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Title

Digital angiography: the implementation of computer technology for cardiovascular imaging.

Permalink

<https://escholarship.org/uc/item/3zp71396>

Journal

Progress in cardiovascular diseases, 28(3)

ISSN

0033-0620

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Publication Date

1985-11-01

DOI

10.1016/0033-0620(85)90015-5

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Digital Angiography: The Implementation of Computer Technology for Cardiovascular Imaging

Jonathan Tobis, Orhan Nalcioglu, and Walter Henry

THERE HAVE BEEN significant improvements in computer technology over the past five years that have resulted in dramatic clinical applications of digital angiography.¹⁻³ Although digital angiography was initially developed as a means for obtaining intravenous first-pass angiograms, it has proven to be most beneficial as an adjunct to invasive cardiac catheterization. One reason for this rapid development is the computer's unique capacities to manipulate images and obtain functional information about blood flow, iodine contrast density, and ventricular performance.⁴⁻⁶ In the area of cardiovascular diagnosis, digital angiography has been used to obtain left ventriculograms with a lower dose (12 mL) of iodinated contrast media than is used during standard film-based angiography. This permits multiple left ventriculograms to be performed, which, in turn, facilitates the performance of interventional studies such as atrial pacing to assess the functional significance of coronary artery stenosis. During selective coronary angiography, digital acquisition of the images has been shown to yield diagnostic information equal to cineangiography using 35 mm film.⁷ In addition, the digital format provides immediate access to enhance the coronary images through computer processing techniques such as edge sharpening, contrast amplification, and fourfold image magnification. Computer software programs are also readily applied to facilitate quantitation of coronary lesions either by edge detection or videodensitometric analysis. Computer processing of selective coronary angiograms has also been used to study the relative appearance time of iodinated contrast as a measure of coronary flow reserve across stenotic vessels.⁸ An exciting application of digital angiography has been the development of digital roadmapping, which uses computer processing to provide a continual image of the coronary anatomy to act as a guide during angioplasty.⁹

As advances in computer technology improve and the speed of acquisition and storage of data increases, the medical applications of this science will continue to have profound effects. This

review will describe these recent innovations in the application of computers to cardiovascular imaging.

CAPABILITIES OF DIGITAL PROCESSING

Digitization Process

Computers are typically used to process radiologic images by transforming the continuous black and white gradations of an x-ray picture into a matrix in which the shade of gray in each small segment of the image is assigned a number that corresponds to the intensity of x-ray absorption in that small image segment.¹⁰ Instead of recording the x-ray image on radiographic film, the x-rays that penetrate the body and strike the image intensifier are transformed by a television camera into a television image as is commonly performed during fluoroscopy.¹¹ Each television frame is created by a rapidly moving electron beam that traces out 512 horizontal lines from the top to the bottom of the image. This television or video image is described as an analog image because there is a continuous change in electric voltage along each horizontal line corresponding to the varying light intensity across the image. Digital image-processing computers take this analog video image and convert it or digitize it into a series of binary numbers that can be utilized by the computer for manipulating the image. Each television frame is digitized by breaking up each of the 512 horizontal lines in the image into 512 bins. This process establishes the x-y coordinates of each bin (also referred to as a picture element or pixel) in the new computer image. In a 512 × 512 matrix, there are

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Supported in part by grants from the American Heart Association, California Affiliate, and by grant No. RO 1-HL31440-01 from the National Institutes of Health.

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0033-0620/85/2803-0002\$05.00/0

262,144 pixels. Each pixel is assigned an integer number that corresponds to the intensity of the electrical signal in each small region of the analog or video image.¹² The scale of integer numbers used depends upon the number of bits of information that are available for storing information in each pixel. For current applications, there are usually eight bits available per pixel. Since the computer uses a binary system, this translates into 2^8 or 256 numbers that can be used to describe the black and white intensity of each pixel in the image. In terms of human perception, our visual system can differentiate approximately 15 to 20 shades of gray so that the digital image with 256 shades of gray appears to us as a continuous or smooth gradation of gray from pure black (digital number of 0) to pure white (digital number of 256). In addition, our perception of the sharpness of the image or spatial resolution depends on the number of boxes or pixels that are used to form the digital image. If only 64×64 pixels are used, the image has an obvious checkered pattern, which is referred to as "pixelization" of the image. However, when denser matrices are used, such as the 512×512 format, then the pixels become so small that our visual system does not recognize the borders of the individual pixels (unless highly magnified), and we perceive a continuous function of smooth spatial outlines. As the size of the object that is imaged decreases, the need for finer spatial resolution increases. However, the amount of numbers that have to be handled by the computer limit the speed with which the x-ray images can be processed so that one must strike an appropriate balance between image resolution and processing speed.

The fact that there are computers available to perform these numerical feats attests to the dramatic improvements in computer capabilities that have occurred over the last 20 years. In 1968 when computers were initially applied in medicine for analyzing the pressure recordings from a cardiac catheterization laboratory, a room full of computers was required to perform 200 analog-to-digital conversions per second.¹³ By 1981 computers were available that were the size of a large tape recorder and could process 8 million analog-to-digital conversions per second. Translated into images, this meant that a 512×512 pixel matrix

could be processed 30 times per second, which is equivalent to television framing rates and usual cineangiographic rates.

Mask Mode Subtraction

Once the x-ray image has been transformed into a digital format, enhancement of the image is possible because the computer treats each image as a series of numbers that can be varied with such mathematic functions as addition and multiplication or more complicated functions such as logarithmic amplification or Fourier transformation.¹⁴ Different mathematic functions can be used to enhance the image or to extract more information from the image than can be obtained from radiographic film alone.¹⁵ For example, an intravenous injection of contrast media is less invasive than a direct arterial injection for obtaining an angiogram of the carotid arteries. However, contrast concentration decreases markedly during its transit from the veins and through the pulmonary circulation so that when the contrast material finally reaches the carotid arteries it is too diluted to be recorded with traditional radiographic film techniques. A similar problem occurs when attempting to visualize contrast in the left ventricle following an intravenous injection. Digital image-processing techniques have been used to improve visualization of low concentrations of iodinated contrast media. One of the earliest methods of digital image processing was mask mode subtraction described by Mistretta.¹⁶⁻¹⁷ During this process, an attempt is made to subtract out extraneous structures in the angiographic image such as soft tissue and bone densities. In order to accomplish this, an initial x-ray image of the neck or thorax is taken, digitized by the computer, and stored in the memory of the computer for subsequent use. This stored image is referred to as a mask. Another x-ray image of the neck or thorax can be taken and digitized and then compared with the original image in the computer memory. The two images are compared pixel by pixel for the intensity of the gray scale information contained within each corresponding pixel. If the gray scale information in each pixel in the two images is equivalent, then the pictures will cancel each other out during the subtraction process. The resulting image will have a uniform

gray scale value. In addition, there will be no bones or soft tissue visualized provided there was no motion of the patient between the time that the mask and the subsequent image were acquired. If a diluted amount of iodinated contrast media is present in the carotid arteries or the heart at the time the second image is obtained, it will be more easily visualized because soft tissues and bone densities will be subtracted out and no longer obscure the contrast-filled artery or ventricle. This process of mask mode subtraction has been effectively used with intravenous injections to visualize the cardiac chambers and the aorta and to screen patients for atherosclerotic involvement of the carotid, renal, or iliac arteries.¹⁸⁻²² Adequate studies can be obtained in approximately 75% of cases.

