

Failure of intravascular ultrasound to predict dissection after balloon angioplasty by using plaque characteristics

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Intravascular ultrasound (IVUS) is more sensitive than angiography in the assessment of plaque characteristics before intervention and vascular damage after balloon angioplasty. On the basis of IVUS data, this finding may improve clinical treatment by reducing the incidence of severe dissections after balloon angioplasty. We therefore studied the relation between plaque characteristics and dissections after balloon angioplasty. First, an *in vitro* study on atherosclerotic arteries ($n = 42$) was performed in which IVUS images were compared with histologic sections to validate the IVUS technique; second, the *in vitro* findings were compared with IVUS findings obtained *in vivo* ($n = 73$). Dissections were observed in 37 histologic sections and visualized on IVUS in 22 (59%) of the corresponding ultrasonic cross-sections; *in vivo* dissections were demonstrated by IVUS in 46 (63%) cases. Dissections were generally seen at the thinnest region of the plaque on both histologic sections (92%) and IVUS cross-sections (*in vitro* 83%; *in vivo* 93%). No significant relation was found between pre-interventional plaque characteristics such as composition features and eccentricity and the incidence, location, and extent of postinterventional dissections. Thus IVUS is able to identify dissections after balloon angioplasty, generally occurring at the site of the thinnest plaque diameter. However, neither the incidence nor the severity of these dissections was related to any of the preinterventional plaque characteristics. (*Am Heart J* 1997;134:1075-81.)

Intravascular ultrasound (IVUS) is a tomographic imaging technique that allows determination of plaque characteristics before and the presence, location, and extent of dissection after catheter-based interventions.¹⁻¹² It has been suggested that plaque characteristics, including plaque composition and eccentricity, may be determinants of the incidence and location of vascular damage after vascular interventions.¹³⁻¹⁷ Elucidation of this relation is an important issue because it may result in a more targeted strategy for the treatment of atherosclerotic disease. In this *in vitro* and *in vivo* study IVUS was used before and after balloon angioplasty of atherosclerotic arteries to document the presence, location, and extent of postinterventional dissection and to evaluate a possible relation with plaque characteristics. Histologic sections were used to validate the *in vitro* IVUS findings.

Methods

IVUS

A mechanical 30 MHz IVUS imaging system was used (DUMED, Rotterdam, The Netherlands) mounted on a 4.1F catheter. The axial resolution of the system is 80 μm ; lateral resolution is 225 μm at a depth of 1 mm. Images were displayed on a video monitor by a video-scanned memory and stored on an SVHS recorder. Both the *in vitro* and *in vivo* study were approved by the Local Committee on Human Research.

***In vitro* studies.** Atherosclerotic human vascular specimens, including coronary ($n = 33$) and iliofemoral arteries ($n = 9$) were harvested at autopsy and stored at -20°C . The specimens were thawed, side branches were tied off with sutures, and proximal and distal ends were connected to sheaths and fixed to a waterbath at room temperature. Distally, a reference segment was indicated with a needle at the 12 o'clock position (Fig. 1). During the study the arteries were pressurized at 100 mm Hg by a fluid reservoir containing water connected to the side arm of the proximal sheath. The specimens were studied with IVUS before and after balloon angioplasty. The largest lumen diameter seen in the segment by IVUS was used as reference site for the balloon diameter; the balloons were sized 1:1 to the lumen diameter. Balloon angioplasty was performed for 2 minutes, with a manometer-controlled pressure of 8 to 10 atm. Intervention was judged successful if the lumen area at the narrowest lumen site as seen on IVUS increased; otherwise a larger balloon was used. A displacement-sensing device was used to

