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Experimental Validation of Geometric and Densitometric Coronary Measurements on the New Generation Cardiovascular Angiography Analysis System (CAAS II)

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Computer-assisted contour detection and videodensitometric cross sectional area assessment of coronary artery obstructions on the CAAS II system were validated in vitro and in vivo by angiographic cinefilm recording and automated measurement of stenosis phantoms (luminal diameter 0.5, 0.7, 1.0, 1.4, 1.9 mm) which were first inserted in a plexiglass model and then serially implanted in swine coronary arteries. "Obstruction diameter" (OD) and "obstruction area" (OA) values obtained from 10 in vitro and 19 in vivo images at the site of the artificial stenoses were compared with the true phantom dimensions. The in vitro assessment of OD yielded an accuracy of 0.00±0.11 mm (correlation coefficient: r = 0.98, y = 0.18 + 0.82x, standard error of estimate: SEE = 0.08), whereas the in vivo measurement of OD gave an accuracy of −0.01 ± 0.18 mm (r = 0.94, y = 0.22 + 0.82x, SEE = 0.15). The assessment of OA gave an accuracy of −0.08 ± 0.21 mm² in vitro (r = 0.97, y = 0.08 + 0.99x, SEE = 0.22) and −0.22 ± 0.32 mm² in vivo (r = 0.95, y = 0.21 + 1.01x, SEE = 0.33). The mean reproducibility was ±0.09 mm for geometric measurements and ±0.21 mm² for videodensitometric assessments, respectively. Thus, due to inherent limitations of the imaging chain, the reliability of geometric coronary measurements is still far superior to videodensitometric assessments of vessel cross sectional areas.

Key words: quantitative coronary angiography, anesthetized pigs, coronary artery disease

INTRODUCTION

Since automated edge detection techniques diminish the variability from visual assessments of coronary artery dimensions or hand-held calipers [1], the use of quantitative coronary angiography has gained ground in the field of invasive cardiology allowing on-line measurement of vessel diameters using digital systems [2] and off-line application of geometric as well as videodensitometric algorithms on cinefilms [3,4]. While previous validation studies already demonstrated that geometric measurements of coronary arteries potentially represent a reliable approach [5–12], the value of videodensitometric assessments remains controversial [13–21]. Moreover, the comparative validation of current quantitative coronary analysis systems has shown that new software development for quantitative coronary measurement requires separate validation studies to maintain quality control [22].

The present investigation was performed to define accuracy, reliability, and reproducibility of geometric as well as videodensitometric assessments of the new version of the Cardiovascular Angiography Analysis System (CAAS II). Stenosis phantoms of known diameter mimicking the narrowings of human coronary arteries were used as a reference both in an in vitro plexiglass model as well as after serial insertion in the coronary arteries of anesthetized pigs. Geometric validation was assessed by measuring the absolute value of "obstruction diameter" within the artificial stenoses which has already been shown to be more reliable than relative measures of coronary artery dimensions based on the definition of a ref-

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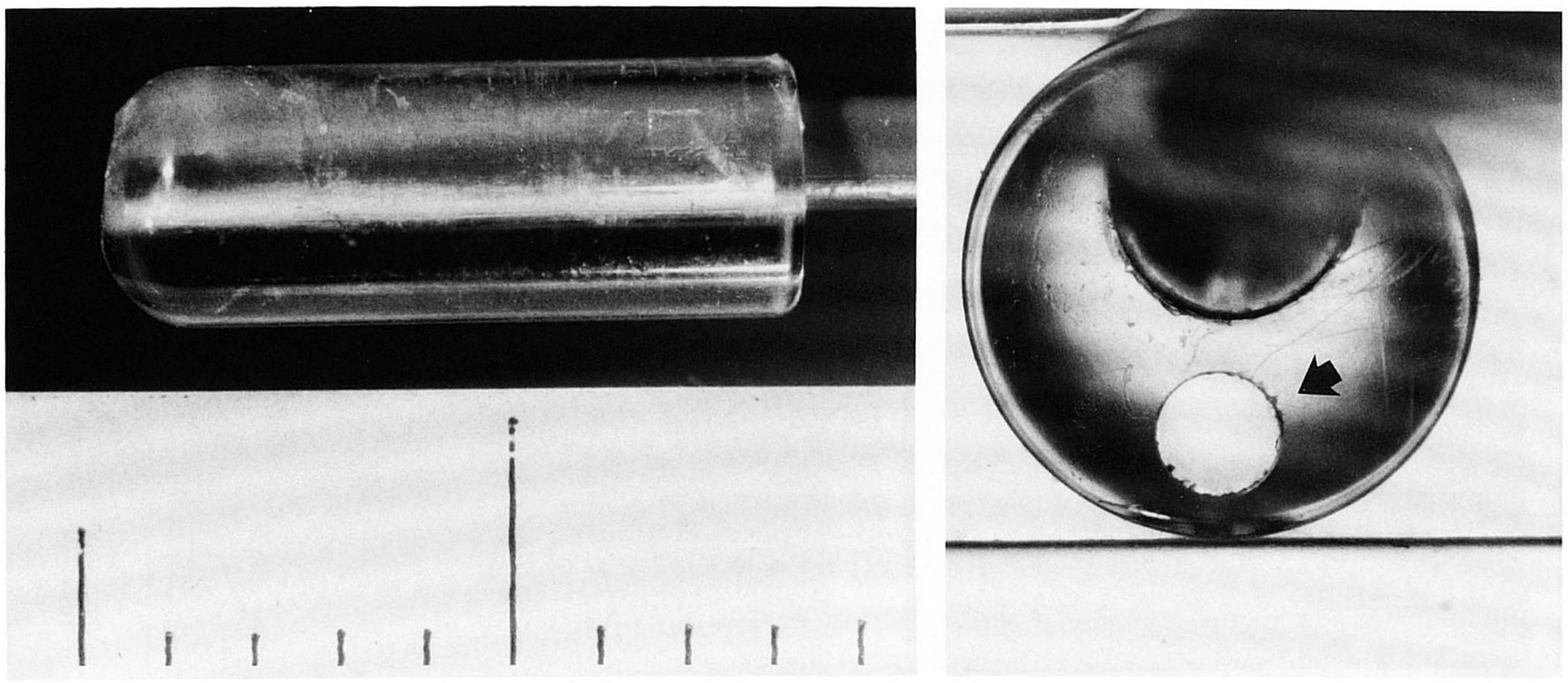


Fig. 1. Catheter mounted cylindrical plexiglass stenosis phantom (length 8.4 mm, diameter 3.0 mm) in two projections. On the short axis view (right hand side) the entrance of the 0.7 mm stenosis channel is indicated by an arrow.

erence contour [23–26]. To assess the influence of different calibration techniques on the outcome of geometric measurements in vivo, calibration at the isocenter was compared with catheter calibration as conventionally used in clinical practice. Finally, the densitometric measurement of the ''obstruction area'' computed with digital subtraction of background density, was used for a comparison with the true phantom cross sectional areas. The reliability of video-densitometric measurements was studied with and without application of an algorithm which corrects for the contribution of side branches to background density.

