Assessment of short-, medium-, and long-term variations in arterial dimensions from computer-assisted quantitation of coronary cineangiograms

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ABSTRACT A computer-assisted technique has been developed to assess absolute coronary arterial dimensions from 35 mm cineangiograms. The boundaries of optically magnified and video-digitized coronary segments and the intracardiac catheter are defined by automated edge-detection techniques. Contour positions are corrected for pincushion distortion. The accuracy and precision of the edge detection procedure as assessed from cinefilms of contrast-filled acrylate (Perspex) models were −30 and 90 μm, respectively. The variability of the analysis procedure itself in terms of absolute arterial dimensions was less than 0.12 mm, and in terms of percentage arterial narrowing for coronary obstructions less than 2.74%. Short-, medium-, and long-term variability measurements were assessed from repeated coronary angiographic examinations performed 5 min, 1 hr, and 90 days apart, respectively. For all studies the mean differences in absolute diameters were less than 0.13 mm. The variability in obstruction diameter ranged from 0.22 mm for the best-controlled study (medium-term) to 0.36 mm for the least-controlled study (long-term); variability in reference diameter ranged from 0.15 to 0.66 mm, respectively. It is concluded that the biological variations are a source of major concern and that further attempts toward standardization of the angiographic procedure are seriously needed.
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CONVENTIONAL visual evaluation of the severity of coronary obstructions from 35 mm cineangiograms has been limited by relatively large interobserver and intraobserver variations.[1–4] Moreover, by this technique the degree of luminal narrowing can be determined only in terms of percentage diameter narrowing assessed from one or more views. To evaluate the efficacy of modern therapeutic procedures in the catheterization laboratory,[5–8] the effects of vasoactive drugs,[9, 10] and the effects of short- and long-term interventions on the regression or progression of coronary artery disease,[11] an objective and reproducible technique for the assessment of coronary arterial dimensions is seriously needed.

Over the last few years there has been an increasing interest in quantitation of coronary cineangiograms. The various systems used to date vary to a great extent, from manual procedures that implement a vernier caliper or comparable device[12–17] to a computerized manual edge-tracing procedure[18] and methods that make use of computer edge detection algorithms to determine arterial dimensions in a two-dimensional projection.[19–29] Several investigators have also applied densitometric procedures in an attempt to derive cross-sectional area measurements from single-view coronary cineangiograms.[30–36] Finally, methods have been proposed for the three-dimensional representation of coronary arterial segments assessed from two orthogonal views.[18, 20, 37] A detailed overview of the different computer techniques developed has been published elsewhere.[38]

The purposes of this article are (1) to briefly describe the basic principles of a new computerized analysis procedure for coronary arterial segments, (2) to present the results from a validation study of this technique, and (3) to discuss the overall short-, medium-,

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and long-term variability in the assessment of arterial dimensions from repeated coronary angiographic and computer analysis.

Materials and methods

Analytic procedure. The procedures for quantitative analysis of coronary arterial segments have been implemented on the computer-based Coronary Angiography Analysis System (figure 1).[21–23] The cinefilm is mounted on a specially constructed cinevideo converter.[32] The selected cineframe is projected onto the target of a high-resolution video camera via a drum with six different lens systems, which allows for six different optical magnifications. The video camera is attached to a movable x-y stage, so that any area of interest in the cineframe can be selected with the appropriate magnification factor. The center square of the resulting analog video image is digitized in matrix size of 512 × 512 picture elements (pixels) with eight bits (256 levels) brightness resolution and displayed on a video monitor. At several crucial moments in the analysis procedure, user-interaction is possible by means of a writing tablet.

To analyze the dimensions of a coronary arterial segment quantitatively, the following steps are performed: (1) computation of the calibration factor on the basis of the contrast catheter displayed in the images, (2) boundary detection of the arterial segment, (3) computation of the diameter function from the detected and pincushion-corrected contour positions, (4) determination of the severity of a coronary obstruction in terms of absolute and relative parameters, and (5) determination of the mean diameter over one or more user-defined nonobstructed portions of this segment. The different steps will be described briefly.

Contour detection. Calibration of the diameter data of the vessels in absolute values (mm) is achieved by computer detection of the outer boundaries of a user-selected portion of the optically magnified contrast catheter (optical magnification factor $2\sqrt{2}$). The contour data are corrected for the pincushion distortion in the image. From the corrected contour positions a mean diameter value is determined in pixels; the calibration factor is then expressed in millimeters per pixel from the known size of the catheter.

Pincushion distortion from the image intensifier results in a position-dependent magnification of an object. Since the distortion cannot be described by a simple analytic function, a cineframe of a centimeter grid placed against the input screen of the image intensifier is used to assess the distortion. A correction vector for each pixel in the image can be obtained from the automatically computer-processed cineframe of the grid.

