Edge detection versus densitometry in the quantitative assessment of stenosis phantoms: An in vivo comparison in porcine coronary arteries

The aim of this study was the in vivo validation and comparison of the geometric and densitometric technique of a computer-assisted automatic quantitative angiographic system (CAAS system). In six Landrace Yorkshire pigs (45 to 55 kg), precision-drilled phantoms with a circular lumen of 0.5, 0.7, 1.0, 1.4, and 1.9 mm were percutaneously introduced into the left anterior descending or left circumflex coronary artery. Twenty-eight coronary angiograms obtained with the phantom in a wedged intracoronary position could be quantitatively analyzed. Minimal lumen diameter, minimal cross-sectional area, percent diameter stenosis, and cross-sectional area stenosis were automatically measured with both the geometric and densitometric technique and were compared with the known phantom dimensions. When minimal lumen diameter was measured using the geometric approach, a nonsignificant underestimation of the phantom size was observed, with a mean difference of -0.06 ± 0.14 mm. The larger mean difference observed with videodensitometry (-0.11 ± 0.20 mm) was the result of the failure of the technique to differentiate the low lumen videodensities of two phantoms of smaller size (0.5 and 0.7 mm) from a dense background. Percent cross-sectional area stenosis measured with the two techniques showed a good correlation with the corresponding phantom measurements (mean difference between percent cross-sectional area stenosis calculated from the quantitative angiographic measurements and the corresponding phantom dimensions was equal to $2 \pm 6\%$ for both techniques, correlation coefficient = 0.93 with both techniques, SEE = 5% with the geometric technique and 6% with the densitometric approach). In an in vivo experimental setting mimicking diagnostic coronary angiography, single-plane quantitative angiography showed a high accuracy and precision in the measurement of stenosis hole phantoms with both the geometric and the densitometric approach. The failure of densitometry in the measurement of some of the most severe stenoses explains the better results obtained with the geometric technique. (AM HEART J 1992;124:1181.)

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Computer-based automatic edge detection angiographic analysis systems have reduced the variability resulting from visual and caliper-determined vessel sizing.[1] The accuracy of the measurements with edge detection, however, can be impaired by the presence of eccentric lesions or of lesions of complex lumen geometry. Under these conditions, densitometry has a potential advantage because it is not governed by the shape of the lesion. In vitro studies have demonstrated a high accuracy of videodensitometry in the measurement of hole phantoms[2-6] and its superiority to edge detection in the measurement of eccentric stenoses.[7,8] The clinical application of this technique, however, has produced conflicting reports on its reliability as an alternative to the geometric approach.[7-15] To determine the accuracy and to un-

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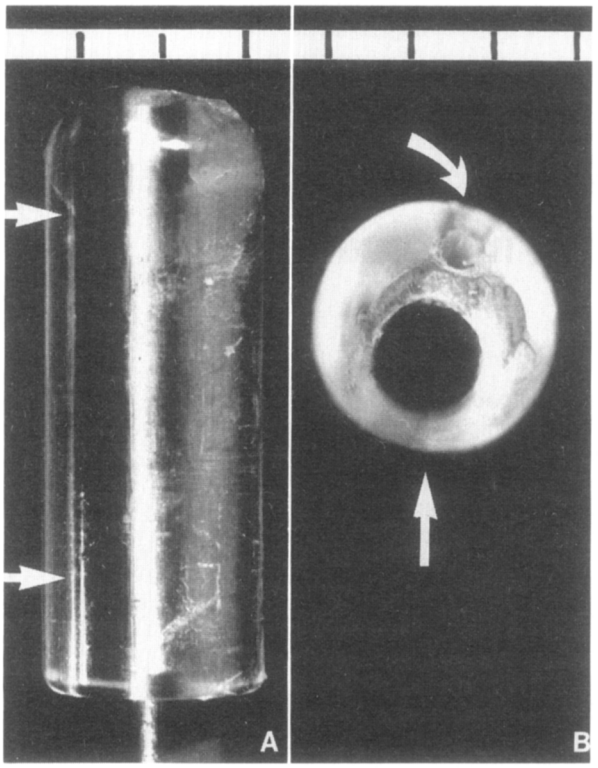

Fig. 1. A, Magnified tip of one of the catheters used for mounting the stenosis phantom and a millimeter ruler for orientation. Note the transparent radiolucent cylinder connected to the tip of the catheter, with a channel of 0.7 mm diameter indicated by *arrowheads*. **B,** Catheter tip photographed perpendicular to the long-axis of the phantom lumen. Note the almost perfect circularity of the precision-drilled lumen (diameter 1.4 mm, *arrow*). The catheter lumen used for guide wire insertion is indicated with *a curved arrow*.

derstand the limitations of these two quantitative angiographic techniques, the comparison must be performed with lumens of known sizes.

