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An Explanation for Discrepancy Between Angiographic and Intravascular Ultrasound Measurements After Percutaneous Transluminal Coronary Angioplasty

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Objectives. This study attempted to determine why there is a discrepancy between angiographic and intravascular ultrasound measurements after coronary balloon angioplasty.

Background. Previous studies have shown a poor correlation between angiographic and intravascular ultrasound measurements after percutaneous coronary balloon angioplasty.

Methods. After successful balloon angioplasty, 91 lesions in 84 patients were studied by intravascular ultrasound. Plaque morphology on intravascular ultrasound was classified as demonstrating a superficial injury if there was either no fracture or only a small tear that did not extend to the media versus a deep injury defined as the presence of a plaque fracture that reached the media. Measurements of minimal lumen diameter were compared between angiography and intravascular ultrasound.

Results. On ultrasound imaging, a superficial injury pattern was observed in 44 lesions, whereas a deep injury was seen in 47 lesions. There were no statistical differences at baseline in patient or lesion characteristics. In the superficial injury group there was a significant correlation between angiography and intravascular ultrasound for minimal lumen diameter ($r = 0.67$) and lumen cross-sectional area ($r = 0.69$). In the deep injury group there was a poor correlation for minimal lumen diameter ($r = 0.05$) and lumen cross-sectional area ($r = 0.28$). After balloon angioplasty, the angiographic appearance showed a normal contour in 34%, the presence of dissection in 38% or a hazy appearance in 23%. On ultrasound imaging after angioplasty, the superficial injury group comprised 65% of lesions with a normal angiographic appearance and 67% of lesions with a hazy appearance, whereas 77% of lesions with an angiographic diagnosis of dissection were in the deep injury group by ultrasound ($p = 0.0005$).

Conclusions. These observations suggest that the discrepancies between angiographic and ultrasound measurements are due to differences in plaque morphology created by balloon dilation. Superficial injuries demonstrate similar results by angiography or ultrasound, whereas a deep injury to the plaque produces a difference in measurements between angiography and ultrasound. When angiography reveals a dissection, there is a high probability that intravascular ultrasound will demonstrate a plaque fracture extending to the media.

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Previous studies (1–5) have shown poor correlation between angiographic and intravascular ultrasound measurements after successful angioplasty. Plaque fracture with passage of contrast material through a dissection plane may cause an overestimation of lumen diameter on angiography (6). The accuracy of making this diagnosis is important because the presence and extent of plaque fracture may influence the restenosis rate (7). Therefore, this study attempted to determine the reason for the discrepancy between the angiographic and intravascular ultrasound assessment of lumen dimensions and appearance after coronary angioplasty.

Methods

From October 12, 1989 to December 31, 1992, 91 lesions in 84 patients were successfully treated with coronary balloon angioplasty and underwent an intravascular ultrasound study. All patients had coronary artery stenosis with objective evidence of ischemia. Patients with total occlusions were excluded from the study. Baseline angiograms were recorded in at least two projections before angioplasty. Standard coronary angioplasty was performed from the femoral artery approach. Angioplasty balloons were chosen with an inflated diameter approximately equal to the angiographic lumen diameter immediately proximal to the site to be dilated. The number of balloon inflations and pressure exerted were determined by the operator to achieve an optimal angiographic result. Although

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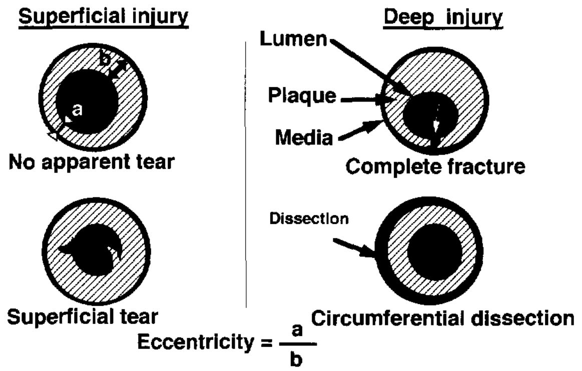


