

# Future Directions in Echocardiography

Arthur E. Weyman, MD, FACC

Harvard Medical School, Massachusetts General Hospital, Boston, MA

*Future developments in echocardiography will likely focus on the continued evolution of existing techniques, such as real-time 3-dimensional (RT3D) imaging and contrast-enhanced imaging; higher resolution imaging; and greater flexibility in imaging systems due to miniaturization, enhanced connectivity, and integration with other techniques. Improvements in RT3D image quality may include expanded parallel processing and use of transesophageal matrix arrays. Two areas of future clinical potential for contrast-enhanced echocardiography/ultrasound are the use of targeted microbubbles for diagnostic and therapeutic applications and expanded vascular imaging. Although molecular imaging holds great promise for the future, in the short-term, it is likely that contrast will be used more extensively for vascular imaging to assess both the effects of interventions on local perfusion and the activity of atherosclerotic plaque based on the size/density of the vasa vasorum. The widespread use of ultrasound will be facilitated by the development of a convenient portable or readily available ultrasonic equivalent of the stethoscope.*

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To understand the future directions in echocardiography, it is first important to understand where we are now and how we got here. Most of the basic echocardiographic techniques we use today were initially described many years ago. In most cases, however, their broader clinical application awaited improvements in image processing or the development of suitable recording devices or analysis techniques. For example, the original M-mode echoes were recorded on 35-mm film by a camera aimed at the oscilloscope. The 35-mm film was eventually replaced by Polaroid film, which eliminated the development time. However, it was not until the introduction of the strip

chart, more than 15 years later, that M-mode recording became truly practical. Likewise, the growth of 2-dimensional (2D) imaging paralleled the introduction of the digital scan converter and the progression from movie film/large reel-to-reel video tape decks, to portable VCRs, and, finally, digital recorders. The clinical analysis Doppler flow recording, first described in the late 1950s, was still based on the auditory analysis of signals by the expert ear into the mid 1970s. It was not until the introduction of the real-time spectrum analyzers in the early 1980s that the technique became clinically useful.

These basic echocardiographic tools (2D and M-mode imaging along with pulsed, continuous wave and color Doppler) are now mature, and improvements should be small and incremental. It is unlikely that completely new diagnostic approaches will be forthcoming. As a result, future development will likely focus on the continued evolution of existing techniques, such as real-time 3-dimensional (RT3D) imaging and contrast-enhanced imaging; higher resolution imaging; and greater flexibility in imaging systems due to miniaturization, enhanced connectivity, and integration with other techniques. This article will examine how these developments will likely benefit clinical practice.

### Three-Dimensional Echocardiography

The first attempts to create 3-dimensional (3D) reconstructions from echocardiographic data occurred in the 1970s,<sup>1,2</sup> but it was not until the late 1980s that position-sensing devices and computer reconstructive techniques matured to the point at which 3D imaging could be used to answer important diagnostic questions.<sup>3-8</sup> Although studies based on the spatial and temporal reconstruction of

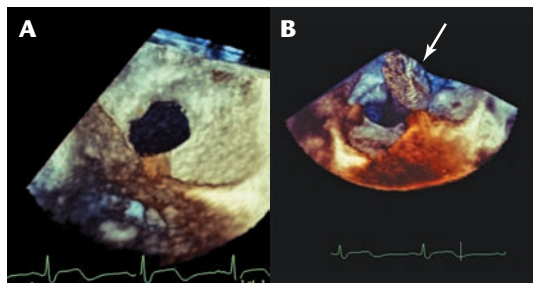
2D images demonstrated the importance of 3D imaging in a variety of clinical situations, the complexity of the reconstruction approach limited application to the research environment. The recent development of matrix array transducers capable of RT3D imaging and Doppler imaging addresses many of the problems encountered with 3D reconstruction because volumetric imaging does not require external registration of imaging planes, permits shorter scanning time, and allows full volume images to be recorded during a single breath hold. Unfortunately, to date, the widespread application of RT3D has been prevented by the limited spatial resolution/image quality that occurs when a limited amount of data are spread over a larger area, the low frame rate, and the lengthy analysis time. Therefore, the incremental value of this approach in clinical practice is still being defined. Solutions to these problems are important short-term goals of instrument development.