The aim of this study was the validation and the comparison of the videodensitometric and geometric techniques of a computer-based automatic quantitative angiographic analysis system (CAAS system) in an in vivo experimental setting simulating a diagnostic coronary angiogram. For this purpose, stenosis phantoms with circular lumens covering the entire range of clinically relevant coronary stenoses (diameter: 0.5 to 1.9 mm) were inserted into the coronary arteries of six closed-chest pigs, and a standard selective cineangiogram was performed.

METHODS

Coronary phantoms. Precision drills of 0.5, 0.7, 1.0, 1.4, and 1.9 mm were used to create circular holes in a series of cylinders of acrylate (Plexiglas, Rohm and Haas Co., Philadelphia, Pa.) and polyamide with a diameter of 3.0 and 3.5 mm and a length of 8.4 mm. This material was chosen because of its extremely high radiolucency and its suitability for precision drilling. An optical calibration with a fortyfold magnification showed a mean difference of 3 ± 23 μm between the drills used and the resulting lumens, with an almost perfect circularity of the lumens. The cylinders were mounted at the tip of 4F radiolucent catheters containing a movable radiopaque guide wire for catheter insertion (Fig. 1).

Animal preparation. Studies were performed in accordance with the position of the American Heart Association on research animal use and under regulations of Erasmus University Rotterdam. After sedation with intramuscular ketamine and intravenous metomidate, six cross-bred Landrace Yorkshire pigs (HVC, Hedel, The Netherlands) of either sex (45 to 55 kg) were intubated and connected to a respirator for intermittent positive pressure ventilation with a mixture of oxygen and nitrous oxide. Anesthesia was maintained with intravenous pentobarbital. The right carotid artery was cannulated with a 12F valved sheath for the insertion of the stenosis phantoms. The left carotid artery was used for the insertion of the angiographic coronary catheter and the left jugular vein was used for administration of drugs or fluids when necessary. To prevent clot formation, all animals were treated with an intravenous bolus of acetylsalicylic acid (500 mg) and heparin (10,000 I.U.) and a continuous intravenous infusion of 10,000 I.U./hr of heparin.

Image acquisition. After intracoronary administration of 1 mg of isosorbide dinitrate and performance of preliminary left coronary angiography for orientation, the catheter with the stenosis phantom mounted was advanced into the left coronary artery until a wedge position in either the left anterior descending or the left circumflex artery was obtained. The guide wire used for the insertion of the radiolucent catheter was then totally removed. An 8F El-Gamal guiding catheter (Schneider AG, Zürich, Switzerland) was engaged in the ostium of the left coronary artery and selective coronary arteriography was performed by power injection of 10 ml of iopamidol (iodine content 370 mg/ml) at 37° C with an injection rate of 10 ml/sec (Mark V pressure injector, Medrad Inc., Pittsburgh, Pa.). Ventilation was transiently interrupted during the acquisition of the angiograms. Before the angiogram, the catheter was filmed unfilled for calibration purposes. To increase the calibration accuracy, a catheter with minimal distal tapering and a highly radiopaque polyurethane jacket (Soft-Touch, Schneider AG.) was chosen and the tip was measured at the end of the procedure with a micrometer.

A single-plane Philips Poly Diagnost C2 machine was used, equipped with an MCR x-ray tube and powered by an Optimus CP generator (Philips Medical Systems International BV, Best, The Netherlands). The 0.8 mm focal spot and the 5-inch (12.5 cm) field of view of the image intensifier were used for all angiograms. The pulse width was maintained unchanged at 5 msec. The kVp and mA range were automatically adjusted according to the thickness of the imaged object (mean 76 kVp), and cinematography was performed using the "lock in" mode. Angiograms were

filmed at 25 frames/sec using an Arritechno 90 cine camera (Arnold & Richter, Munich, Germany) with an 85 mm lens. A Kodak CFE cine film (Eastman Kodak, Rochester, N.Y.) was used and was developed with a Refinal (M) developer (Agfa-Gevaert, Leverkusen, Germany) for 4 minutes at 28° C. The film gradient was measured in all cases to ensure that the optical densities of interest were on the linear portion of the sensitometric curve. The insertion of the entire range of stenosis phantoms was attempted in all animals. The choice of the radiographic projection was aimed at avoiding foreshortening and overlapping of contiguous vessels on the stenotic segment.