MATERIALS AND METHODS

Stenosis Phantoms

The stenosis phantoms used in the in vitro as well as in vivo model consisted of radiolucent acrylate or polyimide cylinders with precision-drilled eccentric circular lumens of 0.5, 0.7, 1.0, 1.4, and 1.9 mm in diameter (Fig. 1). The outer diameters of the cylinders were 3.0 or 3.5 mm, and the length was 8.4 mm. Acrylate was used to produce the phantoms with small stenosis diameters (0.5, 0.7 mm), whereas the less fragile polyimide was better suited to the drilling of large stenosis diameters (1.0, 1.4, 1.9 mm). Optical calibration of the stenosis channels using 40-fold magnification gave a tolerance of 0.003 mm. Parallel to the stenosis lumen a second hole of 1.3 mm in diameter was drilled in the cylinders to attach them to the tip of 4F Fogarty catheters (Vermed, Neuilly en Thelle, France). The central lumens of these catheters contained a removable metal wire, which was used for intracoronary insertion of the phantoms as well as for their positioning in the radiographic isocenter.

In Vitro Experiments

The stenosis phantoms were serially inserted in the center of cylindrical acrylate models (diameter 25 mm, length 120 mm) with a concentric channel of 3.0 mm in diameter. The plexiglass channel including the artificial stenosis was then filled with contrast medium (iopamidol 370, Bracco, Milano, Italy; 370 mg iodine/ml) at a concentration of 100%. Digital as well as cinefilm acquisition was performed with an additional thickness of plexiglass blocks (12.5 cm anterior and 5 cm posterior to the models) to approximate the density of water. The addition of plexiglass blocks results in a more appropriate kV-level (75 kV) and in a scatter medium which more closely approximates the X-ray scatter in the human thorax during fluoroscopy. Each phantom filled with contrast medium was recorded on cinefilm which was processed routinely and analyzed off-line on the Cardiovascular Angiography Analysis System II (Pie Medical, Maastricht, The Netherlands).

In Vivo Experiments

The experimental approach employing the catheter mounted stenosis phantoms in normal coronary arteries of anesthetized pigs has already been described in a recent study from our group [12]. Two different calibration methods were applied to geometric measurements. Calibration at the isocenter was carried out by radiographic

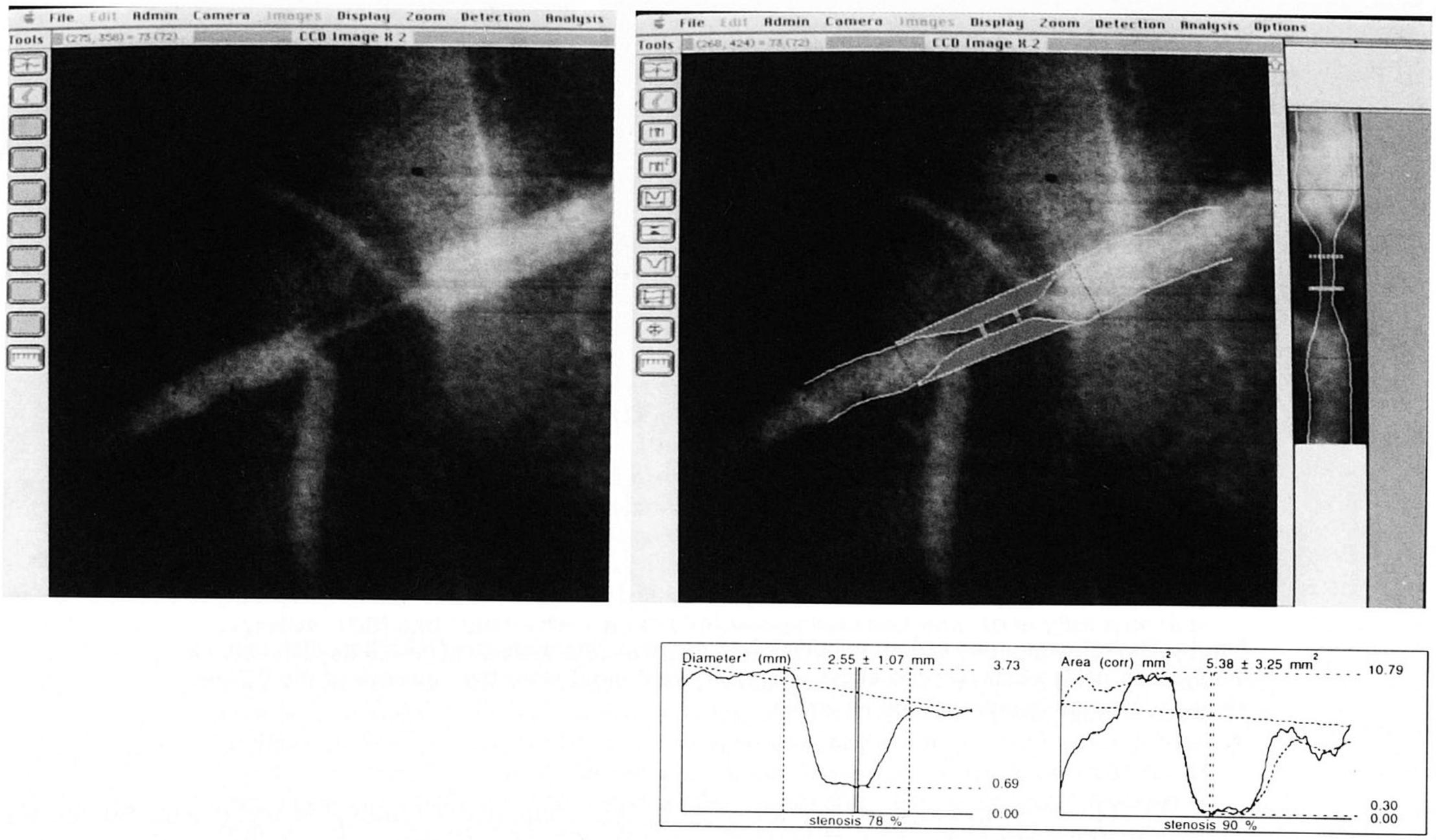


Fig. 2. Angiographic visualization of a 0.7 mm stenosis phantom in coronary wedge position (left hand side) with consecutive geometric and videodensitometric analysis (right hand side). Vessel diameter function and cross sectional area function with background correction are displayed in the bottom graphs. The dotted curve in the right graph displays calculated cross sectional area values as derived from the geometric vessel diameter function.

acquisition of a drill-bit (diameter 3 mm) within the isocenter of the X-ray system before angiography. Catheter calibration was performed by acquisition of the unfilled tip of the contrast catheter as conventionally recommended for clinical routine [27]. The diameter of the non-tapering part of this catheter was assessed with a precision micrometer (No. 293-501, Mitutoyo, Tokyo, Japan; accuracy 0.001 mm), resulting in the respective calibration factor (mm/pixel). Using these two methods of calibration, two series of results were obtained allowing an estimation of the potential geometric error introduced by non-isocentric calibration.