To understand the loss of resolution that occurs when moving from a 2D format to a 3D format, it is important to remember that all echocardiographic images are formed by assembling a fixed number of B-mode lines. The B-mode line is formed when the echoes from a sound pulse are displayed as dots along a line, with the brightness of the dot corresponding to the strength of the reflected echo and the distance along the line to the distance traveled through tissue. Because only 1 pulse can travel unambiguously through tissue at any time, the depth of field to be examined limits both the number of pulses that can be transmitted per unit time and, hence, the B-mode lines available for image formation. For example, because sound travels in tissue at about 1.5 mm/ $\mu$ sec, it takes 200  $\mu$ sec

for a sound pulse to travel to a depth of 15 cm and for the resulting echoes to return to the transducer. As a result, at this depth of field, a maximum of 5000 pulses can be transmitted (the pulse repetition frequency) and B-mode lines recorded each second. These lines must then be divided by the number of frames assembled per second (at 50 frames/sec, this would leave 100 lines per frame). For a 90° sector, this would be about 1.1 lines/degree. When these lines are used to form a 2D image, the image quality is reasonable and the space between lines filled in by interpolation. However, when spread throughout a volume, the line separation becomes much greater and the spatial resolution and resultant image quality deteriorate significantly. In the sector format, the line spacing increases as the distance from the transducer increases, so image quality also deteriorates with depth.

### *Approaches to Improving RT3D Image Quality*

**Expanded parallel processing.** To increase line density at a fixed pulse repetition frequency, parallel processing was developed several years ago for 2D imaging to increase the frame rate while maintaining image quality. Parallel processing is based on the ability of array transducers to control the path along which reflected echoes are preferentially received by altering the delays of the signals returning to the different elements of the array. In the standard format, the delays are optimized to receive the echoes arising from the center of the transmit beam where the transmit beam intensity and resulting echocardiograph strength are the greatest. However, if there are 2 separate receive pathways operating in parallel, they can be optimized to receive echoes from either side of the transmit beam and thus



**Figure 1.** Transesophageal matrix array 3-dimensional image of an atrial septal defect (A) during percutaneous closure with an Amplatzer device (AGA Medical, Plymouth, MN). The catheter can be seen crossing the defect (B), and the left atrial side of the device (arrow) has been deployed.  
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double the number of B-mode lines for each transmit pulse. Because the matrix arrays used in 3D volumetric imaging can transmit and receive in multiple directions, in the future, it should be possible to greatly expand the number of parallel pathways to increase the number of B-mode lines per transmit pulse and, thus, improve image quality. Introduction of a larger number of parallel pathways obviously increases complexity and requires that the transmit pulse be defocused to allow enough separation between lines to avoid redundancy. Defocusing leads to energy dispersion and, hence, to decreased sensitivity necessitating an increase in output power that can lead to excess transducer and tissue heating—but these problems should be solvable.<sup>9</sup>

**Transesophageal matrix arrays.** Another way to improve image quality is to limit recording to the apex of the sector/pyramid where the B-mode lines are most densely packed. RT3D imaging from the esophagus has a number of advantages because it permits the use of higher frequencies, which provides improved axial resolution and places the structures of interest in the near field of the transducer where the B-mode lines are more closely spaced, so spatial resolution is improved.<sup>10</sup> This approach has yielded excellent 3D images of structures in close apposition to the transducer, such as the left atrium, interatrial septum, and mitral valve (Figure 1), but as with transthoracic 3D recordings, image

quality tends to deteriorate in the far field. However, the combination of enhanced parallel processing and near field imaging should greatly improve image quality.<sup>11</sup>

