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Basic Investigations

Quantification of Intracoronary Volume by Videodensitometry: Validation Study Using Fluid Filling of Human Coronary Casts

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Changes in intracoronary volume reflect the hemodynamic significance of progression or regression of diffuse coronary artery disease where intracoronary catheters cannot be applied for direct measurements due to small vessel dimensions. We have validated the videodensitometric measurement of intracoronary volume with epoxy casts of postmortem human coronary arteries. The volume of 31 coronary segments (cross-sectional areas in a range of 2–13 mm^2) measured by fluid-filling using a precision dispenser was compared with the respective single plane intracoronary volume assessments obtained by the videodensitometric algorithm of the new generation Cardiovascular Angiography Analysis System (CAAS II). The true and measured values of volume were compared by calculation of the mean of the signed differences ± standard deviation and by linear regression analysis. Videodensitometric measurement of intracoronary volume correlate well with fluid-filling of human coronary artery casts (correlation coefficient: r = 0.99, y = 1.96 + 0.99x, standard error of estimate: SEE = 3.96) with a significant trend towards overestimation of true volume values (mean difference = 1.73 ± 3.64 mm^3, $P<0.05$). Intracoronary volume estimations can be used to measure changes of luminal dimensions of coronary arteries and may offer a new approach to assessment of progression or regression of diffuse coronary artery disease. © 1994 Wiley-Liss, Inc.

Key words: intracoronary volume, quantitative coronary angiography, coronary artery disease

INTRODUCTION

Since the introduction of computerized quantitative angiography (QCA), the progression and regression of coronary artery disease have been assessed by two-dimensional measurement of luminal diameter and cross-sectional area [1]. Two-dimensional measurements of luminal dimension at the site of focal atherosclerotic lesions can be used to assess alterations in coronary flow reserve [2,3]. The progression or regression of atherosclerosis as well as the functional significance of diffuse coronary artery disease, however, cannot always be adequately evaluated by two-dimensional measurements. Diffuse intimal hyperplasia, for example, reduces intracoronary volume without focal stenosis [4]. Theoretically three-dimensional reconstruction of coronary arteries by intracoronary ultrasound imaging should enable the quantification of changes in intracoronary volume when diffuse coronary atherosclerosis is present [5]. However, the caliber and stiffness of intracoronary ultrasound catheters remain strong limitations to the investigation of coronary arteries with small diameters [6]. By contrast, videodensitometry has been shown to be a potentially reliable technique for the assessment of intracoronary dimensions [7].

In the present investigation, the volume of epoxy phantoms produced by a negative cast technique from human coronary arteries was used as a reference to in-

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vestigate the potential of videodensitometry for the quantification of intracoronary volume.

MATERIAL AND METHODS

Epoxy Phantoms

The coronary arteries of three human hearts removed postmortem were flushed thoroughly with saline and then injected in situ with a fluid silicon paste to obtain positive luminal casts [8]. After hardening, the main arteries were dissected and put into a potassium hydroxide solution for removal of tissue. The positive casts of four atheromatous coronary arterial segments were selected. After removal of all ramifications, each segment was suspended in a Teflon mold and cast with epoxy resin. Four epoxy blocks with negative casts of diffusely diseased human coronary arteries were thus obtained (Fig. 1).

Assessment of Cast Volume

A radiopaque scale with metal markers was attached to each epoxy block, producing a series of subsegments (length, 5–9 mm; cross-sectional area, 2–13 mm^2), and the cast lumen was filled with colored water using a precision microdispenser (Fig. 2). The tolerance of the microdispenser was <0.01 mm^3 (Microlab M, Hamilton Bonaduz AG, Bonaduz, Switzerland). The precise volume of each cast segment delineated by the scale was recorded. Thus, a series of 31 volumetric segments was obtained, serving as a reference for videodensitometric analysis.