The procedure for arterial contour detection requires the user to indicate a number of center positions in the optically magnified arterial segment (optical magnification factor 2). A smoothed version of this centerline determines regions of interest of size 96 × 96 pixels encompassing the arterial segment to be transferred to the host processor (PDP 11/44) for edge definition. To decrease spatial fluctuations due to quantum noise, the digital data are smoothed spatially with a 5 × 5 median filter. Subsequently, the digital data are resampled along straight lines, denoted scanlines, perpendicular to the local centerline directions. Contours of the arterial segment along the scanlines are determined on the basis of the weighted sum of first and second difference functions applied to the resampled brightness information by so-called minimal cost criteria. If the user does not agree with part of the detected contours, these erroneous positions may be corrected interactively with the writing tablet. Figure 2 shows the intermediate steps in the edge detection procedure for the obtuse marginal branch of figure 3.

Since the tentative centerline was initially defined by the user, the detected contours may be slightly dependent on the given centerline positions, particularly at sections with high curvature. To minimize this influence as much as possible, a final centerline is determined automatically as the midline of the detected and possibly corrected contours. The digital data are resampled and the minimum cost algorithm for contour detection is applied again. Finally, a smoothing procedure is applied to each of the detected contours and the resulting positions are corrected for pincushion distortion. Figure 3 shows the finally detected contours along the obtuse marginal branch.

Contour analysis. The diameter function D(i) of the arterial segment, calibrated in absolute millimeters, is determined by computing the distances between corresponding contour points to the left and right of the centerline. From the minimal value D_m of the diameter function and the mean diameter value D_r at a

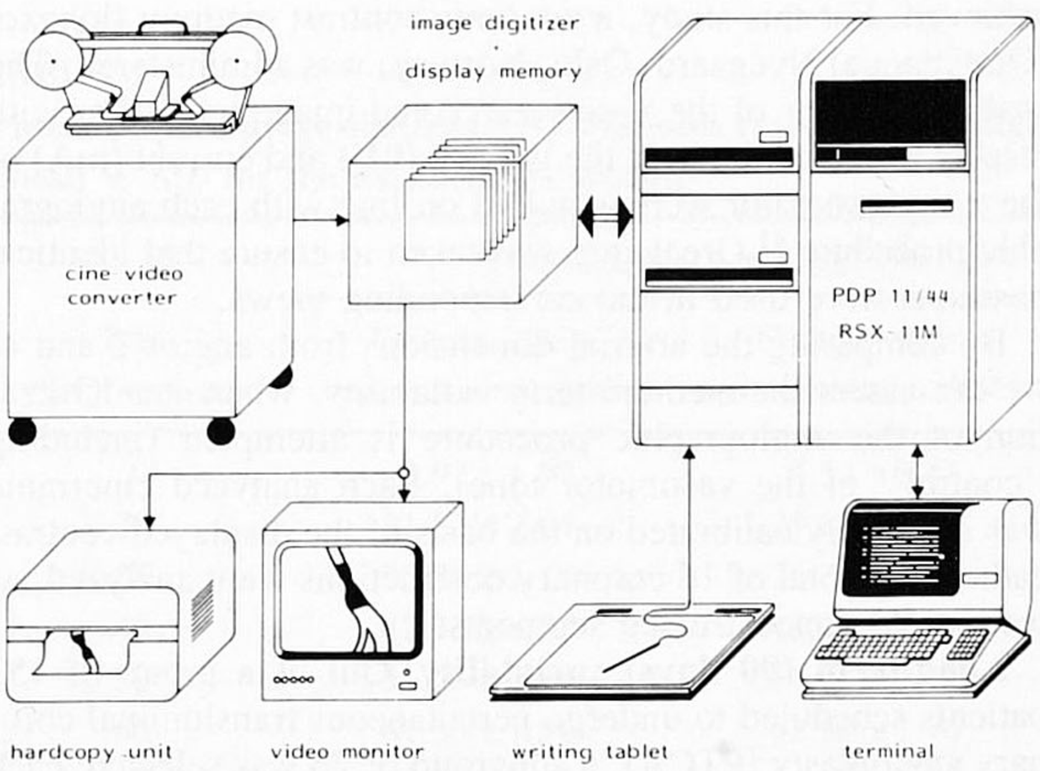

FIGURE 1. Block diagram of the Coronary Angiography Analysis System.

