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Cardiac applications of digital subtraction angiography

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Abstract

Recent developments in digital computer technology have enabled direct digital acquisition of radiographic images at spatial and temporal resolutions similar to that of cineradiography. Initially intended as a means of performing peripheral angiography, digital subtraction angiography has been increasingly applied to cardiac catheterization procedures. Advantages of cardiac digital subtraction angiography include the capabilities to: immediately replay, magnify and enhance angiographic studies during coronary artery interventions, perform left ventriculography with peripheral contrast injections and direct left ventriculography with substantially reduced contrast doses, perform bypass graft visualization using aortic root contrast injection, assess relative regional coronary blood flow and facilitate the quantification of ventriculographic and coronary stenosis parameters. Clinical comparisons of standard cineradiographic and digital angiographic studies have demonstrated very similar results.

Introduction

Although both intravenous contrast administration cardiac and peripheral angiography and analogue image subtraction were first employed decades ago [1], only recently, following the development of efficient digital computers, has direct digital subtraction angiography been made possible. Pioneering efforts at the Universities of Winsconsin, Arizona and Kiel and the Mayo Clinic [2–5] in this area have resulted in the availability of commercial systems and their widespread clinical use. Initially, digital angiography was intended as a means of enabling the visualization of peripheral arterial structures using intravenous contrast administration, thus reducing the invasiveness of angiography. This approach was successful for ventriculographic imaging [6] because of the relatively large vascular volumes of these chambers. Coronary arteries and saphenous vein bypass grafts, however, cannot be visualized in sufficient detail by this tech-

nique, requiring aortic root and selective contrast injections for their clinical visualization [7, 8]. This trend toward the use of intra-arterial contrast administration has also been followed in peripheral digital angiography because of the resulting superior spatial and contrast resolution. Cardiac applications have increasingly differed from peripheral studies by their frequent use of quantification and parametric imaging [9, 10]. The technical aspects of cardiac digital angiography and its application to clinical ventriculography are summarized in this paper. Clinical applications to coronary arteriography are detailed in a companion paper.

Instrumentation

Digital radiography employs the conversion of fluoroscopic or radiographic images into digital format for subsequent image enhancement and storage. Important technical features of this process

include radiographic and video scanning techniques, image matrix size and framing rate, storage medium, enhancement methods, and image analysis and quantification. In opposition to standard angiography, digital imaging is performed at constant radiographic parameters (kV, mA and pulse width), so as to allow image enhancement [11–13]. Ideal cardiac systems employ automated determination of the optimal radiographic parameters within a few milliseconds, obviating the need for 'test exposures'. In general, digital ventriculography is performed in 256×256 pixel matrix resolution at 30 or 60 frames per second. Both low to moderate level continuous fluoroscopy and pulsed radiographic exposures have been found sufficient for these low resolution studies.

Coronary artery and saphenous vein bypass graft imaging requires greater spatial resolution of at least 512×512 , although a slower framing rate may be employed. Increased spatial resolution is achieved with use of 1024×1024 pixel matrices if either radiographic exposure is increased above clinical cineradiographic levels (approximately 25 uR/frame) or when field sizes larger than 10 to 15 cm are employed [14]. The rapid translational movement of coronary arteries necessitates the use of pulsed radiographic exposures (<10 ms) and progressive rather than interlaced video scanning. Exposure rates of 2–10 frames per second provide clinical information similar to that of 30 frames per second cineradiography [8], although considerable 'jitter' is observed at the slower framing rates. Electrocardiographically-gated coronary artery image acquisition can be employed to eliminate discontinuous movement [15]. Lastly, direct digital memory or disk storage of the digitized plumbicon signal clearly provides superior signal-to-noise ratios than does use of video disk or tape.

Subtraction techniques

A major advantage of digital radiography is that unwanted densities such as overlying bone and soft tissues can be subtracted allowing visualization of very low concentrations of contrast media. Most enhancement techniques employ subtraction of

frames which differ by one (first-order) or two (second-order) variables. The characteristics of several techniques have been extensively reviewed by Reiderer & Kruger [16]. The most commonly used enhancement technique is mask-mode subtraction which is performed by subtracting similarly positioned frames obtained prior to (mask) and following contrast administration. By this process, only radiographic densities not common to the two frames remain. The mask can be either a time averaged frame or single frame, although optimal subtraction is achieved through use of electrocardiographically-gated mask matching [15]. Due to the exponential attenuation of the x-ray beam, logarithmic analogue-to-digital conversion must be employed [12]. Even with this, due to non-linearity of the image intensifier and plumbicon transfer functions and veiling glare, mask-mode subtraction does not totally eliminate overlying tissues.