Figure 1. Schematic representation of intravascular ultrasound morphology after percutaneous transluminal coronary angioplasty.

there was no rigid dilation protocol, the usual approach was to use two to three inflations at 4 to 6 atm for 45 to 90 s in duration each. After the coronary balloon angioplasty was considered to be successful by angiography, an intravascular ultrasound examination was performed. An angioplasty success was defined as a diameter stenosis after angioplasty <50%. The ultrasound catheter was either a 4.3F 20-MHz or 3.9F 25-MHz device (Interpret, InterTherapy/CVIS). Continuous ultrasound images were obtained at 30 frames/s as the catheter was moved back and forth through the dilated area. The fluoroscopic picture that displayed the position of the ultrasound catheter was shown on the same video screen as the cross-sectional ultrasound images to correlate the ultrasound image with the position on the angiogram along the length of the artery. All patients signed a written informed consent approved by the Human Subjects Review Committee of the University of California–Irvine.

Intravascular ultrasound morphology and quantitative measurements. Although a detailed description of the various morphologic patterns observed after balloon angioplasty has been reported from our laboratory (7), for the purpose of this analysis, a simplified classification was used. The intravascular ultrasound lesion morphology was categorized as a superficial or deep injury at the angiographic center of the lesion. *Superficial injury* was defined as a plaque that either did not have a fracture or, if a small tear was present, did not extend to the media. *Deep injury* was defined as the presence of a plaque fracture that reached the media. A sonolucent zone behind the plaque greater than two times the medial thickness was classified as a dissection with deep injury even if a plaque fracture was not visualized. Diagrams of plaque classifications are shown in Figure 1. Morphologic classification was performed by two experienced intravascular ultrasound reviewers. When there was a disagreement about the morphology, a third intravascular ultrasound reviewer who was not informed about the procedure or the purpose of the study judged the morphology.

Minor and major lumen diameters, lumen cross-sectional area, minor and major vessel diameter and vessel cross-sectional area (defined as the area bounded by the media) were measured. The atheroma cross-sectional area was calculated as vessel cross-sectional area minus lumen cross-sectional area. Plaque eccentricity was calculated as the thinnest plaque width divided by the opposite plaque dimension (7). Plaque calcification was quantified as 0 if absent or +1 if it subtended 1° to 90°, +2 if 91° to 180° and +3 if >180° of arc.

Angiographic morphology and quantitative measurements. Digital coronary angiograms were recorded in at least two projections before and after coronary balloon angioplasty. These angiograms were stored on a digital acquisition X-ray system (DCI Philips, Inc.) and were also archived on 35-mm cine film. Angiographic morphology was classified as a normal or hazy contour, a dissection or "other" if it could not be categorized into the previous three types (8). A *normal contour* was defined as a smooth lumen surface throughout the length of the lesion site. A *hazy contour* was defined as a ground-glass appearance of the contrast agent in the lumen at the dilated site or an irregular edge at the lumen border. A *dissection* was defined as either a linear intraluminal lucency, a collection of contrast external to the main lumen, or a long circumferential intraluminal lucency (*spiral dissection*). A *filling defect* or *ulceration* was classified in the "other" group. Angiographic classification was performed by two experienced operators. When there was disagreement between reviewers, another operator who was not informed about the study independently interpreted the angiograms. The minimal lumen diameter and the proximal angiographically normal segment were measured. Lumen cross-sectional area was calculated from orthogonal projections as an ellipse. Measurements were made from the digital angiograms by an operator who did not know the purpose of the study, using digital calipers from end-diastolic frames or the frame that best demonstrated the stenotic area. The diameter of the guiding catheter was used for calibration (9,10). Postprocedural minimal lumen diameter was determined from the tightest visual lumen dimension from multiple projections. For comparison with the ultrasound measurements, the angiographic minimal lumen diameter was determined from the angiogram with the smallest dimension from at least two projections. Lesions that were visualized in only one view were excluded from the regression analysis.