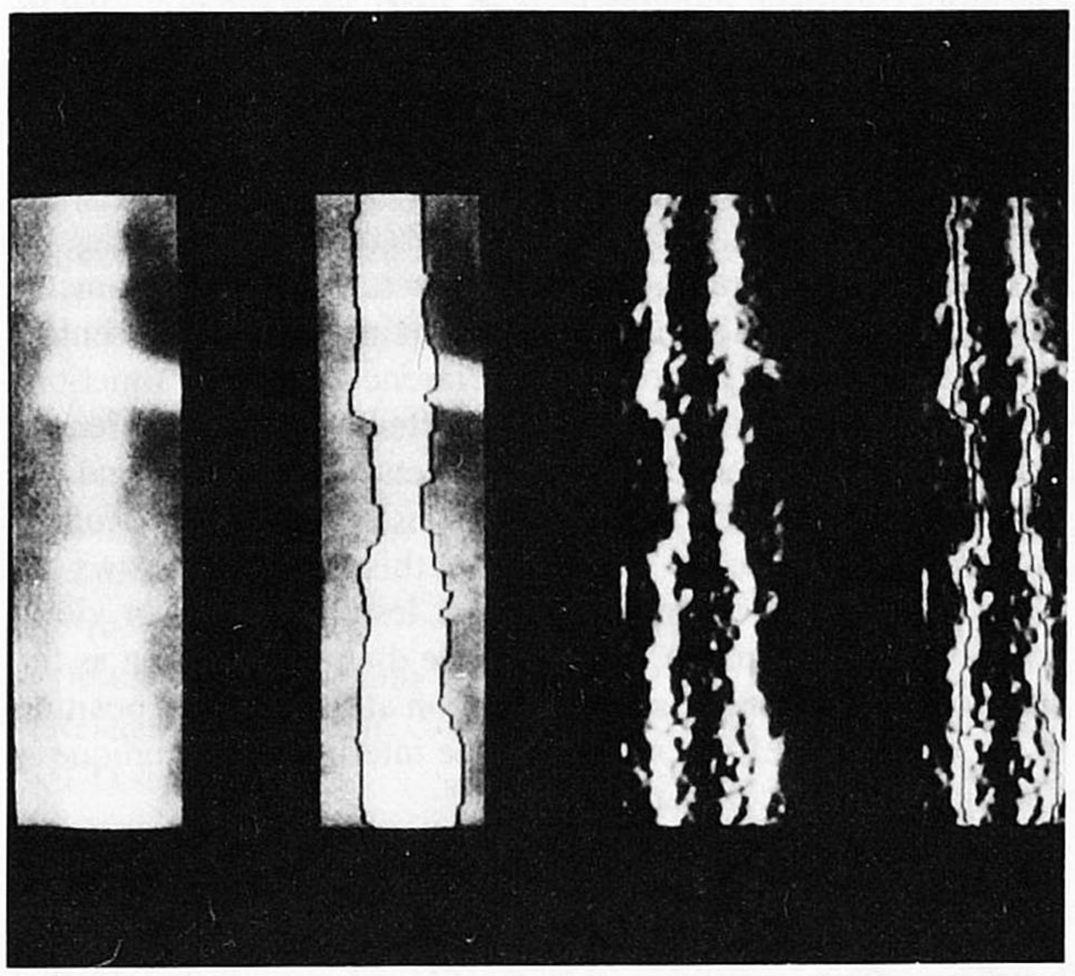

FIGURE 2. Illustration of the intermediate steps in the edge detection procedure for the obtuse marginal branch shown in figure 3. *A*, Transformed intensity matrix. *B* Transformed intensity matrix with contours superimposed. *C*, Cost matrix with the brightness level of each pixel being a measure for the weighted sum of the first and second difference functions for that particular pixel. *D*, Cost matrix with detected contour (minimal cost paths) superimposed.

