Simpson's rule for the volumetric ultrasound assessment of atherosclerotic coronary arteries: a study with ECG-gated three-dimensional intravascular ultrasound

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Background Volumetric intravascular ultrasound (IVUS) assessment provides complementary information on atherosclerotic plaques. The volumes can be calculated by applying Simpson's rule to cross-sectional area data of multiple IVUS images, acquired with a fixed sample spacing, which is the distance (along the vessel's axis) between two images.

Objective To evaluate the effect of different sample spacings on the results of volumetric IVUS measurements.

Methods A stepwise electrocardiographically gated IVUS image-acquisition and automated three-dimensional analysis approach was applied to 26 patients. Twenty-eight coronary segments with mild-to-moderate coronary atherosclerosis were examined. Volumetric measurements of five images per mm (i.e. sample spacing 0.2 mm), representing a complete scanning of the coronary segment, were considered the optimal standard, against which volumetric measurements of three, one, and one-half images per mm (i.e. larger sample spacings) were compared.

Results The lumen, total vessel, and plaque volumes obtained with five images per mm were 183.3 ± 2.8, 350.6 ± 141.6, and 167.3 ± 89.2 mm^3. There was an excellent correlation ($r = 0.99$, $P < 0.001$) between these data and volumetric measurements with larger sample spacings. The volumetric measurements with larger sample spacings differed on average only by a little ($< 0.7\%$) from the optimal standard measurements. However, a relatively small, but significant, increase in SD of these differences was associated with the wider sample spacings ($< 3.6\%$, $P < 0.05$).

Conclusions The width of the sample spacing has a relatively small but significant impact on the variability of volumetric intravascular ultrasound measurements. This should be considered when designing future volumetric studies. The electrocardiographically gated acquisition of five IVUS images per mm axial length during a stepwise transducer pull-back is an ideal approach, particularly when addressing with IVUS volumetric changes that are assumed small, such as those expected in studies of the progression and regression of atherosclerosis.

Introduction

Intravascular ultrasound (IVUS) imaging depicts the coronary lumen and vessel wall, and permits the evaluation of atherosclerosis *in vivo* [1-5]. Volumetric data can be obtained with the use of motorized devices for controlled pull-back of the IVUS transducer [6], and allow a more comprehensive assessment of the distribution and therapy of coronary plaques [7-10]. The pioneers of volumetric IVUS assessment performed the volume calculation by applying Simpson's rule to the results of laborious manual analyses of cross-sectional IVUS images (one image per mm), acquired during a uniform transducer pull-back [8-10].

Three-dimensional IVUS and automated analysis systems have recently been developed [11-20]. Such approaches permit the automated analysis of a larger number of images. Accordingly, volumetric measurements can be performed on a larger number of IVUS images, acquired at a smaller sample spacing, which is the distance (along the vessel's axis) between two IVUS images used for volume calculation. However, the effect of different sample spacings on the results of volumetric IVUS measurements was not known. In the present study we evaluated this problem, using three-dimensional sets of IVUS images acquired with an electrocardiographically gated approach [21-23] for 28 atherosclerotic coronary segments of 26 patients. Volumetric measurements of five

images per mm (i.e. sample spacing 0.2 mm), acquired at the same phase of the cardiac cycle, were considered the optimal standard, insofar as they represented a complete scanning of the coronary segment. The purpose of this study was to evaluate the difference between the volumetric measurements obtained using the optimal standard method (five images per mm) and those with three, one, and one-half images per mm.

Methods

Study population

We examined 26 patients [of whom 21 (81%) were men] aged 54.9 ± 9.1 years during diagnostic (n = 19; 73%) and follow-up catheterization procedures after previous catheter-based interventions (n = 7; 27%) with IVUS, using an electrocardiographically gated three-dimensional image-acquisition station and a dedicated pull-back device [21–23]. In total 28 atherosclerotic coronary segments with mild-to-moderate atherosclerosis were studied. These segments were relatively straight on at least two angiograms from opposite angiographic projections. Segments with severe calcification were excluded from the study. The investigation was approved by the Medical Ethics Committee of the University Hospital Dijkzigt. All of the patients gave their written informed consent to participate in the study.