Quantitative analysis. An end-diastolic cine frame was selected for off-line analysis with the CAAS System (Pie Medical, Maastricht, The Netherlands). A 6.9 × 6.9 mm region of interest was selected from the 18 × 24 mm image area on the 35 mm cine frame and was digitized into a 512 × 512 pixel matrix with 256 grey levels. The image calibration factor was calculated using the catheter as a scaling device in each projection.

Contour analysis. The diameter of the coronary arteries and of the lumen of the stenosis phantoms was calculated with an automatic contour detection technique. A weighted first and second derivative function with predetermined continuity constraints was applied to the brightness profile of each scan line perpendicular to the vessel centerline.[16] Manual corrections of the automatically determined contours were allowed by the system but were never performed for these measurements. In four measurements the automatically determined distal or proximal ends of the stenotic segments were modified to avoid the measurement of the minimal luminal diameter at the site of a discrete intraluminal filling defect (thrombus) or of a localized spasm distal to the phantom lumen. The obstruction diameter was defined by the minimal value in the diameter function. The geometric cross-sectional area was computed from this obstruction diameter assuming a circular cross section. A user-defined diameter was selected in a normal coronary segment distal to the stenosis as a reference diameter for the calculation of percent diameter and cross-sectional area stenosis and as a calibration of the densitometric measurement (Fig. 2). The automatic mode for the calculation of this reference diameter from the integration of the segments proximal and distal to the stenosis (interpolated technique) could not be used because of the bias for the densitometric measurements induced by the presence of the phantom-mounting catheter in the proximal segment of the vessel.

Videodensitometry. The brightness profile of each scan line perpendicular to the centerline of the vessel lumen was transformed into an absorption profile by means of a simple logarithmic transfer function to correct for the Lambert-Beer law. The background contribution was estimated by computing the linear regression line through the background points directly left and right of the detected contours.[17] Subtraction of this background portion from the absorption profile yielded the net cross-sectional absorption profile. By repeating this procedure for all scan lines, the cross-sectional area function was obtained. An absolute reference densitometric area value was calculated using the diameter measurements obtained from the edge detection technique assuming a circular configuration in a user-defined reference segment distal to the stenosis (Fig. 2). The densitometric minimal cross-sectional area could then be calculated by the ratio of the density levels at the reference area and at the narrowed segment. The densitometric minimal lumen diameter was calculated from the densitometrically determined cross-sectional area assuming a circular model. Densitometric percent diameter and cross-sectional area stenosis were calculated from the densitometric measurements of stenosis and reference segment. The phantom-derived corresponding values were calculated from the known dimensions of the phantoms and the geometric measurements of the reference segment.

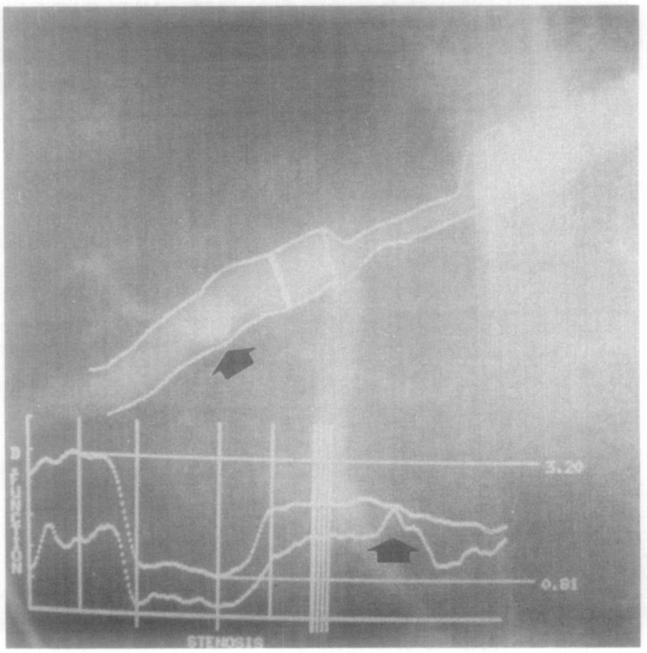

Fig. 2. Magnified image of the middle segment of the left anterior descending artery in the left anterior oblique view (60 degrees angulation). The automatically detected vessel contours are displayed in the segment analyzed and the *graph below* shows the segment length, from proximal to distal, on the x-axis and the lumen diameter on the y-axis. The lumen of the stenosis phantom (diameter: 1.00 mm) was underestimated with the edge detection technique (minimal lumen diameter: 0.81 mm), as shown in the intermediate curve of the graph. The densitometric profile, shown by the *lower curve*, strictly followed the diameters detected with the geometric technique, with the exception of a localized increase at the site of a side branch (*arrows* in the graph and in the angiographic image) and of the proximal segment of the vessel in which the videodensity was reduced because of the presence of the phantom-mounting radiolucent catheter. Because of this, for all measurements a user-defined reference diameter was selected immediately distal to the stenosis (multiple line in the graph and superimposed on the coronary angiogram).

