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New Developments in Ultrasound Systems for Contrast Echocardiography

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Summary: Contrast echocardiography (CE) has evolved significantly in the past decade. Contrast agents and the hardware and software used to detect them and display optimal images have developed in tandem. Not only are hardware and contrast agents available that allow left ventricular cavity enhancement, but recent research points to the usefulness of CE for the evaluation of myocardial perfusion in the cardiac catheterization laboratory and operating room. Advances in ultrasound technology, such as transient harmonic imaging and integrated backscatter, coupled with the development of newer contrast agents that contain smaller, more stable microbubbles capable of transpulmonary passage for intravenous injection, promise a vast increase in the applications of CE in clinical practice.

Key words: ultrasound, contrast echocardiography, contrast agents, myocardial perfusion, harmonic imaging, backscatter, microbubbles, transpulmonary, Doppler, gray scale

The Limitations of Myocardial Contrast Echocardiography

Contrast echocardiography (CE) has developed rapidly in recent years, with equipment manufacturers continuing efforts to overcome current limitations. Standard echocardiographic equipment lacks a full dynamic range or linear gray scale for processing the amplitude of reflected echoes.[1] Rather than quantifying the actual amount of ultrasound energy, scanners compress the initial signal to a relatively narrow range to produce a video display.[1–4] Scan conversion, postprocessing, and data storage on videotape further distort the original backscattered ultrasound signal. These distortions, as well as electronic thresholding, which establishes a level below which systems will not register to suppress noise, further decrease the dynamic range and system sensitivity. They likely explain the lack of sensitivity of commercial scanners to low microbubble concentrations.[5]

Instrument limitations, notably limited frequency resolution, also appear to explain an increase in detected maximum velocity during contrast-enhanced Doppler examinations. In particular, a large change in signal strength can alter the estimated maximum frequency derived from the spectral Doppler.[6]

Artifacts induced by contrast agents also frequently degrade image quality. In some cases, the amount of backscatter is so overwhelming that the enhancement appears to extend beyond the limits of the region being evaluated.[7] At higher contrast agent concentrations, regional flow assessment is also compromised by myocardial shadowing due to attenuation in regions behind the left ventricular (LV) cavity.[8] In addition, increasing the amount of microbubbles injected does not correct for attenuation because this creates a nonlinear relationship between concentration and videointensity.[9] Methods of time-gain compensation, intended to compensate for attenuation, do not change transit time calculation because both background and microbubble signals increase.[10] Physiologic pressures can also alter the reflected ultrasound signal and bubble size, limiting the success of myocardial perfusion imaging and quantification of flow based on time intensity curves.[11–14] In addition, some microbubbles appear to be susceptible to ultrasonic destruction by acoustic pressure;[15–17] reducing exposure to ultrasound pulses by using intermittent harmonic imaging can significantly decrease the rate of destruction.[15, 16]

Intermittent Imaging

To generate echocardiographic images, the transducer must emit an ultrasound signal and then receive the returning one. Since ultrasound emissions destroy microbubbles,[15] the scattering characteristics of the agent and its echogenic duration are adversely affected. To overcome this problem, higher doses of contrast can be given; however, higher doses can have hemodynamic effects and, therefore, are undesirable.[18] Thus, methods to detect lower doses of contrast are necessary.

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Intermittent imaging—gating the frame rate to one or two images per cardiac cycle—can yield significantly improved and longer-lasting contrast.[15, 19] The videointensity of the microbubbles is greater when exposed to triggered ultrasound pulses (0.5–1.0 Hz) instead of constant ultrasound pulsing.[15, 16] The doses required to achieve myocardial contrast are also lower and, thus, safer than those required for conventional imaging, reducing the amount of attenuation (loss of ultrasound energy as it passes through tissue) in the LV cavity. This effect of intermittent imaging is even greater with harmonic imaging where bubble destination is greater because of the longer pulse length,[15, 16] which provides a much improved signal-to-noise ratio.[15, 20]