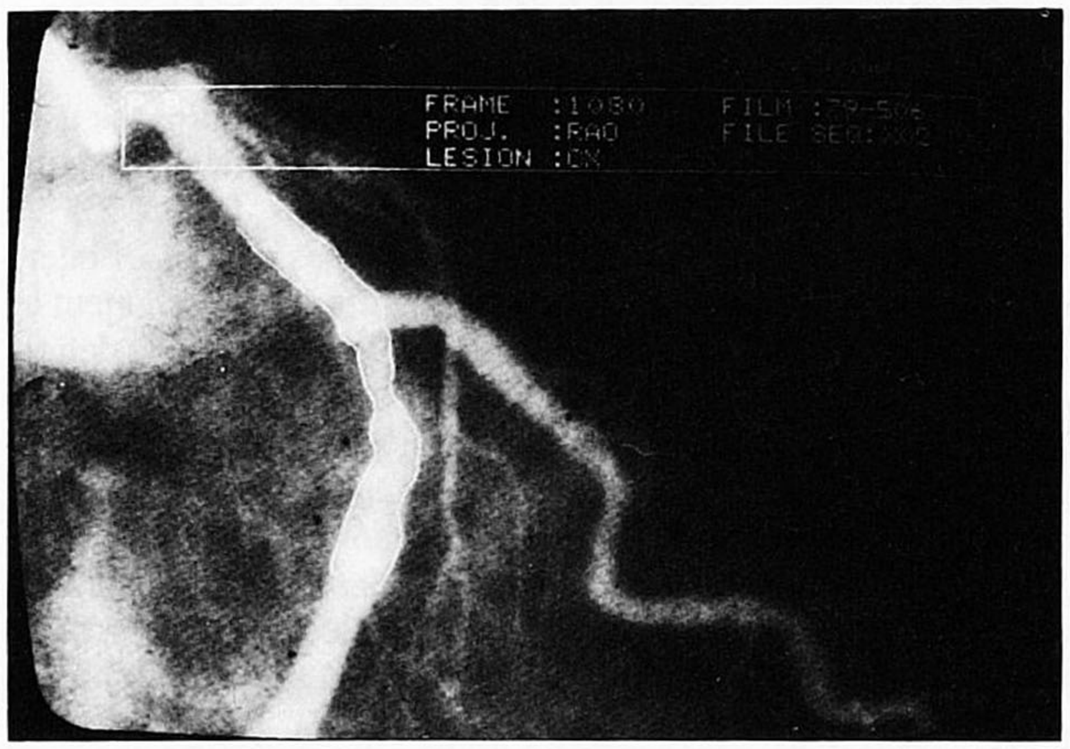

FIGURE 3. Example of 2:1 magnified window from original cineframe showing obtuse marginal branch with focal obstruction. The contours detected according to the procedure illustrated in figure 2 have been transformed back toward the digitized image; an administrative data block is displayed at the top.

user-indicated reference position, the percentage diameter (%-D) reduction is computed as

$$\%\text{-D stenosis} = \left(1 - \frac{D_m}{D_r}\right) \times 100\%$$

The mean diameter D_r is computed as the average of 11 diameter values in a symmetric region with the center at the user-defined reference position. A typical example of such an analysis is illustrated in the companion article.[8] The extent of the obstruction is determined from the diameter function D(i) on the basis of curvature analysis and expressed in millimeters.[22]

The computed percentage diameter stenosis may depend heavily on the selected reference position. To minimize these variations, we have implemented an alternative method, denoted interpolated percentage diameter stenosis, which is not dependent on a user-defined reference region.

The basic idea behind this technique is the computer estimation of the original diameter values over the obstructed region (reference diameter function, assuming there was no coronary disease present) from the actual luminal diameter function.[8, 21–23] On the basis of the proximal and distal centerline segments and the computed reference diameter function, the reference contours over the obstructed region can be reconstructed. The difference in area between the reference and the detected contours over the obstructive lesion is a measure for the "atherosclerotic plaque"; in addition, this technique allows the assessment of the eccentricity of the lesion in a given view. Following this approach, the reference diameter is taken as the value of the reference diameter function at the minimal position of the obstruction. An example of the interpolated technique is illustrated in the companion article.[8]

The total time required for the analysis of a single coronary obstruction from a cineframe in terms of user-defined percentage diameter stenosis is 10 min. This time includes all necessary handling, from mounting the cinefilm, locating the desired frame, and performing the described contour detection and analysis procedures, until the moment that the results are obtained on hardcopy output. To analyze a second arterial segment in the same cineframe requires an additional 4.5 min.

Accuracy and precision of the contour detection technique. To determine the accuracy and precision of the contour detection process, cinefilms of nine acrylate (Perspex) models of coronary arteries with circular cross sections filled with contrast medium were analyzed. Absolute dimensions of the models were known with an accuracy of ±0.01 mm. The percentage diameter narrowing for this set of models ranged from 0% to 70%. The models were filmed in the center of the image intensifier field-of-view under 10 cm of water with various settings of the quality (range 60 to 110 kV) of the x-ray system; different concentrations (50% and 100%) of the contrast agent (diatrizoate [Urografin-76] Schering AG, Berlin) were used.

Variability data analysis. The variability of repeated analyses of cineangiograms was assessed from a total of 13 end-diastolic cineframes of 13 routinely obtained coronary angiograms. These cineframes were analyzed twice by one technical analyst with a medium time interval of 28 days.

For all studies described in this article, cineframes were selected at end-diastole, if possible. In cases of overlap of a segment to be analyzed with other vessels, the frame was selected at another instant in time near end-diastole. The user-determined beginning and end points of the major coronary segments were standardized according to the definitions of the American Heart Association.[39]

Short-term (5 min) variability. The short-term variability was defined as that in measured arterial dimensions from repeated acquisition and analysis of coronary cineangiograms taken 5 min apart with unchanged positions of x-ray source and image intensifier. Data were collected from 12 patients catheterized for suspected coronary artery disease; an ionic contrast medium, Urografin-76, was used.

A total of eight coronary lesions and 39 nonobstructed segments were selected for quantitative angiographic analysis. Since the views were unchanged during the repeat angiographic examinations, calibration was performed only for the first set of angiograms.

