

Usefulness of Repeat Coronary Angiography 24 Hours After Successful Balloon Angioplasty to Evaluate Early Luminal Deterioration and Facilitate Quantitative Analysis

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Because of the unavoidable occurrence of vessel disruption after successful coronary balloon angioplasty, the reliability of quantitative angiographic analysis in that setting has been questioned. For this reason and the suggested occurrence of delayed elastic recoil, repeat angiography at 24 hours has been advocated in clinical interventional trials. In this study, these issues are confronted by performing comprehensive quantitative analysis (Cardiovascular Angiographic Analysis System) of coronary angiograms, acquired in multiple identical projections immediately after and 24 hours after angioplasty, in 102 patients with 110 successfully dilated lesions. Vasomotion was controlled by intracoronary nitrate before angiography and all patients were fully anticoagulated (activated partial thromboplastin time 85 to 120 seconds) for >24 hours. Paired Student's *t* tests applied to angiographic measurements revealed that there was no significant deterioration in minimal luminal diameter or cross-sectional area from immediately after angioplasty to 24 hours later. It can thus be inferred that there is no phenomenon of delayed elastic recoil, at least during this time period. Measurement accuracy and precision of the Cardiovascular Angiographic Analysis System from the postangioplasty angiogram are highly acceptable, at <0.01 and ± 0.20 mm, respectively. Therefore, it is concluded that routine repeat 24-hour angiography is not indicated after successful angioplasty. A highly significant increase (*p*

<0.001) in reference diameter ($+0.11 \pm 0.18$ mm) was responsible for the apparent increase in percent diameter stenosis ($2.4 \pm 7\%$), a finding that demonstrates the potential for error by selective application of percent diameter stenosis measurements alone. Preferential use of absolute luminal measurements is thus strongly recommended for clinical trials with angiographic monitoring.

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Computer-assisted quantitative analysis systems have become the gold standard for measuring coronary angiographic luminal dimensions, as demonstrated in clinical studies of interventional devices and pharmacologic agents aimed at "restenosis prevention".¹⁻⁵ However, one of the main criticisms of quantitative angiography has been the potential measurement inaccuracy and imprecision immediately after apparently successful balloon angioplasty.⁶ Disruptions of vessel luminal contour almost always occur,⁷⁻⁹ although only seen angiographically as "dissection" in one third of cases.¹⁰ It could thus be hypothesized that angiography 24 hours after intervention might provide a better substrate for the measurement of luminal dimensions in clinical studies.¹¹ Moreover, because up to 50% of achievable luminal increase may be lost immediately after balloon deflation, due to elastic recoil,¹² it could be suggested that repeat early angiography should be performed to assess the probability of further delayed elastic recoil. Such practice could lead to prolonged hospitalization and additional risk of morbidity, an increase in the work load of the medical staff of catheterization laboratories, and ultimately, increased health care costs. Furthermore, routine angiography at 24 hours could reduce the likelihood of informed consent for percutaneous interventions, especially in clinical trials. This study investigates the need for repeat angiography 24 hours after successful balloon angioplasty and provides an opportunity to examine the postangioplasty measurement variability of the Cardiovascular Angiographic Analysis System, hitherto unpublished.

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TABLE I Flow Chart from Randomization in the Safety Trial to Suitability for This Quantitative Angiographic Ancillary Study

	Number of Patients
Patient enrolled in randomized study	118
Patients excluded after enrollment	
No angioplasty performed	
Failure to cross lesion	4
Previously unrecognized left main lesion	1
Took heparin during previous 24 hours	3
Randomized to receive heparin or hirudin	110
Failure to successfully dilate all target lesions	2
Major adverse cardiac events within 24 hours	
Death	0
Myocardial infarction	1
Emergency bypass graft surgery	3
Myocardial infarction + emergency surgery	1
Repeat angioplasty	0
Complete (thrombotic) occlusion at 24 hours without major adverse event	1
Successful angioplasty + satisfactory quantitative analysis postangioplasty + 24 hrs	102

METHODS

Patients: The study population comprised 102 patients who underwent successful balloon angioplasty of 110 lesions and had quantitative coronary angiography performed before, immediately after, and 24 hours after angioplasty as part of a safety and efficacy trial of a new anticoagulant preparation, details of which are published elsewhere.¹³ The study was performed in full accordance with the principles of the "Declaration of Helsinki," as well as specific local laws and regulations of each participating center. Before randomization, each patient gave written informed consent according to the requirements of the local institution.

Table I displays the source of the 102 patients assessed in this study. The aim of this study was to focus on luminal dimensional changes occurring during 24 hours, and assess the reliability of the angiogram immediately after angioplasty for quantitative analysis. Therefore, only patients with successfully dilated lesions and quantitative angiographic analysis both immediately after, and 24 hours after angioplasty were included in the study. Successful angioplasty was defined according to the conventionally applied method in clinical practice and trials^{4,5}—a diameter stenosis <50% after angioplasty, as visually assessed by the interventionalist. Clinical outcome of the remaining 16 patients in the safety and efficacy trial, who were not included in this study, has been described elsewhere.¹³ The patient population is, in general, demographically representative of modern clinical experience with coronary balloon angioplasty^{4,5} in patients with stable angina (Table II). All patients had symptomatic obstructive coronary artery disease of at least 1 vessel, which was deemed suitable for treatment by angioplasty. The angioplasty procedure itself was performed according to the routine practice of the individual interventionalist.