Statistical analysis. The minimal lumen diameter, min-

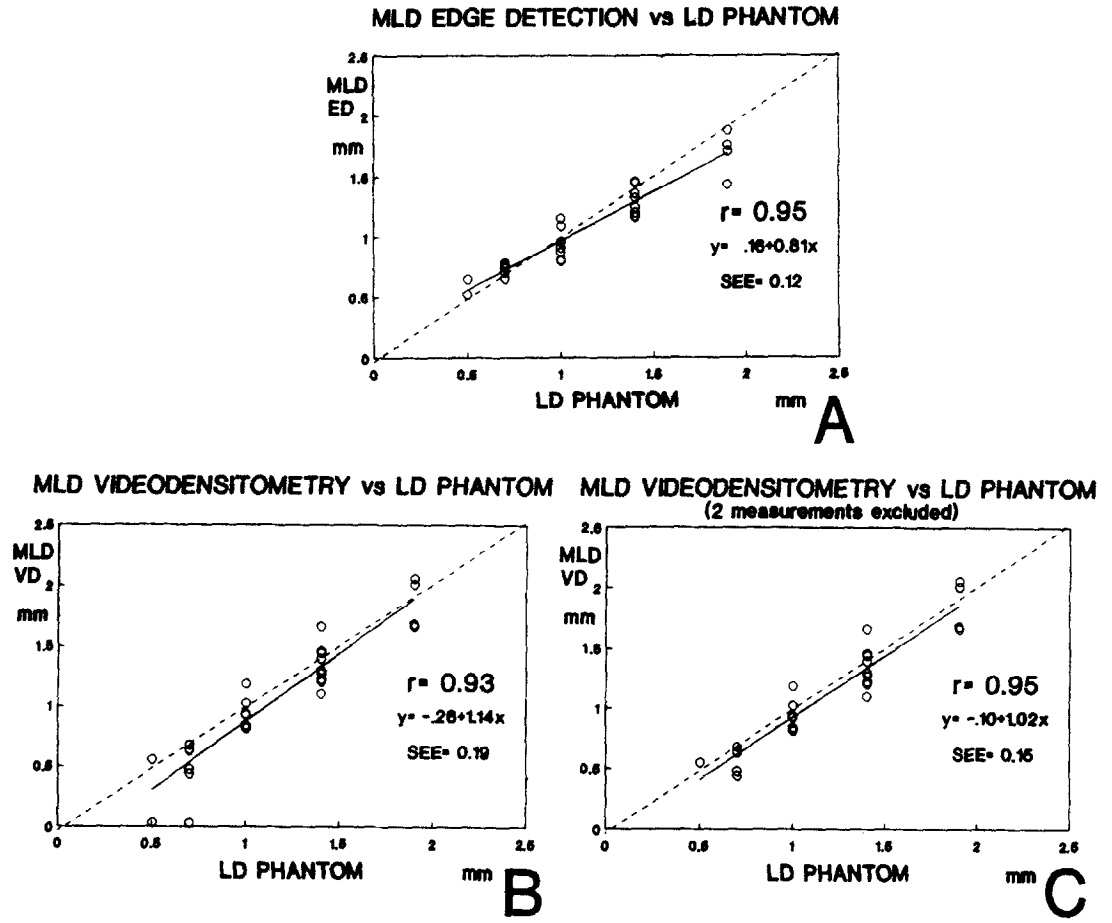

Fig. 3. Linear regression analysis of the phantom lumen diameter *(LD)* versus the minimal lumen diameter *(MLD)* measured with edge detection *(ED)* **(A)** and videodensitometry *(VD)* **(B)**. *Dashed lines* and *continuous lines* correspond to the line of identity and the line of regression, respectively. **C** shows the videodensitometric results when the two failed measurements (aligned on the x axis in **B**) are excluded.

imal cross-sectional area, and percent cross-sectional area stenosis measured both with the geometric and the densitometric technique were compared with the corresponding values of the stenosis phantoms using a paired *t* test (two-tailed) and linear regression analysis. The mean differences between geometric and densitometric minimal lumen diameter and cross-sectional area and corresponding phantom dimensions were calculated and were considered an index of the accuracy of the measurements, while the standard deviation of the differences was considered an index of precision. These differences were also plotted against the size of the phantoms according to the method proposed by Bland and Altman[18] (modified). The standard deviations of the differences with the geometric and densitometric technique were compared using the Pitman's test. A p value < 0.05 was considered statistically significant.