One of the major reasons for inadequate studies is misregistration artifact. This degradation in the quality of the subtracted image occurs when there is movement in the image between the time that the mask is acquired and the subsequent contrast-filled images are obtained. The motion of background tissues creates misregistration of bone and soft tissue densities. There will be unequal subtraction or cancellation of the digital numbers within certain pixels near the boundaries of bone and soft tissues. The resulting subtracted images will have light or dark streaks in the image and will produce decreased visualization of the diluted iodine. In addition, these streaks can be confused with arterial stenoses; thus, the recognition of misregistration is important. Fortunately, postprocessing techniques can be used to improve image quality and reduce problems because of misregistration artifact. One of the advantages of digital angiography is that unlike film-based radiography in which the image cannot be altered after development, digital images can be restored from the computer memory and manipulated after the angiogram is acquired. For example, if there is a significant misregistration streak in the subtracted image, then a new mask can be recalled from computer memory and subtracted from the frames with iodine. A series of different masks can be tried until one is found that has a minimum of misregistration (Fig 1). In addition, the mask can be moved by the computer relative to

the second image in postprocessing the digital angiogram to further reduce misregistration artifact. More recent software programs have been developed that use a continuous update of the mask, synchronous to the cardiac cycle. This process, which is called dynamic mask subtraction, produces images with a minimum of misregistration artifact and thus further enhances iodine contrast.

Cardiac Imaging With Digital Angiography

In order to take advantage of the benefits of digital imaging, it was first necessary to compare cardiac images obtained during standard film-based angiography with digitally acquired images to determine whether ventricular volumes and ejection fraction correlated well between the two imaging techniques. Comparison studies were initially performed with intravenous administration of iodine contrast media, and the left ventricle was imaged in a first-pass mode after the iodine bolus traveled through the right ventricular and pulmonary phases.²³⁻²⁹ As distinguished from digital acquisition of peripheral arterial studies in which the framing rates are two to eight per second, for cardiac ventricular imaging the digital images had to be acquired at 30 frames per second. The image-processing computers available in 1981 did not have the computer storage capacity to store in a digital format images at this rapid framing rate. Therefore, initial comparison studies were performed by acquiring the images at 30 frames per second, subtracting a mask image in real time, and reconvert the digital information into an analog format for storage on videotape. Computer technology advanced rapidly so that by 1983 complete digital storage of 512×512 matrix images at 30 frames per second was accomplished. Digital storage made it easier for images to be recalled for postprocessing without degradation of the image by videotape noise.

There were several routes for administration of intravenous contrast media such as the superior or inferior vena cava, or the femoral or brachial vein. Our initial comparison studies were performed in the catheterization laboratory following routine cardiac catheterization; therefore, the femoral vein was used as the venous access.⁶ For the first-pass angiograms, 30 to 40

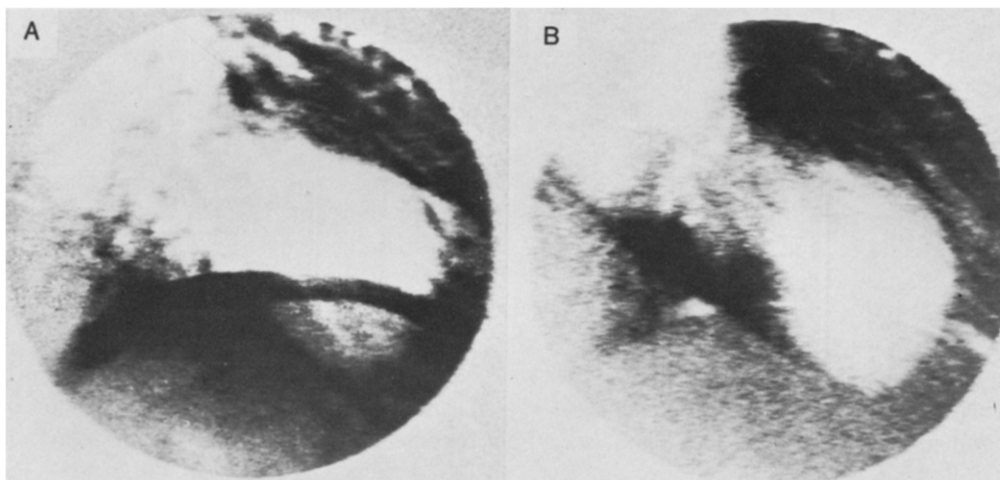


Fig 1. The first-pass digital subtraction angiogram demonstrates some of the postprocessing capabilities of digital imaging. In Panel A (end-diastole), there is a large misregistration artifact due to respiratory motion of the diaphragm between the time the mask image was taken and the subsequent left ventricular phase. In Panel B (end-systole), a new mask has been chosen after the study was performed, and the boundaries of a large anterior apical aneurysm are more clearly defined. (Reprinted with permission from *Modern Concepts of Cardiovascular Disease* 53:32, 1984.)

mL of meglumine diatrizoate (Hypaque 75 [Winthrop-Breon, New York]) or meglumine iohalamate (Vascoray [Mallinckrodt, St Louis]) were injected by hand over two to three seconds through a 6F introducing sheath placed in the femoral vein. The angiograms were obtained with fluoroscopic exposure of 8 mA and 70 to 90 kilovolts (peak) with 4 mm of aluminum filtration to diminish low-energy x-ray penetration. The angiograms could be obtained in either a continuous mode, or just the right and left ventricular phases could be isolated. Standard 35 mm film-based cineangiograms were obtained in the 30-degree RAO projection with direct left ventricular injection of 40 mL of contrast media. Left ventricular volumes were measured by the area-length technique from both the digital and film angiograms. Initial studies demonstrated good correlations in the measured volumes at end-diastole and end-systole and for the calculated ejection fractions. In addition, there were no premature ventricular contractions during the left ventricular phase of digital angiograms, whereas six of 33 (18%) patients had ventricular tachycardia during the standard intraventricular injection of contrast with the film-based angiograms.