Image Acquisition

The phantoms were filled with 100% contrast medium (Iopamidol 370, Bracco, Milan, Italy; 370 mg iodine/ml) and positioned in a water bath between Plexiglass blocks (12.5-cm anterior and 5-cm posterior), to approximate the X-ray scatter in the human thorax with an energy level of 75 kV during fluoroscopy. Subsequently, each phantom was recorded on 35-mm cinefilm, using a Philips DCI system with a focal spot of 0.8 mm, a focus-to-object distance of 90 cm, and an object-to-image intensifier distance of 13 cm. The cinefilms were obtained at a frame rate of 25 images/sec using an Arritechno 90 cinecamera (Arnold & Richter, Munich, Germany) with an 85-mm lens. A Kodak CFE cinefilm (Eastman

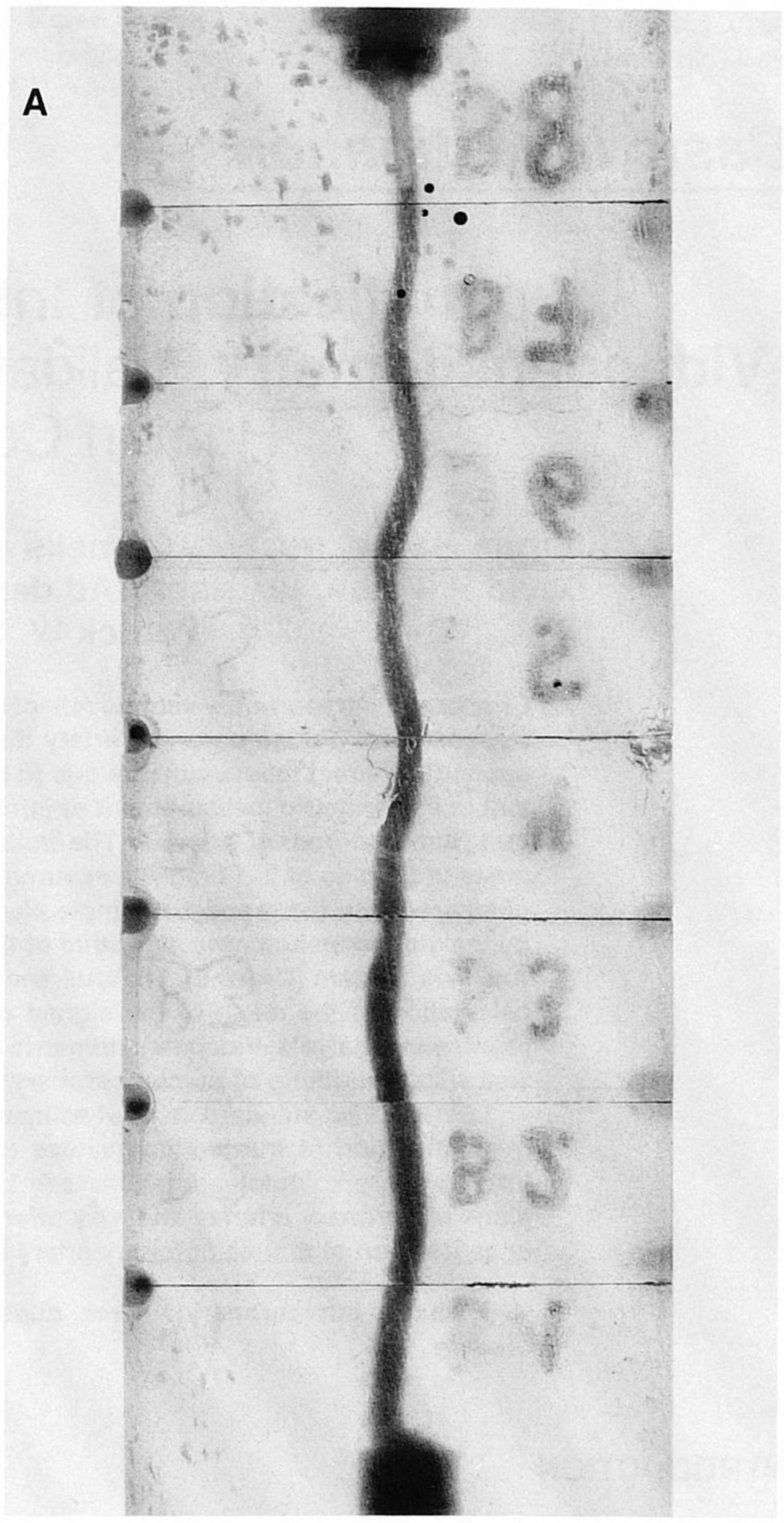

Fig. 1. A: Four epoxy blocks with negative casts of diffuse diseased human coronary arteries were used as a reference for videodensitometric assessment of intracoronary volume. B: The volume of each coronary segment of the epoxy blocks was measured by fluid filling using a precision micro dispenser (tolerance <0.01 μl).