IVUS image acquisition

The coronary segments were examined with a mechanical IVUS system (ClearView; CardioVascular Imaging Systems Inc., Sunnyvale, California, USA) after standard intravenous premedication with 10 000 U heparin and 250 mg aspirin, and intracoronary administration of nitrates. Sheath-based IVUS catheters with 30 MHz single-element transducers (MicroView; CardioVascular Imaging Systems Inc.) were used. This catheter design is equipped with a 2.9Fr 15 cm long transparent distal sheath, which has a common distal lumen that houses the guide wire during catheter introduction and the transducer during imaging when the guide wire has been pulled back [24]. Electrocardiographically gated image acquisition was performed by using a three-dimensional image-acquisition station (EchoScan; TomTec, Munich, Germany), which also steered the dedicated pull-back device (stepping motor) to withdraw the IVUS transducer through the stationary imaging sheath [21]. After each 0.2 mm step, one IVUS image was acquired 40 ms after the peak of the R wave, assuring a complete scanning of the vascular segment. If the length of the R–R interval fell within the preset range, which was checked retrospectively by the acquisition station, the image was stored in the computer memory of the IVUS image-acquisition station. After an image had been stored, the following cardiac cycle was used to automatically move the transducer to the adjacent image-acquisition site, where the same procedure was repeated.

Automated contour analysis

The gated three-dimensional IVUS acquisition technique allowed measurements without systolic and diastolic artifacts and thus without gaps and overlaps between adjacent images. The IVUS analysis was performed off-line using a computerized contour-detection system [18,19,21,23,25] that permits the digitization of a maximum of 200 IVUS images and the automated detection of the luminal and external vascular boundaries (Fig. 1). It operates on the basis of the concept that longitudinal contours facilitate automated contour detection on the tomographic cross-sectional IVUS images by defining the center and the range of the boundary-detection process (Fig. 2). An analyst checked each detected contour and performed corrections, when this was required. The algorithm (the minimum-cost algorithm) has previously been described, and both its validation and its reproducibility have been reported [18,19,21,22,25].

In the present study, the entire contour-detection process (aiming at maximum accuracy) required 25 ± 5 min for five image samples per mm; at this sampling of five images per mm the 'interactive' component accounted for approximately 20 min of the overall analysis time. The different sample spacings did not affect the analysis time required for the automatic steps, but they did affect the time required for editing and visual checking of the contours. By increasing the sample spacing, the latter component could gradually be reduced to approximately 5 min (at one-half image per mm); the detection of the longitudinal contours appeared less feasible with a very large sample spacing (one-half image per mm). We experienced no adverse effects of the plaque morphology (e.g. calcium) on the computerized analysis, using wider sample spacings.

Comparisons between volumetric measurements in three-dimensional IVUS *in vitro* and measurements on the

Fig. 1
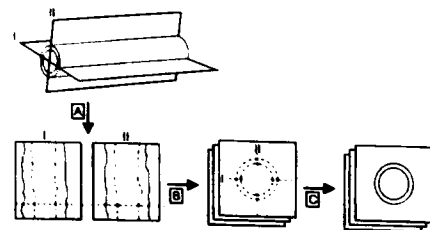
Principle of the intravascular ultrasound (IVUS) analysis system used. The stack of cross-sectional IVUS images is stored in the computer memory and sliced to provide two perpendicular longitudinal sections (I and II). Automated detection both of the luminal and of the external vascular contours is performed on these sections (A). The longitudinal contours are represented as individual edge points on the entire stack of cross-sectional IVUS images (B). They define the center and range of the final automatic contour-detection step, which is then performed on the cross-sectional IVUS images (C).