The spatial resolution of the intravenous angiograms was not as good as the direct intra-

ventricular angiograms. However, there were occasional patients with large apical aneurysms who had better visualization of the left ventricle on the digital study because there was improved mixing of the blood pool with the iodine contrast following intravenous administration. It is perhaps more appropriate to compare first-pass digital angiograms with first-pass radionuclide studies. From that perspective, digital angiograms have ten times the spatial resolution of radionuclide images and therefore are very useful for assessing ventricular wall motion at rest and during stressful intervention.³⁰⁻³³

Direct Intraventricular Studies

The concept of ventricular imaging with intravenous administration of contrast was intriguing because of the less invasive nature of the method. The next step in understanding the capabilities of digital processing was to obtain left ventriculograms with direct injection of contrast using significantly lower doses than those injected during standard film-based angiograms.³⁴ This could offer several important advantages in performing angiograms, including greater safety when studying children or patients who cannot tolerate large volumes of hyperosmolar contrast media. Our initial study compared angiograms in 30 patients taken in the 30-degree RAO pro-

jection.³⁵ Standard film-based ventriculograms were obtained with a total of 40 mL of Hypaque 75 injected at 30 mL/s over three seconds. Digital angiograms were obtained in the same projection using a total of 10 mL of contrast media injection at 5 mL/s over two seconds. During the standard film-based acquisition, six of 30 (20%) patients had ventricular tachycardia and no reliable volume data could be obtained. In contrast, no patient had sustained premature ventricular contractions during the 10-mL digital angiogram, and only four patients had a single premature ventricular contraction. Left ventricular volumes measured by the area-length technique at end-diastole and end-systole and the calculated ejection fractions correlated well between the digital and film-based angiograms. In addition, the 10-mL injection did not increase the mean left ventricular end-diastolic pressure, whereas the 40-mL injection increased the mean left ventricular end-diastolic pressure by an average of 6 mm Hg ($P < .01$). In order to improve mixing within the left ventricle, we currently use a total of 12 mL of iodine contrast, diluted 1:1 in water and injected into the left ventricle at 8 mL/s over three seconds. Because of the lower iodine dose, three to four digital subtraction left ventriculograms can be obtained with the equivalent contrast dose of one film-based angiogram (Fig 2). This permits catheterization studies to be performed with a lower total of iodine in

diabetic patients and in patients with renal or cardiac dysfunction. In routine cases, multiple left ventriculograms can be obtained, thus obviating the need for a biplane laboratory. Alternatively, multiple lower-dose digital angiograms can be used to assess left ventricular function during intervention studies. Because of these significant advantages, in 1982 we stopped using 35 mm cinefilm for obtaining left ventriculograms and began to use low-iodine-dose digital ventriculograms for all of our routine clinical catheterization studies.

VIDEODENSITOMETRY

An angiogram is a two-dimensional projection image or shadowgram of a three-dimensional object. The outline of a left ventriculogram or a coronary angiogram only demonstrates the widest boundary in the x - y plane that is filled by iodine contrast media. Digital angiograms also contain this information as well as information about the depth of the object of interest in the plane perpendicular to the imaging plane. The process that measures density values within an angiogram is called videodensitometry.³⁶

Digital acquisition of angiograms facilitates densitometric counting because the digital number assigned to each pixel in the image corresponds to the depth of the iodinated contrast material that the x -ray beam traversed.³⁷ In order to obtain a linear relationship between

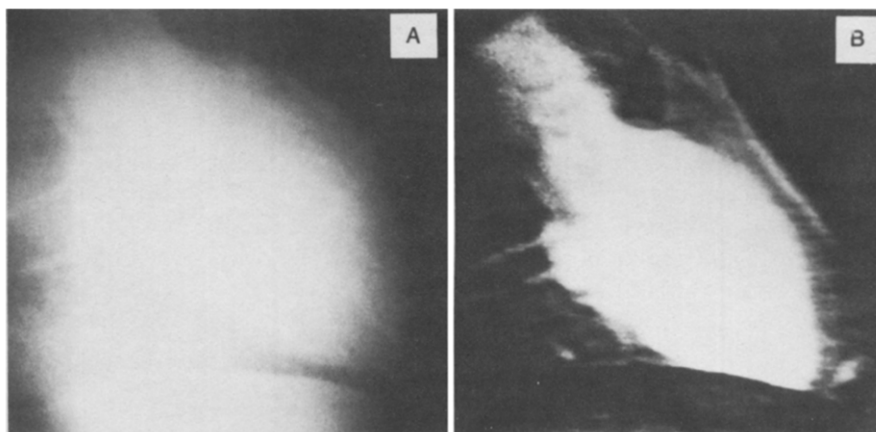
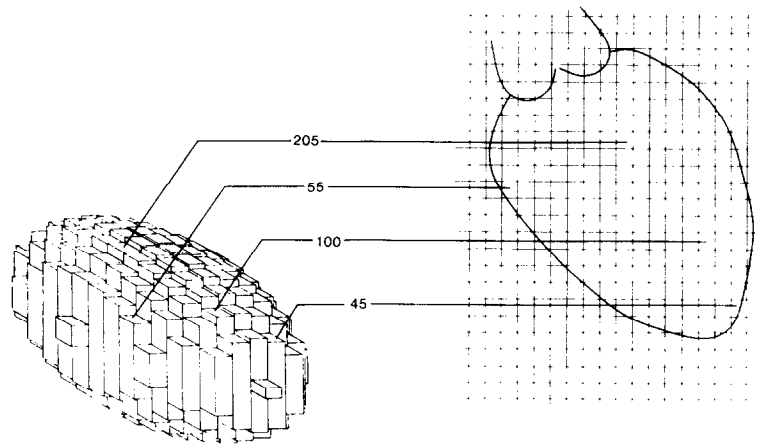


Fig 2. Low dose ventriculography. This composite photograph demonstrates a cineangiogram (A) of 12 mL of contrast medium injected directly into the left ventricle compared with a digital angiogram (B) of the same amount of contrast medium. Contrast enhancement is significantly better with the digital subtraction technique. (Reprinted with permission of the publisher from *Digital Subtraction Angiography* by Tobis J, et al, in Rappaport E (ed) *Cardiology Update: Review for Physicians*, 1984, p 206. © 1984 by Elsevier Science Publishing Co., Inc.⁸⁵)

digital number and contrast depth, the electronic signal from the absorbed x-rays must be logarithmically amplified.³⁸ Logarithmic amplification is necessary because x-rays are absorbed as an exponential function of the depth of the tissue or contrast material. This kind of information is lost when film is used because logarithmic amplification is not performed, and the gray scale of the film is often chosen to saturate the white levels of iodine to improve contrast visualization. The result of saturation is that very white, high-contrast images are obtained on film, but information is lost about relative amounts of iodinated contrast material within the vasculature.

Since the image in digital angiography is represented by a matrix of numbers, the information within each pixel can be logarithmically amplified very quickly. The digital numbers within each pixel then correspond to the depth of iodine in that pixel. By adding up the digital numbers over an area of interest such as the left ventricle, a number is obtained that corresponds to the total volume of the ventricle (providing there is equal mixing of the iodine throughout the blood volume of the ventricle and that background densities are properly accounted for) (Fig 3).