Anticoagulation: Patients were randomly allocated to receive intravenous heparin or recombinant hirudin at doses sufficient to maintain activated partial thromboplastin time (monitored before, after, and 6, 12 and 24

TABLE II Clinical Data and Target Lesion Distribution in 102 Patients

Age (years)	58 (35–74)
Men (%)	83 (78)
Previous MI (%)	39 (37)
Diabetes mellitus (%)	5 (5)
Hypertension (%)	32 (30)
Current smokers (%)	25 (24)
Angiographic coronary disease pattern	
1-vessel disease (%)	87 (82)
2-vessel disease (%)	17 (16)
3-vessel disease (%)	2 (2)
CCS functional classification	
I or II (%)	59 (56)
III or IV (%)	47 (44)
Medication	
Long-acting nitrates (%)	51 (48)
β blockers (%)	80 (75)
Calcium antagonist (%)	72 (68)
Acetylsalicylic acid (%)	88 (83)
Angiographic lesion location of dilated segments	
Left anterior descending	40%
Circumflex	30%
Right coronary artery	29%
Left main stem	1%

CCS = Canadian Cardiovascular Society; MI = myocardial infarction.

hours after angioplasty) at 85 to 120 seconds for 24 hours. Dosage adjustments were made accordingly if levels were outside this target therapeutic range. Assays of prothrombin fragments F₁ and F₂, fibrinopeptide A, thrombin-antithrombin III complexes, anti-factor IIa and Xa activity, D-dimer, tissue-type plasminogen activator and plasminogen activator inhibitor antigen were performed. The collectively analyzed findings illustrated that, in general, thrombin generation was effectively inhibited by both anticoagulants throughout the 24-hour study period.¹³ Thus, it would appear that the anticoagulant dosage regimens were adequate in each patient group.

Coronary angiographic procedures to facilitate quantitative analysis: Angiograms were carefully recorded according to the requirements of the computer-assisted Cardiovascular Angiographic Analysis System: (1) avoidance of projections in which the spine or other structures, or closely parallel or overlapping side-branches, obscure the vessel segment of interest; (2) filming of the lesion and segment of interest as close to the field center as possible, and in ≥ 2 , preferably orthogonal, projections for the right coronary artery, and ≥ 3 projections (separated by $\geq 30^\circ$) for the left coronary artery, ideally at the end of a full inspiration; (3) vasomotion controlled by intracoronary nitrate (isosorbide dinitrate 1 to 3 mg or glycerol trinitrate 0.1 to 0.3 mg) before angiography, and before, immediately after, and 24 hours after balloon angioplasty; (4) to ensure exact comparability of angiographic measurements, angiography was performed in exactly similar projections (which are precisely recorded at each catheterization session) using a fixed-table approach before, immediately after, and 24 hours after angioplasty; (5) coronary arteries were optimally opacified using nonionic contrast which had been prewarmed to 37°C for ≥ 3 complete cardiac cycles; (6) guidewire and balloon catheter were removed before the final postangioplasty

TABLE III Quantitative Angiographic Measurements Before, Immediately After and 24 Hours After Angiography Given as Means of the Multiple Matched Projections \pm SD

	Before	Immediately After	24 Hours After	Mean Diff. 24 Hours After (accuracy)	SD of Mean Diff. 24 Hours After (precision)	p Value of Mean Diff. (paired t test)
Minimal luminal diameter (mm)	1.03 \pm 0.40	1.72 \pm 0.36	1.72 \pm 0.39	0.007	\pm 0.20	0.74
Minimal luminal cross-sectional area (mm ²)	0.92 \pm 0.85	2.57 \pm 1.51	2.64 \pm 1.53	0.07	\pm 0.85	0.42
% area stenosis (%)	84.9 \pm 10.3	57.9 \pm 12.8	59.8 \pm 14.1	1.9	\pm 14.1	0.17
Lesion length (mm)	5.91 \pm 1.95	5.71 \pm 1.78	5.75 \pm 1.79	0.05	\pm 1.3	0.72
Lesion symmetry (ratio)	0.57 \pm 0.20	0.50 \pm 0.20	0.49 \pm 0.18	-0.02	\pm 0.20	0.37
Interpolated reference diameter (mm)*	2.67 \pm 0.64	2.72 \pm 0.58	2.83 \pm 0.59	0.11	\pm 0.18	<0.0001
% diameter stenosis (%)	60.6 \pm 12.9	36.3 \pm 7.9	38.7 \pm 8.7	2.4	\pm 7.0	0.0005
Reference area (mm ²)	5.95 \pm 3.02	6.10 \pm 2.73	6.61 \pm 2.93	0.51	\pm 0.84	<0.0001
Plaque area (mm ²)	6.40 \pm 3.39	4.30 \pm 2.35	4.92 \pm 2.82	0.62	\pm 1.48	<0.0001

*The interpolated reference diameter is the computer reconstruction of the original "disease-free" vessel dimensions over the analyzed segment. The actual diameter measurement taken as the reference diameter, and thus as the "vessel size," is the interpolated diametric measurement at the site of the most severe narrowing (minimal luminal diameter), thus providing an objective and user-independent estimation of the actual "normal" diameter at that site, in the absence of any disease.¹⁵⁻¹⁷
Diff. = difference.