Harmonic Imaging

One of the newest and most promising techniques in CE is harmonic imaging, which exploits the nonlinear emissions of harmonics by resonant microbubbles.[21–23] Microbubbles have specific resonant frequencies, depending largely on particle size.[7] When exposed to ultrasound, the resonating microbubbles emit fundamentals and harmonics of the frequency to which they are exposed. The imaging frequency can be set to detect only the harmonics ( ).[1, 19] Thus, use of the harmonic mode (with either B-mode imaging or Doppler) when tracking an injected echo-enhancer through the myocardium, increases the intensity of the blood echo image relative to the tissue echo because the bubbles resonate significantly more than tissue.[24] The improved signal-to-noise ratio of harmonic imaging may allow for on-line definition of risk area and infarct size during acute myocardial infarction (MI).[24] Using harmonic imaging, detection of low concentrations of microbubbles is enhanced.[1] Contrast enhancement lasts significantly longer in harmonic than in conventional modes, and images are less susceptible to artifacts such as acoustic shadowing.[25] Harmonic imaging is becoming the procedure of choice for CE.

One animal study suggests that harmonic imaging, coupled with aortic root injection of a contrast agent, provides accurate on-line assessment of risk area and infarct size during acute MI.[20] Myocardial perfusion imaging has been accomplished noninvasively in animal studies with the use of harmonic imaging during intravenous injection of a contrast agent. The improved contrast signal can be used to delineate resting and stress-induced coronary flow changes.[26] It can also be used to visualize the risk area or regions of relative hypoperfusion more easily, improving detection of coronary artery disease (CAD), and quantifying the spatial extent of ischemic burden.[27] By delineating regions of no-reflow after successful reperfusion, the improved contrast signal may also dramatically improve assessment of myocardial viability.[28]

Studies in animals and in an in vivo coronary flow model found that harmonic imaging increased myocardial videodensity from 12 to 35%. For three new transvenous contrast agents, harmonic imaging was also shown to enhance visualization of blood flow in small intramyocardial vessels and offer the potential to distinguish between normal and ischemic areas.[29] A harmonic transducer has been used to show that intermittent imaging produces myocardial contrast in multiple views with a single intravenous injection, allowing detection of regional perfusion abnormalities.[30] Because they require lower doses of contrast agents and increase diagnostic contrast, the combination of harmonic and intermittent imaging may profoundly expand future applications of ultrasound contrast media.

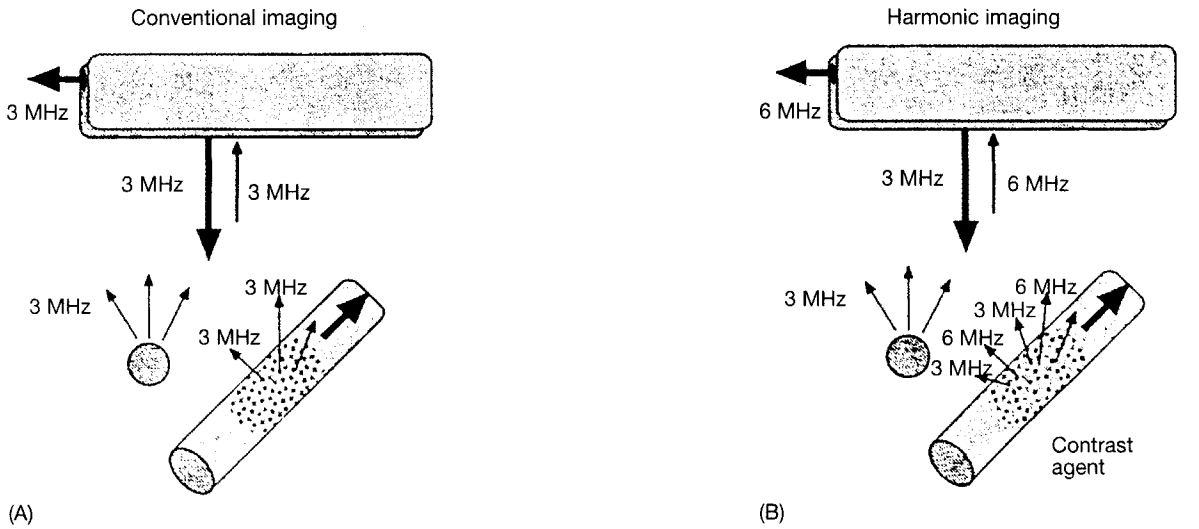

FIG. 1 Harmonic imaging. When exposed to the ultrasound beam, microbubbles resonate at a harmonic frequency approximately twice that of the transmitted one.[1, 19] In conventional imaging (A), ultrasound is transmitted and reflected back by tissue and microbubbles at the same frequency. Only the transmitted frequency is received. In harmonic imaging (B), the imaging equipment is set to detect only the harmonic frequency; thus, only the contrast agent is imaged. From Ref. No. 42 with permission.