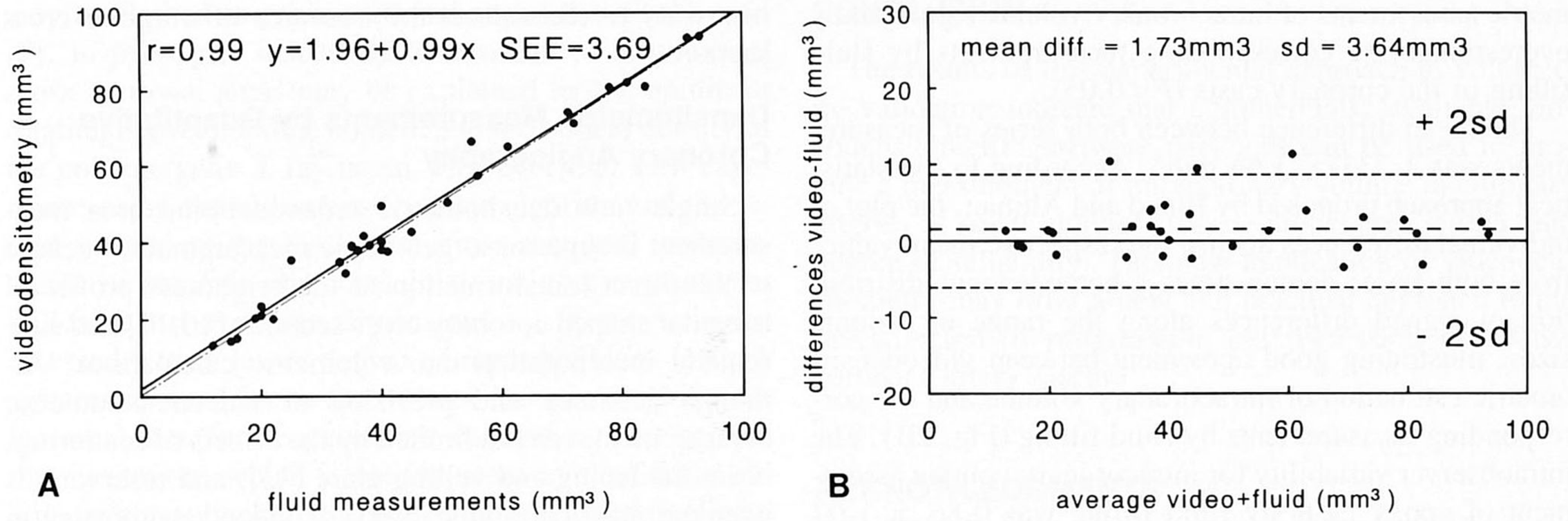

Fig. 2. A: Videodensitometric assessments of the volume of each coronary segment are plotted against the values obtained by fluid measurements (range of cross-sectional areas: 2–16 mm^2). B: Differences between volume measurements using videodensitometry and fluid filling plotted against the mean values from both methods.

Kodak, Rochester, NY) was used and processed by a Refinal (M) developer (Agfa-Gevaert, Leverkusen, Germany) for 4 min 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 densitometric curve.

Image Processing

The cinefilm images of each coronary phantom were analyzed using geometric and videodensitometric algorithms by the new version of the Cardiovascular Angiography Analysis System (CAAS II, PieMedical, Maastricht, Netherlands). This procedure is based on the digital selection of a 6.9×6.9-mm region-of-interest out of the 18×24-mm cineframe for digitization into a 512×512 pixel matrix, using a CCD camera with 8 bits (256 gray levels). Effectively, this means that the entire cineframe of 18×24 mm can be digitized at a resolution of $1{,}329 \times 1{,}772$ pixels.