The theory behind videodensitometry is similar to the photon-counting technique of radio-nuclide imaging. Therefore, similar software algorithms have been used for performing the densitometric computations. First, an approximate region of interest around the left ventricle is chosen. A background area is also described by the operator, which is used to subtract out background densities from the region of interest that are not coming from the iodinated blood volume (Fig 4). In order to test the clinical validity of this technique, a comparison study was performed with first-pass intravenous digital angiograms in which measurements of the left ventricular volume were made with the area-length method and by videodensitometry.³⁹ In order to determine absolute ventricular volumes, the concentration of iodine within the ventricle would have to be known. This is not feasible at the current time. However, the digital numbers represent relative ventricular volumes at end-diastole and end-systole. Ejection fraction can be calculated densitometrically because these relative volumes can be used to compute a relative change in volume from end-diastole to end-systole. In 25 patients who had first-pass digital left ventriculograms, the ejection fraction by



RELATION BETWEEN CONTRAST DEPTH AND PIXEL DENSITY VALUE

Fig 3. The relation between contrast depth and pixel density value is demonstrated in this diagram. On the left is a three-dimensional model of a left ventriculogram that has been sectioned into boxes. The two-dimensional surfaces of these boxes correspond to the x - y coordinates of pixels on the digital angiographic image shown on the right. The density value of each pixel corresponds to the depth of the box represented in each pixel. By adding the density values on the digital image within the region of interest, a number is obtained that corresponds to the total volume of contrast media within that region. (Reprinted with permission from *Medical and Biological Engineering and Computing*, Vol 10, Trenholm et al: Computer Determination of Left Ventricular Volume Using Videodensitometry, © 1972, Pergamon Press, Ltd.³⁶)

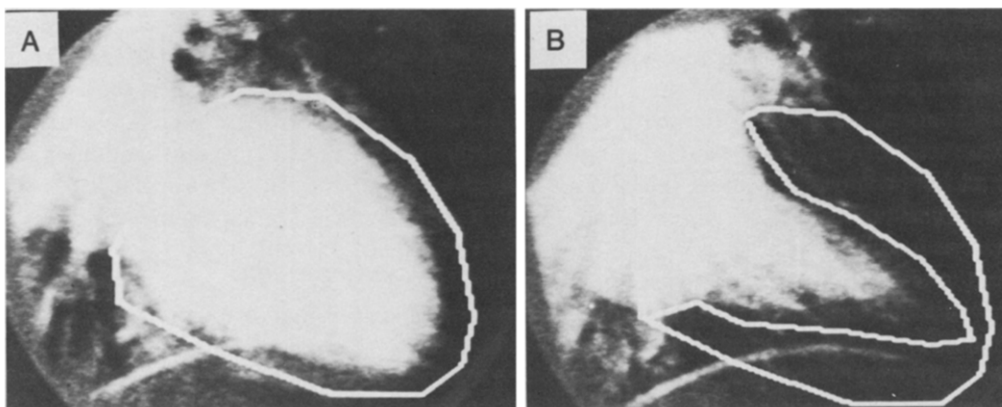


Fig 4. The technique for obtaining the background area during a videodensitometric analysis is depicted in this figure of a first-pass digital subtraction angiogram. The end-diastolic frame (A) is outlined to include all of the iodine within the left ventricle, and the boundary of the aorta and mitral valve plane is used as the medial boundary. The end-systolic frame (B) is then chosen, and the area around the end-systolic border is outlined. The background region of interest is taken as the area between the end-diastolic and end-systolic regions of interest. (Reprinted with permission.³⁹)

videodensitometry correlated well with the ejection fraction by the area-length method ($r = .88$).

The videodensitometric approach offers unique advantages for assessing right ventricular ejection fraction. One of the difficulties in trying to measure right ventricular volumes by angiography is that the right ventricle does not conform to a simple geometric shape. In addition, the right ventricle has numerous trabeculae and interstices, which make it difficult to use a mathematic formula to derive its volume from a two-dimensional angiogram. The densitometric method can be used to derive the relative volume of any irregular object without using any assumptions about its three-dimensional geometry. Radionuclide imaging of the right ventricle has gained widespread support because the photon-counting technique is based on densitometric principles. However, a major problem of radionuclide imaging is its limited spatial resolution. During intravenous first-pass digital studies, it was noted that the tricuspid valve annulus moves toward the apex and shortens the long axis of the right ventricle by about 20%. Densitometric methods such as radionuclide angiography, which use only one fixed region of interest to outline the right ventricle at end-diastole, must by necessity neglect the apical displacement of the tricuspid valve annulus. The result of using one fixed region of interest is that some right

atrial counts are included in the end-systolic volume calculation. The increased spatial resolution of digital angiograms permits excellent visualization of the tricuspid annulus and allows identification of the proper boundary of the right ventricle at end-diastole and at end-systole. In our study of 19 patients who had first-pass digital right ventriculograms, we found that a videodensitometric analysis with two separate regions of interest gave a closer correlation with the ejection fraction calculated by the area-length technique than did the method using only one region of interest, whereas the radionuclide data did not correlate very well with either the digital or area-length methods.⁴⁰

Another application of videodensitometry for cardiovascular imaging is its potential for studying cardiac physiology. The densitometric analysis of an iodine bolus as it passes through the left ventricle yields a density-time curve. The points on this curve represent relative volume in the ventricle. The filling pattern during diastole can be used to derive a relative measure of ventricular filling. In preliminary studies, the densitometric filling curves have correlated with Doppler velocity patterns of flow across the mitral valve. In addition, left ventricular compliance can be assessed using the density-time curves. If a catheter is placed in the left ventricle during a first-pass digital ventriculogram, then simultaneous pressure and density curves can be

generated. The area-length method can be used to scale the density curve at end-diastole and end-systole corresponding to the maxima and minima of the curve. The resulting data can be used to derive a pressure-volume curve to analyze left ventricular compliance without the laborious task of calculating ventricular volume frame by frame from cinefilm.

Although there are no geometric assumptions in the densitometric approach, as with any methodology there are certain assumptions and potential problems inherent to the technique. With x-ray imaging systems there are physical limitations that could create nonlinear absorption in the system. These include veiling glare from the image intensifier screen, x-ray beam scatter from the patient, and beam hardening since x-rays without a uniform energy are used. A significant amount of physics research in digital imaging is being devoted to understanding these issues of videodensitometry and minimizing their effect.^{41,42}

ASSESSMENT OF LEFT VENTRICULAR FUNCTION WITH DIGITAL IMAGING

Bicycle Stress Testing

Digital angiography has been applied to the evaluation of left ventricular function using different methods and under various conditions. First-pass intravenous digital ventriculograms have been obtained at rest and immediately following supine bicycle exercise.^{43,44} In an analogous manner to first-pass radionuclide exercise stress testing, changes in global ejection fraction and the development of segmental wall motion abnormalities are taken as a measure of exercise-induced ischemia in patients with coronary artery stenoses. In one study of 19 patients who underwent coronary angiography for evaluation of chest pain, the development of wall motion abnormalities and a fall in ejection fraction was more sensitive than the development of chest pain or S-T segment response on the electrocardiogram for identifying patients with coronary disease.⁴⁵ Adequate first-pass ventriculograms could not be obtained in three of the 19 patients (16%) because of significant misregistration artifact created by the increased respiratory motion following exercise. Although our study as well as

the larger experience of Yianakis and co-workers at the Cleveland Clinic and Goldberg and Borer at New York Hospital suggest the clinical usefulness of this method, we have recently used the method infrequently and instead have used pacing in conjunction with cardiac catheterization as our method of inducing myocardial stress.

