Characteristics of Coronary Segments

The minimal lumen CSA as measured by the contour detection system was  $6.4 \pm 1.7$  mm<sup>2</sup> (3.5 to 9.7 mm<sup>2</sup>). The maximum and average CSA plaque+media burden were  $60.5 \pm 10.2\%$  (31.7% to 77.7%) and  $46.5 \pm 9.9\%$  (22.8% to 65.9%).

## Manual Tracing Versus Automated Contour Detection

In the 200 randomly selected image slices, the measurements of the lumen, EEM, and plaque+media CSAs and the CSA plaque+media burden obtained with the automated contour detection system ( $9.37 \pm 3.09$  mm<sup>2</sup>,  $18.33 \pm 6.70$  mm<sup>2</sup>,  $8.95 \pm 5.16$  mm<sup>2</sup>, and  $46.03 \pm 13.46\%$ , respectively) were similar to the results obtained by manual tracing ( $9.35 \pm 3.18$  mm<sup>2</sup>,  $18.37 \pm 6.62$  mm<sup>2</sup>,  $9.02 \pm 5.08$  mm<sup>2</sup>, and  $46.53 \pm 13.41\%$ ; n=200). Between-method differences were  $0.4 \pm 4.3\%$ ,  $-0.4 \pm 3.6\%$ ,  $-1.6 \pm 9.1\%$ , and  $-1.2 \pm 6.8\%$ , respectively (all *P*=NS). The correlations between the measurements provided by both methods were high ( $r \geq .98$ ; Fig 3).



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### **Figure 3.**

Correlation between results of measurements of lumen, EEM, and plaque+media (P+M) CSA and CSA P+M burden by automated contour detection (Ia) and conventional manual tracing (MA-III).

## **Reproducibility of the Contour Detection Analysis**

For measurements of lumen, EEM, and plaque+ media CSA and the CSA plaque+media burden (n=3421), both intraobserver ( $-0.4\pm 2.7\%$ ,  $-0.4\pm 1.8\%$ ,  $-0.4\pm 5.1\%$ , and  $-0.0\pm 4.2\%$ ) and interobserver ( $0.4\pm 5.2\%$ ,  $-0.9\pm 2.7\%$ ,  $-1.5\pm 7.2\%$ , and  $-1.5\pm 6.9\%$ ; all  $P<.001$ ) differences were low. Correlation coefficients were high for repeated measurements by the same observer ( $r=.99$ ) and measurements by the two observers ( $r\geq .97$ ; Fig 4↓). For the corresponding volumetric measurements (n=30), the intraobserver ( $-0.4\pm 1.1\%$ ,  $-0.4\pm 0.6\%$ ,  $-0.3\pm 1.0\%$ , and  $0.0\pm 0.4\%$ ) and interobserver ( $0.6\pm 2.9\%$ ,  $-0.8\pm 1.0\%$ ,  $-2.5\pm 3.2\%$ , and  $0.8\pm 1.5\%$ ;  $P<.05$ ) differences were also low, and high correlations were found for both intraobserver and interobserver comparisons ( $r=.99$ ; Fig 5↓).



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#### **Figure 4.**

Intraobserver variability (left; first [Ia] vs second [Ib] observation) and interobserver variability (right; first [Ia] vs second [II] observer) of measurements of lumen, EEM, and plaque+media (P+M) CSA and CSA P+M burden by automated contour detection analysis system.



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### **Figure 5.**

Intraobserver variability (left; first [Ia] vs second [Ib] observation) and interobserver variability (right; first [Ia] vs second [II] observer) of measurements of lumen, EEM, and plaque+media (P+M) volume and volumetric P+M burden by automated contour detection analysis system.

## **Discussion**

The present study demonstrates that (1) ECG-gated acquisition of 3D IVUS images is feasible, (2) there is a good agreement between the results provided by the automated contour detection method and manual border tracing, and (3) the automated contour detection analysis can be performed in a relatively short analysis time with a high degree of reproducibility.