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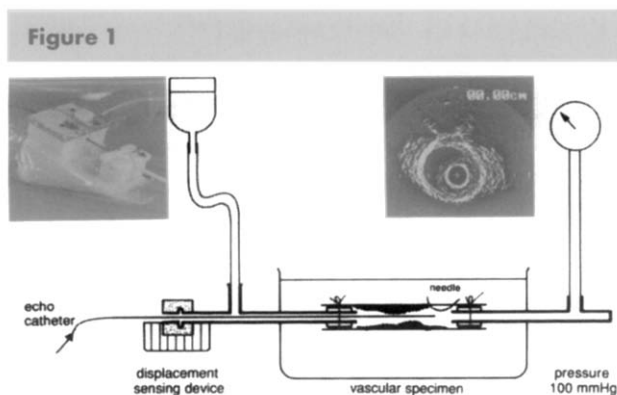


Figure 1

In vitro setup showing IVUS catheter advanced through sensing unit of displacement-sensing device and sheath toward pressurized vascular specimen. Needle attached distally to artery used as reference is seen at 12 o'clock position in ultrasound cross-section (arrow). Catheter tip position in relation to needle (00.00 cm) is indicated in right upper corner. *Left upper panel*, displacement-sensing device. Calibration = 1 mm.

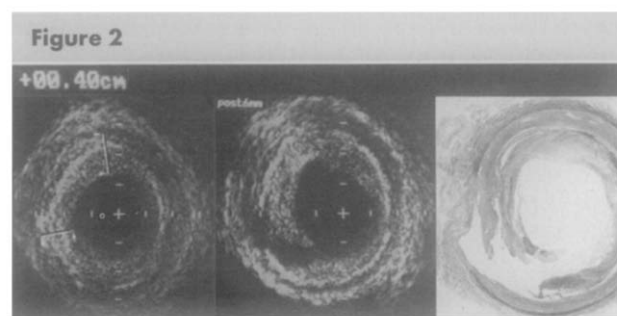


Figure 2

Corresponding IVUS cross-sections obtained in vitro at level 0.4 cm before and after balloon angioplasty and histologic counterpart. Minimum (8 o'clock position) and maximum (12 o'clock position) plaque thicknesses are indicated by arrowheads. Dissection is seen at thinnest region of plaque (arrow). +, Catheter. Calibration = 1 mm.

ensure reliable comparison of IVUS images before balloon angioplasty, with the same segment obtained after intervention.¹⁸ The ultrasound catheter was advanced through the displacement sensing unit by the sheath distally into the artery. A series of images was obtained during a manual pullback of the IVUS catheter. The distance between the tip of the ultrasound catheter and the reference needle in steps of 0.01 cm was automatically mixed with the IVUS images on the video screen (Fig. 1).

For histologic comparison the arteries were fixed under pressure (100 mm Hg) in 10% buffered formalin for 2 hours and subsequently decalcified in a standard rapid decalcifier solution (Ampex, Plainfield, Ill.) for 5 hours. The arteries were then processed for routine paraffin embedding. The site of the reference needle was marked with Indian ink.



Figure 3

Corresponding IVUS cross-sections obtained in vitro at level 1.8 cm before and after balloon angioplasty and histologic counterpart. Minimum (3 o'clock position) and maximum (9 o'clock position) plaque thicknesses are indicated by arrowheads. After balloon angioplasty dissection is seen at thickest region of plaque (arrow). +, Catheter. Calibration = 1 mm.

Transverse sections, 5 μ m thick perpendicular to the long axis of the vessel, were obtained at 1 mm intervals. The sections were arranged from proximal to distal with notation of the 12 o'clock position indicated by ink. The sections were stained with the elastic van Gieson and the hematoxylin eosin techniques. Qualitative and quantitative analysis of the histologic sections and the corresponding IVUS images was performed (interval 2 mm). From each vascular specimen studied, the IVUS cross-section at the narrowest lumen area (target site) before intervention and its corresponding ultrasound image after intervention were selected for comparison with the histologic sections. The ultrasound images and the histologic sections were analyzed by two independent and blinded observers.