Fig. 2
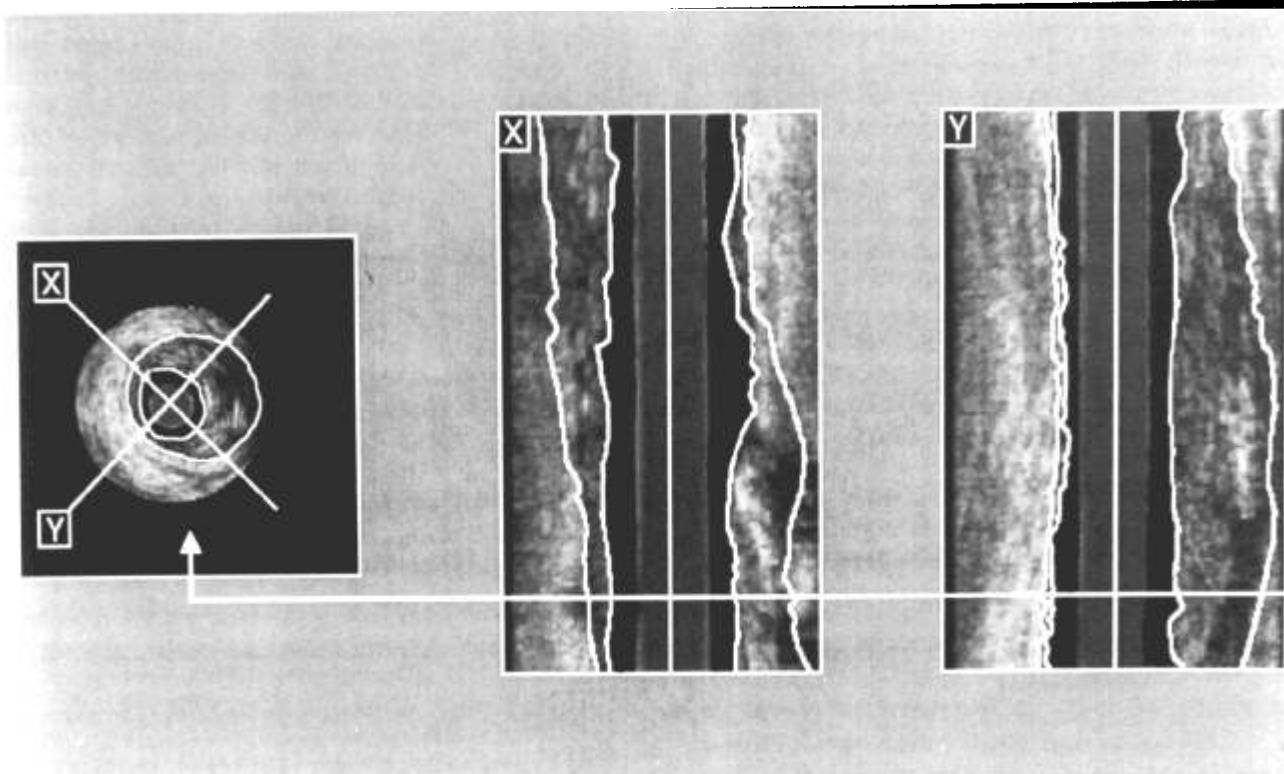
Example of a coronary segment analyzed by the automated intravascular ultrasound analysis system. The arrowhead indicates the position of the cross-sectional intravascular ultrasound image (left-hand panel) on the perpendicular longitudinal sections (X and Y).

corresponding histologic sections revealed high correlations (r = 0.83–0.98) [18], and the intra- and inter-observer differences of volumetric measurements *in vivo* were less than 1% with SD not exceeding 3.2% [21].

Data analysis

The lumen and total vessel cross-sectional areas were measured by the automated analysis system on each digital planar IVUS image. The area within the border between hypoechoic media and echoreflective adventitia has been shown to be a reproducible measure of the total cross-sectional area of the vessel. Because ultrasound cannot measure media thicknesses accurately [26], the plaque plus media dimensions were used as measures of the plaque burden, just like in many previous studies using IVUS. The plaque cross-sectional area was calculated as the total cross-sectional area of the vessel minus the cross-sectional area of the lumen. Lumen, total vessel, and plaque volumes were calculated by integrating all of the cross-sectional area measurements multiplied by the slice thickness (Simpson's rule), using the cross-sectional area measurements of five, three, one, and one-half images per mm (i.e. sample spacings of 0.2, 0.33, 1.0, and 2.0 mm). Volumetric measurements of five images per mm (i.e. a sample spacing of 0.2 mm), representing

a complete scanning of the vascular segment, were used as the optimal standard against which to evaluate the effect of larger sample spacings on the results of volumetric IVUS measurements.

Statistics

Values are expressed as means ± SD; qualitative data as prevalences. The volumetric measurements of five images per mm were compared with measurements using three, one, and one-half images per mm, using Student's paired t test. According to the method of Bland and Altman [27], the agreement between these volumetric measurements was assessed by determining the mean and SD of the between-measurement differences. The variances of these differences were tested against each other with Pitman's test [28]. Linear regression analysis was performed to evaluate the strength of the relation between the volumetric measurements of five images per mm and measurements with fewer images per mm. $P < 0.05$ was considered statistically significant.