TABLE IV Quantitative Angiographic Measurements from a Total of 308 Individual Projections, Identically Reproduced (matched) After Angioplasty and at 24 Hours

	After	24 Hours After	Mean Diff. 24 Hours After	p Value of Mean Diff.
Subsegmental lesion location (subsegment 1-6)*	2.44 \pm 1.1	2.43 \pm 1.2	-0.01 \pm 0.73	0.75
Minimal luminal diameter (mm)	1.70 \pm 0.40	1.71 \pm 0.41	0.0008 \pm 0.27	0.60
Minimal luminal cross-sectional area (mm ²)	2.45 \pm 1.63	2.50 \pm 1.63	0.05 \pm 1.3	0.50
% area stenosis (%)	59.0 \pm 18.4	61.3 \pm 19.6	2.2 \pm 21.2	0.07
Lesion length (mm)	5.72 \pm 2.35	5.81 \pm 2.42	0.09 \pm 2.07	0.45
Lesion symmetry (ratio)	0.50 \pm 0.27	0.49 \pm 0.26	0.01 \pm 0.31	0.70
Interpolated reference diameter (mm)	2.70 \pm 0.60	2.82 \pm 0.59	0.12 \pm 0.29	<0.0001
Reference area (mm ²)	6.01 \pm 2.81	6.55 \pm 2.95	0.54 \pm 1.35	<0.0001
% diameter stenosis (%)	36.5 \pm 10.4	39.0 \pm 11.0	2.5 \pm 10.0	<0.0001
Plaque area (mm ²)	4.29 \pm 2.92	4.91 \pm 3.55	0.62 \pm 2.49	<0.0001

*The Cardiovascular Angiographic Analysis System approach automatically subdivides the arterial segment to be analyzed (defined from side branch to side branch) into 6 subsegments of equal length; a minimal, mean and maximal diameter are determined (as well as a range of additional parameters) for each subsegment. The subsegmental location of the minimal luminal diameter within the arterial segment can thus be identified and compared over sequential analyses.
Values are expressed as mean \pm SD.
Diff. = difference.

angiographic recordings; and (7) to enable accurate calibration, the contrast-empty angiographic catheter¹⁴ (at least 7Fr) was filmed before each contrast injection and after the procedure, and the distal 20 cm of each catheter used was enclosed with the angiogram for micro-metric measurement at the core laboratory.

Quantitative and qualitative angiographic analysis:

In the core laboratory, quantitative angiographic analysis was performed by independent analysts without any knowledge of clinical details, using the Cardiovascular Angiographic Analysis System, which has been previously described in detail elsewhere.¹⁵⁻¹⁷ To facilitate the provision of objective, reliable and reproducible measurements, end-diastolic cine-frames were selected for analysis from non- or minimally foreshortened projections by 2 experienced observers. To confirm that each lesion was quantitatively analyzed in the same projections on the pre-, and post- and 24-hour angiograms, a Polaroid® print was made of each analysis. Absolute luminal measurements were obtained using the known diameter of the angiographic catheter.¹⁴ Corrections were automatically made for so-called pincushion distortion, in nonisocentrically filmed catheter or target lesion positions. Comprehensive lesion measurements were provided, including minimal luminal diameter (MLD), interpolated reference diameter, lesion length, plaque area

and percent diameter stenosis derived as: $[(1 - \text{MLD}) / \text{interpolated reference diameter}] \times 100\%$). In addition, videodensitometric measurements of minimal luminal cross-sectional area (MLCA), reference area and area stenosis were produced. In this study, the averaged values separately presented for each measurement parameter are means of the multiple projections filmed for each lesion and of the individual projections.

Statistical analysis: Since the focus of the study is on potential changes in lesion severity during the 24 hours after successful angioplasty, a lesion-specific approach was applied to evaluation of the results. Quantitatively measured and derived values are given as mean \pm SD. Paired Student's *t* tests are used to compare angiographic measurements immediately after and 24 hours after angioplasty. Accuracy and precision of measurements obtained from the immediate postangioplasty angiogram are defined according to the method suggested by Bland and Altman,¹⁸ i.e., accuracy is the mean difference between the measurement immediately after and 24 hours after angioplasty, and the precision (or measurement variability) is the standard deviation of this mean difference using the 24-hour measurement as the standard against which to compare the measurements obtained immediately after angioplasty. Linear regression analysis and Pearson's product moment correlation

coefficient are used to further evaluate the relation between these measurements.