In vivo studies. After giving informed consent, patients ($n = 73$) undergoing balloon angioplasty of the iliofemoral artery were studied with IVUS before and after intervention. An introducer sheath was placed into the femoral artery; the ultrasound catheter was advanced through the sheath in a retrograde manner into the iliac artery ($n = 10$) and in an antegrade manner into the femoral artery ($n = 63$). A series of IVUS cross-sections of the treated segment was recorded before and after intervention with 1 cm interval during manual pullback of the IVUS catheter. Corresponding IVUS cross-sections obtained before and after balloon angioplasty were analyzed. From each patient studied, the cross-section with the narrowest lumen area (target site) before balloon angioplasty was selected for comparison with the corresponding image obtained after intervention.

Data and statistics

IVUS cross-sections obtained before intervention were assessed for plaque composition and eccentricity. Plaque composition was divided into soft (echodense without shadowing) and hard (bright echoes with shadowing). Minimum and maximum plaque thickness was measured to determine plaque eccentricity (Figs. 2 and 3). Plaque thickness was calculated as the perpendicular distance between the plaque

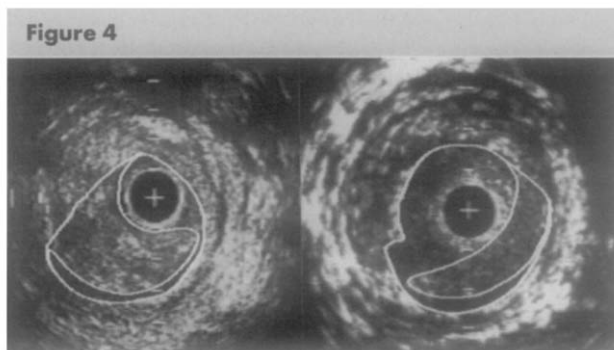


Figure 4
IVUS cross-sections obtained after balloon angioplasty in vivo. Lumen and dissection arm are contour traced. Dissection arm index is 59% and 31% in left and right panel, respectively. +, Catheter. Calibration = 1 mm.

surface, (intimal leading edge) and the internal elastic lamina; in the absence of a distinct internal elastic lamina on ultrasound, the transition between plaque and media or adventitia was used. An eccentric plaque was defined as a ratio between maximum and minimum plaque thickness ≥ 3 ; a concentric plaque as a ratio < 3 .

After intervention the presence, location, and extent of dissection on the IVUS cross-sections was scored. Dissection was defined as the presence of a tear in the intimal surface separating a part of the plaque from the rest of the underlying arterial wall.⁴ The location of the dissection in relation to the plaque thickness was scored; a nominal yes or no score indicated whether the dissection occurred at the thinnest region or not. The extent of dissection was graded in three ways. First, the extent of dissection was graded as an arc of the circumference with the center of the lumen as reference point; dissections were graded as minor (≤ 90 degrees) or major (> 90 degrees).¹⁹ In case of multiple dissections the total arc of the dissection was considered. Second, the depth of a dissection was graded as superficial or deep.⁹ A superficial dissection was defined as one that leaves some remaining plaque intact between the dissection and the underlying media; a deep dissection was defined as one that extends through the plaque to the media. Third, the dissection area index was assessed by comparing the area of the dissected arm to the neolumen area.⁸ The measurements of the dissection arm and neolumen area were performed with a digital video analyzer (Fig. 4).²⁰ In the corresponding histologic sections the presence, location and extent (minor or major; superficial or deep) of dissection was scored.

To test the reproducibility of plaque thickness and dissection arm index measurements in the in vitro and in vivo IVUS images, measurements were repeated by a second blinded observer. The mean and standard deviations of the paired differences between the two observers were calculated. The significance of the interobserver differences was

Table I. Incidence and location of dissections seen in the histologic sections and on IVUS

| | Total | Thinnest site |
|---------------------------|----------|---------------|
| In vitro (<i>n</i> = 42) | | |
| Histology | 37 (88%) | 34 (92%) |
| IVUS | 22 (52%) | 18 (82%) |
| In vivo (<i>n</i> = 73) | | |
| IVUS | 46 (63%) | 43 (93%) |

determined by a paired *t* test; the degree of observer variability was presented with a coefficient of variation defined as the standard deviation of paired differences divided by the mean of the absolute values. Interobserver variability of IVUS to assess the presence of hard plaque and the presence and extent of dissection in vivo has been previously assessed (hard plaque: kappa value 0.67, agreement 85%; dissection: kappa value 0.69, agreement 85%; paired difference of the extent of dissection 18 ± 48 degrees).²¹ The chi-squared test was used to assess differences in categorical variables and the Mann-Whitney test to assess differences in continuous variables. A *p* value < 0.05 was considered significant.