Statistical analysis. Group data were tabulated as mean value ± 1 SD. Categoric variables were analyzed using the chi-square analysis. Unpaired, two-sided *t* tests were used for continuous data. Differences were considered statistically significant at $p < 0.05$. The minimal lumen diameter and lumen cross-sectional area by angiography were compared with ultrasound measurements using linear regression analysis and by the method of Bland and Altman (11).

To assess interobserver variability of intravascular ultrasound measurements, 20 lesions in each group were randomly chosen. Minimal lumen diameter, lumen cross-sectional area, minimal vessel diameter and vessel cross-sectional area were measured by two observers (S.N., J.M.T.). Intraobserver (S.N.) variability was assessed 6 months after the initial measurements.

Table 1. Clinical Characteristics of 84 Study Patients

	Superficial Injury (n = 41)	Deep Injury (n = 43)	p Value
Male gender	31 (76%)	30 (70%)	0.55
Age (yr)	60 ± 12	60 ± 12	0.74
Unstable angina	19 (46%)	22 (51%)	0.82
Acute MI	6 (15%)	6 (14%)	0.91
Previous MI	13 (32%)	11 (26%)	0.53
CABG	5 (12%)	7 (16%)	0.59
Diabetes	7 (17%)	10 (23%)	0.48
Hypertension	18 (44%)	14 (32%)	0.28
Hyperlipidemia	16 (39%)	23 (53%)	0.18
Smoking	10 (24%)	14 (33%)	0.41
Family history	14 (34%)	9 (21%)	0.17

Data presented are mean value ± 1 SD or number (%) of patients. CABG = coronary artery bypass graft surgery; MI = myocardial infarction.

Results

Intravascular ultrasound morphology. After successful coronary balloon angioplasty, 44 lesions (48%) were classified as having superficial injury by intravascular ultrasound assessment. In this group, 38 lesions (42%) had no evidence of plaque fracture, and 6 (7%) had a superficial plaque tear that did not reach the media. There were 47 lesions (52%) classified as having a deep injury. In this group, a deep plaque fracture that extended to the media was observed in 43 lesions (47%), and 4 (4%) had a circumferential dissection. The baseline characteristics of the patients were similar in the two groups (Table 1). The vessel distribution and lesion characteristics of the two groups are shown in Table 2. There was no statistical difference between the two groups for vessel distribution, percent diameter stenosis at baseline, lesion length, calcium detected by angiogram or incidence of a restenosis lesion.

Table 2. Characteristics of 91 Lesions Studied

	Superficial Injury (n = 44)	Deep Injury (n = 47)	p Value
Lesion location			
LAD	18 (41%)	19 (40%)	
RCA	15 (34%)	16 (34%)	
LCx	9 (20%)	11 (23%)	0.53
SVG	2 (5%)	0 (0%)	
LMCA	0 (0%)	1 (2%)	
% diameter stenosis	71 ± 18	73 ± 15	0.92
Reference lumen diameter (mm)	2.9 ± 0.8	3.1 ± 1.0	0.35
Lesion length (mm)	12.7 ± 9.3	13.7 ± 9.7	0.65
Angiographic Ca	7 (16%)	5 (11%)	0.45
Restenosed lesion	9 (20%)	8 (17%)	0.67

Data presented are mean value ± 1 SD or number (%) of lesions. Ca = calcium; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; RCA = right coronary artery; SVG = saphenous vein graft.