RESULTS

Angiographically visible dissection was present in 31% of lesions immediately after successful angioplasty. Of these, 15% were type A, 9% type B and 7% type C dissections.

Table III shows that no significant change was observed in MLD or in MLCA immediately after or 24 hours after angioplasty. Because of the significant increase in reference diameter, a significant increase was also observed in percent diameter stenosis: from 36% immediately after to 39% 24 hours after angioplasty

($p = 0.0005$). Despite the significant increase in reference area, percent area stenosis did not change significantly during the 24-hour period, although a trend toward increase was observed. The increase in reference diameter was also responsible for the observed significant increase in plaque area, because the edge-detection algorithm calculates plaque area automatically from the reference diameter function and the actual detected arterial contours. There was no significant change in lesion length or symmetry immediately after to 24 hours after angioplasty.

The postangioplasty accuracy and precision of the MLD measurement was found to be <0.01 and ± 0.20 mm, respectively (Table III).

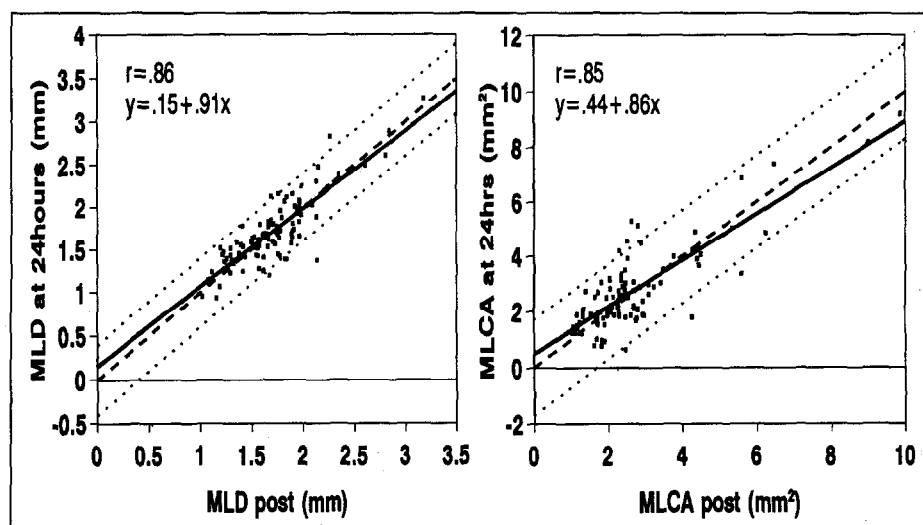


FIGURE 1. Linear regression analysis ($y = a + bx$) of minimal luminal diameter (MLD) and minimal luminal cross-sectional area (MLCA) after angioplasty and at 24 hours. r is Pearson's correlation coefficient. The identity line is the dashed line and the parallel dotted lines above and below are \pm twice the measurement variability (i.e., 95% confidence limits for detecting a real change in MLD or MLCA from postangioplasty to 24 hours). The actual regression line is represented by the bold line. Excellent correlation between MLD and MLCA measurements from the postangioplasty and 24-hour angiograms is demonstrated. Only one clear "outlier" can be considered to have undergone significant deterioration in MLD (2 in MLCA) during the 24 hours.

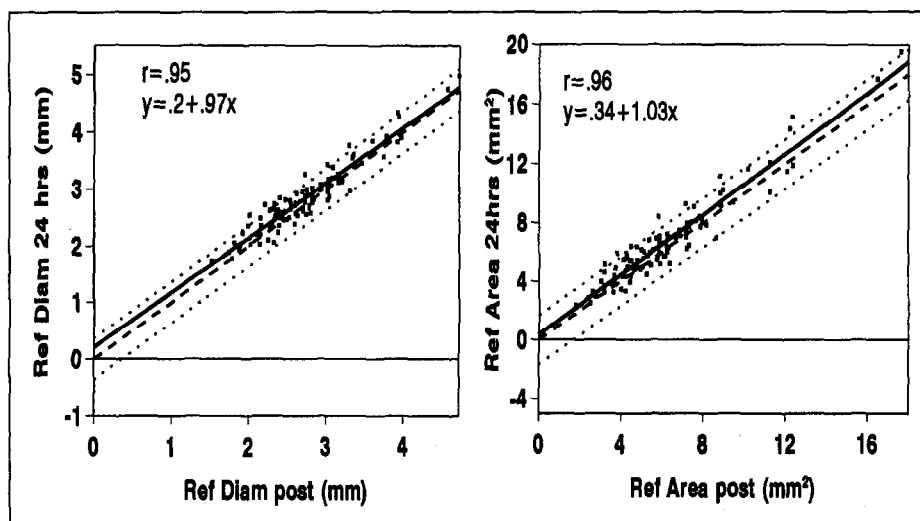


FIGURE 2. Linear regression analysis of reference diameter (Ref Diam) and area after angioplasty and at 24 hours. The format is the same as in Figure 1. Again excellent correlation is observed between measurements from the postangioplasty and 24-hour angiograms. However a systematic increase in dimensions is apparent from postangioplasty to 24 hours from the almost parallel course of the regression line above the identity line for both reference diameter and area.