Medium-term (1 hr) variability. As part of a pharmacologic intervention study, we assessed the 1 hr variability in the measurements of coronary arterial dimensions with repeated coronary angiographic examination and analysis in a group of 11 patients. Immediately after control cineangiographic examinations in multiple views (angio 1), the first metabolite of molsidomine (Cassella, Frankfurt am Main, Federal Republic of Germany) (SIN 1) was administered in the left main stem; 2 min thereafter, coronary angiograms were obtained in the same multiple views to study the immediate effect of the drug on the dimensions of the coronary arteries (angio 2).[40] One hour later these angiograms were repeated to assess the long-term effect of the drug (angio 3). A fourth angiographic procedure (angio 4) was carried out after a second intracoronary administration of the drug to determine whether further dilatation could be achieved. For this study, a nonionic contrast medium (iohexol [Omnipaque] Nyegaard, Oslo, Norway) was administered. The spatial positions of the x-ray source and image intensifier with respect to the patient and the voltage (kV) and current (mA) of the x-ray generator were acquired on-line with each angiographic procedure.[41] Great care was taken to ensure that identical positions were used in the corresponding views.

By comparing the arterial dimensions from angios 2 and 4, we can assess the medium-term variability, when standardization of the angiographic procedure is attempted (including "control" of the vasomotor tone). Each analyzed cineframe was separately calibrated on the basis of the displayed contrast catheter. A total of 16 coronary obstructions were analyzed, as well as 90 nonobstructed segments.

Long-term (90 days) variability. Out of a group of 153 patients scheduled to undergo percutaneous transluminal coronary angioplasty (PTCA), a subgroup of 26 was selected; each subject had two cineangiograms of good quality in a number of standard views that were suitable for paired analysis of the

stenotic lesions.[7] The first film was the diagnostic angiogram, while the second measurements were obtained from cineframes acquired immediately before the actual PTCA procedure. At the time of the angiographic investigations, no attempt was made to standardize inspiratory level, volume, and rate of injection of the contrast agent or technical characteristics of the x-ray system. More importantly, the vasomotor tone in both conditions was unknown and neglected. The median delay between the diagnostic and the PTCA angiogram was 90 days (range 1 to 250 days).

Statistical analysis. The results from the various studies were analyzed for significant differences with Student's t test for paired values (border of significance, $p = .01$).

The accuracy of the contour detection technique was defined by the average difference of the computed results with the true values and the precision was defined by the pooled SD of the differences.

Results

Accuracy and precision of the contour detection technique. For the obstructions in the acrylate models the diameter reduction percentages and the absolute obstruction dimensions were measured. For each model with a given concentration of the contrast agent, the mean ± SD of all the measurements at the various kilovolt levels of the x-ray tube were determined (tables 1 and 2). The overall accuracy and precision for the percentage diameter stenosis measurements equaled 2.00% and 2.68%, respectively, and for the obstruction diameters −30 and 90 μm, respectively.

Variability data analysis. A total of 13 coronary obstructions and 25 nonobstructed segments were analyzed twice. The mean differences ± SD of the repeated measurements as well as the overall mean values of the parameters are presented in table 3. With the exception of the interpolated reference diameter measurement and the mean diameter of nonobstructed segments, no significant differences were found between the repeated measurements. The SD of absolute measurements was less than 0.12 mm; SDs of percentage diameter stenosis measurements for the user-defined and interpolated procedures were 2.74% and 3.94%, respectively.

Short-term variability. The mean differences in the measured parameters from the repeat angiograms were all nonsignificant (table 4). The short-term variability in the obstruction diameter (SD = 0.34 mm) was about twice that of measurements at nonobstructed portions of the segments (reference diameter, SD = 0.17 mm; mean diameter of nonobstructed segments, SD = 0.16 mm). These last two variability measurements were about 50% higher than the values obtained from repeated analyses of cinefilms only (table 3).

Medium-term variability. The results on the x-ray gantry settings are presented in table 5. The angular variability, computed from the absolute differences of angular settings, was less than 4.2 degrees and the

TABLE 1
Measured percentage diameter (%-D) stenosis vs true %-D stenosis (mean ± SD) for the nine acrylate models

True %-D stenosis	Measured %-D stenosis: Contrast agent concentration 100%	Measured %-D stenosis: Contrast agent concentration 50%
0	0.92 ± 1.90	3.33 ± 3.41
20	21.83 ± 2.04	21.83 ± 2.48
25	25.33 ± 3.14	26.33 ± 1.21
40	42.33 ± 3.27	43.17 ± 4.12
50	51.50 ± 3.27	54.83 ± 2.93
60	61.33 ± 1.51	62.50 ± 1.76
62.5	63.33 ± 2.42	64.67 ± 3.27
70	70.50 ± 1.97	73.33 ± 2.25

TABLE 2
Measured vs true obstruction diameters (mean ± SD) for nine acrylate models

True size (mm)	Measured size (mm): Contrast agent concentration 100%	Measured size (mm): Contrast agent concentration 50%
5	4.90 ± 0.10	4.97 ± 0.12
4	3.95 ± 0.10	3.94 ± 0.09
3	2.99 ± 0.09	3.00 ± 0.11
2	1.97 ± 0.11	1.98 ± 0.09
1.5	1.50 ± 0.06	1.50 ± 0.10