Table 3. Angiographic and Intravascular Ultrasound Measurements After Percutaneous Transluminal Coronary Angioplasty

	Superficial Injury	Deep Injury
Angiography		
Minimal lumen diameter (mm)	1.9 ± 0.5	2.0 ± 0.5
Lumen CSA (mm^2)	3.5 ± 1.7	3.8 ± 1.6
% stenosis	30 ± 14	32 ± 16
Balloon/vessel ratio	1.13 ± 0.47	1.06 ± 0.35
Intravascular Ultrasound		
Minor lumen diameter (mm)	2.1 ± 0.5	2.0 ± 0.6
Major lumen diameter (mm)	2.5 ± 0.5	2.5 ± 0.6
Lumen CSA (mm^2)	4.8 ± 2.5	4.6 ± 1.6
Minor vessel diameter (mm)	3.8 ± 0.7	3.7 ± 0.8
Major vessel diameter (mm)	4.0 ± 1.0	4.1 ± 0.8
Vessel CSA (mm^2)	13.6 ± 5.5	13.1 ± 4.2
% atheroma	64 ± 13	62 ± 17
Atheroma CSA (mm^2)	8.8 ± 4.3	8.5 ± 4.2
Eccentricity index	0.45 ± 0.08	0.27 ± 0.05*

*$p < 0.005$. Data presented are mean value ± 1 SD. CSA = cross-sectional area.

Quantitative angiographic and intravascular ultrasound measurements. Average balloon/vessel ratio, quantitative angiographic measurements and intravascular ultrasound measurements are shown in Table 3. After angioplasty, minimal lumen diameter was 1.9 ± 0.5 and 2.0 ± 0.5 mm ($p = 0.51$), angiographic percent diameter stenosis was 30 ± 14% and 32 ± 16% ($p = 0.56$), and balloon vessel ratio was 1.13 ± 0.47 and 1.06 ± 0.35 ($p = 0.70$) in the superficial and deep injury groups, respectively.

Intravascular ultrasound measurements after coronary balloon angioplasty showed no statistical difference in lumen and vessel diameters; lumen, vessel and atheroma cross-sectional areas; and percent atheroma occupied between the two groups. The eccentricity index was significantly lower in the deep injury group (0.27 ± 0.05) than the superficial injury group (0.45 ± 0.08, $p = 0.003$).

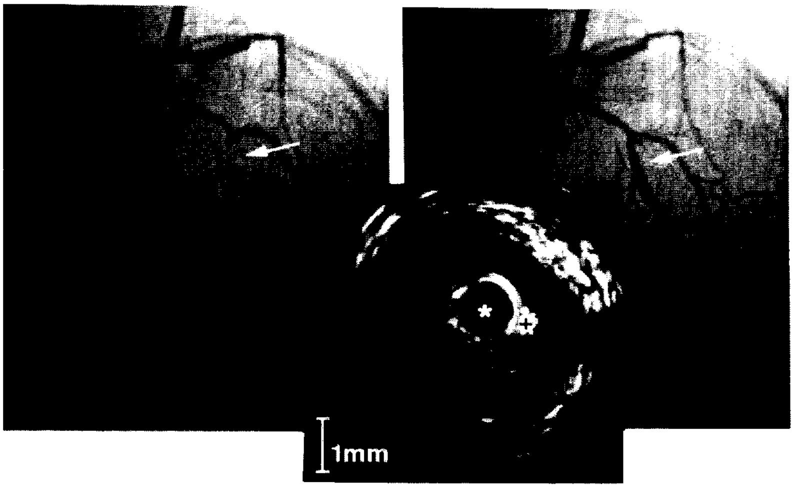
Angiographic morphology. Table 4 compares the results of the angiographic and intravascular ultrasound classifications. By angiography, a normal contour was observed in 31 lesions (34%), a hazy appearance in 21 (23%) and evidence of a dissection in 35 (38%). Four lesions could not be classified among the three categories; two were ulcerated; and two

Table 4. Relation Between Angiographic and Intravascular Ultrasound Morphology

Angiographic Characterization	IVUS Classification: Superficial Injury	IVUS Classification: Deep Injury	Total
Normal	20 (65%)	11 (35%)	31
Hazy/irregular	14 (67%)	7 (33%)	21
Dissection	8 (23%)	27 (77%)	35

$p = 0.0005$, intravascular ultrasound (IVUS) classifications compared across categories. Data presented are number (%) of lesions.