Videodensitometric Analysis

The videodensitometric volume measurement of 31 coronary segments (mean length 0.5 ± 0.1 cm) was calibrated using a circular cross-sectional area calculation at the tubular inlet of each epoxy block by an edge-detection technique [9]. Calibration of diameter measurements by the edge-detection technique was performed using a 3-mm drill bit as a scaling device. The cross-sectional area derived from the diameter was thus used as a measure for videodensitometric cross-sectional area assessment. Subsequently, each coronary segment underwent separate videodensitometric analysis. Thereby, the brightness profile of each scanline perpendicular to the centerline of the lumen is transformed into an absorption 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 at two positions located 2 and 3 pixels outside the left and right detected contours [9]. Subtraction of this background portion from the absorption profile yields the net cross-sectional absorption profile allowing the calculation of the cross-sectional area and the cross-sectional volume by multiplication with the distance between the scanlines. Subsequently, the segment volume is calculated by the summation of all contained cross-sectional volumes.

Statistical Analysis

Videodensitometric measurements of volume were compared with the directly measured volumes by fluid filling using a *t*-test as well as calculation of the mean of the signed differences and the respective standard deviations. A linear regression analysis was applied and individual differences were plotted against the mean values from both measurements using the statistical approach of Bland and Altman [10]. Finally, interobserver and intraobserver variability of volume measurements by fluid filling was assessed by calculation of the mean of signed differences ± SD.

RESULTS

The individual data of videodensitometric volume calculations on 31 coronary segments have been plotted against the direct measurements using fluid filling with a precision microdispenser in Figure 2A. Both series of measurements show excellent correlation ($r = 0.99$, $y = 1.96 + 0.99x$, $SEE = 3.69$), although videodensito-

metric assessments of intracoronary volume significantly overestimate the corresponding measurements by fluid filling of the coronary casts ($P<0.05$).

The mean difference between both series of measurements was 1.733 ± 3.64 mm^3. According to the statistical approach proposed by Bland and Altman, the plot of individual differences against the respective mean values from both series demonstrates a homogeneous distribution of signed differences along the range of volume sizes, illustrating good agreement between videodensitometric estimation of intracoronary volume and the corresponding measurements by fluid filling (Fig. 2B). The intraobserver variability for intracoronary volume assessment of epoxy casts by fluid filling was 0.86 ± 1.07 mm^3, while the interobserver variability was 1.0 ± 1.41 mm^3.

DISCUSSION

Intracoronary Ultrasound

Despite the potential value of quantification of luminal volume in the study of progression and regression of diffuse coronary artery disease, previous attempts at the measurement of arterial volume have been limited to the three-dimensional reconstruction of intracoronary ultrasonic examinations [5]. An inherent limitation of quantification by intracoronary ultrasound, however, is the obligatory intraluminal insertion of an ultrasonic catheter that wedges in severe coronary stenoses as well as in coronary vessels of small diameter (6). This results in stretching of the vessel wall, restricting the application of three-dimensional intracoronary ultrasound to large vessels without severe stenoses.

Geometric Measurements by Quantitative Coronary Angiography

Quantitative coronary angiography (QCA) offers two approaches to the assessment of intracoronary volume: geometric and densitometric coronary measurements. Single-plane geometric measurements of vessel diameters by an edge-detection technique can be used to calculate luminal cross-sectional areas, assuming a circular model. If the length and the local cross-sectional area for a given segment of a coronary artery are known, an estimation of intracoronary volume can be derived. In principle, the use of edge-detection algorithms provides highly reliable measurements [11–13]; however, the assumption of a circular model does not take into account the irregular shape of human coronary arteries in the presence of intimal hyperplasia and obstructive atherosclerosis [14]. Averaging of area values from two orthogonal planes reduces the error introduced by the assumption of a circular cross-sectional area from one single view [15], but multiple-view analysis would be necessary to reconstruct the true area of irregular cross sections.