Results

In vitro studies

Dissections were seen in 37 of the 42 histologic sections occurring at the thinnest site of the plaque circumference in 34 (92%) specimens (Table I). In the corresponding IVUS cross-sections the dissection was correctly detected in 22 cases (sensitivity 59%); 18 of these 22 dissections were seen at the thinnest plaque site (Fig. 2). The occurrence of dissections not seen at the thinnest region on IVUS were histologically confirmed in three of the four cases (Fig. 3). Histologic review of these three sections demonstrated fibrous plaques; in two of these specimens the dissection was seen at the thinnest region in a nearby cross-section both on IVUS and on the histologic section.

Dissections were graded as minor in 19 and as major in 18 histologic sections. IVUS revealed minor and major dissections in 15 and seven cases, respectively (Table II). The extent of dissections measured in the histologic sections was larger (median 90 degrees; range: 0 to 270 degrees) than in the corresponding IVUS images (median 30 degrees, range 0 to 180 degrees) ($p < 0.001$).

In 15 cases dissections demonstrated on histologic examination (seven minor and eight major) were not identified by IVUS because of one of the following reasons: (1) the dissected portion of the plaque remained adherent to the vessel wall, (2) the ultrasound catheter

Table II. Incidence of minor and major dissections seen in the histologic sections and on IVUS

| IVUS | Histology | | | Total |
|------------------|---------------|------------------|------------------|-------|
| | No dissection | Minor dissection | Major dissection | |
| No dissection | 5 | 7 | 8 | 20 |
| Minor dissection | 0 | 9 | 6 | 15 |
| Major dissection | 0 | 3 | 4 | 7 |
| Total | 5 | 19 | 18 | 42 |

Table III. Relation between plaque characteristics (composition and eccentricity) and the incidence and extent of dissection seen on IVUS in vitro and in vivo

| | Dissection | | | | | | |
|-----------------------------|------------|-----------|----------|----------|-------------|------------|------------|
| | Present | Absent | Minor | Major | Superficial | Deep | DAI |
| IVUS in vitro | | | | | | | |
| Plaque composition | | | | | | | |
| Soft (<i>n</i> = 24) | 11 (46%) | 13 (54%)* | 5 (45%) | 6 (55%)* | 0 (0%) | 11 (100%)* | 29% ± 17%* |
| Hard (<i>n</i> = 18) | 11 (51%) | 7 (39%) | 10 (91%) | 1 (9%) | 1 (9%) | 10 (91%) | 20% ± 11% |
| Plaque eccentricity | | | | | | | |
| Eccentric (<i>n</i> = 21) | 9 (43%) | 12 (57%)* | 6 (76%) | 3 (33%)* | 0 (0%) | 9 (100%)* | 26% ± 18%* |
| Concentric (<i>n</i> = 16) | 10 (52%) | 6 (38%) | 8 (80%) | 2 (20%) | 1 (10%) | 9 (90%) | 26% ± 13% |
| IVUS in vivo | | | | | | | |
| Plaque composition | | | | | | | |
| Soft (<i>n</i> = 38) | 25 (66%) | 13 (34%)* | 17 (68%) | 8 (32%)* | 3 (12%) | 22 (88%)* | 45% ± 51%* |
| Hard (<i>n</i> = 35) | 21 (60%) | 14 (40%) | 16 (76%) | 5 (24%) | 3 (14%) | 18 (86%) | 44% ± 33% |
| Plaque eccentricity | | | | | | | |
| Eccentric (<i>n</i> = 47) | 28 (60%) | 19 (40%)* | 19 (68%) | 9 (32%)* | 4 (14%) | 24 (86%)* | 50% ± 51%* |
| Concentric (<i>n</i> = 26) | 18 (69%) | 8 (31%) | 14 (78%) | 4 (22%) | 2 (11%) | 16 (89%) | 35% ± 25% |

DAI, Dissection arm index.