TABLE 3
Variability in measurements of parameters of coronary arterial segments from repeated analysis of 13 cineframes

	Overall mean value	Mean diff.	p value	SD diff.
Calibration factor (mm/pixel)	0.096	0.0003	NS	0.002
User-defined reference (n = 13)				
Obstruction diam. (mm)	1.52	0.00	NS	0.10
Reference diam. (mm)	2.97	0.005	NS	0.12
%-D stenosis (%)	48.4	0.23	NS	2.74
Extent (mm)	8.42	−0.38	NS	1.89
Interpolated reference (n = 13)				
Reference diam. (mm)	2.87	−0.10	<.004	0.10
%-D stenosis (%)	47.9	−2.08	NS	3.94
Nonobstructed segments (n = 25)				
Mean diam. (mm)	2.42	0.07	<.005	0.11
Length segment (mm)	17.72	0.02	NS	0.97

%-D = percentage diameter.

TABLE 4
Short-term variability in measurements of various parameters of coronary arterial segments for the two control cineangiograms

	Overall mean value	Mean diff.	p value	SD diff.
User-defined reference (n = 8)				
Obstruction diam. (mm)	1.66	0.05	NS	0.34
Reference diam. (mm)	3.33	−0.10	NS	0.17
%-D stenosis (%)	46.5	−2.46	NS	8.01
Extent (mm)	6.6	0.5	NS	1.31
Interpolated reference (n = 8)				
Reference diam. (mm)	3.17	0.02	NS	0.21
%-D stenosis (%)	44.9	−0.90	NS	8.30
Nonobstructed segments (n = 39)				
Mean diam. (mm)	2.82	−0.005	NS	0.16
Length segment (mm)	11.37	−0.33	NS	1.36

%-D = percentage diameter.

variability in the various positions of image intensifier and x-ray source was less than 3.0 cm. There were no significant differences between the repeated x-ray system settings. These results show that the x-ray system settings can be reproduced accurately in routine clinical practice.

The mean differences in the measured parameters from angios 2 and 4 were all nonsignificant (table 6). The overall mean values were computed from angio 2. The medium-term variabilities in the obstruction diameters were 35% lower than those for the short-term study, while the variabilities in mean diameter and user-defined reference diameter increased by 50% and 65%, respectively. The variability in the interpolated reference diameter decreased by 29% with respect to the 5 min study.

Long-term variability. The nonsignificant mean differences in the obstruction diameters suggest that no detectable progression or regression of atherosclerotic

TABLE 5
Variability in x-ray gantry settings with repeated cineangiographic studies (n = 25)

	Overall mean value	Mean diff.	p value	SD diff.
Rotation U-arm (degrees)	31.2	0.3	NS	4.2
Rotation pat./C-arm (degrees)	26.4	0.3	NS	2.2
Isocenter-image intensifier distance (cm)	22.6	1.1	NS	3.0
Focus-isocenter distance (cm)	72.8	−0.3	NS	0.8
Object-isocenter distance (cm)	5.3	0.2	NS	1.4

TABLE 6
Medium-term variability in measurements of various parameters of coronary arterial segments from repeated coronary angiographic studies and analysis[A]

		Angio 4 − 2		
	Overall mean	Mean diff.	p value	SD diff.
Calibration factor (mm/pixel) (n = 25)	0.094	−0.001	NS	0.002
User-defined reference (n = 16)				
Obstruction diam. (mm)	2.13	0.00	NS	0.22
Reference diam. (mm)	3.57	0.06	NS	0.28
%-D stenosis (%)	41.3	0.75	NS	8.09
Extent (mm)	6.28	−0.15	NS	2.03
Interpolated reference (n = 14)				
Reference diam. (mm)	3.32	0.05	NS	0.15
%-D stenosis (%)	38.1	1.21	NS	7.23
Nonobstructed segments (n = 90)				
Mean diam. (mm)	3.05	0.07	NS	0.24
Length segment (mm)	14.03	−0.03	NS	1.02

%-D = percentage diameter.

[A]Angiograms 2 and 4 were performed immediately after administration of a vasodilative drug. Time between angios 2 and 4 was approximately 1 hr (see text).

lesions had occurred over the period of 90 days (table 7). These paired data provide some insight in the total variability of the cineangiographic procedure and the computer analysis under worst-case circumstances, since no special care had been taken to reduce the potential sources of variability (x-ray system settings, vasomotor tone, etc.).

Under these particular conditions, the variations in absolute measurements were 0.36 mm for the obstruction diameter and 0.66 mm for the interpolated reference diameter, and in relative measurements 6.5% for the interpolated percentage diameter stenosis.