Atrial Pacing Studies

Pacing the atrium at incremental heart rates is a form of stress that can reproducibly create ischemic conditions in patients with coronary artery disease.⁴⁶⁻⁵⁶ This technique has been combined with digital acquisition of left ventriculograms in order to assess the functional significance of coronary artery stenoses. Although the coronary anatomy is defined angiographically during cardiac catheterization, there is often disagreement in interpretation of the severity of a specific lesion.⁵⁷⁻⁶¹ As a result, stenoses can be underestimated or overestimated depending on the position of the lesion, its internal contour, and the radiographic projection used. A functional assessment of the hemodynamic effect of a coronary lesion provides an independent measure of the severity of the stenosis by allowing one to evaluate the effect that the lesion has on reserve ventricular performance.⁶² Digital ventriculograms are very beneficial in performing atrial pacing studies because the low dose of iodine contrast permits multiple ventriculograms to be obtained.

In an initial study of 21 patients who were referred for cardiac catheterization to evaluate symptoms of chest pain, digital left ventriculograms were obtained at rest and at the peak heart rate achieved.⁶³ The pacing protocol involved increasing the atrial rate by ten beats per minute until the patient developed chest pain or until 85% of the maximum predicted heart rate was obtained. Of the 21 patients, 15 had coronary artery disease with greater than 50% diameter narrowing documented by angiography and six patients had angiographically normal coronary arteries. The development of S-T segment changes on the electrocardiogram (three of 15 patients) or chest pain (eight of 15 patients) were insensitive markers of ischemia. However, the ejection fraction fell or did not increase in 14 of the 15 patients (93%) with coronary artery dis-

ease, whereas it increased in five of six patients (83%) without coronary artery disease. In addition, segmental wall motion abnormalities developed during pacing that corresponded to myocardial areas supplied by specific stenotic arteries.

The atrial pacing studies were useful as a means to assess the amount of myocardial dysfunction that occurs under stress because of diminished flow through a stenotic artery. This study influenced the way we presently perform cardiac catheterization, and the results of atrial pacing studies are frequently used to help in the clinical management of our patients.

In addition to providing information that is useful in clinical decision making, digital angiography can be used during other intervention studies to answer questions of cardiac physiology. One of the concerns about exercise or pacing stress tests is the time at which the analysis of left ventricular function should be performed. Should radionuclide or digital angiograms be

obtained at the peak heart rate or shortly thereafter? Is it correct to compare ejection fraction at rest to values obtained at peak heart rates when preload and afterload are significantly different from baseline values? Low-dose digital ventriculograms were used to answer these physiologic questions because three to four ventriculograms can be performed with the same iodine contrast dose as one standard film-based left ventricular angiogram. Two separate studies were performed with atrial pacing.⁶⁴ In the first group of 21 patients, 12-mL digital ventriculograms were obtained at rest, at the peak pacing rate, and within ten seconds after the pacemaker was discontinued (Fig 5). In a second group of 19 patients, digital ventriculograms were obtained at rest, peak pacing, and at 30 seconds after pacing was stopped. In all 11 patients in the two groups without coronary artery disease by angiography, the left ventricular volume decreased at end-diastole and end-systole during atrial pacing

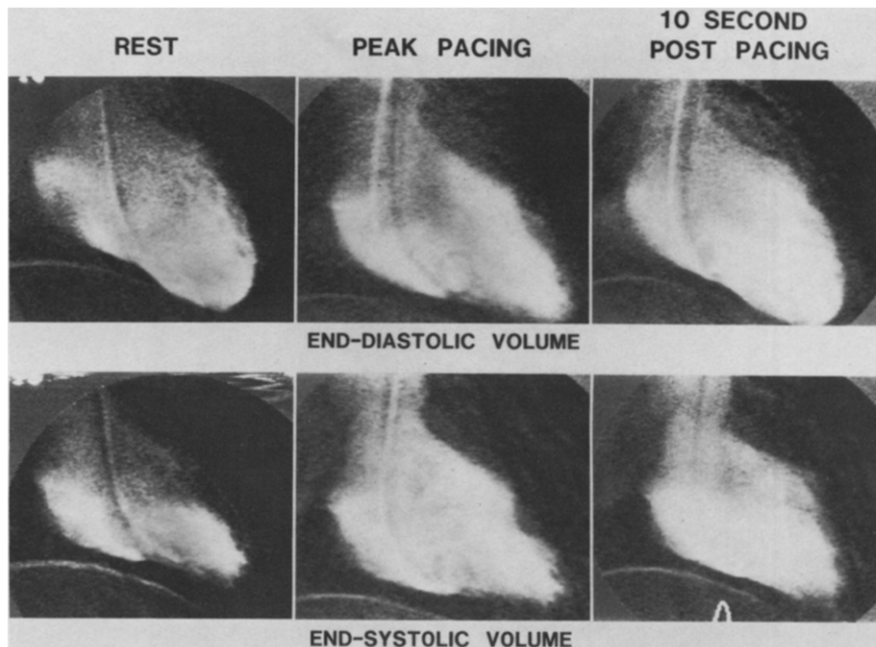


Fig 5. Isolated frames from digital subtraction left ventriculograms obtained with 12 mL of contrast material during an atrial pacing study are demonstrated above. Frames at end-diastole (top row) and end-systole (bottom row) are shown for the studies obtained at rest, peak pacing, and ten seconds after pacing was stopped. The baseline study revealed inferior wall hypokinesis with a global ejection fraction (EF) of 40%. At peak atrial pacing to a heart rate of 140, the patient had an abnormal ECG response but experienced no chest pain. However, the left ventricle demonstrates diffuse akinesis of the anterior, apical, and inferior walls with an EF of 16%. In the ten-second postpacing study, there is still significant hypokinesis of the anterior and inferior walls, and the EF is still depressed below rest at 34% but has improved compared to the peak pacing study. (Reprinted with permission from the American Journal of Cardiology 56, Sept 1985.⁶⁴)

and returned to baseline values by ten seconds after pacing stopped. The ejection fraction increased or did not fall by more than two percentage points in ten of the 11 patients (91%). In patients with coronary artery disease, the end-diastolic volume decreased as expected during pacing. However, the end-systolic volume did not decrease as much or even increased, thereby causing a decrease in ejection fraction. In the patients with coronary artery disease, the ejection fraction fell by more than two percentage points in 25 of 29 patients (86%). The sensitivity of the atrial pacing study was highest when the ventriculogram was obtained at the peak pacing rate compared with a sensitivity of 52% during the postpacing studies. This result was found despite the fact that the preload and afterload (as measured by left ventricular end-diastolic pressure and systemic blood pressure) were unchanged from baseline during the 10- or 30-second postpacing studies. In addition, 21 of the 40 patients had treadmill stress tests performed prior to cardiac catheterization. The double product achieved during atrial pacing was not significantly different from that during the treadmill stress test in the patients with coronary artery disease. However, the sensitivity and specificity of the pacing study was superior to those obtained with the treadmill stress test in this selected population. Thus, digital angiography has proven to be very useful in performing intervention studies to understand physiologic questions of ventricular function during ischemia in patients.

Digital Coronary Angiography

There have been many important advances in performing coronary angiography with digital processing. When this technology was initially applied to cardiac imaging, it was hoped that a method could be developed for obtaining coronary angiograms following intravenous administration of contrast material. This possibility does not appear feasible with present technology. However, digital acquisition following selective injection of contrast into the coronary arteries has proven in our experience to be one of the most important benefits of the clinical application of digital angiography.