Considering quantitative measurements obtained from each individual projection immediately after and 24 hours after angioplasty separate measurements, there were a total of 308 matched pairs of projections of the 110 lesions analyzed (Table IV), giving an average of 2.8 views per lesion. The subsegmental location of the MLD of the lesion did not vary during this time. Similar to the mean overall findings, there was no significant difference in MLD, MLCA, lesion length or symmetry immediately after angioplasty to 24 hours after angiography. A significant increase in reference diameter, reference area and percent diameter stenosis was observed, as well as a trend toward an increase in area stenosis, confirming the mean overall results.

The correlation between quantitative angiographic measurements immediately after and 24 hours after angioplasty was excellent for absolute luminal measurements of MLD and cross-sectional area (Figure 1), reference diameter and reference area (Figure 2). However, the correlation was not as good for the relative measurements of percent diameter and area stenoses (Figure 3).

Although 4 lesions had detectable deterioration (a statistically significant decrease from the time immediately after to 24 hours after angioplasty) in MLD (3 in the cross-sectional area), only 1 lesion had a clear deterioration in MLD (Figure 1, left) and 2 in MLCA (Figure 1, right) (from postangioplasty to 24 hours). No successfully dilated lesion was considered to require redilatation during or after the 24 hours.

DISCUSSION

In this study we have addressed the issues of reliability of the angiogram immediately after angioplasty for quantitative analysis and the occurrence of delayed elastic recoil in the first 24 hours after angioplasty by performing repeat angiography immediately after and 24 hours after angioplasty. To maximize objectivity in the evaluation of the occurrence of a real phenomenon, we

attempted to perform the study under "ideal" angiographic conditions. Thus, the angiographic table height is kept constant at all stages and exactly the same angiographic projections are repeated for each individual patient at 24 hours as done immediately after angioplasty. In addition, to avoid the potentially confounding influence of vasomotion and thrombosis, intracoronary nitrate was administered before angiography, and all patients underwent complete anticoagulation for the 24-hour period.

Whether the mean of the multiple matched projections was considered or each projection was considered as a separate measurement, no change in MLD (measured by an edge detection approach) or in MLCA (measured by videodensitometry) was detected from immediately after to 24 hours after balloon angioplasty, which leads to the following interpretative statements.

1. There is no need for routine 24-hour angiography: After successful balloon angioplasty, immediate angiography is just as reliable a substrate for quantitative analysis as angiography at 24 hours. Thus, the presence of angiographically visible but nonocclusive dissection in 31% of lesions (similar to previous reports^{10,11}) clearly does not unduly interfere with the quantitative analysis. A recent study, examining reliability of post-angioplasty angiography, stratified patients according to whether or not angiographic complications after angioplasty occurred, and found a significant difference in MLD (measured by a hand-tracing technique from magnified angiographic images) between post- and 24-hour angioplasty in the complicated versus uncomplicated groups.¹¹ Although apparently similar, that study and this present study are in fact difficult to compare overall since our study was intended to answer the question of whether routine repeat angiography is necessary at 24 hours in patients with successful balloon angioplasty, and the previous study examined the effect of angiographic complications on reliability of quantitative an-

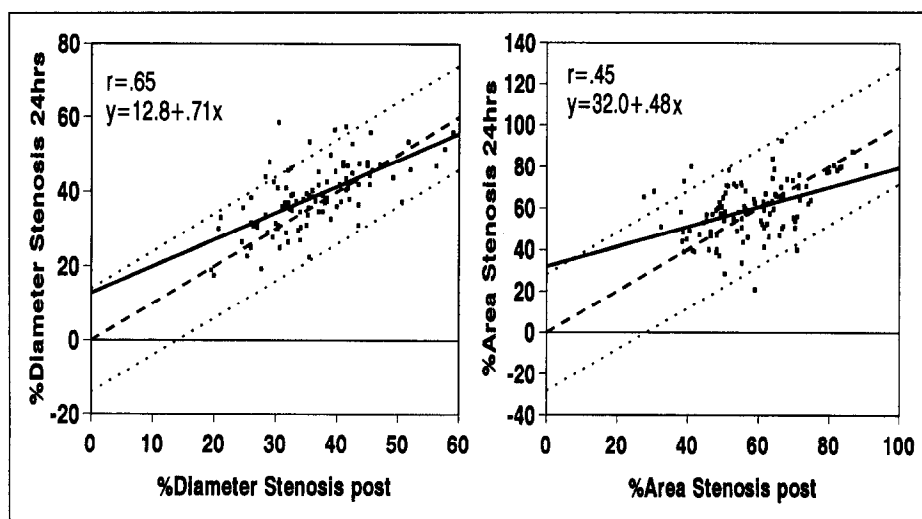


FIGURE 3. Linear regression analysis of percent diameter and area stenosis after angioplasty and at 24 hours. The format is the same as in Figure 1. Note the much greater degree of scatter of individual data points for these relative measurements compared with the absolute measurements shown in Figures 1 and 2. In addition, from the percent diameter stenosis display, it would appear that 6 lesions underwent significant early deterioration in lesion severity ("early restenosis"). This discrepancy with the absolute minimal luminal diameter measurements is due to the increase in reference diameter (Figure 2, left), as described in the text.