Integrated Backscatter, Radiofrequency Imaging, and Ultrasound Tissue Characterization

Ultrasound passing through or reflected from tissue yields sufficient information about the tissue to help characterize it.[4] The identification of physical or physiologic abnormalities depends on this interaction of beam and tissue.[4] For example, calcific tissue reflects more brightly than normal myocardium, and thus is interpreted as increases in ultrasound amplitude. These appearances, however, can be greatly altered by the time-gain compensation settings, nonlinear image processing, and reject settings.[31]

One such tissue property is the scattering of the ultrasound based on the type of tissue and the signal wavelength. When an ultrasound beam encounters an interface smaller than the beam's wavelength, scatter occurs.[32] This low-intensity scatter is generally filtered out by two-dimensional (2-D) echocardiography, which relies on specular echoes created when the beam contacts surfaces larger than its wavelength.[32] Only the scatter aimed back at the transducer (backscatter) is detected. Integrated backscatter identifies these echoes and assigns decibel values to them.[32] One advantage is to minimize the subjective alteration of images.

Calculation of integrated backscatter can be done on processed data or by analysis of unprocessed radiofrequency data returning from the heart. Attempts have been made to quantitate the radiofrequency signals produced by the interaction of integrated backscatter, representing the energy of the ultrasound returned from the heart. More stable contrast agents under development will overcome the systolic destruction of contrast for radiofrequency integrated backscatter quantitation of myocardial blood flow.

Further quantitative analysis can be performed with acoustic densitometry. This permits quantitation of time domain-derived integrated backscatter power. Close correlation was found with radiofrequency integrated backscatter signals.[33] This method brings tissue characterization into a clinical setting.[33]

Three-Dimensional Imaging

Facilitated by advances in digital technology and techniques for image acquisition and display,[34] three-dimensional (3-D) echocardiography can measure the volume and mass of the myocardium[35, 36] and the progression and regression of atherosclerosis.[37] Three-dimensional images are acquired by reconstructing objects from a consecutive series of static 2-D images.[38] A real-time, multiprocessor, 3-D reconstruction system has been formated that allows 3-D reconstruction of successive B-scan ultrasound images at fine intervals (30 frames) of the cardiac cycle.[36] In an experimental study, 3-D echocardiography, using a contrast agent, was employed to display the infarcted myocardial mass.[35, 39] The technique appears to be feasible even in small children with complex congenital heart disease.[38] With the added dimension of time, dynamic 3-D imaging (i.e., 4-D imaging) can create the perception of motion while displaying small cardiac structures and myocardial backscatter texture.[34] Such 4-D reconstructions can produce reasonable estimates of LV volumes and have been used to study both normal and diseased mitral valves.[34] Focus on a specific area of interest, called segmentation, remains difficult despite the availability of automatic computer algorithms for image processing.[34]

Digital Processing

Optimal contrast images are those that show small changes in videointensity which accurately reflect the relative microbubble concentration in tissue. The human eye cannot distinguish these subtle variations in gray levels, but can differentiate many hues of color. Thus, color coding of images is helpful in discerning videointensity. To achieve accurate conversion to color codes, the gray scale values in the image must be established prior to conversion. This is accomplished by digital image processing, which requires proper alignment of the pixels to correct for translation and rotation. Videointensities are scaled and then converted to color schemes which can be customized. This same process is used in the calculation of time-intensity curves.[40] Digitally recording data prior to compression and processing may provide a more accurate transit rate calculation by avoiding the threshold effect.

Conclusion

During the past decade, rapid coevolution has occurred in the development of ultrasound equipment and contrast agents for use in cardiac assessment. The coupling of advanced echocardiographic equipment with a new generation of contrast agents may enhance the role of contrast echocardiography in clinical practice. The most exciting and promising prospect is the use of intravenous contrast agents for the noninvasive assessment of myocardial imaging.[41]

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