Image Acquisition and Processing

The 5″-field mode of the image intensifier (focal spot 0.8 mm) was selected and the radiographic system settings were kept constant (kV, mA, X-ray pulse width) in each projection. All phantoms were imaged isocentrically in two projections and acquired on 35-mm cinefilm (CFE Type 2711, Kodak, Paris, France) using a frame rate of 25 images/s. Particular care was taken to minimize foreshortening of the segment of interest and to avoid overlap with other vessels or structures. The cinefilms were routinely processed and used for off-line analysis on the CAAS II system [28]. From each angiogram that fulfilled the requirements of quantitative analysis (no superimposition of surrounding structures, no major vessel branching at the site of the phantom position), a homogeneously filled end-diastolic coronary image was selected and geometric as well as densitometric analysis was carried out after cine-video conversion in the CAAS II system (Fig. 2). This procedure allows the digital selection of a 6.9 × 6.9 mm region-of-interest (ROI) out of the 18 × 24 mm cineframe for digitization into a 512 × 512 pixel matrix using a CCD camera (8 bits = 256 density levels). Effectively, this means that the entire cineframe (18 × 24 mm) can be digitized at a resolution of 1329 × 1772 pixels. A correction for pincushion distortion was not yet available in the evaluated experimental version of the CAAS II software package.

Edge Detection Analysis

Ten in vitro and 19 in vivo frames were suitable for quantitative analysis of the artificial stenoses. A sufficiently long segment of the contrast filled lumen including the stenosis phantom was selected on all images.

On the CAAS system, the edge detection algorithm is based on the first and second derivative functions applied

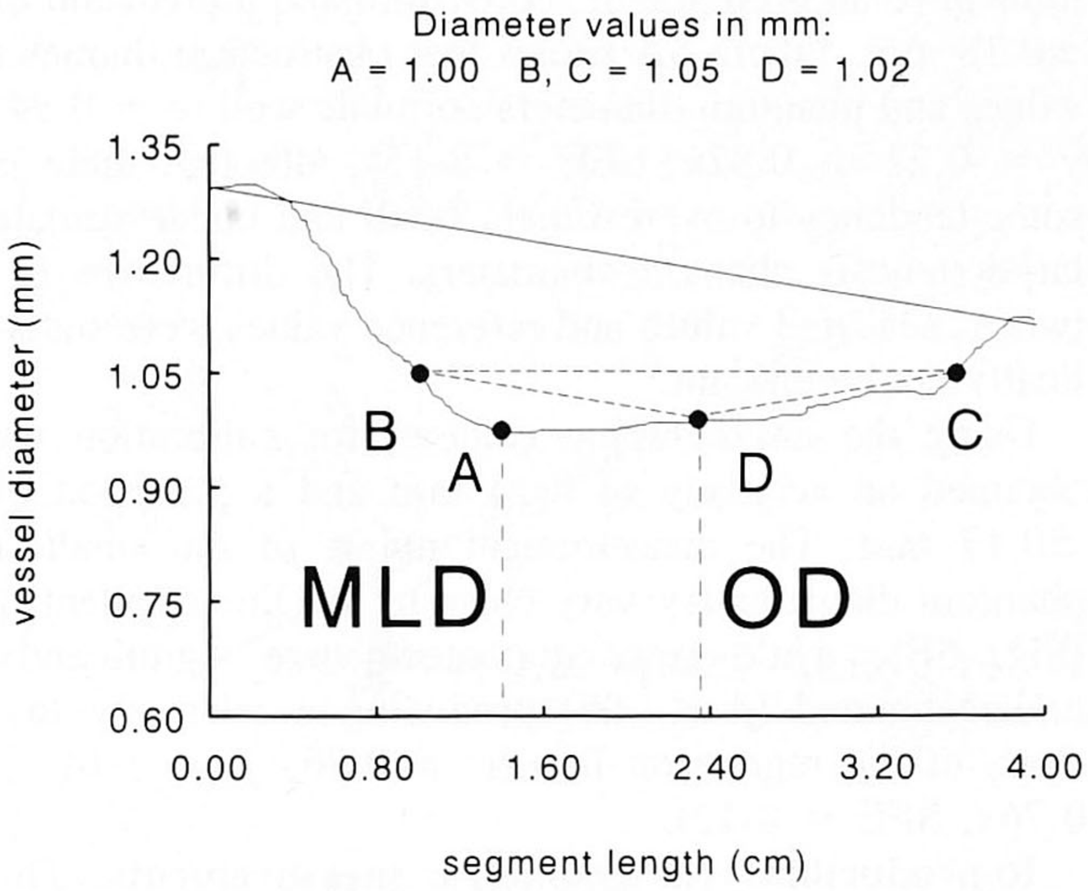


Fig. 3. Definition of "obstruction diameter" on CAAS II: Schematic display of the diameter function curve of a coronary artery stenosis with illustration of the so-called "geometric center" of the obstruction, defined as the middle (D) between the two closest diameter values which exceed the minimal luminal diameter (A) of the stenosis by 5% (B,C). At position D, the "obstruction diameter" is calculated (OD = obstruction diameter; MLD = minimal luminal diameter).

to the brightness profiles along scanlines perpendicular to a model using minimal cost criteria [3,28]. The contour definition is carried out in two iterations. First, the user defines a number of centerline points within the arterial segment which are interconnected by straight lines, serving as the first model. Subsequently, the program recomputes the centerline, determined automatically as the midline of the contour positions which were detected in the first iteration. Smoothing of the contours and derived diameter function is as in the previous CAAS [3]. In the new version of the CAAS system (CAAS II), the edge detection algorithm is modified to correct for the limited resolution of the entire X-ray imaging chain. This modification is based on a look-up table derived from edge detection of simulated density profiles. These profiles are convolved with a Gaussian shaped point spread function (PSF) to reflect the limited resolution of X-ray imaging [32]. It was shown that smaller diameter values are overestimated by the influence of the PSF. The used preliminary version of the correction algorithm converts an observed diameter value into a true diameter value assuming a PSF size of 0.4 mm.

Manual corrections to the automatically detected contours were found to be unnecessary, with the position of the obstruction diameter in the stenosis phantom being defined satisfactorily by the automatic measurement system. The obstruction diameter is determined as the value measured at the "geometric center" of the obstruction, which is defined as the middle between the two closest diameter values that exceed the minimal luminal diameter of the stenosis by 5% (Fig. 3). When a degree of obstruction due to cellular material or partial thrombosis was obvious within the phantom channel, the position of obstruction diameter assessment was then user-defined. This happened in three out of 20 angiographic images obtained during the in vivo experiments.

Videodensitometric Analysis

In the videodensitometric analysis modality, the brightness profile of each scanline perpendicular to the centerline of the lumen is transformed into an absorbtion profile according to the Lambert-Beer law by means of a simple logarithmic transfer function. The background contribution is estimated by computing the linear regression line through the mean of the brightness in two positions located 2 and 3 pixels outside the left and right detected contours [30]. Subtraction of this background portion from the absorption profile yields the net cross sectional absorption profile. By repeating this procedure for all scanlines the cross sectional area function is obtained. The new version of the CAAS provides the operator with two cross sectional area functions, one with a correction of the background densities for vessel branching, and one without such correction [28].

In the clinical setting, an absolute reference for densitometric area values is calculated using the diameter measurements obtained from edge detection technique assuming a circular vessel geometry in a user defined reference segment outside the stenosis. In our experiments, the circular cross sections of the phantoms served as a reference where the minimal cross sectional areas were directly calculated using the automated computer program. In the event of artifactual obstruction within the phantom channel, calibration for the densitometric brightness profile was carried out manually within an unaffected portion of the stenosis phantom. Finally, the values of obstruction diameters were calculated from the cross sectional areas assuming a circular model.