giography. Patients in whom balloon angioplasty was not satisfactorily successful, for whatever reason, need to be managed differently (perhaps including repeat angiography), and is not an issue in this report. In lesions without important angiographic complications, Preisack et al¹¹ also found no significant change in absolute minimal luminal dimensions during 24 hours, in general agreement with our findings and a previous report from Laarman et al.¹⁹

Thus, it must be concluded that the additional risk of patient morbidity (\pm mortality) prolonged hospitalization, as well as health care worker and specialist time, labor and cost involved in carrying out routine repeat 24-hour angiography would yield no extra information or benefit and is clearly not warranted.

2. Postangioplasty measurement variability is highly acceptable: The postballoon angioplasty lesion measurement accuracy of the Cardiovascular Angiographic Analysis System is <0.01 mm and the variability is ± 0.2 mm, which in our estimation is eminently acceptable. Twice this lesion measurement variability (± 0.4 mm) identifies (with 95% confidence) lesions in which a real, detectable ("significant") luminal decrease (or increase) occurs over time. Three times the variability (± 0.6 mm) will provide 99% confidence for the detection of a real change in luminal dimensions. Thus, in this study, 4 lesions showed a detectable deterioration during 24 hours (Figure 1, left). Although we do not advocate the application of a categorical approach to evaluating long-term angiographic outcome of interventions,² it may occasionally be desirable to stratify patients or lesions according to the degree of luminal change developing over time. To this end, the application of lesion measurement variability of the particular measurement system involved is recommended as the stratification method. Measurement variability may vary from system to system, and is a vital piece of information necessary for the purpose of objective comparison of the results of intervention trials using different angiographic measurement systems.

The measurement variability reported here is considerably different from that previously reported in patients undergoing diagnostic coronary angiography a mean of 90 days apart, without therapeutic intervention (0.72 mm).¹⁶ The reasons for this difference need to be highlighted: In the original study published in 1985, mean vessel size was 3.7 mm, compared with 2.7 mm in this study (which is representative of current experience^{4,5}). The former study was performed under a self-proclaimed "worst-case scenario," i.e., unmatched angiographic projections, no particular care taken in recording angiograms suitable for quantitative analysis, no vasomotor control, and so forth, whereas the current study was performed under ideal angiographic conditions, as outlined previously. Because such procedures are routinely performed in all important angiographic studies,^{4,5} the lesion measurement variability previously reported is no longer relevant. It is worth noting, however, that the medium term measurement variability (obtained using vasomotion control and matched projections) previously reported was 0.20 mm,¹⁶ exactly the same as found in this study. Recent experimental inves-

tigations of the accuracy and precision of off-line and on-line quantitative angiographic analysis (using digital and cineangiographic recording of swine "phantom" coronary stenoses of known dimensions) revealed a measurement accuracy of -0.07 mm and a precision of ± 0.2 mm (measured dimension of the phantom stenoses versus actual phantom dimension).²⁰ These findings are collectively indicative of the high level of accuracy and precision of the MLD measurement by the Cardiovascular Angiographic Analysis System, even in the aftermath of balloon angioplasty.

3. There is no delayed elastic recoil after successful angioplasty: Previous reports^{12,21} that elastic recoil is an instantaneous phenomenon occurring immediately after balloon deflation and that no additional recoil occurs during the next 24 hours are confirmed. Nobuyoshi et al²² previously reported a 16% incidence of "early restenosis" based on the measurement variability of their quantitative angiographic measurement system, in accordance with a significant decrease in MLD during 24 hours after successful angioplasty. In our patient group, only 4 lesions (3.6%) had a significant luminal decrease from postangioplasty to 24 hours. The reasons for this disagreement may lie in the methodologic and quantitative angiographic approaches. For example, intracoronary nitrate may not have been consistently administered before angiography by Nobuyoshi et al, who also used only a videodensitometric approach to estimate diameter, a method better suited to cross-sectional area measurements.^{17,23} In addition, it is worth noting the apparent increase in MLD between 1 day and 1 month (almost to the level of the postangioplasty result), and the lack of correlation between the change within 24 hours and the long-term change at 6 months, which could not be explained. Either the reliability of their 24-hour measurements must be questioned, or the possibility of early mural thrombus formation with later resolution (since their patients were not anticoagulated for 24 hours) must also be considered as a possible explanation for the early luminal deterioration and subsequent improvement. According to biochemical and angiographic evidence, with adequate anticoagulation control in this study (having excluded patients with complicated angioplasty or major adverse cardiac events), there appeared to be no significant thrombus formation during the first 24 hours after successful balloon angioplasty.