NORMAL ANGIOGRAPHIC APPEARANCE



PLAQUE STRETCHED WITHOUT FRACTURE

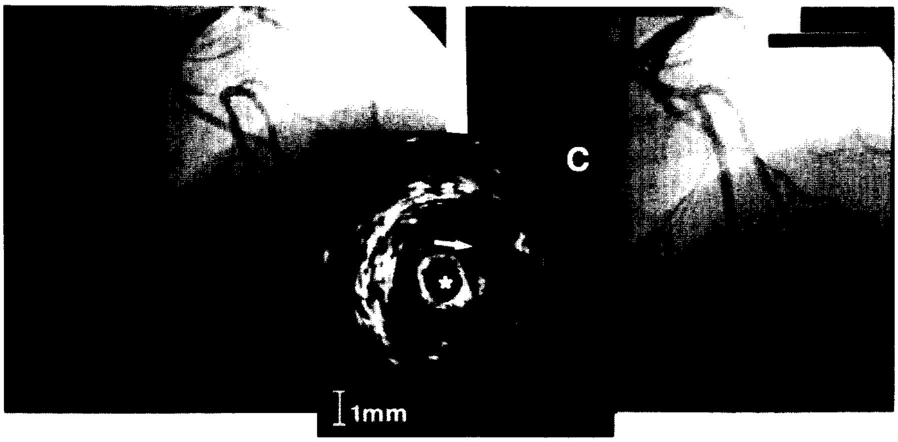
Figure 2. A, Severe stenosis in the midportion of the left anterior descending coronary artery (LAD). **B,** After balloon angioplasty, the angiographic appearance of the lumen shows smooth borders without evidence of dissection. The **ultrasound image (bottom)** obtained at the level of the **arrow** shows the centrally placed ultrasound catheter (*) and the monorail guide wire (+). The plaque is seen as a homogeneous speckled pattern of echoreflections without evidence of a tear or dissection.

showed an intraluminal defect that was considered to be a thrombus. In the superficial injury group, 20 lesions had a normal appearance, 14 a hazy appearance and 8 evidence of a dissection by angiography. In the deep injury ultrasound group, 11 lesions had a normal angiographic appearance, 7 a hazy appearance and 27 evidence of a dissection. Only 35% of normal and 33% of hazy angiographic lesions, but 77% of angiographic dissections, had evidence of deep injury by intravascular ultrasound ($p = 0.0005$). Examples of angiographic images and their corresponding ultrasound morphology are demonstrated in Figures 2 to 4.

By ultrasound criteria, 71 lesions (78%) had calcified plaque at the dilated site. The presence and extent of calcification showed no difference ($p = 0.87$) between the two groups and did not appear to influence plaque morphology after coronary angioplasty. In the superficial injury group, 10 lesions had 0 calcification, 20 had +1, 10 had +3, and 4 had +4. In the deep injury group, 10 lesions had 0 calcification, 20 had +1, 14 had +3, and 3 had +4.

Correlation of angiography and intravascular ultrasound. Comparison of angiographic and intravascular ultrasound measurements was performed separately for each group according to the extent of plaque fracture. Thirty-seven lesions (84%) in the superficial injury group and 39 lesions (83%) in the deep injury group had at least two projections and were eligible for comparison (Fig. 5 and 6). In lesions with superficial injury by ultrasound, there was good correlation between intravascular ultrasound and angiography for minimal lumen diameter ($y = 0.68x + 0.81$, $r = 0.67$, SEE 0.36, $p = 0.001$) and lumen cross-sectional area ($y = 0.90x + 1.53$, $r = 0.69$, SEE 1.62, $p = 0.001$). However, in lesions with deep injury to the plaque, there was poor correlation between intravascular ultrasound and angiography for minimal lumen diameter ($y = -0.06x + 2.11$, $r = 0.05$, SEE 0.47, $p = 0.74$) and lumen