RESULTS

Forty-two coronary cineangiograms were obtained after intracoronary insertion of the stenosis phantoms. Three cineangiograms (7%) were excluded because of the presence of dye streaming around the incompletely wedged stenosis phantom. Eleven angiograms (26%) were considered to be of insufficient diagnostic quality for quantitative analysis because of side-branches overlapping the stenotic segment (3), foreshortening of the stenotic segment (4), or inadequate arterial filling (4). This last finding was observed in three phantoms with a lumen diameter of 0.5 mm and in one 0.7 mm stenosis phantom. The results of the quantitative analysis of the remaining 28 cineangiograms (67%) are reported below.

Minimal lumen diameter. In Fig. 3 the minimal lumen diameters measured with the geometric and densitometric techniques are compared with the phantom diameters using a linear regression analysis. The lower correlation coefficient and higher SEE of videodensitometry (Fig. 3, *B*) were largely the result of the inability of this technique to detect a difference between mean intraluminal density and density of the adjacent background in two angiograms of the smaller phantoms (0.5 and 0.7 mm). In both cases a precise measurement was possible with the geomet-

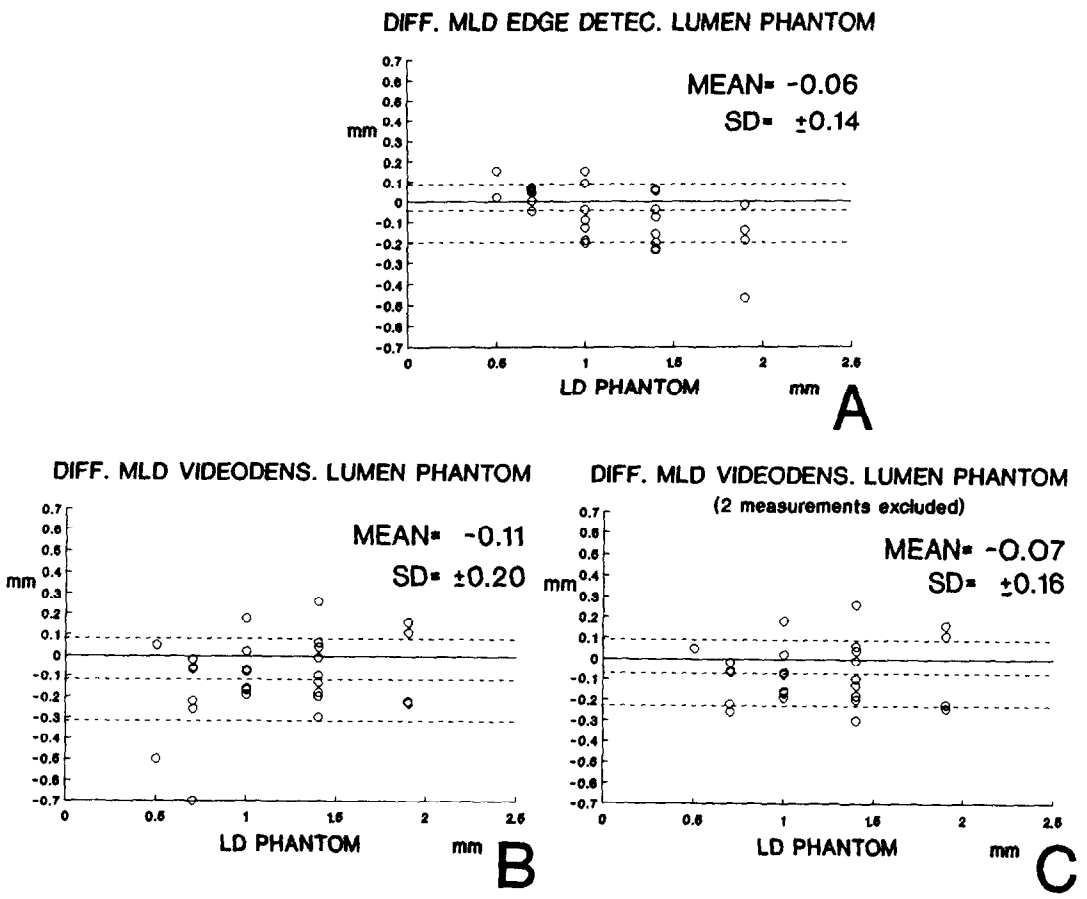

Fig. 4. Differences between minimal lumen diameter *(MLD)* measured with edge detection **(A)** and with videodensitometry **(B)** and phantom lumen diameter *(LD)* are plotted against the lumen diameter of the phantoms (on the x axis, 0.5, 0.7, 1.0, 1.4, and 1.9 mm). *Dashed lines* indicate the mean difference and the standard deviation of the signed differences, respectively. In **C** the two failed measurements with videodensitometry, shown in the *lower left corner* in **B**, are excluded.