Assessment of Reproducibility

To assess the variability of repeated obstruction diameter and minimal cross sectional area measurements carried out with the CAAS II system, one representative cineangiographic frame of each size of the stenosis phantoms (0.5, 0.7, 1.0, 1.4, 1.9 mm) was analyzed 15 times by the same operator using the fully automated software without any user interaction on contours of the artificial lesion and on the position of obstruction diameter assessment.

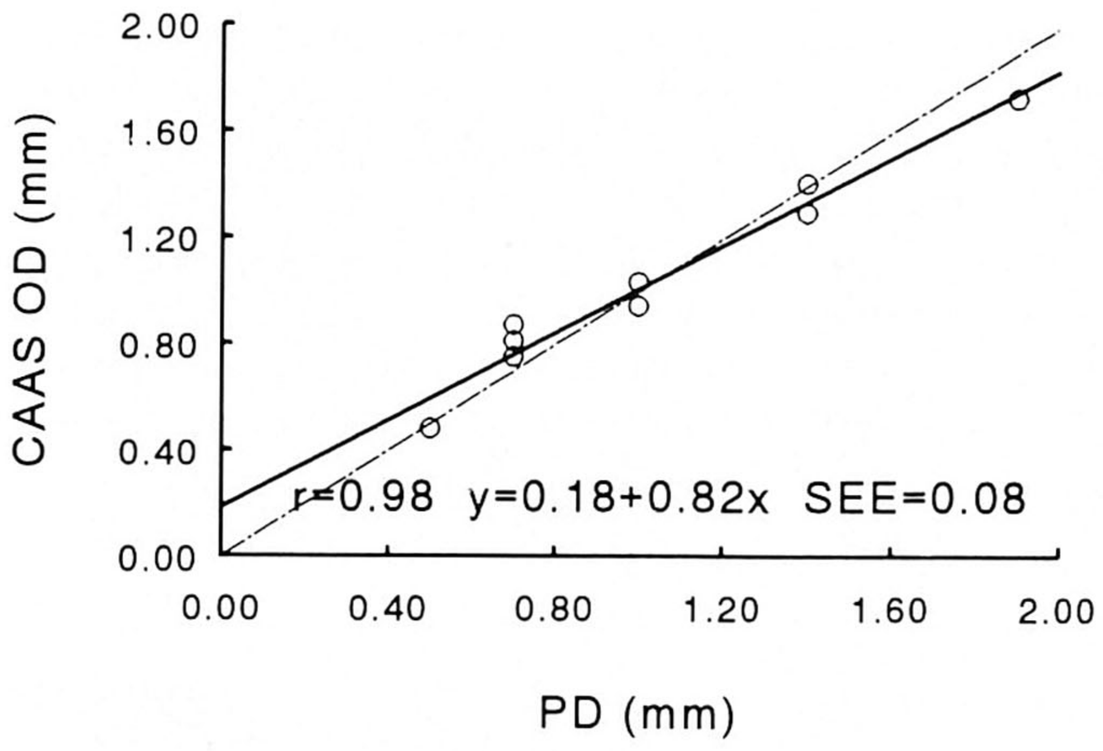


Fig. 4. Plot of obstruction diameter (OD) measurements versus true phantom diameters (PD) using stenosis phantoms (diameter 0.5, 0.7, 1.0, 1.4, 1.9 mm) inserted in a plexiglass model to mimic the radiographic scatter of the human thorax. The graph includes the line of idendity as well as the result of the linear regression analysis.

Statistical Analysis

The individual data for obstruction diameter and minimal cross sectional area were compared with the true phantom diameters as well as the derived cross sectional areas using paired t-test and linear regression analysis. A similar comparison was performed for the obstruction diameter values derived from the densitometric cross sectional areas with the respective phantom diameter data. The mean of the signed differences between measured values or mathematically derived values with the respective reference data was considered an index of accuracy and the standard deviation of the differences an index of precision. The standard deviation of the mean value from 30 geometric and 15 videodensitometric measurements on the same angiographic phantom was considered a measure of reproducibility. These values were calculated separately for all five stenosis phantoms. The mean reproducibility was defined as the mean value from those five reproducibility values.

RESULTS

Validation of Geometric Measurements

In vitro measurements of phantom diameters. Measurements of the obstruction diameters in vitro yielded an accuracy of 0.00 mm and a precision of ±0.11 mm. As demonstrated in Figure 4, there was a high correlation between obstruction diameter and phantom diameter values (r = 0.98, y = 0.18 + 0.82x, SEE = 0.08), with a slight tendency to underestimate large phantom diameters (p = N.S.)

In vivo measurements of obstruction diameters. With calibration at the isocenter, the in vivo assessments of obstruction diameters at the site of the stenosis phantoms gave an accuracy of −0.01 mm and a precision of ±0.18 mm. Figure 5A shows that obstruction diameter values and phantom diameters correlate well (r = 0.94, y = 0.22 + 0.82x, SEE = 0.15), although there is some tendency to overestimate small and underestimate large stenosis phantom diameters. The differences between measured values and reference values were statistically not significant.

Using the angiographic catheter for calibration we obtained an accuracy of 0.14 mm and a precision of ±0.17 mm. The measurement points of the smallest phantom diameter lay very close to the line of identity (Fig. 5B), while large diameters were significantly underestimated ($p < .05$) producing a relatively low slope of the regression line (r = 0.96, y = 0.14 + 0.76x, SEE = 0.12).