HAZY ANGIOGRAM POST PTCA



SUPERFICIAL INJURY

Figure 3. A, Severe stenosis of a proximal left anterior descending coronary artery. **B,** Balloon dilation was successful; however, the lumen has a hazy angiographic appearance. This corresponds to the **intravascular ultrasound image (C)**, which demonstrated a tear in the substance of the plaque (**arrow**), but the plaque tear did not extend to the media. PTCA = percutaneous transluminal coronary angioplasty. Symbols as in Figure 2.

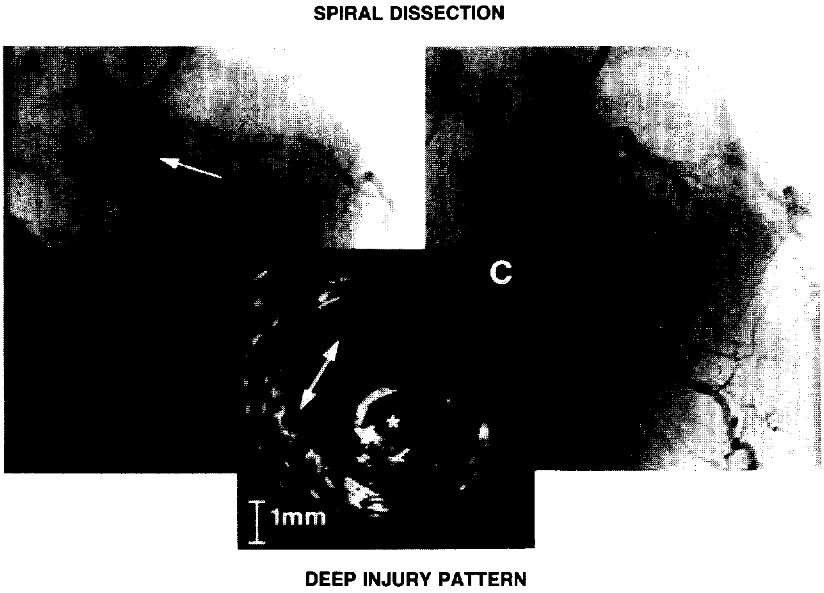


Figure 4. **A,** Severe stenosis of a large obtuse marginal branch **(arrow)** before balloon angioplasty. **B,** After balloon angioplasty there is a spiral dissection that extends halfway down the obtuse marginal vessel. The **ultrasound image (C)** obtained at the level of the stenosis shows a wide lumen area associated with a tear and plaque fractures that extend to the media. Symbols as in Figure 2.

cross-sectional area (y = 0.29x + 3.44, r = 0.28, SEE 1.56, p = 0.08). As a measure of agreement, the mean difference between angiography and ultrasound was −0.35 ± 0.25 and −0.54 ± 0.45 mm for minimal lumen diameter and −1.48 ± 1.33 and −1.64 ± 1.21 mm^2 for lumen cross-sectional area in the superficial and deep injury groups, respectively.

Reproducibility of intravascular ultrasound measurements. In the superficial injury group, the correlation coefficients for intraobserver and interobserver variability of minimal lumen diameter and lumen cross-sectional area were r = 0.99 (SEE 0.14) and r = 0.99 (SEE 0.25) and r = 0.97 (SEE 0.21) and r = 0.98 (SEE 1.10), respectively. In the deep injury group, these were r = 0.85 (SEE 0.15) and r = 0.96 (SEE 0.46) and r = 0.77 (SEE 0.32) and r = 0.91 (SEE 1.56), respectively (all statistically significant at $p < 0.0005$).