Results

IVUS segment characteristics

The coronary segments examined with three-dimensional IVUS measurements were located in the left anterior

descending (n = 15), right circumflex (n = 11), and left circumflex coronary arteries (n = 2); they were on average 21.2 ± 7.3 mm long. The SD per segment of the lumen, total vessel, and plaque cross-sectional area measurements were on average 1.52 ± 0.98, 2.03 ± 1.46, and 1.81 ± 1.06 mm², and 5.56 ± 3.04 mm²; the corresponding ranges per segment (maximum minus minimum values) were 5.56 ± 3.04, 7.45 ± 4.46, and 6.94 ± 3.58 mm², respectively. All of the segments exhibited mild-to-moderate atherosclerotic lesions and the minimum cross-sectional area of the lumen was on average 6.7 ± 2.5 mm². The percentage of the total vessel cross-sectional area that was covered with plaque (the percentage cross-sectional area plaque burden) varied by 30 ± 10% along individual coronary segments; at the minimum lumen site the percentage cross-sectional area plaque burden was 56 ± 11%.

## Volumetric data and results of linear regression analyses

The lumen, total vessel, and plaque volumes of five IVUS

images/mm (the optimal standard) were 183.3 ± 62.8, 350.6 ± 141.6, and 167.3 ± 89.2 mm³. Volumetric measurements of fewer images per mm (i.e. larger sample spacings) correlated excellently with these optimal standard measurements: values of 0.99 for Pearson's correlation coefficient were found for the lumen, total vessel, and plaque volumes of each sample spacing compared (slopes: 0.99 for all; intercepts: between −0.1 and 1.5 mm³). However, the increase in sample spacing was often associated with an increase in the standard error of the estimate (lumen 0.7, 2.6, and 3.6 mm³; total vessel 1.2, 3.0, and 4.6 mm³; plaque 0.9, 3.2, and 4.1 mm³).

## Agreement between volume measurements using different sample spacings

The agreement between volumes of three, one, and one-half images per mm and the optimal standard volumes (five images per mm) is shown in Figure 3. The volumetric measurements of the larger sample spacings differed on average only by a little (< 0.7%) from the

Fig. 3
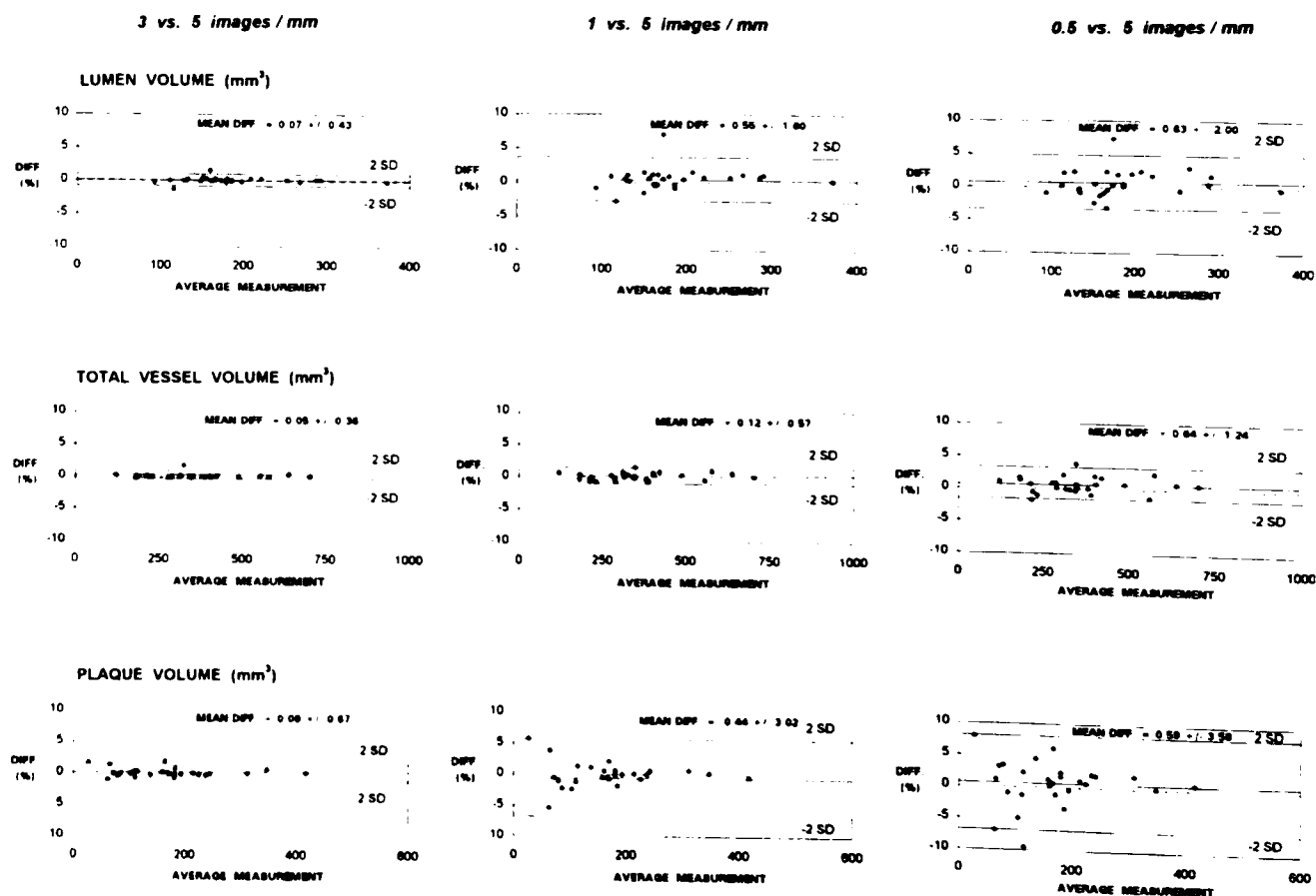
Volumetric measurements of three, one, and one-half images per mm compared with the optimal standard of five images per mm. The between-measurement differences (DIFF) were plotted against the averages of corresponding measurements, obtained at different sample spacings. Unbroken lines indicate the mean between-difference and the range ±2SD. Mean values of the between-measurement differences ±SD are given.