**p* value not significant.

pushed the dissected plaque against the vessel wall, or (3) calcium hindered the visualization.

In 21 of 22 cases IVUS revealed a deep dissection; this was confirmed in the corresponding histologic sections.

Plaque composition assessed on IVUS images before intervention was soft in 24 cases and hard in 18 cases. Thirty-seven of the 42 IVUS cross-sections were available for analysis of eccentricity (calcification hampered quantitative assessment of plaque thickness in five cases); 21 eccentric plaques and 16 concentric plaques were observed. No significant relation was found between plaque characteristics and the incidence, location, and extent of dissection. Table III summarizes data on the relation between plaque characteristics and the incidence and extent of dissection obtained in the in vitro study. A larger number of major dissections were observed in soft plaques than in hard plaques ($p = 0.06$). However, in the histologic sections, a larger number of major dissections were found in plaques with calcification than in soft plaques (11 (63%) of 18 and 7 (37%) of 19, respectively; $p = 0.19$).

In vivo studies

In 46 (63%) of the 73 cases a dissection was evidenced at the target site (Table I). Dissections were seen at the thinnest region of the plaque in 43 of 46 cases (Fig. 5). Dissections were minor in 33 and major in 13 cases. The majority of dissections present were deep: 28 of 33 minor dissections and 12 of 13 major dissections.

The plaques were classified as soft in 38 cases and hard in 35 cases. Plaques were eccentric in 47 cases and concentric in 26 cases. Table III summarizes data on plaque characteristics and the incidence and extent of dissection in the in vivo study. No significant relation was found between plaque composition and eccentricity and the incidence and extent of dissection.

Interobserver analysis

There was good agreement between the two observers for the IVUS measurements. There were no significant differences for the minimum and maximum plaque thickness and ratio. For in vitro IVUS images the mean differences for minimum thickness, maximum

thickness, and ratio were low (0.00 ± 0.05 mm, 0.02 ± 0.08 mm, and 0.06 ± 0.88 , respectively); for in vivo the mean differences were similar (0.01 ± 0.08 mm, 0.01 ± 0.09 mm, and 0.07 ± 0.63 , respectively). The coefficient of variation for these measurements did not exceed 17%.

The mean difference for dissection arm index measured in the in vitro and in vivo study was $1.2\% \pm 2.7\%$ ($p = 0.052$) and $2.3 \pm 5.0\%$ ($p = 0.003$), respectively; the coefficient of variation was 11.2% and 11.5%, respectively.

Discussion

IVUS enables study of the lumen and the vessel wall before and after intervention; this explains the superiority of IVUS over angiography in assessing plaque characteristics and the presence of vascular damage.^{3,6,7,9} Previous histologic studies have shown that the presence and extent of dissection were related to lesion characteristics,^{13,14,16} which may improve clinical treatment by reducing the incidence of severe dissections after vascular interventions with IVUS-derived parameters of plaque characteristics.

This study investigated the potential of IVUS to detect the presence, location, and extent of dissection after balloon angioplasty and also examined the relation between these findings and plaque characteristics.