The greatest problem with mask-mode subtraction is, however, the need for patients to remain completely motionless for up to 10 to 15 seconds. Failure to achieve this results in registration artifact. Motion artifact is especially problematic for cardiac applications because of the need to totally cease respiration. The cyclical cardiac motion can be almost totally eliminated by electrocardiographic-gating [17], with some additional success being reported with the use of respiratory gating [18]. Various other techniques have been used to reduce motion artifact including mask reselection and shifting [15]. Mask frames obtained after the clearance of contrast have been used successfully, since patient motion tends to occur either early during the breath-holding period or at the time of contrast administration. Alternately, linear shifting or 'rubber-sheeting' of the mask can be used to correct for some degree of misregistration. Continuously updated masking in the form of matched and recursive filtering [19, 20] has been applied successfully for cardiac applications, especially for those using fluoroscopy. These techniques are considerably less sensitive to patient motion which has a different frequency than the appearance and disappearance of the contrast bolus. Most forms of mask-mode subtraction have proven adequate for

digital ventriculography and coronary arteriography, but, electrocardiographic-gating is required for optimal coronary quantification and parametric image generation.

Time-interval differencing is another 'first-order' subtraction technique which employs subtraction of post-contrast administration frames temporally separated by a short fixed interval of usually about 30 to 60 ms. This technique has been most widely used for ventriculography in which outwardly and inwardly moving segments are displayed respectively as bright and dark densities. Thus, a functional, phasic display results. Dyskinetic segments and the atrioventricular valve planes are readily identified. One advantage of this technique over mask-mode subtraction is that it is less subject to patient motion artifact because of the short time interval between the frames being differenced. Two of the techniques disadvantages are it does not provide quantitative data on the actual amount of contrast media contained within the ventricles and that akinetic ventricular segments are not visualized.

One of the most promising enhancement techniques for cardiac applications is dual-energy subtraction in which the energy of the x-ray beam is rapidly alternated above and below the k-edge of iodine [21]. Subtraction of closely spaced frames obtained at different energies results in enhanced visualization of the contrast media and significant suppression of the bones and soft tissues. Although this approach requires some modification of the x-ray system, it holds particular promise for cardiac applications because it is the least sensitive of any of the enhancement methods to patient motion.

Contrast administration

Although intravenous contrast administration digital angiography reduces the invasiveness of standard methods, the side-effects and hemodynamic consequences of contrast media remain. Generally, the information gathered far outweighs the procedural risk, but, the systemic, vascular, renal and cardiac effects of contrast media cannot be ignored [22, 23]. For cardiac studies, the hemodynamic

effects also must be considered. The usual 20 to 60 ml contrast dose used for intravenous studies increases right and left ventricular diastolic pressures, cardiac output and heart rate, and reduces arterial pressure [24, 25]. With the increasing need for repetitive ventriculography during exercise and coronary interventions, these contrast load effects become problematic. Most centers, therefore, have begun using direct left ventricular injections of 5 to 10 ml of contrast media, with enhancement by the above described subtraction procedures [26, 27]. Additionally, this approach allows detection of mitral insufficiency, better localization of the mitral valve plane and reduced motion artifact because of the shorter time between the mask and contrast-containing frames. Another development has been the use of nonionic contrast media, which have shown reduced patient toxicity, hemodynamic consequences, hypocalcemia and hypokalemia [28–30]. Patient discomfort during the contrast injection is also lessened, which may reduce motion artifact [31].

The quality of cardiac images obtained by digital subtraction angiography depends significantly on the site and nature of the contrast bolus. In general, image quality is closely related to the total amount of iodine contained within the vascular structure, higher concentrations being necessary for the imaging of smaller vessels such as coronary arteries. Hardware and enhancement routines also affect image quality. For intravenous administration, centrally injected contrast is preferable to peripheral technique owing to the higher concentrations obtained and the lesser chance of extravasation [32, 33]. Little difference has been found between superior vena caval and right atrial administration [34–36]. Further increases in iodine concentration can be obtained with pulmonary artery, aortic root and selective left ventricular and coronary artery injections [7, 8, 27]. An average central venous bolus is 40 ml of full strength contrast injected rapidly (about 2 seconds) [33], although patients with large central circulatory volumes caused by congestive heart failure or valvular insufficiency may require a larger bolus. Most investigators have found 10 to 20 ml of 50% contrast medium sufficient for direct left ventricular injections [37]. For

such studies, complete mixing is a greater problem than opacification.