ric technique. When these measurements were excluded from the analysis (Fig. 3, *C*), videodensitometry showed a regression coefficient and SEE similar to the geometric approach, with the regression line almost aligned with the line of identity ($y = 1.02 \times -0.10$). Both edge detection and videodensitometry underestimated the phantom diameter (mean difference = -0.06 ± 0.14 mm and -0.11 ± 0.20 mm, respectively; p = ns) (Fig. 4). However, when the results were compared without the two previously described failures of the densitometric approach, the mean difference of the densitometric technique (-0.07 ± 0.15 mm) was comparable with the previously reported mean difference obtained using the geometric approach.

Minimal cross-sectional area. The absolute cross-sectional areas (in mm^2) of the stenosis phantoms were correlated with the quantitative angiographic measurements of minimal cross-sectional area (Fig. 5). The discrepancies between corresponding geometric and densitometric measurements occurred mainly in the range of the smaller phantom sizes and had therefore a reduced impact on the calculated correlation coefficient (0.94 with both techniques). A slightly larger SEE, however, was observed with the densitometric technique (0.31 mm^2 versus 0.24 mm^2 with the geometric technique). The mean difference of the angiographically measured minimal cross-sectional areas and the phantom lumen cross-sectional area was -0.15 ± 0.30 and -0.12 ± 0.31 mm^2 for the geometric and densitometric techniques, respectively.

Percent cross-sectional area stenosis. The percent cross-sectional area stenosis calculated for the phantoms and the corresponding geometric and videodensitometric measurements showed a high correlation, with a correlation coefficient of 0.93 for both techniques (SEE = 5% with the geometric technique and 6% with the densitometric technique). Edge detection and videodensitometry overestimated the

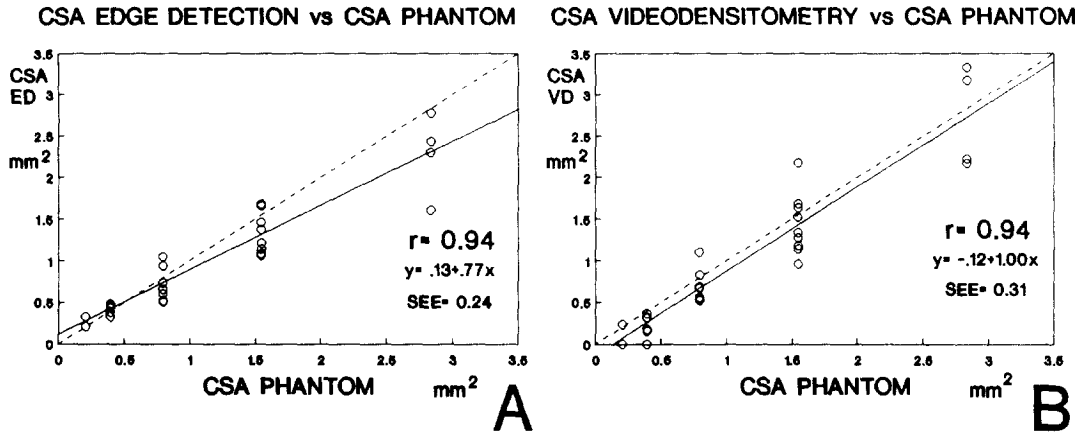

Fig. 5. Linear regression analysis of the phantom cross-sectional area *(CSA)* measured with edge detection *(ED)* **(A)**, and videodensitometry *(VD)* **(B)**. *Dashed lines* and *continuous lines* correspond to the line of identity and the line of regression, respectively.

phantom-derived percent cross-sectional area stenosis, with a mean difference between angiographic and phantom-derived percent cross-sectional area stenosis of 2 ± 6% for both techniques.