The incidence of dissection at the target site was 88% in the histologic sections and 52% and 63% in the in vitro and in vivo IVUS images, respectively. Reviewing the IVUS images obtained in the whole vascular specimen showed that the frequency of dissection increased in vitro from 22 (52%) to 30 (71%) and in vivo from 45 (63%) to 72 (99%) dissections. This finding raises the question of whether dissections at the target site are in fact absent or rather not visualized by IVUS. It has been suggested that histologic processing may have induced dissections, leading to false-negative results by IVUS; this situation is not likely because our previous experience showed that dissections did not occur in histologic sections far from the dilation site.²²

Moreover, comparison of the histologic sections and corresponding IVUS images revealed that IVUS underestimates the extent of dissections. This finding is particularly evident in hard plaques in which calcification may prevent imaging of the dissection cleft: the median difference in the extent of dissection in the histologic sections and IVUS images was 15 degrees (range -30 to 150 degrees) for soft plaques and 105 degrees (range 0 to 270 degrees) for hard plaques ($p < 0.01$).

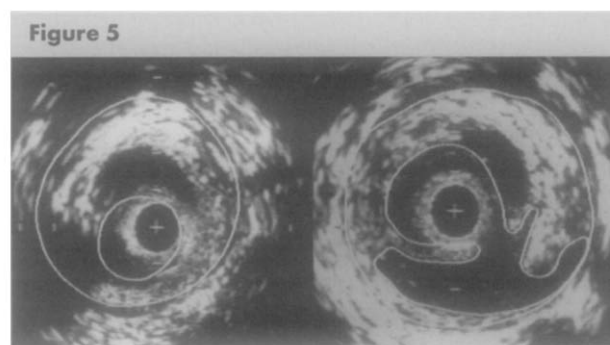


Figure 5
Corresponding IVUS cross-sections obtained before and after balloon angioplasty in vivo. Cross-sections are contour traced off-line, facilitating recognition of lumen area (inner contour) and media-bounded area (outer contour). Before intervention plaque was defined as eccentric and soft. After intervention dissection was seen. Note distinct hypoechoic region inside plaque that did not rupture during angioplasty. The guide wire present before intervention caused dropout at 7 o'clock position. +, Catheter. Calibration = 1 mm.

In this study dissections were generally found at the thinnest site of the plaque. Lee et al.²³ used a computational structural analysis based on IVUS images to identify regions of high stress in the atherosclerotic vessel wall. They concluded that by using this computational method it was possible to predict the location of plaque fracture after angioplasty but that IVUS may not be useful for predicting the ultimate balloon inflation pressure necessary to cause plaque fracture. Lee et al.²³ found that these high stress regions were generally located near the junction of plaque with a more normal vessel wall, which corresponds with the thinnest plaque regions in our study. Our findings are also in agreement with histologic study findings after balloon angioplasty showing a separation of the relatively inelastic plaque from the arterial wall near the edges of the plaque, together with a stretching of the arterial wall.²⁴⁻²⁶

We found no relation between plaque composition and eccentricity and the incidence, location, and extent of dissection in vitro or in vivo. These results differ from findings of other IVUS studies in which a relation was established between hard (calcified) plaque and the incidence or extent of dissection after balloon angioplasty,⁷⁻⁹ whereas others found a trend toward more postangioplasty dissections in soft (non-calcified) plaque than in hard (calcified) plaque.⁴ In our study the underestimation of the extent of dissection in calcified plaques may partly explain the absence of a relation between plaque composition and dissection.

as a larger number of major histologically confirmed dissections were found in plaques containing calcium (hard plaques) than in soft plaques. The latter result is in agreement with the previously mentioned histologic studies, which established a relation between calcification and the presence of dissection.^{14,16}

Similarly, contradictory IVUS results regarding plaque eccentricity and dissection were encountered: Tenaglia et al.⁵ found 50% dissections in both eccentric and concentric plaques, while Honye et al.⁷ found fractures predominantly in eccentric plaques (77% vs 22%). Because these contradictory results might be explained by different definitions of plaque eccentricity, we searched for a relation between dissection and plaque eccentricity based on the presence of a partly disease-free wall; however, no significant relation was found except for the dissection area index, which was larger in concentric than in eccentric lesions ($56\% \pm 51\%$ versus $28\% \pm 22\%$; $p = 0.04$).