Fig. 4
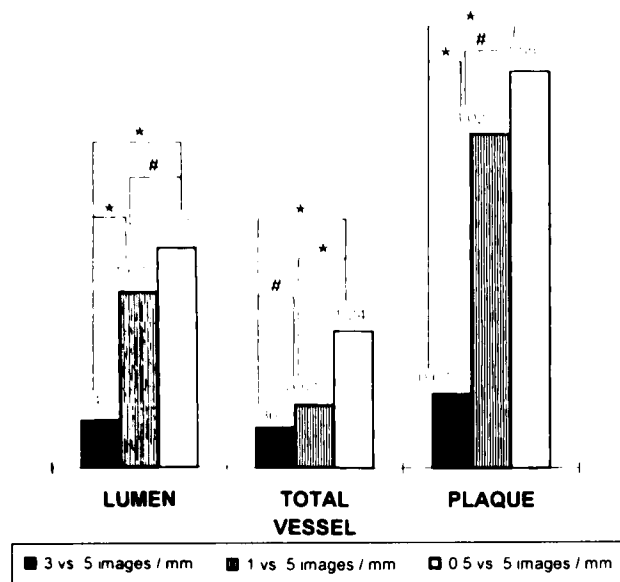
SD (%) of the between-measurement differences (five images per mm as the optimal standard versus three, one, and one-half images per mm). The SD were relatively low, but increased significantly ($*P < 0.05$, $*P < 0.01$) coincident with the increase in sample spacing (i.e. decrease in number of images per mm), which indicated that there was a larger variability of the agreement with the optimal standard measurements.

optimal standard. However, a relatively small but significant increase in SD of these between-measurement differences ($< 3.6\%$, $P < 0.05$) was associated with the increased width of the sample spacing (Fig. 4).

Discussion

Although quantitative angiographic techniques permit only the interpolated measurement of the diameter stenosis and plaque dimensions [29], direct cross-sectional visualization and measurement of the coronary lumen and plaque can be obtained from IVUS assessment [1–5]. Initially, most IVUS studies were restricted to the measurement of diameters and cross-sectional areas, but accumulated evidence has shown that volumetric IVUS measurements provide important complementary information [7–10,16,18,19,21].

Volumetric data can be obtained by applying Simpson's rule to the cross-sectional area data of multiple IVUS images, acquired at a fixed sample spacing, which is the distance (along the vessel's axis) between two image samples. Sampling of a huge number of image samples would theoretically be ideal, but currently it is not realistic, for such an approach is limited by the large computer memory and increased analysis time required. The present study was the first to quantify the consequences

of different sample spacings on volumetric three-dimensional IVUS measurements in vivo. An electrocardiographically gated stepwise image-acquisition approach [20] permitted the acquisition of a reliable standard for the volume measurements: five images per mm (i.e. a sample spacing of 0.2 mm), acquired during the same phase of the cardiac cycle, represented a complete scanning of the arterial segment because the mean width of the IVUS beam in the long vessel axis (out-of-plane resolution) was known to be 0.2 mm [30].