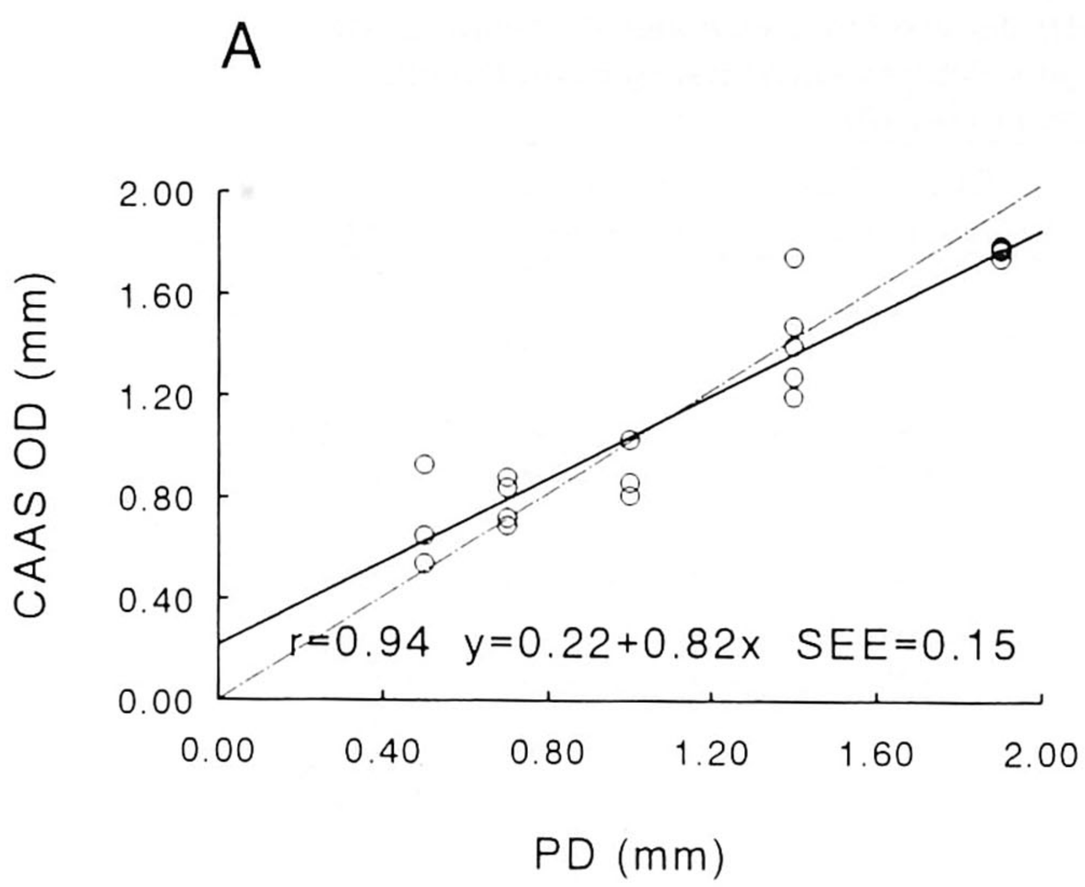
Reproducibility of geometric measurements. The results of 30 repeated analyses of obstruction diameter on each stenosis phantom using one angiographic image per phantom size are depicted in Figure 5C. The variability of measurements was ±0.07 mm for the 1.4 mm phantom, ±0.09 mm for the 0.5 mm, 0.7 mm, and 1.0 mm phantoms, and ±0.10 mm for the 1.9 mm stenosis phantom. Thus, the mean reproducibility of geometric measurements for all phantom sizes was ±0.09 mm.

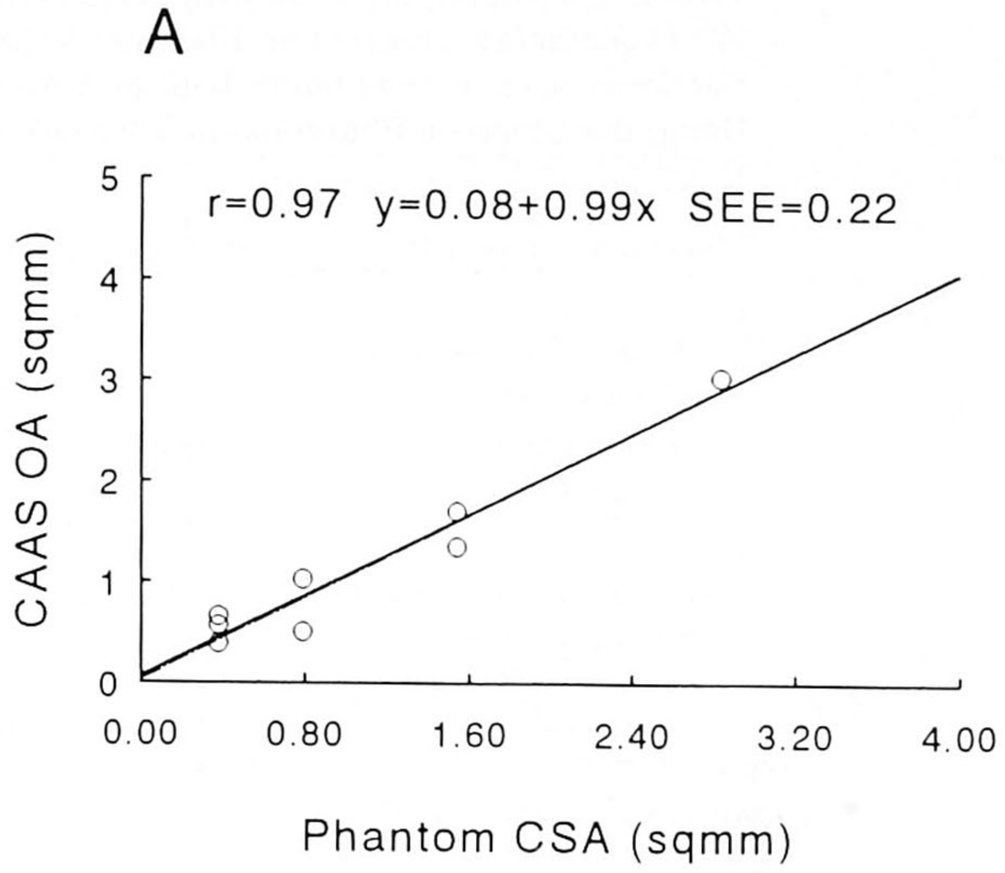
Validation of Videodensitometric Measurements

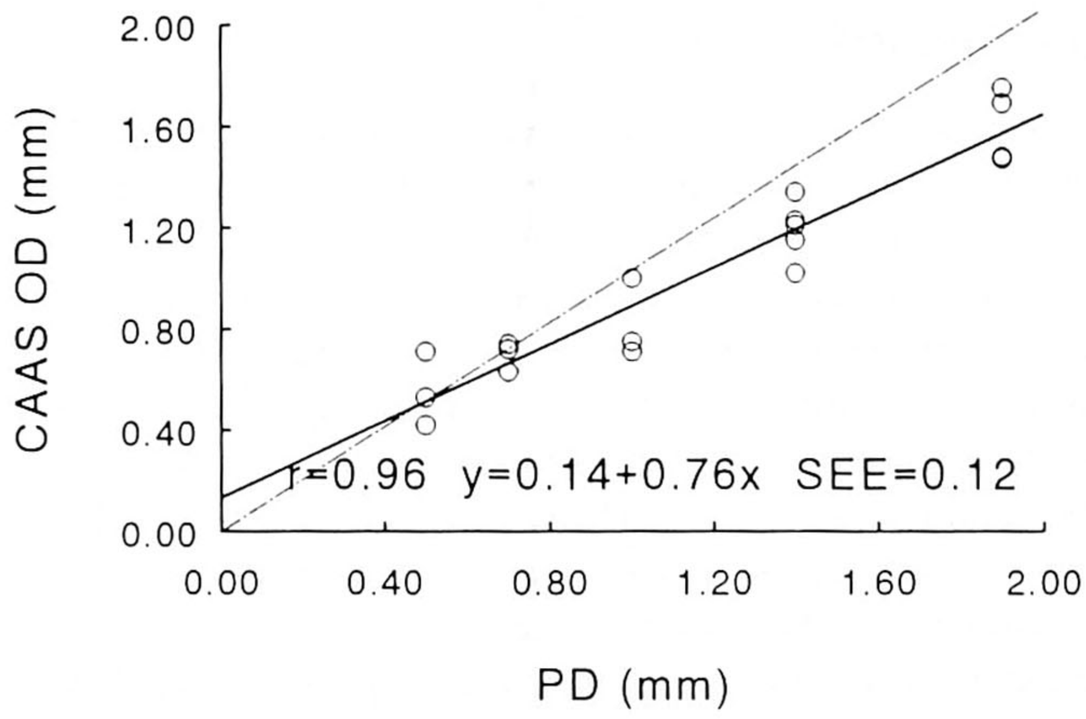
In vitro measurements of minimal cross sectional areas. In Figure 6, the measurements of obstruction areas (OA) in vitro are plotted against the true phantom cross sectional areas (CSA) with correction of the background for vessel branching (Fig. 6A) and without such correction (Fig. 6B). Using the correction of the digitally subtracted background density, these measurements yielded an accuracy of -0.08 mm^2 and a precision of ±0.21 mm^2. As illustrated by Figure 6A, the videodensitometric assessment of phantom obstruction areas correlated very well with the true cross sectional area values (r = 0.97, y = 0.08 + 0.99x, SEE = 0.22). Without correction of background (Fig. 6B), the videodensitometric measurements yielded an accuracy of -0.09 mm^2 and a precision of ±0.23 mm^2 and showed a similar high correlation of measured values and reference values (r = 0.97, y = 0.05 + 1.03x, SEE = 0.24).