Limitations

The number of segments investigated in the in vitro study was smaller compared with the in vivo study and was perhaps too small to allow firm conclusions to be drawn. The sensitivity of IVUS in detecting dissections at the target site in the in vitro study may have been lower compared with the in vivo study because mainly coronary arteries were studied, in which a stenting effect of the catheter may occur.⁸ The incidence of dissection increased when the whole dilated segment rather than the target site was studied. In this study the relation between plaque characteristics and dissection was studied at the target site because plaque morphologic characteristics and eccentricity significantly vary throughout the artery. The technical development of three-dimensional IVUS may result in an axial assessment of plaque morphologic characteristics in atherosclerotic segments and in a classification of plaque eccentricity based on volumetric measurements.²⁷⁻²⁹ Tissue identification by radiofrequency signal processing may in the future permit the classification of plaques that are prone to severe dissection.³⁰

Conclusion

Thus IVUS is able to identify dissections after balloon angioplasty, generally occurring at the site of the thinnest plaque. However, neither the incidence nor the severity of these dissections was related to any of the preinterventional plaque characteristics.

References

- Gussenhoven EJ, Essed CE, Lancée CT, Mastik F, Frielman P, van Egmond FC, et al. Arterial wall characteristics determined by intravascular ultrasound imaging: an in vitro study. *J Am Coll Cardiol* 1989;14:947-52.
- Tobis JM, Mallery JA, Gessert J, Griffith J, Mahon D, Bessen M, et al. Intravascular ultrasound cross-sectional arterial imaging before and after balloon angioplasty in vitro. *Circulation* 1989;80:873-82.
- Davidson CJ, Sheikh KH, Kisslo KB, Phillips HR, Peter RH, Behar VS, et al. Intracoronary ultrasound evaluation of interventional techniques. *Am J Cardiol* 1991;68:1305-9.
- The SHK, Gussenhoven EJ, Zhong Y, Li W, van Egmond F, Pieterman H, et al. The effect of balloon angioplasty on the femoral artery evaluated with intravascular ultrasound imaging. *Circulation* 1992;86:483-93.
- Tenaglia AN, Buller CE, Kisslo K, Stack RS, Davidson CJ. Mechanisms of balloon angioplasty and directional coronary atherectomy as assessed by intracoronary ultrasound. *J Am Coll Cardiol* 1992;20:685-91.
- Gerber TC, Erbel R, Görges G, Ge J, Rupprecht HJ, Meyer J. Classification of morphologic effects of percutaneous transluminal coronary angioplasty assessed by intravascular ultrasound. *Am J Cardiol* 1992;70:1546-54.
- Honye J, Mahon DJ, Jain A, White CJ, Ramee SR, Wallis JB, et al. Morphological effects of coronary balloon angioplasty in vivo assessed by intravascular ultrasound imaging. *Circulation* 1992;85:1012-25.
- Fitzgerald PJ, Ports TA, Yock PG. Contribution of localized calcium deposits to dissection after angioplasty: An observational study using intravascular ultrasound. *Circulation* 1992;86:64-70.
- Potkin BN, Keren G, Mintz GS, Douek PC, Pichard AD, Satler LF, et al. Arterial responses to balloon coronary angioplasty: an intravascular ultrasound study. *J Am Coll Cardiol* 1992;20:942-51.
- Hodgson JM, Reddy KG, Suneja R, Nair RN, Lesnfsky EJ, Sheehan HM. Intracoronary ultrasound imaging: correlation of plaque morphology with angiography, clinical syndrome and procedural results in patients undergoing coronary angioplasty. *J Am Coll Cardiol* 1993;21:35-44.
- Braden GA, Herrington DM, Downes TR, Kutcher MA, Little WC. Qualitative and quantitative contrasts in the mechanisms of lumen enlargement by coronary balloon angioplasty and directional coronary atherectomy. *J Am Coll Cardiol* 1994;23:40-8.
- Friedrich GJ, Moes NY, Muhlberger VA, Gabl C, Mikuz G, Hausmann D, et al. Detection of intralumenal calcium by intracoronary ultrasound depends on the histologic pattern. *Am Heart J* 1994;128:435-41.
- Zarins CK, Lu CT, Gewertz BL, Lyon RT, Rush DS, Glagov S. Arterial disruption and remodelling following balloon dilation. *Surgery* 1982;92:1086-95.
- Chin AK, Kinney TB, Gregory MS, Rurik GW, Shoor PM, Fogarty TJ. A physical measurement of the mechanisms of transluminal angioplasty. *Surgery* 1984;95:196-200.
- Davies MJ. Pathology of atherosclerosis, plaque disruption, and thrombus formation. *Curr Opin Cardiol* 1989;4:464-7.
- Farb A, Virmani R, Atkinson JB, Kolodgie FD. Plaque morphology and pathologic changes in arteries from patients dying after coronary balloon angioplasty. *J Am Coll Cardiol* 1990;16:1421-9.
- Virmani R, Farb A, Burke AP. Coronary angioplasty from the perspective of atherosclerotic plaque: morphologic predictors of immediate success and restenosis. *Am Heart J* 1994;127:163-79.