Our data demonstrate that the width of the sample spacing has a significant impact on the variability of volumetric IVUS measurements, even for lesions with mild-to-moderate atherosclerotic disease. An increased sample spacing width was associated with a higher variability of the agreement between these volume measurements and the optimal standard results. Although this effect remained relatively small, it should be considered when designing future volumetric IVUS studies, particularly when addressing volumetric changes that are assumed small, such as those expected, for instance, in studies evaluating the progression and regression of atherosclerosis.

Previous volumetric IVUS studies

The first clinical volumetric IVUS studies of Matar et al. [8] and Weissman et al. [9] addressed the mechanisms of the improvement of the lumen after directional coronary atherectomy, whereas Dussaillant et al. [10] investigated plaque ablation by rotational atherectomy of noncalcified coronary lesions. In these IVUS studies, interesting mechanistic and pathophysiologic insights were gained by computing volumes from the cross-sectional area information of one end-diastolic image per mm, acquired during continuous motorized pull-backs (at 0.5 and 1.0 mm/s) [8–10]. The application of dedicated algorithms for automated boundary detection in three-dimensional IVUS image sets allowed volume measurements using a much higher number of IVUS images. A validation of lumen volume measurements by a threshold-based three-dimensional IVUS system has been reported by Matar et al. [16]. Our group has validated a contour-detection-based three-dimensional IVUS analysis system that permits the measurement of lumen and vessel volumes [18,19]. As performed in the present study, the latter analysis system can be used in combination with a stepwise electrocardiographically gated image-acquisition approach [21,22]. The electrocardiographic gating improved the performance of the algorithm for automated contour detection, the efficacy of which had also been demonstrated by Sonka et al. [17] and Dhawale et al. [31,32].

Limitations and potential sources of error

Curvatures of the transducer pull-back trajectory, as seen in curved vessel segments, may cause errors in volumetric

IVUS measurements. Therefore, IVUS volume measurements from linear approaches (by manual as well as automated methods) actually represent estimates of the true volumes. To minimize the curve-induced error, we studied only segments that were straight on angiograms obtained from at least two opposite projections. Consequently, our data can not simply be transferred to lesions in significantly curved vascular segments. Combined processing of IVUS and biplane angiographic data [33] has the potential to overcome this problem in the future, but these approaches are still very laborious and only limited data are available [24]. Nevertheless, the combined approaches are beneficial, insofar as they may permit one to determine the curve-induced error in volumetric measurements. This problem is practically interesting and should be addressed in another study, using such combined methods. The data of this study were obtained for atherosclerotic lesions with mild-to-moderate disease (a 'progression–regression study population'); the use of larger sample spacings for more stenotic lesions (e.g. pre-intervention) could result in even more significant increases in measurement variability.

Implications for clinical trials

The present study demonstrated the effect of different sample spacings on the results of volumetric IVUS measurements, but no 'blanket' recommendation, valid for any volumetric IVUS study, can be given. The choice of sample spacing must be considered in the light of the study population examined and the analysis technique used. The additional variability introduced by the use of larger sample spacings might be negligible if a study addresses volumetric differences that are assumed large, or uses an analysis approach with a relatively high measurement variability, or both.

The coronary segments evaluated in this study exhibited mild-to-moderate coronary artery disease, of a degree typical of that in progression–regression studies. In such studies, potentially small changes in plaque or lumen volume may occur [7]. Therefore we may consider the use of automated analysis systems that permit both a rapid analysis of a large number of IVUS images at inherently low measurement variability, and volumetric measurements at a very low sample spacing. The acquisition of five images per mm axial length during electrocardiographically gated image acquisition and electrocardiographically triggered stepwise transducer pull-backs is ideal, and allows complete scanning of an entire arterial segment without any 'gap' or 'blind spot'. When other, nongated methods are used, complete scanning of the vessel segment cannot be guaranteed with five images per mm (and even with more images per mm). It was not the objective of this study to address the complex problems arising from nongated image acquisition, but it has been our experience that at least 10 images per mm (ideally even more) should then be acquired.

In conclusion, the width of the sample spacing has a relatively small but significant impact on the variability of volumetric intravascular ultrasound measurements. This should be considered when designing future volumetric studies. The electrocardiographically gated acquisition of five IVUS images per mm axial length during a stepwise transducer pull-back is an ideal approach, particularly when addressing with IVUS volumetric changes that are assumed small, such as those expected in studies of the progression and regression of atherosclerosis.

References

1 Ge J, Erbel R, Zamorano J, Koch L, Kearney P, Gorge G, et al.: Coronary artery remodeling in atherosclerotic disease: an intravascular ultrasonic study in vivo. Coron Artery Dis 1993, 4:981–986.