3D reconstruction of IVUS images was first used to visually assess the spatial configuration of plaques, dissections, and stents and to perform basic measurements.<sup>16 17 19</sup> More recently, the 3D reconstruction systems have included algorithms for automated quantification of lumen dimensions.<sup>16 17 18 19 20 21 25 26 27</sup> The contour detection system used in the present study can be used for the detection of both the tissue-lumen boundary and the media-adventitia (EEM) boundary, and therefore plaque volume can be measured.

## **Feasibility**

Non-ECG-gated image acquisition is frequently marred by cardiac cycle-linked coronary artery vasomotion and IVUS catheter motion, which produce sawtooth artifacts in the reconstructed 3D images that can interfere with automated contour detection (both the ease of use and, presumably, reproducibility). Conversely, in the present ECG-gated image sets, the longitudinal contours were smooth and without such artifacts. Therefore, there was much less need to manually edit the automatically detected longitudinal contours. Moreover, the accuracy of the derived edge information improved the performance of the second automated contour detection step on the planar IVUS images. This reduction in manual editing time on both longitudinal and planar images accounts for the low time of analysis compared with a previous study using nongated image acquisition<sup>30</sup> (34 minutes and 69 minutes, respectively). Indeed, this represents a significant reduction in analysis time and as a consequence reduces the cost of the analysis. However, the ECG-gated 3D IVUS acquisition in the present study required a longer acquisition time than conventional motorized pullback (eg, non-ECG-triggered pullback at 0.5 mm/s). On average, only a 6-mm-long coronary segment could be imaged in 1 minute.

## Reproducibility of the Contour Detection

In the present study, the measurement of the lumen, EEM, and plaque+media CSA differed little from the results obtained by manual contour tracing of these borders; there were only small interobserver and intraobserver differences in both the planar and volumetric analyses. However, the reproducibility of the plaque+media measurements was lower than for the other measures, which may reflect the combined variability of both the luminal and the EEM contours, confirming previous *in vitro*<sup>31</sup> and *in vivo* data (nongated patient data)<sup>30</sup> and findings of others.<sup>38</sup> The reproducibility of the volumetric measurements was higher than for the CSA measurements, which may be a result of an averaging of the differences between the individual CSA measurements.

Although the segments in this ECG-gated contour detection study were nonselected and included calcified segments with some side branches, the reproducibility of the CSA measurements was consistently better than observed in a previous study using nongated contour detection.<sup>30</sup> We believe that the key factors explaining the overall high reproducibility of automated contour detection observed in this study are (1) the integrated analyses of the conventional cross-sectional image slices with two longitudinal sections and (2) the facilitated and improved detection as a result of the smoothness of the contours on the ECG-gated longitudinal IVUS sections.

## Reproducibility of Alternative Methods of Quantitative 3D IVUS

There is very little information on the reproducibility of 3D IVUS measurements using other measurement systems and algorithms. Matar and colleagues<sup>21</sup> reported a Pearson's correlation coefficient of .98 for an intraobserver study of lumen volume measurement by an automated threshold-based IVUS analysis system, confirming the low variability of the volumetric measurements observed in the present study. Another acoustic quantification system<sup>25</sup> performs measurements of lumen CSA and volume, based on the automated detection of the blood pool in single IVUS images acquired at random during the cardiac cycle.<sup>21 25</sup> Because the measurements are based on single-frame analysis, ECG-gated image acquisition may not influence the reproducibility of such systems.

Conversely, 3D contour detection-based analysis approaches benefit from an ECG-gated image acquisition.<sup>20</sup> Sonka and associates<sup>39 40</sup> developed an alternative 3D contour detection system that performs computerized detection of the luminal and external vascular boundaries in 3D sets of planar

IVUS images without the additional information provided by the longitudinal contours. In their study,<sup>39</sup> the correlation between automated and manually traced CSA measurements was quite good ( $r=.91$  and  $.83$  for lumen and plaque CSA, respectively). Using ECG-gated 3D IVUS, they found significantly improved results ( $r=.98$  and  $.94$  for lumen and plaque+media CSA, respectively),<sup>40</sup> underlining the significance of ECG-gated IVUS image acquisition. Most likely, other promising contour detection algorithms<sup>41 42</sup> for 3D analyses may also benefit from an ECG-gated image acquisition.