Densitometric Measurements by Quantitative Coronary Angiography

Single-view densitometric cross-sectional area measurement is superior to geometric measurement, because of the direct transformation of the brightness profile of irregular shaped coronary cross sections [16,17] and subsequent incorporation into volumetric calculations. Although accuracy and precision of videodensitometric measurements remain limited by the effects of scattering, beam hardening and veiling glare [13], and reservations over the practical applicability of videodensitometry in clinical cardiology have been raised [15–23], recent validation studies have shown that small-vessel cross-sectional areas can be assessed with a high degree of reliability and reproducibility [7,13]. It would appear that videodensitometry offers potentially an effective method of quantification of intracoronary volume in patients with diffuse coronary artery disease.

Experimental Model for Validation

An experimental approach to the validation of intracoronary volume measurements by videodensitometry must accommodate the irregular shape of atherosclerotic coronary arteries. Smooth regular-shaped phantoms, appropriate for the assessment of edge-detection algorithms [12], are inadequate for this purpose.

To imitate the asymmetric geometry of coronary arteries in patients with coronary atherosclerosis, we used epoxy phantoms produced by a negative cast technique from postmortem human coronary arteries [8] directly reflecting luminal irregularities and vessel tortuosity. The calibration of 31 volumetric segments by fluid filling with a precision microdispenser (accuracy <0.01 mm^3) provided a series of reference values for comparison with volumetric measurements derived from videodensitometry. The low interobserver and intraobserver variability in the assessment of intracoronary volume using fluid filling enhanced the suitability of this experimental approach to volumetric validation.

The results of this study show that the videodensitometric algorithm of the new version of CAAS provides highly reliable measurements of intracoronary volume in vitro, at least for cross-sectional areas of 2.00–13.00 mm^2. Within this range, a low mean difference (1.73 mm^2) and standard error of estimate (SEE = 3.64) indicated good agreement between measured values and reference volumes (Fig. 2), although the trend toward overestimation of reference values was statistically significant ($P<0.05$).

Recent in vitro studies have demonstrated that reliable videodensitometric assessment of luminal dimensions

may be limited to cross-sectional areas of <13.00 mm^2 [7]. In principle, inaccurate assessment of large-vessel cross-sectional areas may be explained by the nonlinear relation between iodine content and the optical density of the polyenergetic X-ray beam. However, our own experience using the videodensitometric algorithm of the recent version of the CAAS for cross-sectional measurements of stenosis phantoms in swine coronary arteries indicated that even area dimensions >1.00 mm^2 may be assessed with a lower degree of reproducibility [13]. A systematic error due to the isolated use of a single cross-sectional area for densitometric calibration may explain this limitation, which is clearly more evident when inhomogeneous background has to be processed by digital subtraction in vivo.

Limitations

The use of circular-shaped cross-sectional areas for the purpose of videodensitometric calibration may hamper the transformation of the present volumetric validation to conditions present in the clinical situation. In our study using human coronary casts, videodensitometric calibration of CAAS was performed at the conically shaped inlet of the epoxy phantoms. Thus, a higher degree of accuracy was produced than could be obtained in clinical practice, where a coronary segment that appears to have an approximately homogeneously circular cross section is recommended for calibration.

By contrast, the experimental approach of densitometric calibration may have introduced some systematic error that could lead to the small but significant degree of overestimation. Because of vignetting, cinefilm exposure is somewhat less near the edges of the frame when compared to its center. The fact that calibration of the densitometric curve was performed at the inlet of the phantoms, located closer to the edge of the image, could have influenced the outcome of the calibration.

Finally, the use of angiographic catheters for the calibration of geometric measurements by an edge-detection technique may introduce additional errors due to out-of-plane magnification of the catheter tip [24], which can affect the outcome of videodensitometric volume assessments. However, at least for the volumetric assessment of coronary artery segments with small cross-sectional area, these systematic errors should be negligible. Another limitation of our experimental study is the use of casts from coronary arteries that show a relatively homogeneous reduction of intracoronary lumen. Although the potential of videodensitometry to assess intracoronary volume could be adequately documented, additional experimental measurement series would be required to prove similar reliability of densitometric volume assessment at the site of irregular-shaped coronary lesions.

CONCLUSION

The results of this experimental approach to volumetric validation indicate that commercially available videodensitometric software packages can be used to provide a measurement of intracoronary volume in coronary arteries of small luminal cross-sectional area with a high degree of reliability. This new application of videodensitometry may offer a new and practical approach to the investigation of progression and regression of diffuse coronary artery disease.

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