2 Pinto FJ, Chenzbraun A, Botas J, Valantine HA, St Goar FG, Alderman EL, et al.: Feasibility of serial intracoronary ultrasound imaging for assessment of progression of intimal proliferation in cardiac transplant recipients. Circulation 1994, 90:2348–2355.

3 Mintz GS, Painter JA, Pichard AD, Kent KM, Satler LF, Popma JJ, et al.: Atherosclerosis in angiographically "normal" coronary artery reference segments: an intravascular ultrasound study with clinical correlations. J Am Coll Cardiol 1995, 25:1479–1485.

4 Erbel R, Ge J, Bockisch A, Kearney P, Görge G, Haude M, et al.: Value of intracoronary ultrasound and Doppler in the differentiation of angiographically normal coronary arteries: a prospective study in patients with angina pectoris. Eur Heart J 1996, 17:880–889.

5 Alfonso F, Macaya C, Goicolea J, Hernandez R, Segovia J, Zamorano J, et al.: Determinants of coronary compliance in patients with coronary artery disease: an intravascular ultrasound study. J Am Coll Cardiol 1994, 23:879–884.

6 Fuessl RT, Mintz GS, Pichard AD, Kent KM, Satler LF, Popma JJ, et al.: In vivo validation of intravascular ultrasound length measurements using a motorized transducer pullback system. Am J Cardiol 1996, 77:1115–1118.

7 von Birgelen C, Slager CJ, Di Mario C, de Feyter PJ, Serruys PW: Volumetric intracoronary ultrasound: a new maximum confidence approach for the quantitative assessment of progression–regression of atherosclerosis? Atherosclerosis 1995, 118 (suppl):S103–S113.

8 Matar FA, Mintz GS, Farb A, Douek P, Pichard AD, Kent KM, et al.: The contribution of tissue removal to lumen improvement after directional coronary atherectomy. Am J Cardiol 1994, 74:647–650.

9 Weissman NJ, Palacios IF, Nidorf SM, Dinsmore RE, Weyman AE: Three-dimensional intravascular ultrasound assessment of plaque volume after successful atherectomy. Am Heart J 1995, 130:413–419.

10 Dussaillant GR, Mintz GS, Pichard AD, Kent KM, Satler LF, Popma JJ, et al.: Effect of rotational atherectomy in noncalcified atherosclerotic plaque: a volumetric intravascular ultrasound study. J Am Coll Cardiol 1996, 28:856–860.

11 Rosenfield K, Losordo DW, Ramaswamy K, Pastore JO, Langevin RE, Razvi S, et al.: Three-dimensional reconstruction of human coronary and peripheral arteries from images recorded during two-dimensional intravascular ultrasound examination. Circulation 1991, 84:1938–1956.

12 Coy KM, Park JC, Fishbein MC, Laas T, Diamond GA, Adler L, et al.: In vitro validation of three-dimensional intravascular ultrasound for the evaluation of arterial injury after balloon angioplasty. J Am Coll Cardiol 1992, 20:692–700.

13 Mintz GS, Pichard AD, Satler LF, Popma JJ, Kent KM, Leon MB: Three-dimensional intravascular ultrasonography: reconstruction of endovascular stents in vitro and in vivo. Clin Ultrasound 1993, 21:609–615.

14 Evans JL, Ng KH, Wiet SG, Vonesh MJ, Burns WB, Radvany MG, et al.: Accurate three-dimensional reconstruction of intravascular ultrasound data: spatially correct three-dimensional reconstructions. Circulation 1996, 93:567–576.

15 von Birgelen C, Kutryk MJB, Gil R, Ozaki Y, Di Mario C, Roelandt JRTC, *et al.*: **Quantification of the minimal luminal cross-sectional area after coronary stenting by two- and three-dimensional intravascular ultrasound versus edge detection and videodensitometry.** *Am J Cardiol* 1996, 78:520-525.

16 Matar FA, Mintz GS, Douek P, Farb A, Virmani R, Saturnino PJ, *et al.*: **Coronary artery lumen volume measurement using three-dimensional intravascular ultrasound: validation of a new technique.** *Cathet Cardiovasc Diagn* 1994, 33:214-220.

17 Sonka M, Liang W, Zhang X, De Jong S, Collins SM, McKay CR: **Three-dimensional automated segmentation of coronary wall and plaque from intravascular ultrasound pullback sequences.** In *Computers in Cardiology 1995.* Los Alamitos: IEEE Computer Society Press; 1995:637-640.