The initial studies with selective coronary

artery injections were performed in 1982 with computer systems that did not have large digital storage capacity. Images were obtained at 30 frames per second, digitized and subtracted in real time from a stored mask, and then reconverted to an analog format for storage on videotape. In order to decrease motion artifact resulting from the movement of the heart itself, a blurred mask was used that summated 16 frames (one-half second) of the thorax prior to the injection of contrast material. Continuous fluoroscopic energy levels were used at 20 mA with 75 to 90 kV(p). Because of the analog storage and other variables in the imaging chain, these images had a moderate amount of electronic noise. Nevertheless, a comparison study of 31 patients demonstrated that coronary stenoses were well visualized, and quantitative measurements of the stenoses correlated well with measurements made from cinefilm angiograms.⁶⁵ These initial studies indicated that contrast visualization within the arteries and during the myocardial blush phase was improved about fourfold over cinefilm (Fig 6).

A videodensitometric analysis was applied to these early digital coronary angiograms in an effort to assess myocardial blood flow as reflected in the distribution of iodine contrast material. Various regions of interest were placed over epicardial coronary arteries or over regions of myocardium perfused by specific coronary branches. The digital angiogram was replayed through the computer to derive density:time curves within the various regions of interest. These perfusion-washout curves yielded information about the time of arrival and distribution of iodine contrast within the myocardium. Whiting and co-workers have found similar results in animal experiments using radiolabeled microspheres.⁶⁶ In addition, they have shown that quantitative information can be obtained about the hemodynamic effect of coronary stenoses by performing densitometric flow analyses at rest and after the hyperemic response induced by contrast media. The results of these analyses of myocardial blood flow using iodine contrast are still preliminary. If they are proven to be predictive of the severity of coronary stenoses, they will have considerable clinical impact since common iodine media is used instead of the more cumbersome

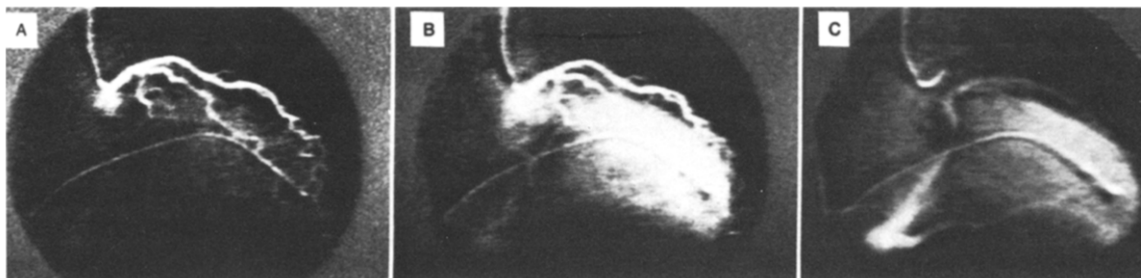


Fig 6. The three phases of a digital coronary angiogram are demonstrated above. This early study was acquired at 30 frames per second, digitized and subtracted in real time from a 16-frame blurred mask, and reconverted to analog format for storage. The first phase (A) reveals the coronary anatomy following selective injection of contrast media into the left coronary artery. The myocardial blush phase (B) demonstrates the muscle perfusion of the contrast media, and the venous phase (C) shows the washout of iodine from the capillary system. By analyzing the density in a specific region over time, a relative assessment of myocardial perfusion can be derived.

some radioactive-labeled gas or particle techniques.⁶⁷

Another approach to understanding the hemodynamic significance of coronary stenoses using selective coronary digital angiography has been developed by Vogel and co-workers.⁶⁸ They obtained coronary angiograms at end-diastole and subtracted sequential images from each other to derive a composite image of the time of arrival of the iodine bolus at each diastolic frame over six cycles. The position of arrival of the bolus peak at each diastole was color coded to improve visualization. Color mapping studies were performed at rest and within ten seconds after the hyperemic stimulus of iodine contrast media. In a nonstenotic artery, the hyperemic response should produce a more rapid peak contrast arrival compared to rest. In a stenotic artery that no longer has the autoregulatory tone to permit the expected increase in flow following a hyperemic stimulus, one would not expect to see a change in the arrival time image. Vogel has shown that these time-of-arrival maps correlate with the angiographic determination of stenoses and that they can be used before and after transluminal angioplasty as an independent measure of the hemodynamic effects of the angioplasty.⁶⁹

Digital Storage of Coronary Angiograms

By 1983 digital-imaging devices were developed that had a digital storage capacity of 80 megabytes. A 512×512 image requires approximately one-fourth megabyte of digital disk space. This meant that approximately 300

images could be stored on the 80 megabyte digital disk. The rate of acquisition of these digital images was also limited to eight frames per second. Despite these temporary technical limitations, the coronary images acquired and stored in a digital format proved to have superior detail as well as other significant clinical benefits compared with analog videotape storage. Since there was no film to develop, digital coronary angiograms were available for review within two minutes of acquisition (Fig 7). The images could be played back in an unsubtracted format or rapidly processed with computer algorithms to enhance contrast with mask mode subtraction, to sharpen coronary boundaries with edge detection algorithms, or to magnify the image fourfold to focus attention on specific lesions (Fig 8). The unsubtracted as well as the postprocessed enhanced images could then be downloaded onto 3/4-inch videotape for replay at conferences. The information could also be stored in a complete digital format on digital magnetic tape. Although the digital archiving was more time consuming, no information was lost because of the introduction of electronic noise. The imaging chain was also used differently compared to the earlier studies with analog storage. The images were obtained in a pulsed radiographic mode using 600 mA at 75 to 85 kV(p). Also, the signal from the image intensifier was transformed by a progressive scan television camera instead of the usual interlaced mode. Progressive scanning permitted multiple scrubbing of the input phosphor between images to diminish "ghost" artifacts.

A study was performed in 19 patients in order

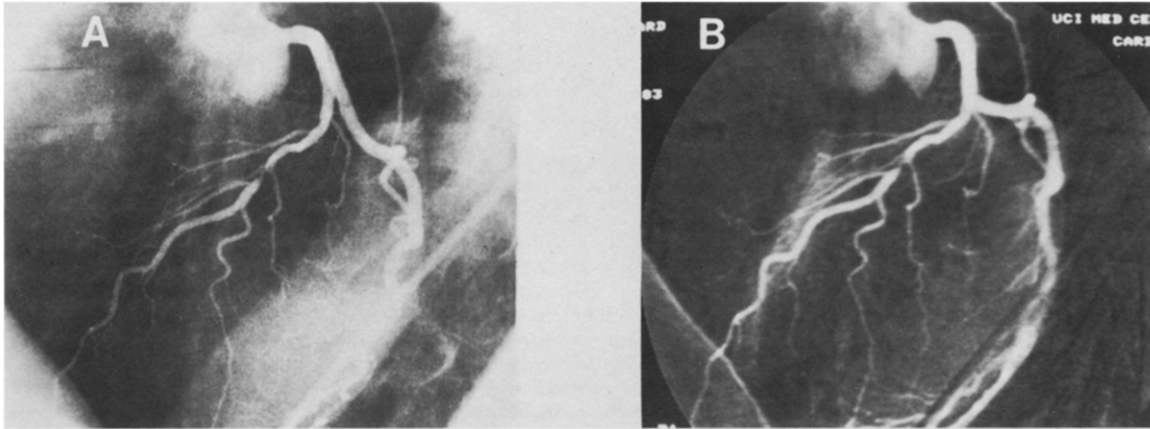


Fig 7. A single frame from a selective coronary angiogram acquired on 35mm film (A) is compared with a digitally acquired image (B). The angiograms were obtained sequentially in the 60-degree LAO projection with 45 degrees of cranial angulation. The digital image was processed with a single-frame mask mode subtraction algorithm to diminish background bone and soft tissue densities. There is a severe stenosis of the mid-left anterior descending coronary artery. (Reprinted with permission from Tobis et al: *American Journal of Cardiology* 54:489-496, 1984.⁷⁰)