DISCUSSION

In vitro studies. Several in vitro studies have confirmed that densitometry has the potential to measure differences in density between large and narrow phantom lumens and that the calculated percent cross-sectional area stenosis is highly correlated with the corresponding phantom-derived measurement.[2-6] Furthermore, these studies have confirmed that videodensitometry has potential advantages in the measurement of eccentric lesions from a single-plane angiogram[7,8] and that absolute values can be obtained from the comparison of the density of a reference area measured with edge detection[17] or of the density of a thin-walled, contrast-filled angiographic catheter.[2] Phantoms with a large lumen diameter were less accurately measured with videodensitometry, most likely the result of the nonlinearity between iodine content and the optical density of the radiographic image induced by the spectral hardening of the polyenergetic x-ray beam. On the contrary, videodensitometry has not shown the overestimation observed with edge detection in the measurement of stenoses sizes < 1 mm.

The in vitro measurement of radiographic phantoms, however, can not reproduce some of the sources of error of the videodensitometric approach in vivo. Arterial branches overlapping or parallel to the analyzed segment impairing the measurement of the density of the lumen or of its background, patient structural noise inducing an inhomogeneous background, lack of orthogonality of the vessel with the radiographic beam, and inhomogeneous filling of the vessel during injection are conditions that can not be assessed in in vitro studies. Some of the most important sources of the nonlinearity of densitometry such as scatter/veiling glare and beam hardening are also accentuated or more difficult to correct for in vivo.[19]

Clinical studies. The promising results of the in vitro application of videodensitometry, the development of interventional techniques inducing complex lumen irregularities of the treated stenosis, and the diffusion of digital angiography with the possibility of on-line videodensitometric measurements have stimulated the interest in this technique of quantitative analysis. Single-plane videodensitometric analysis was found to be an accurate and convenient method for quantifying the relative stenosis of eccentric coronary lesions.[7,8] The shaggy and rough appearance of the dilated segment after balloon angioplasty, with the presence of haziness of the luminal contour, is a challenge to quantitative angiography. Initial reports[10,11] have suggested that the use of videodensitometry can overcome these limitations of the geometric technique in the immediate evaluation of the results of balloon angioplasty. Other reports,[13] however, showed comparable quantitative angiographic measurements with both techniques. Doubts concerning the possibility of reliably assessing vascular dimensions from one projection, and in general of the accuracy of videodensitometry, were raised by the observation of a poor correlation between the videodensitometric measurements of the same segment in two projections after angioplasty.[14] Balloon angioplasty, however, can be considered a critical condition for the application of any quantitative angiographic technique and videodensitometry can also provide unreliable measurements

because of inadequate mixing caused by blood turbulence or intraluminal dissections.[20, 21] Not surprisingly, the large discrepancies of the edge detection and videodensitometric measurements immediately after angioplasty are largely reduced after stent implantation, probably because of remodeling of the stented segment into a more circular configuration and the sealing of wall dissections.[22] Clinical studies, however, can evaluate only the variability of repeated measurements in the same or in different projections. A more complete comparison of the usefulness and limitations of the two techniques is possible only if a lumen of known dimension is measured.

Previous in vivo phantom studies: Comparison with present results. Simons et al.[23] measured with a videodensitometric technique a large series of coronary stenoses induced by the inflation of silicone elastomer cuffs in dogs and compared these results with the measurements of the pressurized histologic cross sections. Although a good correlation between videodensitometry and histology measurements was demonstrated, a relatively large mean difference (18.5% difference in the measurement of the stenosis diameter) was observed. The use of preshaped intracoronary phantoms can reduce the variability induced by the inaccuracies of the measurement of the true stenotic lumen. This approach, however, is outweighted by the more troublesome phantom insertion procedure, thus explaining the limited number of analyzable angiograms in our series (28 corresponding measurements) and in the series reported by Wiesel et al.[24] and by Mancini et al.[25] (14 measurements in 10 dogs and 25 measurements in 16 dogs, respectively). Wiesel et al.[24] observed a mean difference between calculated cross-sectional area and known phantom lumen cross-sectional area of 0.65 mm^2 with videodensitometry and one of 0.54 mm^2 with the geometric technique, with correlation coefficients of 0.76 and 0.70, respectively. The larger differences and lower correlation values in comparison with the results of our study can be explained by the different sizes and shapes of some of the stenotic lumens and by the lower number of pixels per millimeter available in the digitized image. More similar phantoms (circular lumen with a diameter ranging from 0.83 to 1.83 mm) were inserted by Mancini et al.[25] into the coronary arteries of open-chest dogs. When the analysis was performed on the cine film, the SEE of the linear regression analysis of true phantom diameter and corresponding geometric measurements was equal to 0.24 mm ($r = 0.87$). Although no direct data were provided concerning the accuracy of the videodensitometric measurements, the videodensitometric minimal cross-sectional area and percent area stenosis were significantly correlated with the coronary flow reserve assessed using electromagnetic flowmeters, yielding a correlation similar to the geometric measurements.