Discussion

We have developed a computer-based system that facilitates an objective and reproducible approach to the assessment of coronary artery disease. The system combines a number of important features: (1) a region of interest in a selected cineframe encompassing the arterial segment to be analyzed is optically magnified and video converted by means of a specially constructed x-y controlled cinevideo converter; (2) a highly reliable edge detection algorithm has been developed; (3) the boundary information is corrected for magnification and distortion in the images; (4) absolute values of clinically important parameters of lesion severity can be assessed in a reliable manner; and (5) the analy-

TABLE 7
Long-term variability in measurements of various parameters of coronary obstructions (n = 26)

	Overall mean value	Mean diff.	p value	SD diff.
Obstruction diam. (mm)	1.25	0.00	NS	0.36
Extent (mm)	10.04	0.62	NS	4.34
Interpolated reference				
Reference diam. (mm)	3.72	−0.13	NS	0.66
%-D stenosis (%)	66.19	−1.92	NS	6.52

%-D = percentage diameter.

sis procedure has been designed to be user-friendly so that a technical analyst can work with it after a short training period.

Technical characteristics. Since large changes in underlying background densities may occur in a cineframe, it is of great importance that a cineframe is illuminated homogeneously over the entire image. Only then it is possible to fully utilize the dynamic range of the video camera and digitize the optical density changes at the arteries with a maximum number of gray levels. The optical path of the cinevideo converter has been designed for such a homogeneous response; this plays a role not only in accurate edge detection, but even more so in implementation of techniques for densitometric analysis.

The edge detection algorithm is based on the weighted sum of first- and second-derivative functions. From our experience and those of others, it is well known that positions defined by the maximal response of first-derivative criteria lie within the projected arteries.[42] On the other hand, because of the limited frequency response of the entire x-ray/cine/video chain, the maximal response of second-derivative functions will result in detected positions outside the arterial lumen. Therefore the weighted sum of first- and second-derivative functions provides an accurate definition of the arterial lumen. The weighting factor has been derived empirically and has been validated with the acrylate models. One great advantage of the minimal cost algorithm for contour detection is the fact that the edge positions are not determined per individual scanline, but an overall minimal cost path is computed. Side branches and other disturbing structures therefore have only minimal influence on the contour path.

From the evaluation study with the acrylate models it may be concluded that the detected edge positions closely approximate the true positions. For the absolute minimal obstruction diameters the values for the overall accuracy and precision were −30 and 90 μm, respectively. This 30 μm accuracy compares favorably with the accuracy ranges of 59 to 137 μm for the method recently published by Spears et al.[29]

Strictly speaking, the calibration factor computed from a single view is applicable only for objects in the plane of the analyzed catheter segment parallel to the image intensifier input screen. The change in magnification for two objects located at different points along the x-ray beam axis is about 1.5% for each centimeter that separates the objects axially with the commonly used focus-image intensifier distances. For coronary segments lying in other planes, corrections to the calibration factor could be determined from a second, preferably orthogonal, view. However, if one is interested only in the changes of sizes of coronary segments as a result of long- or short-term interventions, acceptable results can be obtained from single-plane views. For these situations one must make sure that for the repeat angiogram, the x-ray system is positioned exactly the same as for the first angiogram. Although the calibration factor used for a particular segment is then only an approximation of the true calibration factor, the same systematic error will be present for the first and the repeat angiograms.

Sources of error in angiographic and analysis procedures. The quality of both the coronary angiographic and the computer analysis procedures is hampered by various sources of variation. In the angiographic data acquisition, the following sources of variation can be distinguished: (1) differences in the angles and height levels of the x-ray gantry with respect to the patient at the time of repeated angiography, (2) differences in vasomotor tone of the coronary arteries, (3) variations in the quality of mixing of the contrast agent with the blood, and (4) deviations in the size of the catheter as listed by the manufacturer from the true size. Variations in the data analysis procedure are caused by (1) quantum noise in the images, (2) electronic noise contributions in the analog video images, (3) quantitation errors in the analog-to-digital conversion, (4) the effects of resampling the data along scanlines through the square grid of the digital data, (5) observer variations in the definition of center positions within the catheter and the selected arterial segment, (6) possible manual corrections to the detected contours, (7) selection of reference positions, and (8) manual definition of starting and end points in nonobstructed arterial segments for measurement of overall mean diameter.

To obtain reliable quantitative results from coronary cineangiograms, these variations should be minimized as much as possible, which requires a number of precautions to be taken. We have developed several ap-

proaches toward such a standardization. By registering the x-ray system settings on-line with a microprocessor system, differences in the angiographic projections can be minimized at the time of repeat angiography (table 5). The variations in vasomotor tone of the arteries can be minimized by the administration of a vasodilative drug immediately before the coronary angiographic study. Unknown deviations in size of the catheter can be circumvented by measuring the actual size after the catheterization procedure with a micrometer.

The variations in density levels in the cinefilm caused by quantum noise can be reduced by filtering the image data. The electronic noise contributions are reduced by recursive digitization of the images. The iterative approach in the edge detection algorithm results in a reduction of the variations due to the factors listed under items 4 through 6. It has been our experience that the position of a reference point can be reproduced accurately by proper documentation of the analysis data on Polaroid photographs or on x-ray sheets by means of a video imager (table 3). Similarly, the reproducibility of the manual definition of the starting and end points of arterial segments can be improved by making use as much as possible of anatomic landmarks such as bifurcations (table 3).