The accuracy and precision values as well as the linear regression analyses of obstruction diameters as derived from measured phantom minimal cross sectional areas with and without background correction compared with the respective results from the direct measurement of obstruction diameters are listed in Table IA.

In vivo measurements of minimal cross sectional areas. The results of in vivo assessments of minimal luminal cross sectional areas at the position of the ste-







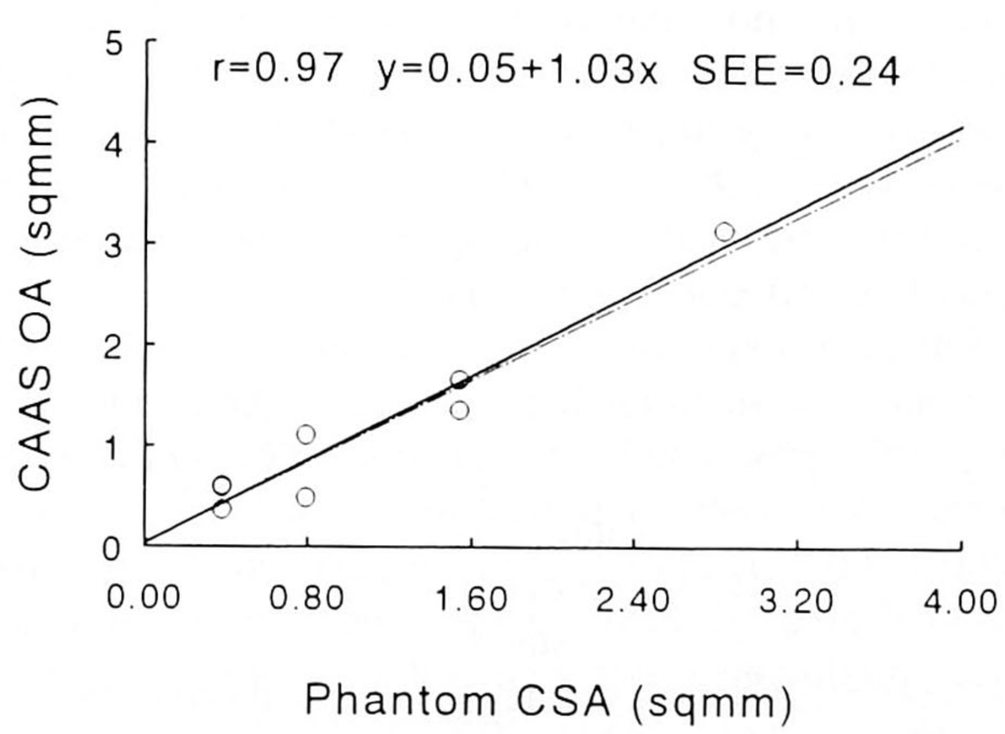


Fig. 6. Videodensitometric assessment of phantom cross sectional areas using the plexiglass model. In graph A individual obstruction area (OA) measurements are plotted against the true phantom cross sectional areas (CSA) using a correction on the background subtraction. In graph B the corresponding values obtained without background correction are displayed. The contour of the 0.5 mm phantom could not be detected automatically owing to overlap with the radiographic shadow of the 4F insertion catheter.

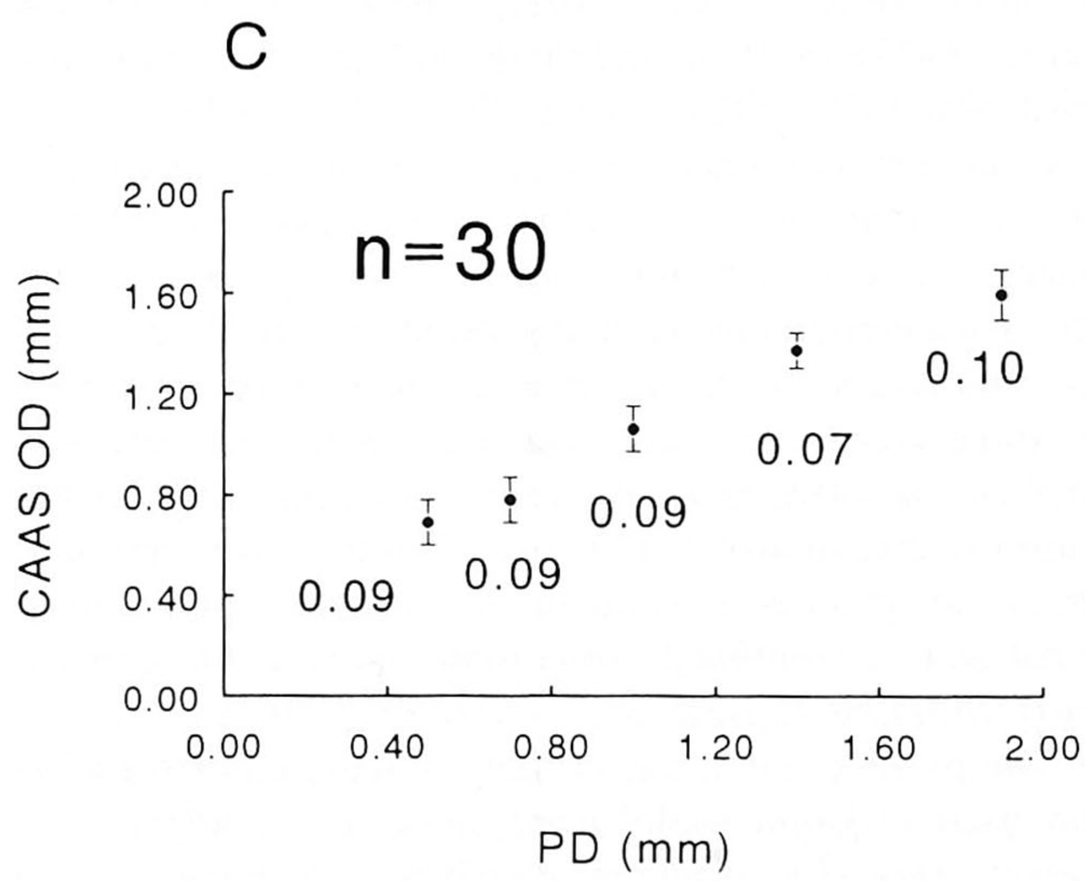


Fig. 5. Obstruction diameter (OD) measurements are displayed versus the true phantom diameters (PD) using percutaneous insertion of the stenosis phantoms in porcine coronary arteries with calibration at the isocenter (A) and catheter calibration (B). The reproducibility of obstruction diameter assessments is reflected by the standard deviation of 30 repeated obstruction diameter measurements on one representative stenosis phantom of each size (C).