4. Percent diameter stenosis is an unreliable measurement: The significant increase in interpolated reference diameter from postangioplasty to 24 hours is responsible for the observed increase in measured percent diameter stenosis. This finding reiterates conclusions of previous studies^{24,25} regarding potential for misinformation by preferential use of percent diameter stenosis for description of the severity of luminal obstructions. Figures 1 to 3 further illustrate the imprecision of percent versus absolute measurement parameters.

The increase in reference vessel dimensions may be due to greater effectiveness of intracoronary nitrate at 24 hours on the relatively disease-free vessel segment. The vasoconstrictive stimulus of the dilatation procedure and the release of vasoactive substances from the damaged

endothelium and platelets may prevent immediate realization of dimensional increase in the relatively undiseased vessel adjacent to the target lesion.

Study limitations: Patients with unstable angina receiving intravenous heparin were excluded. It could be suggested that unstable lesions might "behave" differently during the 24 hours after successful angioplasty, since it is known that unstable angina predisposes to periprocedural and in-hospital major adverse cardiac events.²⁶ This limitation would need to be addressed by further study in "unstable" patients.

Perhaps the ideal test of accuracy and precision of quantitative angiography, according to current technology, would involve comparison with intravascular ultrasound findings.^{7,8,27} However, it must be recognized that intravascular ultrasound is itself fraught by considerable limitations. It cannot be usefully applied to the evaluation of severe stenoses or to extremely tortuous or small vessels, which makes complete preinterventional assessment impossible in a large proportion of lesions treated in daily practice⁸ (average MLD in recent "restenosis prevention trials" was approximately 1 mm^{4.5}). Furthermore, "good" quality images may not be obtainable in certain clinical situations, such as the presence of intimal disruptions after angioplasty.²⁸ Until the vessel wall and lumen areas are more objectively and reproducibly quantifiable by intravascular ultrasound, quantitative angiography must still be considered as the "gold standard."

1. Beatt KJ, Serruys PW, Hugenoltz PG. Restenosis after coronary angioplasty: new standards for clinical studies. *J Am Coll Cardiol* 1990;15:491-498.
2. Serruys PW, Foley DP, de Feyter PJ. Restenosis after coronary angioplasty: a proposal of new comparative approaches based on quantitative angiography. *Br Heart J* 1992;68:417-424.
3. Popma JJ, Califf RM, Topol EJ. Clinical trials of restenosis following angioplasty. *Circulation* 1991;84:1426-1437.
4. Serruys PW, Rutsch W, Heyndrickx GR, Danchin N, Mast EG, Wijns W, Rensing BJ, Vos J, Stibbe J. Prevention of restenosis after percutaneous transluminal coronary angioplasty with thromboxane A2 receptor blockade. A randomized, double blind, placebo controlled trial. *Circulation* 1991;84:1568-1580.
5. The Mercator Study Group. Does the new angiotensin converting enzyme inhibitor cilazapril prevent restenosis after percutaneous transluminal coronary angioplasty? The results of the Mercator study: a multicenter randomized double-blind placebo-controlled trial. *Circulation* 1992;86:100-111.
6. Ellis SG, Muller DWM. Arterial injury and the enigma of restenosis. *J Am Coll Cardiol* 1992;19:275-277.
7. Honye J, Mahon DJ, Jain A, White CJ, Ramsee SR, Wallis JB, Al-Zarka A, Tobis JM. Morphological effects of coronary balloon angioplasty in vivo assessed by intravascular ultrasound imaging. *Circulation* 1992;85:1012-1025.
8. Potkin BN, Keren G, Mintz GS, Douek PC, Pichard AD, Satler LF, Kent KM, Leon MB. Arterial responses to balloon coronary angioplasty: an intravascular ultrasound study. *J Am Coll Cardiol* 1992;20:942-951.
9. Uchida Y, Hasegawa K, Kawamura K, Shibuya I. Angioscopic observation of the coronary luminal changes induced by coronary angioplasty. *Am Heart J* 1989;117:769-776.
10. Hermans WRM, Rensing BJ, Foley DP, Deckers JW, Rutsch W, Emanuelsson H, Danchin N, Wijns W, Chappuis F, Serruys PW, on behalf of the Mercator Study group. Therapeutic dissection after successful coronary angioplasty: no

effect on restenosis or on clinical outcome in 693 patients. *J Am Coll Cardiol* 1992;20:767-780.