Variabilities of acquisition and analysis procedures. Repeated analysis of the set of 13 coronary cineangiograms has shown that the variability of the data analysis procedure is excellent. No significant differences were found between the repeated measurements, while the SD of the differences of absolute measurements was less than 0.12 mm. When one wants to specify the reproducibility of a coronary analysis system, this SD of the differences of replicate absolute measurements is the parameter of choice, since it does not depend on arterial size. The variabilities for the user-defined and interpolated procedures were 2.74% and 3.94%, respectively. These data show that the smallest variations were obtained with the user-defined method, whereby a ''normal'' reference diameter position must be defined by the user. However, at the expense of a small increase (+ 1.2%) in the variability, the percentage diameter stenosis measurements can be automated with the interpolated analysis procedure. In addition, this interpolated approach provides data about the area of the ''atherosclerotic plaque'' and the lesion's eccentricity in a given view. Another very practical advantage of the use of the interpolated technique is that for the analysis of repeated angiograms, knowledge about the exact location of a reference, either proximal or distal to the stenosis, is not required.[7, 10]

From tables 4, 6, and 7, the mean differences and SDs of the differences in the obstruction and interpolated reference diameters, as well as in the interpolated percentage diameter stenosis, have been summarized in table 8 for the short-, medium- and long-term studies. The mean differences in absolute diameters were below 0.13 mm in all studies. The variability in obstruction diameter for these three types of studies ranged from 0.22 mm for the medium-term study to 0.36 mm for the least-controlled, long-term study. Likewise, the variability in the interpolated reference diameter was smallest for the medium-term study (0.15 mm) and largest for the long-term study (0.66 mm). The long-term study clearly demonstrated that the variability in absolute dimensions increases if no special care is taken to reduce the potential sources of variation. Possible reasons for the variability from the medium-term study being smaller than that from the short-term study are (1) controlled vasomotor tone and (2) the use of nonionic vs ionic contrast medium. Bentley and Henry,[43] investigating the effect of meglumine diatrizoate (Renografin-76; 1689 mOsm/liter) on animal arteries, demonstrated that the angiographic dye in concentrations not exceeding those during angiography exert potent, dose- and time-dependent vasomotor effects. In addition, experiments in vivo have shown that intracoronary injection of ionic, hyperosmolar, and hyperviscous contrast media produce direct myocardial depression, followed by an adrenergically mediated reflex effect that potentially could affect the vasomotor tone of the arteries.[44] Bentley et al.[45] have demonstrated that these deleterious effects can be prevented by the use of nonionic, isosmotic angiographic

TABLE 8

Summary of the differences (mean and SD) in the absolute diameter measurements and interpolated percentage diameter-stenosis for the short-, medium-, and long-term studies

	Mean diff.			SD diff.		
	Short-term	Medium-term	Long-term	Short-term	Medium-term	Long-term
Obstruction diam. (mm)	0.05	0.00	0.00	0.34	0.22	0.36
Interpolated ref. diam. (mm)	0.02	0.05	−0.13	0.21	0.15	0.66
Interpolated %-D stenosis	−0.90	1.21	−1.92	8.30	7.23	6.52

%-D = percentage diameter.

dye (such as Omnipaque) and therefore may account for the observed decrease in variability measures, although this last hypothesis has not yet been tested.

The variabilities in the interpolated percentage diameter reduction were all of the same order of magnitude, ranging from 8.30% for the short-term study to 6.52% for the long-term study. Therefore an upper limit of 8.30% for the variability in interpolated percentage diameter stenosis from repeated angiographic examination and analysis could be defined. The mean differences were less than 1.92%.

The data from table 8 also make clear that the variabilities in the obstruction diameters with repeated angiographic studies and analysis were 2.2 to 3.6 times greater than those from repeated analysis alone, and 1.5 to 6.6 times greater for the interpolated reference diameters. This was caused by the sources of variation in the data acquisition procedure described above. Alderman et al.[25] found an increase in variability in absolute sizes with a medium-term study compared with repeated analysis alone by a factor of 3; we found an increase by a factor of 1.5 to 2.2. In their study identical calibration factors, computed from the spacial positions of the image intensifier and x-ray source with respect to the patient,were used for the initial and repeat angiographic studies. This means that their actual variations in arterial size would be greater than the ones reported, if the calibration factor was also assessed repeatedly from the catheter as was done in our study.

In conclusion, we have developed a procedure for the quantitative analysis of coronary cineangiograms that can be applied on a routine basis. This procedure is based on an accurate, automated method for the contour detection of arterial segments. Various dimensional parameters are derived from the diameter data. Our data clearly show that the biological variations are a source of major concern and that further attempts toward standardization of the angiographic procedure are seriously needed.

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