18 von Birgelen C, van der Lugt A, Nicosia A, Mintz GS, Gussenhoven EJ, de Vrey E, *et al.* **Computerized assessment of coronary lumen and atherosclerotic plaque dimensions in three-dimensional intravascular ultrasound correlated with histomorphometry.** *Am J Cardiol* 1996, 78:1202-1209.

19 von Birgelen C, Di Mario C, Li W, Schuurbiers JCH, Slager CJ, de Feyter PJ, *et al.*: **Morphometric analysis in three-dimensional intracoronary ultrasound: an in-vitro and in-vivo study using a novel system for the contour detection of lumen and plaque.** *Am Heart J* 1996, 132:516-527.

20 Roelandt JRTC, Di Mario C, Pandian NG, Li W, Keane D, Slager CJ, *et al.*: **Three-dimensional reconstruction of intracoronary ultrasound images: Rationale, approaches, problems, and directions.** *Circulation* 1994, 90:1044-1055.

21 von Birgelen C, de Vrey EA, Mintz GS, Nicosia A, Bruining N, Li W, *et al.*: **ECG-gated three-dimensional intravascular ultrasound: feasibility and reproducibility of the automated analysis of coronary lumen and atherosclerotic plaque dimensions in humans.** *Circulation* (in press).

22 von Birgelen C, Mintz GS, Nicosia A, Foley DP, van der Giessen WJ, Bruining N, *et al.*: **Electrocardiogram-gated intravascular ultrasound image acquisition after coronary stent deployment facilitates on-line three-dimensional reconstruction and automated lumen quantification.** *J Am Coll Cardiol* 1997, 30:436-443.

23 Bruining N, von Birgelen C, Di Mario C, Prati F, Li W, Den Hood W, *et al.*: **Dynamic three-dimensional reconstruction of ICUS images based on an ECG-gated pull-back device.** In *Computers in Cardiology 1995.* Los Alamitos: IEEE Computer Society Press; 1995:633-636.

24 von Birgelen C, Mintz GS, de Feyter PJ, Bruining N, Nicosia A, Di Mario C, *et al.*: **Reconstruction and quantification with three-dimensional intracoronary ultrasound: an update on techniques, challenges, and future directions.** *Eur Heart J* 1997, 18:1056-1067.

25 Li W, von Birgelen C, Di Mario C, Boersma E, Gussenhoven EJ, van der Putten N, *et al.*: **Semi-automatic contour detection for volumetric quantification of intracoronary ultrasound.** In *Computers in Cardiology 1994.* Los Alamitos: IEEE Computer Society Press; 1994:277-280.

26 Mallery JA, Tobis JM, Griffith J, Gessert J, McRae M, Moussabeck O, *et al.*: **Assessment of normal and atherosclerotic arterial wall thickness with an intravascular ultrasound imaging catheter.** *Am Heart J* 1990, 119:1392-1400.

27 Bland JM, Altman DG: **Statistical methods for assessing agreement between two methods of clinical measurement.** *Lancet* 1986, ii:307-310.

28 Pitman EJG: **A note on normal correlation.** *Biometrika* 1939, 31:9-12.

29 de Feyter PJ, Serruys PW, Davies MJ, Richardson P, Lubsen J, Oliver MF: **Quantitative coronary angiography to measure progression and regression of coronary atherosclerosis: value, limitations, and implications for clinical trials.** *Circulation* 1991, 84:412-423.

30 Benkeser PJ, Churchwell AL, Lee C, Abouelnasr DM: **Resolution limitations in intravascular ultrasound imaging.** *J Am Soc Echocardiogr* 1993, 6:158-165.

31 Dhawale PJ, Griffin N, Wilson DL, Hodgson J McB: **Calibrated 3D reconstruction of coronary arteries using intravascular ultrasound with cardiac gating and catheter motion compensation.** In *Computers in Cardiology 1992.* Los Alamitos: Computer Society Press; 1992:30-33.

32 Dhawale PJ, Wilson DL, Hodgson JMcB: **Optimal data acquisition for volumetric intracoronary ultrasound.** *Cathet Cardiovasc Diagn* 1994, 32:288-299.

33 Slager CJ, Laban M, von Birgelen C, Krams R, Oomen JAF, den Boer A, *et al.*: **'ANGUS': a new approach to three-dimensional reconstruction of geometry and orientation of coronary lumen and plaque by combined use of coronary angiography and IVUS [abstract].** *J Am Coll Cardiol* 1995, 25 (suppl):144A.