## Potential Sources of Error and Study Limitations

Problems related to IVUS in general<sup>43</sup> and to 3D reconstruction in particular<sup>22 23</sup> may influence the contour detection process. The quality of the basic IVUS images is crucial to both planar and 3D image analysis.<sup>22</sup> Incomplete visualization of the vessel wall, for example as caused by acoustic shadowing<sup>6</sup> from lesion-associated calcium, hampers conventional planar IVUS analyses; however, 3D IVUS allows interpretation in the axial dimension and estimated contour tracing of the external vascular boundary. Image distortion caused by nonuniform transducer rotation or noncoaxial IVUS catheter position in the lumen may create artifacts both in planar images and in 3D reconstruction.<sup>22</sup>

Vessel curvatures may cause differences between the movement of the distal transducer tip and the proximal part of the catheter (although the use of sheath-based IVUS catheters reduces the latter problem) and a significant distortion of the 3D image reconstruction.

Most importantly, linear 3D systems such as used in this study can provide only approximate values of the volumetric parameters<sup>44</sup> because they do not account for vascular curvatures and the real spatial geometry. In curved vascular segments, this results in an overestimation of plaque volume at the inner side (expansion) and an underestimation of plaque volume at the outer side (compression) of the curve.<sup>22</sup> Approaches combining data obtained from angiography and IVUS<sup>45 46 47 48</sup> can provide information on the real spatial geometry of the vessel. Unquestionably, the combined approaches have a unique potential, but currently these sophisticated techniques are still laborious, restricted to research applications, and not yet useful for routine off-line analysis of clinical IVUS examinations. In the present study, only relatively straight coronary segments, showing no more than mild vessel curvatures, were included. We felt that this premise was important to limit curve distortion–induced deviation of volumetric measurement,<sup>44</sup> because linear 3D analysis systems do not account for vascular curvatures.

Compared with conventional motorized transducer pullback at a uniform speed, ECG-gated image acquisition takes longer, which may limit its use before intervention, especially in patients with very severe coronary stenoses. Therefore, we currently perform ECG-gated IVUS examinations during diagnostic or follow-up catheterizations and at the presumed end point of coronary interventions.

## Clinical Implications

The examination of coronary arteries by IVUS permits the comprehensive assessment of atherosclerosis<sup>1 2 3 6 7 10 11</sup> and the evaluation of the instantaneous<sup>27 49</sup> and long-term effects of catheter-based interventions on the coronary lumen and plaque. To quantify these changes, anatomic landmarks such as side branches or spots of calcium can be used to define specific anatomic image slices for comparative analysis in serial studies.

The proposed 3D IVUS method, which permits reproducible and reliable contour detection of both lumen and plaque, may facilitate volumetric measurements<sup>10 30 31</sup> and obviate the need for laborious analyses based on Simpson's rule.<sup>15</sup> Furthermore, the use of ECG-gated image acquisition<sup>28</sup> increases the applicability of the contour detection algorithm by shortening the analysis time<sup>49</sup> and increasing the reproducibility of the method. These advantages may be most significant in studies that are expected to show only small changes in plaque and/or lumen over time (eg, in trials evaluating the progression or regression of atherosclerosis during pharmacological therapy<sup>10</sup>). In addition, because the time from the peak of the R wave to image acquisition can be varied, this method can be used to study the cyclic (systole versus diastole) changes in vessel dimensions.

## Conclusions

ECG-gated acquisition of 3D IVUS image sets is feasible and permits the application of automated contour detection to provide reproducible measurements of the lumen and atherosclerotic plaque CSA and volume in a relatively short analysis time.

## Selected Abbreviations and Acronyms

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CSA = CSA

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3D = three-dimensional

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EEM = external elastic membrane

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IVUS = intravascular ultrasound

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