**3D intracardiac imaging.** In addition to transthoracic and transesophageal 3D imaging, more extensive intracardiac 3D applications are also feasible. Current intracardiac imaging is limited in its field of view and penetration. Although attempts at intracardiac and intravascular 3D imaging have been reported, they are largely based on the recording of sequential 2D images during catheter pullback and are limited by registration artifacts due to catheter movement and inconsistent withdrawal rates. More recently, matrix array transducers have been described for intracardiac use in which a single side-looking array is positioned at the tip of a catheter, or multiple arrays (up to 5) are positioned at various angles to one another to record selected subvolumes around the catheter tip that are combined to form a full 360° volume. Combinations of side-looking and forward-looking arrays are also possible. Areas of overlap in the images from multiple arrays are spliced together to form a coherent volume representation.<sup>12</sup> Incorporation of array transducers into catheters designed for therapeutic intervention should permit more selective application and limit complications.<sup>13</sup> The major limitation to date has been the size of the transducer array, and, as a re-

sult, the number of wires that must be housed within the catheter. Newer technologies, such as imbedding thin wires within the walls of the catheter during fabrication, may increase the number of elements available for radial or linear intracardiac matrix array transducers.

#### *RT3D Imaging Combined With Other Approaches*

**3D imaging with contrast.** The use of contrast in conjunction with 2D imaging is well established and has improved border recognition in difficult subjects, particularly during stress studies. The combination of contrast with 3D imaging will likely partly compensate for the limited spatial resolution of the technique and should enhance its value in areas such as stress echocardiography.

**3D speckle tracking.** Potentially more promising in the longer term is the introduction of 3D speckle/feature tracking. Several algorithms have recently been developed that attempt to map the movement of intramyocardial echoes (speckle or features) directly from the radiofrequency data that form the basis for 2D B-mode ultrasound scans. These approaches begin by mapping the intensity distribution of a group of pixels around a defined starting point within a selected region of the myocardium. Moving to the next frame, the algorithm begins at the same initial pixel location and then sweeps the pattern or mask from the preceding frame in a predefined search pattern around that pixel until the optimal correlation between the mask and underlying data is obtained. Using this approach, the displacement of the mask from its starting point, in theory, represents the interframe movement of the underlying tissue. Repeating the processes from frame to frame throughout the cardiac cycle at

multiple points around the ventricle gives the amplitude, rate, and direction of motion of the underlying tissue at all of the selected starting points and, hence, permits the calculation of 2D strain rate and strain.

Unfortunately, 2D speckle is limited by the contraction and rotation of the heart, which shift the area being studied relative to a fixed short axis (contraction) or to apical (rotation and translation) imaging planes from diastole to systole. Tracking speckle/features of the myocardium in 3D dimensions greatly enhances the computational requirements but should overcome the errors produced by translation and rotation of the ventricle, making the technique more robust and providing a 3D map of local myocardial function (tissue velocity, strain, and strain rate) at multiple points within the left ventricle. Initially, this technique would most likely be feasible in conditions where the myocardium is thick and where image quality is good, but application should improve along with image quality.<sup>14</sup>

#### *Improved Display Formats and Approaches to Analysis*

**Display formats.** Another problem with volumetric imaging is the inability of the operator to optimize the alignment between the sampling beams within the volume and all of the targets of interest during data acquisition. Targeting the volume acquisition by a single or orthogonal 2D plane during acquisition helps to optimize this relationship. However, better display formats that permit target definition and image quality to be assessed in multiple planes during recording—such as C-scan imaging and real-time cropping—should improve the operator's ability to appropriately align individual sampling beams within the volume

relative to selected targets to optimize imaging of the structure(s) of interest.

**More robust analysis methods.** Although improvements in RT3D imaging will provide greater detail in the reproduction of cardiac structure, function is typically based on wall motion that is often difficult to record and analyze. Automated border detection algorithms have been studied and gradually improved for decades, and although still imperfect, they offer the promise of more rapid function and real-time volume analysis when combined with 3D data.

#### **Contrast-Enhanced Ultrasound**

To this point, the primary clinical applications of contrast-enhanced echocardiography/ultrasound have been the detection of shunt flow, endocardial border enhancement, and, with more limited clinical success, the assessment of myocardial perfusion. Two areas of future clinical potential are the use of targeted microbubbles for diagnostic and therapeutic applications and expanded vascular imaging.