11. Preisack MB, Athanasiadis A, Voelker W, Karsch KR. Reliability of quantitative coronary angiography of the target lesion immediately and 1 day after coronary balloon and excimer laser angioplasty. *J Am Coll Cardiol* 1993;21:876-884.
12. Rensing BJ, Hermans WRM, Beatt KJ, Laarman GJ, Suryapranata H, van den Brand M, De Feyter PJ, Serruys PW. Quantitative angiographic assessment of elastic recoil after percutaneous transluminal coronary angioplasty. *Am J Cardiol* 1990;66:1039-1044.
13. van den Bos AA, Deckers JW, Heyndrickx GR, Laarman GJ, Suryapranata H, Zijlstra F, Close P, Rijnierse JMM, Buller HR, Serruys PW. Safety and efficacy of recombinant hirudin (CGP 39 393) versus heparin in patients with stable angina undergoing coronary angioplasty. *Circulation* 1993; in press.
14. di Mario C, Hermans WRM, Rensing BJ, Serruys PW. Calibration using angiographic catheters as scaling devices — importance of filming the catheters not filled with contrast medium [Letter]. *Am J Cardiol* 1992;69:1377.
15. Reiber JHC, Booman S, Tan HS, Gerbrands JJ, Slager CJ, Schuurbiens JCH, Meester GT. Computer processing of coronary occlusions from x-ray arteriograms. Proceedings VI International Conference on Information Processing in Medical Imaging (Paris), 1979:79-92.
16. Reiber JHC, Serruys PW, Kooijman CJ, Wijns W, Slager CJ, Gerbrands JJ, Schuurbiens JCH, den Boer A, Hugenoltz. Assessment of short-, medium-, and long-term variations in arterial dimensions from computer assisted quantitation of coronary cineangiograms. *Circulation* 1985;71:280-288.
17. Reiber JHC, Serruys PW. Quantitative coronary angiography. In: Marcus ML, Schelbert HR, Skorton DJ, Wolf GI, eds. *Cardiac Imaging, a Companion to Braunwald's Heart Disease*. New York: WB Saunders, 1991:211-280.
18. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;2:307-310.
19. Laarman GJ, Serruys PW, Suryapranata H, van den Brand M, Jonkers PR, de Feyter PJ, Roelandt JRTC. Inability of coronary flow reserve measurements to assess the efficacy of coronary angioplasty in the first 24 hours in unselected patients. *Am Heart J* 1991;122:631-639.
20. Haase J, de Mario C, Slager CJ, van der Giessen WJ, den Boer A, de Feyter PJ, Verdow PD, Reiber JHC, Serruys PW. In-vivo validation of on-line and off-line geometric coronary measurements using insertion of stenosis phantoms in porcine coronary arteries. *Cath Cardiovasc Diagn* 1992;27:16-27.
21. Hanet C, Wijns W, Michel X, Schroeder E. Influence of balloon size and stenosis morphology on immediate and delayed elastic recoil after percutaneous transluminal coronary angioplasty. *J Am Coll Cardiol* 1991;18:506-511.
22. Nobuyoshi M, Kimura H, Nosaka H, Mioka S, Ueno K, Hamasaki N, Horiuchi H, Oshishi H. Restenosis after successful percutaneous transluminal coronary angioplasty: serial angiographic follow-up of 299 patients. *J Am Coll Cardiol* 1988;12:616-623.
23. Serruys PW, Reiber JHC, Wijns W, van den Brand M, Kooijman CJ, ten Kate HJ, Hugenoltz PG. Assessment of percutaneous transluminal coronary angioplasty by quantitative coronary angiography: diameter versus densitometric area measurements. *Am J Cardiol* 1984;54:482-488.
24. Beatt KJ, Luijten HE, de Feyter PJ, Brand van de M, Reiber JH, Serruys PW. Change in diameter of coronary artery segments adjacent to stenosis after percutaneous transluminal coronary angioplasty: failure of % diameter stenosis measurement to reflect morphologic changes induced by balloon dilation. *J Am Coll Cardiol* 1988;12:315-323.
25. Serruys PW, Luijten HE, Beatt KJ, Geuskens R, de Feyter PJ, van den Brand M, Reiber JH, ten Kate HJ, van Es GA, Hugenoltz PG. Incidence of restenosis after successful coronary angioplasty: a time-related phenomenon. A quantitative angiographic study in 342 consecutive patients at 1, 2, 3 and 4 months. *Circulation* 1988;77:361-371.
26. Hermans WRM, Foley DP, Rensing BJ, Rutsch W, Heyndrickx GR, Danchin N, Maast G, Wijns W, Lablanche JM, Rafflenbeul W, Uebis R, Balcon R, de Feyter PJ, Serruys PW, on behalf of the CARPORT and MERCATOR study groups. Usefulness of quantitative and qualitative angiographic lesion morphology, and clinical characteristics in predicting major adverse cardiac events during and after native coronary balloon angioplasty. *Am J Cardiol* 1993;72:14-20.
27. Waller BF, Pinkerton CA, Slack JD. Intravascular ultrasound: a histological study of vessels during life. The new "gold standard" for vascular imaging. *Circulation* 1992;85:2305-2310.
28. Di Mario C, Madretsma S, Linker D, The SH, Born N, Serruys PW, Gussenhoven EJ, Roelandt JRTC. The angle of incidence of the ultrasonic beam: a critical factor for the image quality in intravascular ultrasonography. *Am Heart J* 1993;125:442-448.