TABLE I. Comparison of Obstruction Diameter (OD) Values Obtained by Direct Measurement With Calculated Obstruction Diameter Values (COD) Derived From Videodensitometric Cross Sectional Area Assessments With and Without Digital Subtraction of Background Density Using the Stenosis Phantoms In Vitro (A) as well as In Vivo (B)

Measurement parameter	Accuracy	Precision	Correlation	Linear regression	SEE
A					
OD: direct measurement	0.14	0.07	r = 0.99	y = −0.05 + 0.92x	0.07
COD (from OA)					
Uncorrected	−0.05	0.14	r = 0.95	y = 0.11 + 0.95x	0.15
Corrected	−0.05	0.14	r = 0.95	y = 0.13 ± 0.92x	0.14
B					
OD: direct measurement	−0.01	0.18	r = 0.94	y = 0.22 + 0.82x	0.15
COD (from OA)					
Uncorrected	−0.09	0.25	r = 0.89	y = 0.19 + 0.91x	0.25
Corrected	−0.12	0.19	r = 0.93	y = 0.21 + 0.92x	0.19

nosis phantoms are plotted against the respective reference values in Figure 7A,B.

Using background correction, the measurements of minimal cross sectional area yielded an accuracy of -0.22 mm^2 and a precision of ± 0.32 mm^2. Figure 7A illustrates that the correlation and standard error of estimate are clearly improved by correction of background density ($r = 0.95$, $y = 0.21 + 1.01$, $SEE = 0.33$). However, true cross sectional area values are significantly overestimated ($p < .01$).

Without background correction, the measurements of minimal cross sectional area gave an accuracy of -0.21 mm^2 and a precision of ± 0.61 mm^2. The measurement points of small obstruction areas lay close to the line of identity (Fig. 7B); however the assessment of large cross sectional areas yielded a large scatter of measurement values producing a high standard error of estimate ($r = 0.82$, $y = 0.37 + 0.87x$, $SEE = 0.61$).

The accuracy and precision values as well as the linear regression analyses of obstruction diameters as derived from measured phantom minimal cross sectional areas, with and without background correction compared with the respective results from the direct measurement of the obstruction diameter, are listed in Table IB.

Reproducibility of videodensitometric measurements. The results of 15 repeated measurements of each phantom minimal cross sectional area with and without background correction are plotted in Figure 7C,D, respectively. Without correction of background density, the variability of measurements was ± 0.09 mm^2 for the 0.5 mm and 1.0 mm phantom, ± 0.14 mm^2 for the 0.7 mm phantom, ± 0.26 mm^2 for the 1.4mm, and ± 0.27 mm^2 for the 1.9 mm stenosis phantom (Fig. 7D). Using background correction, the variability of measurements was ± 0.09 mm^2 for the 0.7 mm, ± 0.13 mm^2 for the 0.5 mm and 1.0 mm phantom, ± 0.26 mm^2 for the 1.4 mm, and ± 0.43 mm^2 for the 1.9 mm phantom (Fig. 7C). Thus, the mean reproducibility of densitometric measurements was ± 0.17 mm^2 without and ± 0.21 mm^2 with background correction.

DISCUSSION

Although several studies have confirmed that videodensitometric assessment of brightness profiles along the cross section of a contrast filled vessel can be used to estimate the cross sectional area of eccentric coronary lesions from a single plane [13,14], the reliability of these measurements remains controversial, particularly when compared with biplane assessment of coronary artery diameters [13–21]. However, it has been found that small vessel cross sectional areas are assessed with considerable accuracy, whereas the assessment of large vessel cross sectional areas produces highly scattered values, a phenomenon which is most likely due to the nonlinear relation between iodine content and the optical density of the radiographic image induced by the spectral hardening of the polyenergetic X-ray beam [31].

Geometric coronary measurements, on the other hand, provide highly accurate and reliable assessments of coronary artery dimensions, although the geometric unsharpness depending on the size of the focal spot is a limiting factor for the accurate assessment of small vessel diameters [32], which is crucial for the evaluation of high grade coronary artery stenoses. Looking at the different ranges at which video-densitometric and geometric coronary measurements have the highest potential of reliability, a combined use of both approaches theoretically could be considered.

The present validation of the new version of the Cardiovascular Angiography Analysis System compares accuracy, precision, and reproducibility of geometric and videodensitometric coronary measurements in order to elucidate the practical value of both techniques.