Discussion

Study findings. The mechanism of coronary balloon angioplasty has been explained as a combination of plaque stretching, fracture, dissection or compression (12–15). When plaque fracture is present, the angiogram may overestimate the lumen diameter. Intravascular ultrasound studies (1–5) have consistently shown a discrepancy between angiographic and intravascular ultrasound measurements after balloon angioplasty. In the present study, 84 patients had balloon angioplasty and intravascular ultrasound studies, and the lesions were categorized according to ultrasound morphology after balloon angioplasty on the basis of the presence and extent of plaque fracture and circumferential dissections: 1) lesions with superficial injury to the plaque either without the presence of a tear or a tear that did not extend to the media, and 2) lesions with a plaque fracture that extended to the media. The significant finding from this analysis was that when there was no tear or only superficial injury to the plaque, there was a significant correlation between angiography and intravascular ultrasound for minimal lumen diameter (r = 0.67). This degree of correlation is similar to a recently reported study (16) of coronary arteries with minimal angiographic disease (r = 0.59).

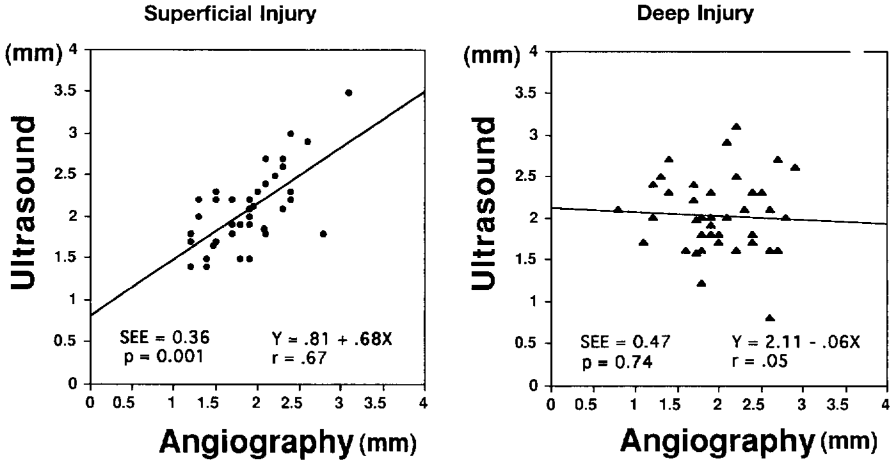


Figure 5. Comparison of angiographic and intravascular ultrasound measurements for minimal lumen diameter after balloon angioplasty in the subset of 37 patients with superficial injury **(left)** versus 39 with a deep injury pattern **(right)** by intravascular ultrasound.

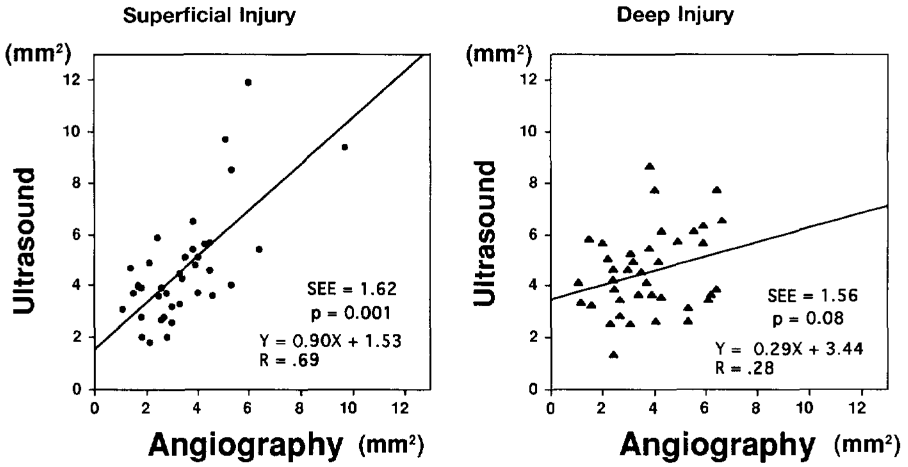


Figure 6. Comparison of angiographic and intravascular ultrasound measurements for minimal lumen cross-sectional area after balloon angioplasty in the subset of 37 patients with superficial injury **(left)** versus 39 with a deep injury pattern **(right)** by intravascular ultrasound.