A peculiarity of our study was that we were able to examine phantoms of small lumen diameter (0.5 and 0.7 mm). The angiographic examination of these high-grade stenosis phantoms, however, was not possible in all cases because the reduced flow rapidly induced ischemic changes and intraluminal thrombosis. Furthermore, in four cases the visualization of these severe stenosis phantoms was so poor as to preclude any quantitative measurement. In two cases correctly analyzed with edge detection, however, videodensitometry could not identify the low density of the small phantom lumen. The results from the data base of our laboratory, where quantitative angiographic measurements from more than 4600 patients included in large multicenter trials[26, 27] have been collected, show that in more than 10% of the cineangiograms before coronary angioplasty densitometry failed to measure the lumen diameter because of the combined effect of low density of a severe stenosis, a dense background, or the presence of parallel vessels interfering with the background subtraction. Edge detection, on the contrary, could be used in almost all cases.

With the exception of some of the measurements of the most severe lesions, the accuracy and precision of the videodensitometric results were comparable with the accuracy and precision of the geometric results. In this study, however, only cineangiograms with an optimal orientation of the incident x-ray beam to the evaluated segment, cineangiograms without overlapping vessels, and cineangiograms with an adequate homogeneous lumen filling were analyzed. It is noteworthy that more than one fourth of the cineangiograms had to be excluded because of the presence of these three conditions, which are likely to reduce to a greater extent the accuracy of the videodensitometric measurement rather than that of the geometric measurements. This finding might suggest a more limited applicability of videodensitometry in comparison with edge detection in the analysis of large series of cineangiograms from clinical investigations.

Limitations of the study. The use of phantoms of regular circular lumina limits the possibility to detect advantages of the densitometric technique in the evaluation of eccentric or irregular stenosis. Although this evaluation is of interest, the aim of this study was more simply to establish whether videodensitometry is able to measure coronary lesions with an accuracy comparable to that of the geometric

technique, despite the well-known limitations of densitometry in the in vivo application and without the cumbersome and still investigational corrections proposed for the scatter and veiling glare.[28, 29] Beam hardening, another well-known limitation of this technique, is a function of iodine density that is proportional to vessel thickness. Consequently, the results obtained in the examination of this series of small-size lumen phantoms are not applicable to larger vessels.

In this study, to obtain a completely automatic measurement the minimal luminal diameter and minimal cross-sectional area and not the *average* of the corresponding values measured over the obstruction segment were chosen for the comparison with the lumen diameter of the stenosis phantom. This approach, however, can probably explain the moderate underestimation with both techniques as a consequence of quantum noise or intraluminal microthrombosis interfering with the angiographic measurements.

Videodensitometry can only detect percent differences between two vascular segments. Therefore the calculation of absolute videodensitometric measurements of the stenosis was based on the geometric measurement of the luminal cross-sectional area of the reference segment. In this study, because of the presence of the catheter mounting the stenosis phantom in the proximal coronary arterial segment, a user-defined reference segment distal to the stenosis was selected. The videodensitometric measurement of minimal cross-sectional area was dependent, as an integration of densitometric and edge detection measurements, on the accuracy of the geometric measurement of the reference segment. Inaccuracies in the geometric measurement can be caused by an erroneous calculation of the magnification factor using the catheter as a scaling device. Catheters not filled with contrast, with a highly radiopaque wall, and without tapering of the measured segments were used to minimize some of the possible sources of error.[30-33] Inaccuracies induced by an out-of-plane position of the catheter, however, can not be easily corrected. More accurate calibration methods such as the isocentric technique[34] have been proposed, but they are more cumbersome and of difficult application in clinical practice.

The correction for pincushion distortion was performed using a square grid filmed in the anteroposterior position as a reference.[16] Another possible source of distortion in image intensifier tubes, determined from the rotational distortion caused by the geomagnetic field,[35] is more difficult to be corrected because it varies in all the different image amplifier positions. The effect of this type of distortion on small object dimensions, however, is normally negligible.

Conclusions. The geometric and videodensitometric techniques of quantitative angiographic analysis showed a high accuracy and precision in the measurement of stenosis hole phantoms of various severity (diameter 0.5 to 1.9 mm) inserted in porcine coronary arteries and filmed with care taken to avoid foreshortening, vessel overlapping, and incomplete filling of the stenotic segment. The minimal lumen diameter and cross-sectional area measured with both techniques slightly underestimated the true phantom diameter and cross-sectional area. The geometric approach more reliably measured the phantom lumens of smaller diameter.

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