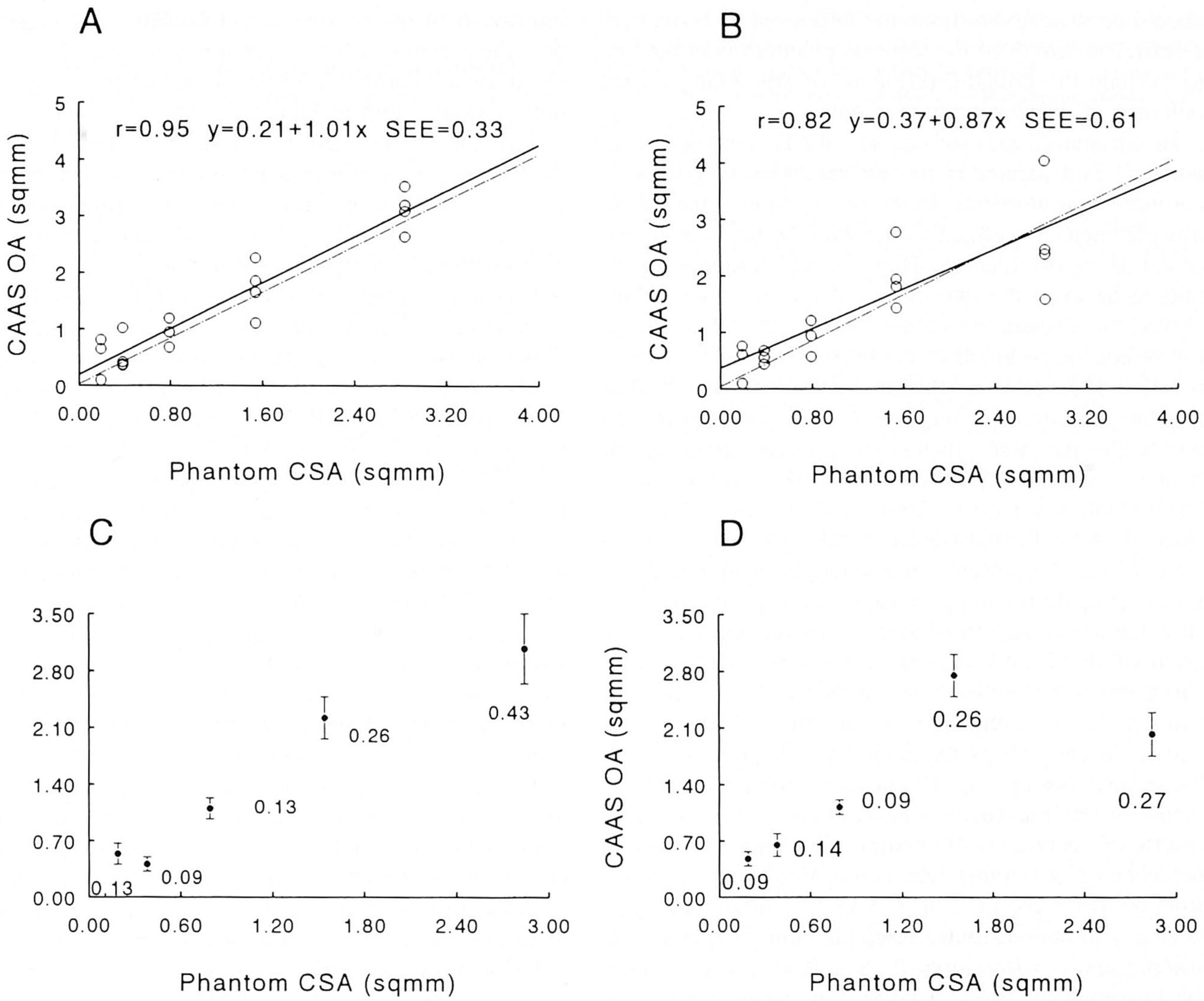


Fig. 7. In vivo validation of videodensitometric cross sectional area assessments using percutaneously inserted stenosis phantoms in swine coronary arteries with (A) and without (B) a correction of the digitally subtracted background density. The reproducibility of 15 repeated measurements on one representative stenosis phantom of each size reflected by the respective standard deviation values shows a high degree of scatter for the assessment of cross sectional areas larger than 1.0 mm^2 for both, measurements with (C) and without (D) background correction.

The variable shape of human coronary artery narrowings [33] has prompted the use of non-circular luminal cross sections in stenosis phantoms as reference for experimental validation of quantitative coronary analysis systems. Under these conditions, the potential of densitometric measurement techniques can be evaluated adequately [34]. For the comparative validation of geometric and videodensitometric assessments, however, the use of circular shaped stenosis phantoms has two advantages. First, the calibration of densitometric measurements, which is normally based on the assumption of a circular vessel cross section proximal to a coronary stenosis, can be carried out correctly at the site of the circular shaped stenosis phantom. And second, the calculation of diameter values derived from the densitometric areas can be compared directly with the respective values obtained by the edge detection technique.

Theoretically, the validation of geometric coronary measurements may be affected by the length of an artificial stenosis, when a smoothing algorithm is applied. The short and abrupt change in vessel diameter without tapering transition cannot necessarily be tracked by an edge detection algorithm incorporating integrated smoothing, so it may result in an overestimation of the obstruction diameter [3]. Thus, if accuracy, precision, and reliability of a specific edge detection algorithm

should be validated as done in the present investigation, a sufficient length of the stenosis phantom is obligatory to exclude the possible influence of smoothing on the outcome of diameter measurements.

In our study, we used the so-called ''obstruction diameter'' as a parameter for the validation of geometric coronary measurements. In the new version of the CAAS this parameter is defined as the value at the ''geometric center of the obstruction'' (Fig. 3), which represents the middle between the two closest diameter values which exceed the absolute minimum by 5% [28]. This averaging offers the potential to circumvent possible underestimation of the phantom diameter caused by the use of an absolute minimum in the presence of microthrombosis within the phantom channel or quantum noise of the imaging system [12]. In contrast to the obstruction diameter obtained by the Automated Coronary Analysis package of the Digital Cardiac Imaging system [35] this parameter still represents an absolute measure and therefore is suitable for the purpose of validation. The ''obstruction area'' as defined in the videodensitometric program of the CAAS II was used as the parameter of validation for densitometric assessments. It equals the ''minimal cross sectional area'' of coronary obstructions which closely reflects the hemodynamic significance of the stenotic lesion [36]. The in vitro geometric measurements of our present validation study yielded superior results of accuracy (0.001 mm) and similar results of precision ($\pm$ 0.11 mm), when compared to initial reports from the first version of the CAAS (3), although a slight tendency to underestimate large phantom diameters was still present ($r = 0.98$; $y = 0.18 + 0.82x$; SEE = 0.08) as illustrated by Figure 4. The superiority of the new software version, however, is more evident from the in vivo results of our investigation using edge detection measurements on the percutaneously inserted stenosis phantoms in swine coronary arteries (Fig. 5).

When calibrated at the radiographic isocenter the new software version yielded an accuracy of -0.01 mm and a precision of ± 0.18 mm ($r = 0.94$, $y = 0.22 + 0.82x$, SEE = 0.15), whereas the identical experimental approach with the previous version of the CAAS (12) gave an accuracy value of -0.07 mm and a precision of ± 0.21 mm ($r = 0.91$, $y = 0.30 + 0.79x$, SEE = 0.19). Using catheter calibration by which geometric conditions similar to clinical routine were simulated, the new software version also demonstrated some improvement although less impressive due to a similar tendency to underestimate true phantom diameters, a phenomenon which may be explained by out of plane magnification of the catheter tip [12]. The high level of reproducibility throughout the range of all phantom sizes (Fig. 5C) is comparable to current digital as well as cinefilm-based quantitative coronary analysis systems [11,22,37]. The improvement of measurement reliability in comparison with the previous software version is based mainly on the experimental correction of the algorithm for overestimation of small stenosis diameters [29].

The videodensitometric software of the new version of the CAAS has been improved in one way. The operator can select a menu option to correct the background density for vessel branching before subtracting it from the cross-sectional absorption profile [28].

It is not surprising that the influence of background correction is minimal with in vitro measurements. This is illustrated by the almost identical results shown in Figure 6A,B. On the other hand, background correction seems to improve the reliability of videodensitometric cross sectional area assessments obtained in our animal model (Fig. 7A,B). However, the assessment of reproducibility based on the standard deviation of 15 consecutive analyses on each phantom clearly demonstrates that even the use of the improved digital subtraction technique to correct for background density cannot overcome the limitation of current videodensitometric measurements of large vessel cross sectional areas due to the effects of beam hardening, scattering, and veiling glare (Fig. 7C). A more sophisticated approach towards calibration of videodensitometric assessments based on the use of reference phantoms with various cross sectional areas to correct for the non-linearity of the entire energy/brightness function possibly could help to solve this problem. At the present stage, however, the potential of highly reliable densitometric assessments is confined to the measurement of cross sectional areas below 1 mm^2 [31].

Calibration with perfectly circular cross sections such as those of the precision-drilled stenosis phantoms used in our experiments provides ideal conditions for the measurement of cross sectional areas. With respect to videodensitometric assessments in clinical practice which uses a ''normally'' shaped portion of the coronary artery as a reference, any morphological irregularities which deviate from the assumed circular shape will affect the reliability of cross sectional assessments at the position of the coronary lesion. Furthermore, the influence of vessel branching and foreshortening of the segment by non-orthogonal imaging are some of the additional sources of error which potentially impair the reliability of videodensitometric measurements.

In conclusion, the experimental validation of the new version of the Cardiovascular Angiography Analysis System demonstrates that the high reliability of geometric coronary measurements based on edge detection technique has been improved further. However, even in the presence of ideal reference cross sections, accuracy and precision of videodensitometric measurements remain limited by the effects of beam hardening, scattering, and veiling glare.

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