#### *Molecular Imaging*

Targeted microbubbles are small (about 1-5  $\mu\text{m}$ ), encapsulated, gas-filled bubbles that, because of their shell composition (lipid or albumin) or the attachment of specific antibodies or other ligands to the shell, can bind to characteristic endothelial or inflammatory cell receptors in areas of disease. Because of their ability to reflect ultrasound, the location, concentration, time/sequence of appearance, and spatial extent of the bubbles can provide insight into the presence, activity, and stage of the disease of interest. Further, the insertion of drugs, proteins, or genes into the bubble can concentrate these agents, along with the bubbles, in

areas of disease, enhancing their effectiveness and reducing the systemic toxicity.

#### *Diagnostic Applications*

There is growing interest in the development of methods for using ultrasound in combination with microbubbles to image disease at the level of its cellular and/or molecular mediators. Molecular imaging with contrast-enhanced ultrasound relies on the detection of novel site-targeted microbubble contrast agents that are retained within or bind to specific components of a disease process, thereby allowing phenotypic characterization. Because microbubbles are pure intravascular tracers, the disease processes must be characterized by antigens that are expressed within the vascular compartment. Accordingly, the pathologic states that have been targeted include inflammation (eg, atherosclerosis, ischemia-reperfusion injury, myocarditis, transplant rejection), tumor-related angiogenesis, neoplasms, and thrombus formation—all of which are mediated in part by molecular events within the vascular space.<sup>15,16</sup> Several strategies have been used to target ultrasound contrast agents to regions of disease. The first takes advantage of the inherent chemical or electrostatic properties of the microbubble shell that promote retention of the microbubbles within diseased organs due to the upregulation of receptors that bind either albumin (Mac-1 on activated leukocytes) or lipid (opsonization with serum complement) components of the shell. Another more selective strategy involves attachment of antibodies, peptides, or other ligands to the bubble surface that recognize and bind to disease-related antigens. Two recent research reports illustrate the potential importance of molecular imaging for

identifying the molecular events that characterize disease. In 1 study, acoustically active, targeted gas-filled microbubbles bearing a selectin-specific ligand on their surface were shown to bind P-selectin on the postischemic endothelium.<sup>17</sup> Because P-selectin is expressed on the endothelial surface within minutes after the onset of ischemia and persists for hours, it potentially provides a marker or “molecular memory” of the prior ischemic event. In addition, a significant linear relationship was shown between risk area size and the size of the region of contrast enhancement. This information could be particularly important in patients presenting to the emergency room with a history of recent chest pain suggestive of myocardial ischemia but without electrocardiographic changes or enzyme elevations at the time of evaluation. In such cases, the ability of this “ischemic memory” to confirm the occurrence of a recent ischemia as well as to define its location and extent could be of enormous clinical significance.<sup>17</sup>

In the second study, targeted molecular imaging was used to define more complex molecular and cellular processes. Using multiple contrast agents targeted to endothelial vascular cell adhesion molecule-1, complement receptors expressed preferentially by activated neutrophils, or the fibronectin receptor ( $\alpha_3\beta_1$ ) on monocytes, the timing of endothelial cell activation and inflammatory cell recruitment during vasculogenesis and ischemia-mediated angiogenesis was defined in models of chronic ischemia. When combined with contrast-enhanced ultrasound perfusion imaging, this allowed the molecular events to be temporally related to new vessel formation and increased blood flow, and this technique can potentially be used to study how vascular

remodeling can be modulated for therapeutic effect.<sup>18</sup> Although these techniques are clearly still in the early phase of development—and it remains to be determined whether similar data would be obtainable in patients with less favorable windows and greater background noise from tissue and circulating bubbles—the potential of such methods is enormous.<sup>17</sup>

#### *Therapeutic Applications*

The therapeutic applications of microbubbles include the localized delivery of genes, drugs, cells, and proteins designed to treat disease or enhance cellular functions. Therapeutic agents can be linked to or dissolved within the microbubble surface shell(s), deposited on sub-surface oil layers, or trapped within the bubbles themselves. Similar to molecular imaging for diagnosis, therapeutic applications are based on the local adherence of bubbles to targets of interest as a result of binding due to the chemical properties of the bubble shell or the attachment of specific ligands or antibodies to the microbubble surface that bind to specific cell surface antigens expressed in regions of disease. After they accumulate at the desired site, the microbubbles can be activated and the agent delivered by ultrasound. Local delivery of therapeutic agents is facilitated by insonification of the microbubbles that generates radiation force, which causes the bubbles to migrate to the vessel wall, promoting interaction with vessel wall ligands and at a higher acoustic power, and causing the bubbles to oscillate, collapse, and disintegrate. Microbubble destruction both releases the therapeutic agent and produces local microstreaming that creates small pores in the adjacent tissue (sonoporation) in the vicinity of the con-