to determine how the digital coronary angiograms compared with standard 35-mm cinefilm angiograms.⁷⁰ These patients had sequential digital and cinefilm angiograms obtained in the same projection. A panel of four cardiologists measured 36 coronary lesions using calipers from both the digital and film angiograms. The mean measurement of all four observers for the 36 stenoses from cinefilm correlated closely with the mean measurements from the digital angiograms ($r = .97$). It is well described that observers

differ in their quantitative measurements of coronary stenoses. In order to test whether the four observers varied in their measurements because of the acquisition technique, a two-factor analysis of variance was performed. This demonstrated that there was no significant difference in the variability of measurements between the cinefilm or the digital techniques. Also, there was no significant difference in variability among the four observers' measurements.

Although the digital angiograms were ob-

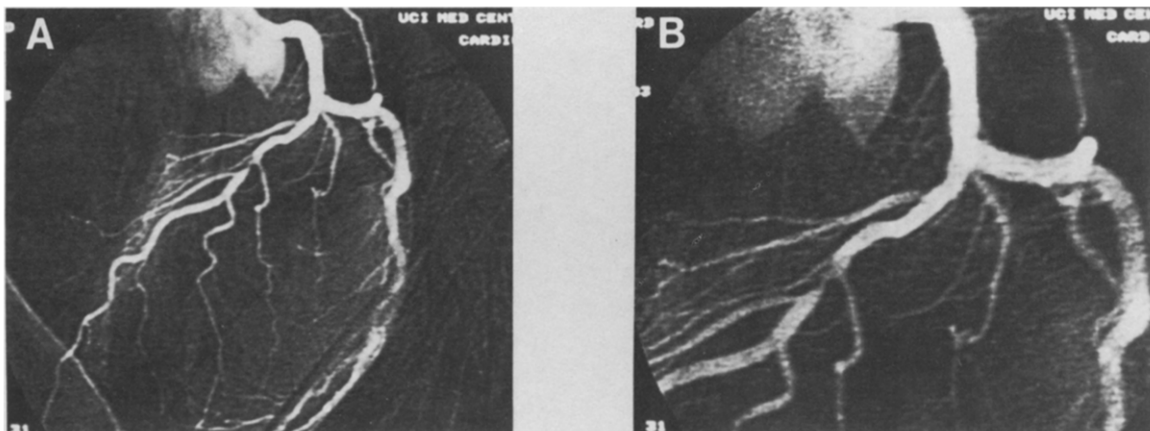


Fig 8. The digital subtraction angiogram shown in Fig 7 was processed by the computer with an algorithm that sharpens vessel boundaries by enhancing contrast differences between pixels (A). A portion of the image can then be digitally magnified fourfold after the operator chooses the region of interest (B). The digital zoom and edge-enhanced image can then be used for quantitation of percent diameter stenosis by other computer programs such as edge detection or videodensitometry. (Reprinted with permission from Tobis et al: *American Journal of Cardiology* 54:489-496, 1984.⁷⁰)

tained at the relatively slow rate of eight per second, there was no effect on the quantitative analysis of percent diameter stenosis. This is due to the cranial-caudal angulated projections that were systematically used to acquire the angiograms. These angulated views demonstrate the proximal bifurcations with less overlap or foreshortening of vessels, and thus faster framing rates are not necessary.⁷¹⁻⁷³ When only nonangulated projections are used, faster framing rates are desirable in order to see a lesion briefly "scissor" into view because of overlap with other vessels. Digital acquisition was found to improve

the angiograms obtained in angulated views since segments of the coronary arteries that are projected over the spine or diaphragm because of the angulation can be enhanced to recover contrast information that is often lost with film-based systems.

In order to improve digital storage capacity, a 475 megabyte digital disk was added to the system in 1984 so that approximately 1,800 images could be acquired before it would be necessary to clear the disk. Additionally, a 475 megabyte parallel transfer disk was recently incorporated into the computer hardware that