Intravenous ventriculography

Digital ventriculography provides three distinct advantages for clinical studies: (1) high-quality resting and exercise left ventriculograms can be obtained using the less invasive intravenous route, although contrast loads need to be similar to those used for standard cineradiography; (2) high-quality left ventriculograms can be obtained using direct contrast injections of considerably reduced volume; and (3) resultant images already reside in computer memory making analysis of global and segmental function quicker and easier to perform. Considerable experimental evidence exists supporting the validity of performing left ventriculography using a rapid central contrast injection (see Fig. 1). Correlations between area-length ejection fractions obtained by digital and standard left ventriculography in a canine model have been reported to be excellent ($r = 0.97$), although some underestimation of end-systolic and end-diastolic volumes were found [38]. Wall motion analyses have also shown close correlations between digital and standard approaches [39], and parametric images generated by time-interval differencing subtraction methods have been shown to be sensitive indices of regional ischemia [40]. Other investigators have demonstrated that wall thickening and wall mass can be determined using digital enhancement techniques [41, 42], although such studies are much more difficult to perform clinically.

Close correlations between digital and standard ventriculographic data have also been reported for clinical validation studies, with left ventricular ejection fraction correlation coefficients ranging from 0.75 to 0.98 [43–48]. Poorer correlations and images were found for ejection fractions less than 35% [49]. Time-interval differencing ejection fractions also correlated less well with standard methodology ($r = 0.81$), even in patients with values greater than 50%. An alternate approach to the area-length method for calculating left ventricular ejection fraction is videodensitometry. Under the

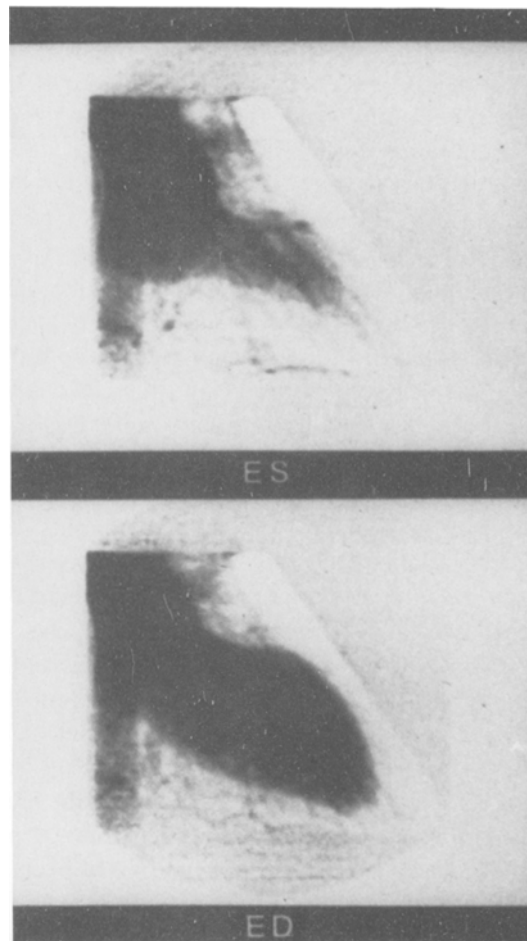


Fig. 1. Two left ventriculographic frames are shown in the RAO projection obtained using mean mask-mode subtraction digital angiography following a central venous injection (top: end-systole, bottom: end-diastole).

assumption that the left ventricle is uniformly opacified with contrast medium, its volume is theoretically proportional to the sum of mask-mode subtracted pixel densities over a ventricular region-of-interest. Advantages of this approach are that assumptions regarding ventricular geometry and precise edge detection are not necessary. Unfortunately, numerous technical factors including nonlinearity of image intensifier and plumbicon transfer functions, beam scatter and hardening, geometric distortion, and veiling glare reduce the validity of this approach [50–54]. Despite these difficulties, several centers have reported accurate