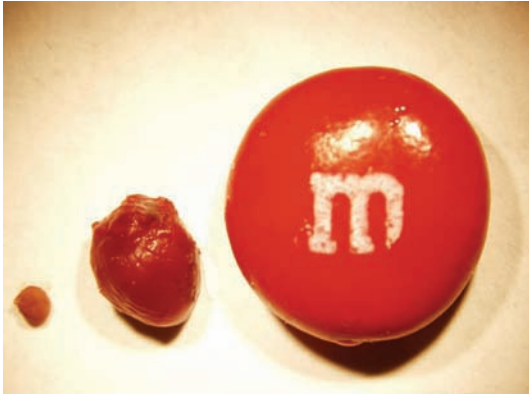
trast agents, facilitating delivery of genes or drugs into the cells. This process can be repeated each time the vasculature refills with the carrier (5-20 sec) until the total volume of injected vesicles has been delivered.<sup>19</sup> Local cavitation due to microbubble destruction can produce other mechanical effects, such as clot fragmentation, which, when combined with local thrombolytic delivery, can enhance thrombolysis. Specific applications of targeted microbubbles that have been demonstrated in experimental models include the promotion and inhibition of angiogenesis, thrombolysis, and the treatment of tumors.<sup>20-22</sup>

Many issues remain to be defined, including the ideal shell composition, the method of drug incorporation into the bubble and the appropriate combination of gas and drug, the necessary concentration of microbubbles to achieve the desired therapeutic effect and the feasibility of achieving this concentration, the ability to activate bubbles within the heart and other organs, and the systemic effects of different agents and their safety in humans. Despite these difficulties, the potential of targeted drug delivery is great and the future realization of even a few of these applications could have enormous clinical potential.

#### *Use of Contrast for Vascular Imaging*

Although molecular imaging holds great promise for the future, in the short-term, it is likely that contrast will be used more extensively for vascular imaging to assess both the effects of interventions on local perfusion and the activity of atherosclerotic plaque based on the size/density of the vasa vasorum. Preliminary experimental studies demonstrate that perfusion imaging





**Figure 2.** This image illustrates the size of the fetal mouse heart (left) and the adult mouse heart (middle) relative to a reference object. (Courtesy of Marielle Scherrer-Crosbie, MD, PhD.) [www.medreviews.com](http://www.medreviews.com)

can be used to assess blood flow and blood flow reserve in the extremities. The greater ease of access of the peripheral circulation to ultrasound imaging (compared with the heart), the incorporation of newer imaging techniques such as time lapse imaging, the ability to assess both small and large vessel perfusion, and the changes with physiologic interventions and the use of perfusion imaging in combination with targeted therapeutic interventions all point to wider clinical application.<sup>23</sup>

Another area of ongoing interest is the development of methods to assess atherosclerotic plaque activity and vulnerability. Angiogenesis and inflammation are characteristic of vulnerable plaque. Immature angiogenic vessels originate from the adventitial surface of the vessel wall (vasa vasorum) and both characterize and contribute to the ongoing inflammatory process. In the carotid vessels, increased plaque neovascularization by contrast-enhanced ultrasound has been shown to correlate with histologic vessel density and is associated with symptomatic disease but unrelated to stenosis severity. A reduction of intraplaque vasculature has been reported following intermediate duration statin therapy.<sup>23,24</sup>