However, when there was deep injury to the plaque, there was poor correlation between angiography and intravascular ultrasound for minimal lumen diameter (r = 0.05). These observations are helpful in clarifying the reasons for the discrepancies that have been reported in previous angiographic and intravascular ultrasound studies.

Comparison with previous studies. In the present study, 38% of lesions had angiographic evidence of dissection, which is similar to the results of a study by Sharma et al. (17), who reported a 30% incidence of dissection after balloon angioplasty. There have been several studies of preprocedural predictors for whether balloon angioplasty of a lesion is likely to result in dissection of the artery. Nichols et al. (18) showed that there was an increased incidence of coronary artery dissection when the balloon/artery ratio was >1.3. Roubin et al. (19) showed a high complication rate as a result of dissection when a large balloon to reference vessel diameter was used. In the present study, there was no distinction between the superficial or deep injury group in balloon/vessel ratio that could be shown to influence the extent of plaque fracture. When the angiogram clearly demonstrated a dissection, 77% of lesions had evidence of a plaque fracture by ultrasound. When the angiogram showed a normal or hazy appearance, there was a low incidence of deep plaque fracture by intravascular ultrasound. However, 23% of angiographic dissections did not demonstrate a deep injury by intravascular ultrasound. One possible explanation for this is that for small tears, the ultrasound appearance is not adequate to resolve the presence of a slitlike dissection. Contrast agent injection under pressure may open these slits and permit better visualization of longitudinal dissections. Previous clinical pathologic studies (20) show that angiographic haziness is frequently due to dissection. A recent report from Naruko et al. (21) suggests that an angiographic smooth wall or a hazy appearance can be associated with laceration limited to the intima. Our ultrasound study showed that 67% of angiographic hazy lesions had a superficial injury pattern.

In the present study, 78% of the lesions demonstrated calcification on ultrasound, which is similar to data from other groups that report that 63% to 76% of target lesions had calcification (22–24). Other investigators (25,26) have described a trend for the development of dissection if there is evidence for calcified plaque. Fitzgerald et al. (25) found that when a tear was present, it frequently began at the interface between the fibrotic tissue and calcification. In the current study, the incidence and extent of calcified plaque was similar in both groups and did not appear to influence the incidence of plaque fracture. The one significant difference between the two study groups was the eccentricity of the lesion. The deep injury group had more eccentric plaques, which suggests that eccentric plaques may be more prone to develop extensive fractures. However, if a stenosis is extremely eccentric, balloon dilation may only stretch the normal free wall and not produce a fracture. Previous pathologic studies (12) suggest that plaque compression does not play a significant role in the mechanism of human coronary artery angioplasty. Previous ultrasound measurements of plaque cross sectional area before and after balloon dilation also did not reveal any evidence for plaque compression (27).

Although all lesions in this study had angiographic evidence of a successful procedure, 48% did not have a deep plaque fracture after balloon dilation. The finding that there was no difference in lumen cross-sectional area between lesions with minimal injury and those with a deep plaque fracture would suggest that a successful angioplasty result can be achieved by a stretching effect and that fracture of the plaque may not be necessary.

The reported discrepancy between intravascular ultrasound and angiographic estimates of the results after balloon angioplasty appear to have a structural basis. When the morphology of the plaque is significantly altered with deep fractures and circumferential dissections, there is poor agreement between the lumen diameter measured by angiography and that by intravascular ultrasound. However, if the plaque is not fractured but is primarily stretched, then the measurements obtained by angiography and intravascular ultrasound correspond closely.

Conclusions. The present intravascular ultrasound findings may be pertinent to the observation that angiographic measurements during follow-up studies for restenosis may not correspond to the incidence of clinical events. Angiography may misrepresent the true lumen dimensions after transcatheter therapies.

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