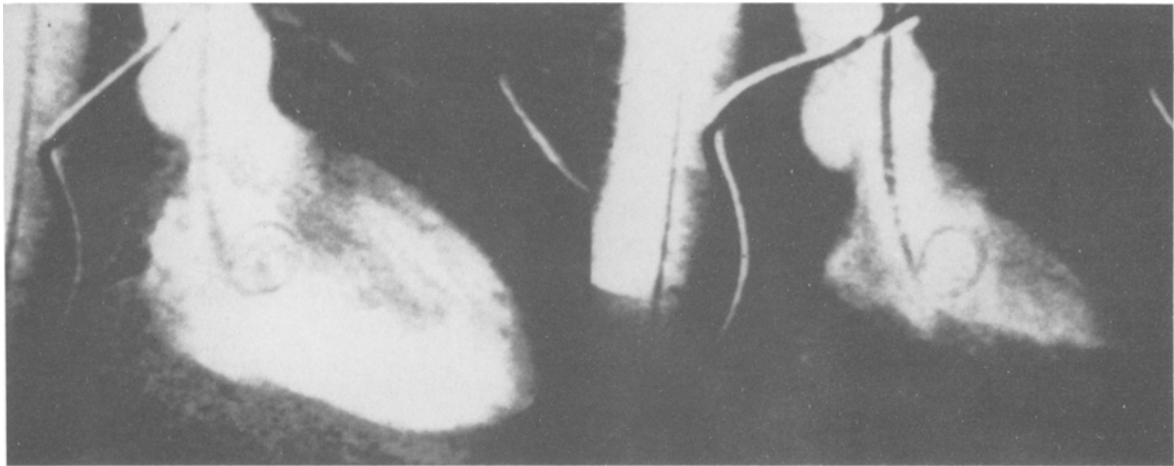


Fig. 2. Two left ventriculographic frames are shown in the RAO projection obtained using electrocardiographic-gated mask-mode subtraction following a low dose direct contrast injection (left: end-diastole, right: end-systole).

estimations of ejection fraction using videodensitometry [55–57], although these methods have not seen wide clinical application.

The interobserver variability of assessing segmental wall motion by visual means is substantial for both digital and standard studies [48, 58]. Automated edge detection programs are under investigation, although none have proven thoroughly reliable. For most clinical applications, the operator is required to visually trace the systolic and diastolic ventricular silhouettes, after which wall motion is analyzed by the computer. Long axis, ventricular centroid and centerline frames of reference and various enhancement techniques have been described [37, 48, 59, 60]. The actual wall motion has been described along radial and perpendicular rays and as segmental areas [39, 44, 60]. Wall motion as assessed by these semiautomated techniques has correlated well with standard ventriculography, although normal apical and basal variability tends to be large, and diaphragmatic artifact can interfere with inferior wall analysis [39, 59]. At present, alternate reference system independent methods for evaluating ventricular function based upon wall curvature are also under investigation, and show promise for increasing the accuracy of ventricular functional analysis [61].

Direct ventriculography

As mentioned above, digital left ventriculography is increasing being performed using direct injection of lesser amount of contrast. This approach allows a better visualization of the mitral valve plane, enables the detection of mitral regurgitation, and shares with intravenous approaches an ease of quantitative analysis and reduction of induced premature ventricular contractions. Motion artifact is also lessened because of the reduced time interval between the mask and contrast containing images. Clinical studies using 5 to 10 ml of contrast, at times diluted to 20% to 50% concentration, have shown good ejection fraction correlations with standard ventriculography ($r = 0.91$ to 0.97) [26, 27, 37, 62]. In general, the quality of low-dose direct ventriculography is equal or superior to that obtained by standard cineradiography and easily permits the use of semiautomated analysis programs [63] (See Fig. 2). Complete opacification of the entire ventricle is the only clinical limitation with optimal results being observed with use of diluted contrast in amounts of at least 20 ml [37, 63]. All investigators using this approach have reported substantially reduced hemodynamic perturbations as compared with the full contrast load necessary for standard cineradiography.

Stress ventriculography

One of the greatest limitations of standard ventriculography is that it does not easily permit the performance of exercise studies. Radionuclide ventriculography, despite its considerably reduced spatial resolution, has found widespread clinical application for this purpose. Exercise intravenous digital ventriculography is a safe alternative to the radionuclide approach over which it has several advantages. Much greater spatial resolution is obtained by digital imaging and the preferable right anterior oblique view or simultaneous biplane imaging are possible without ventricular overlap. Exercise does tend to increase patient motion artifact, however. Clinical experience with exercise digital ventriculography suggests that this problem can be overcome in most instances (approximately 90%), and that ejection fraction changes correlate closely with those obtained by exercise radionuclide ventriculography [64, 65]. The sensitivity for the detection of coronary artery disease appears to be quite high.

Atrial pacing is another form of stress which can be used in conjunction with digital ventriculography. It has the advantage of decreased patient motion over the use of bicycle exercise. Atrial pacing combined with low dose direct digital ventriculography has been reported to have a sensitivity of 93% and a specificity of 83% for the detection of significant coronary disease [66]. In this study, wall motion abnormalities developed or worsened in 80% of case. Many investigators have found the immediate post-pacing period to be the optimal time for performance of the stress study as this allows comparison with the resting ventriculogram at equivalent heart rates. Intravenous digital ventriculography performed immediately post-pacing produces the expected decreases in ejection fraction, increases in end-systolic volume and wall motion abnormalities in coronary disease patients (specificity = 100%, sensitivity = 82%) [67, 68].

Thus, ample clinical trials and experience support the use of digital ventriculography as an equal or preferable substitute for standard cineradiography or radionuclide ventriculography.

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