18. Gussenhoven EJ, van der Lugt A, van Strijen M, Li W, The SHK, van Egmond FC, et al. Displacement sensing device enabling accurate documentation of catheter tip position. In: Roelandt J, Gussenhoven EJ, Bom N, editors. *Intravascular ultrasound*. Kluwer Academic Press, Dordrecht 1993:157-66.
19. Tenaglia AN, Buller CE, Kissio K, Phillips HR, Stack RS, Davidson CJ. Intracoronary ultrasound predictors of adverse outcomes after coronary artery interventions. *J Am Coll Cardiol* 1992;20:1385-90.
20. Wenguan L, Gussenhoven WJ, Zhong Y, The SHK, Di Mario C, Madretsma S, et al. Validation of quantitative analysis of intravascular ultrasound images. *Int J Card Imaging* 1991;6:247-53.
21. van der Lugt A, Gussenhoven EJ, Pasterkamp G, Bom N, Posthuma DJ, Stijnen T. Interobserver reproducibility of qualitative and quantitative analysis of intravascular ultrasound images before and after peripheral balloon angioplasty. *Ultrasound Med Biol* 1996;22:399-404.
22. van der Lugt A, Gussenhoven EJ, Stijnen T, van Strijen M, van Driel E, van Egmond FC, et al. Comparison of intravascular ultrasound findings after coronary balloon angioplasty with histology. *Am J Cardiol* 1995;76:661-6.
23. Lee RT, Loree HM, Cheng GC, Lieberman EH, Jaramillo N, Schoen FJ. Computational structural analysis based on intravascular ultrasound imaging before in vitro angioplasty: prediction of plaque fracture locations. *J Am Coll Cardiol* 1993;21:777-82.
24. Block PC, Myler RK, Stertzer S, Fallon JT. Morphology after transluminal angioplasty in human beings. *N Engl J Med* 1981;305:382-5.
25. Isner JM, Salem DN. The persistent enigma of percutaneous angioplasty. *Int J Cardiol* 1984;6:391-400.
26. Lyon RT, Zarins CK, Lu C-T, Yang C-F, Glagov S. Vessel, plaque and lumen morphology after transluminal balloon angioplasty. *Arteriosclerosis* 1987;7:306-14.
27. 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 (CA): IEEE Computer Society Press; 1994. p. 277-80.
28. von Birgelen C, Di Mario C, Li W, Schurrbijs JCH, Slager CJ, de Feyter PJ, et al. Morphometric analysis in three-dimensional intracoronary ultrasound: an in vitro and in vivo study performed with a novel system for the contour detection of lumen and plaque. *Am Heart J* 1996;132:516-27.
29. 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;70:1202-9.
30. Wilson LS, Neale ML, Talhami HE, Appleberg M. Preliminary results from attenuation-slope mapping of plaque using intravascular ultrasound. *Ultrasound Med Biol* 1994;20:529-42.