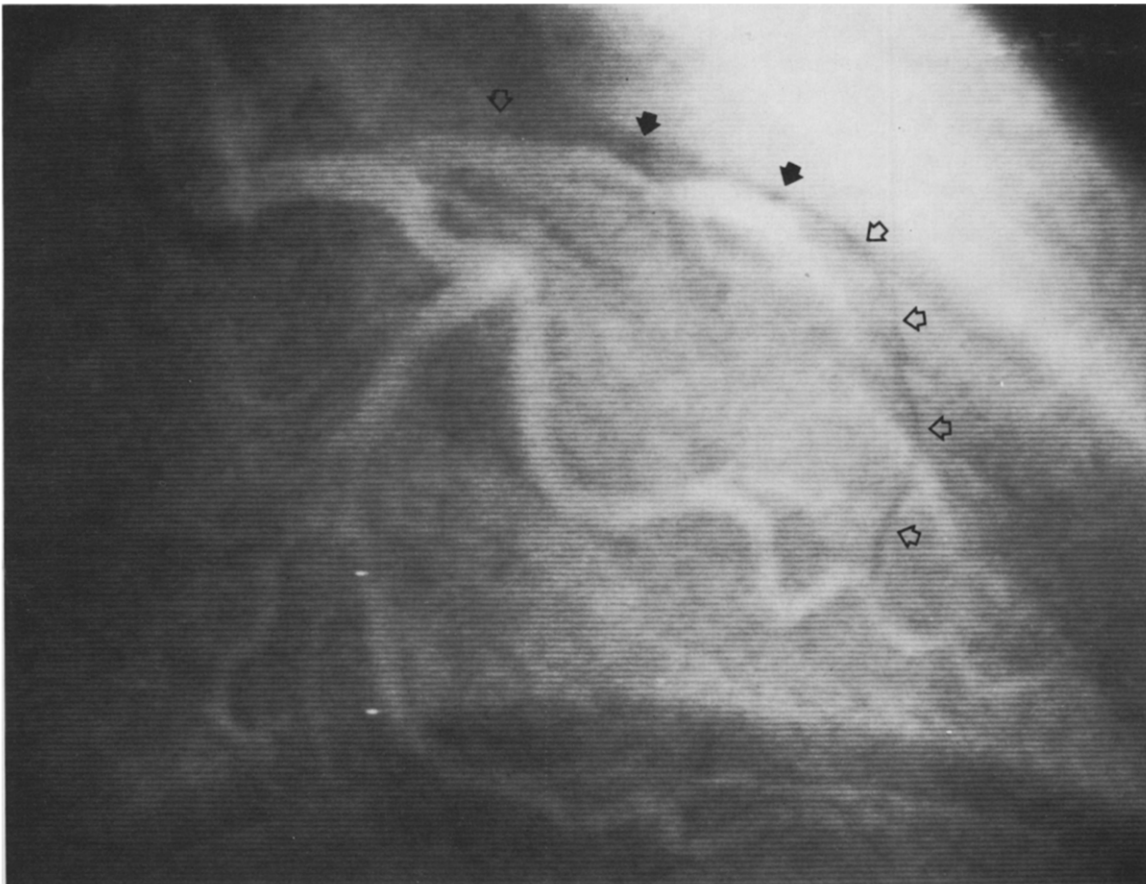


Fig 9. An example of the digital roadmap process is demonstrated above in a photograph taken from a video monitor. The digital subtraction coronary angiogram in white is recalled from computer memory and interlaced through the video mixer with a live fluoroscopic image of the heart. There is a stenosis in the proximal left anterior descending coronary artery at the level of the first septal perforator. The roadmap digital image is kept on the monitor above the catheterization table as the angiographer advances the dilatation guidewire and balloon. In this stop frame image from videotape, the guidewire (open arrows) is seen parallel to the left anterior descending artery and the dilatation balloon metallic markers (closed arrows) are seen approximating the site of the stenosis as visualized on the roadmap. (Reprinted with permission from the American Journal of Cardiology 56, Aug 1985.⁸⁰)

permits 512×512 digital images to be acquired at 30 frames per second. Despite this present capacity for a rapid framing rate equivalent to our cinefilm rate, we have not found additional clinical information has been gained in terms of diagnosis or quantitation of stenotic lesions by using the faster rate.

One of the major advantages of digital acquisition of coronary angiograms is that the computerized format permits rapid quantitative determination of coronary stenoses.⁷⁴⁻⁷⁶ The operator can use computer graphics to outline the boundary of a coronary stenosis in order to quickly calculate the percent diameter narrowing. A second method of measuring stenotic segments uses a videodensitometric approach.⁷⁷ With these algorithms, the operator chooses a region of interest over a nonstenotic segment and a second region over the stenosis.⁷⁸ Exact boundary detection is not necessary since the computer subtracts background information and determines the relative density of contrast between the two areas. Preliminary studies using phantom models suggest that the densitometric technique is independent of the eccentric or irregular geometries often found in atherosclerotic lesions.⁷⁹ The densitometric analysis can be used with the edge detection method following calibration for magnification to derive the absolute minimum lumen diameter in terms of millimeters of a coronary stenosis. Preliminary experience suggests this can be achieved densitometrically even if the boundary of the lesion is too small to accurately measure with boundary detection methods.

Digital Roadmapping

Of the many ways in which digital images can be processed, one of the most exciting techniques has been digital roadmapping. Digital roadmapping is a method to assist visualization of the coronary anatomy during transluminal angioplasty.⁸⁰ Currently, when an angioplasty is performed under fluoroscopy the operator attempts to have a mental image of where the lesion is located. This image may be based upon cineangiograms that were taken at a previous catheterization. Alternately, videotape replays on another monitor are used. During the angioplasty, iodine contrast is injected through the guiding

catheter or the distal balloon catheter.^{81,82} However, there is often poor flow through these catheters and visualization is difficult because of low concentration and the transient nature of the injection.⁸³

Digital angiography can be helpful during angioplasty by providing a constant image of the coronary arteries as a guide or roadmap for the angiographer. Prior to loading the guiding catheter with the dilatation system, a digital coronary angiogram is obtained, processed by mask mode subtraction, and stored in computer memory. An end-diastolic frame is chosen that demonstrates the lesion, and the image is recalled from memory and displayed on the television monitor above the catheterization table for use as the roadmap. The digital coronary roadmap image is then interlaced with the live fluoroscopic video image. When the balloon dilatation catheter and steerable guidewire are advanced under fluoroscopy, the operator sees the catheter and guidewire travel over a superimposed image of the coronary arteries (Fig 9). If a wrong branch is entered, it is easily recognized. The exact placement of the balloon across the stenosis is also aided by the digital roadmap. At the present time, only a single end-diastolic image is used as a roadmap. However, it should be feasible to develop computer programs that could replay the entire digital angiogram triggered from the patient's electrocardiogram and thereby have a continuous roadmap that moves in concert with the motion of the heart as the dilatation catheter is advanced.

Coronary Angiography With Aortic Root Injection

As an alternative to selective coronary artery imaging, the ability to enhance contrast with digital processing can be used to obtain images with aortic root injection of contrast media. At the current time, a prospective study is in progress to determine whether aortic root digital angiograms will be useful for demonstrating left main and proximal right and left coronary artery lesions.⁸⁴ Aortic root digital angiograms have been obtained with a total of 20 to 30 mL of contrast material injected during two diastolic phases. The images are processed within two

minutes and are reviewed before selective coronary angiography is performed. It is hoped that the early recognition of left main lesions with the nonselective digital angiograms will help diminish the incidence of left main dissection during selective coronary angiography.

CONCLUSION

The application of computers for cardiovascular imaging has produced dramatic improvements over the last few years. Digital processing can be used to obtain peripheral or ventricular angiograms with less invasive intravenous injection of iodinated contrast material. Alternatively, lower amounts of contrast material can be used during intra-arterial or direct ventricular angiography. The ability to perform low-dose ventriculograms permits multiple observations to be obtained, which is beneficial for assessing cardiac physiology during intervention studies. Selective coronary digital angiography has proven to have several advantages over film-based systems. The digital images are immediately available for review during the catheterization. The images can be manipulated to improve contrast information and the digital format allows ready access for quantitative analysis

either by edge detection or videodensitometric techniques. The ability to immediately recall images and manipulate the contrast allows digital roadmapping to be performed for guidance of the guidewire and balloon during coronary angioplasty. Because of the improved performance capabilities of the computer hardware and software, the cardiac catheterization laboratory at the University of California, Irvine was transformed in early 1984 to one in which digital acquisition is the predominant method for obtaining left ventriculograms and coronary angiograms. At present, cinefilm is used only as a backup system or for continued research protocols. As further advances are made in computer technology, we expect that clinical applications of digital angiography will increase further and broaden the amount of information that is obtainable during angiography.

ACKNOWLEDGMENT

The authors wish to express their appreciation to our co-workers who have contributed innumerable hours to this research effort: Warren D. Johnston, MD; Lloyd Iseri, MD; Werner Roeck, Eng Grad; Anthony Seibert, PhD; Ellen Mansour, BA; Carol DeBoer, RN; Steve Montelli, CRT; Eunice Henderson, LVN; Marypaull Quick, CRT; Jim Paynter, RCPT.

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