The combination of higher resolution 3D volumetric imaging using

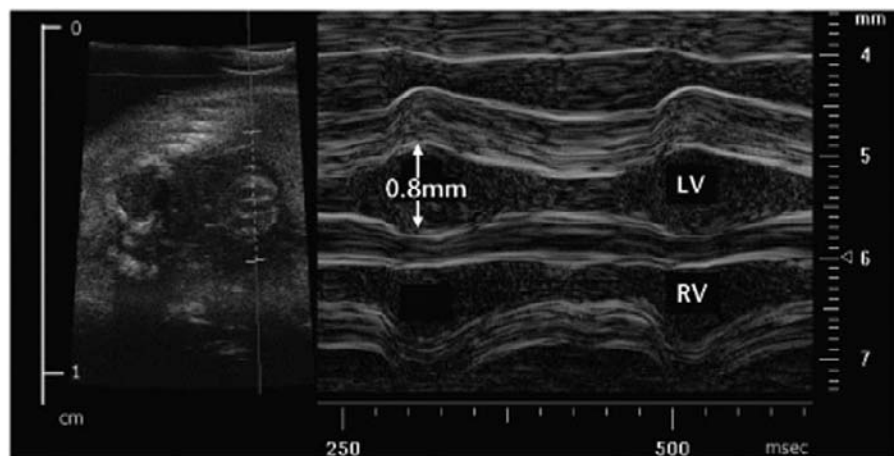
both surface transducers and intracardiac/intravascular matrix array intravascular ultrasound application (IVUS) transducers should improve our assessment of plaque composition and vulnerability.

New imaging approaches will also likely be developed to facilitate the imaging of small vessels and the limited concentration of contrast agents that may occur with molecular targeting. Harmonic imaging (recording signals that are integer multiples of the fundamental or transmitted frequency) is one method that has been proposed<sup>25</sup> to improve contrast detection. However, harmonics also arise from tissue and as such are less specific than might be desired. In contrast, subharmonic resonances (frequencies that are fractions of the transmitted frequency) arise only from microbubbles due to surface modes (nonspherical distortions of the bubble shell) that occur at a threshold intensity level in an ultrasonic field and thus are not produced by tissue.<sup>26</sup> Therefore, subharmonic imaging may prove more sensitive for contrast detection and could be of particular value in selected applications.<sup>27</sup>

### Higher Resolution Imaging

The theoretical limit of resolution of high-frequency ultrasound is in the submicron range, and prototype

ultrasonic microscopes (50 MHz to > 1 GHz) with the capability for imaging at the cellular level were developed more than 3 decades ago. High-frequency ultrasonic imaging has the advantages that tissue/cells can be imaged in vivo without the need for staining or damage to the tissue, and the range of difference in the elastic properties of many tissues (which characterize ultrasound images) is much wider than that of their optical properties, suggesting the potential for the in vivo study of cellular mechanics and, potentially, ultrasonic biopsy of superficial tissues. (In ultrasound, there is a trade-off between frequency and penetration, so that as frequency increases, the ability of the sound wave to penetrate into tissue decreases. Thus, at very high frequencies, it is possible to analyze only the superficial cell layers.) Although to date, acoustic microscopy has been used primarily for nondestructive testing in the electronics industry, there has been a gradual migration of clinical/research imaging frequencies and resolution toward the "microscopic range." For example, high-frequency imaging (20-40 MHz) has been used for the IVUS, but for clinical application, the trade-off between the need for high-performance catheters and disposability has limited image quality. More recently, instruments have been developed with enhanced resolution for transthoracic imaging and have proven enormously valuable in small animal research. Figure 2, for example, illustrates the size of the mouse heart, and Figure 3 is a recording from a mouse fetus recorded in utero. In this example, the whole heart is only 3 mm in diameter, and yet clear images of the LV cavity (the LV internal dimension at end diastole measured 0.8 mm), wall thickness (0.3 mm), and contraction pattern can be obtained. More recently,



**Figure 3.** Two-dimensional and M-mode in utero recordings of the fetal mouse heart. LV, left ventricular; RV, right ventricular. (Courtesy of Marielle Scherrer-Crosbie, MD, PhD, and Helene Thibault, MD.)  
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in vivo imaging of the zebrafish heart was reported using a 75-MHz imaging system with 25- $\mu$ m resolution combined with a 45-MHz pulse wave Doppler device. The system provided real-time delineation of cardiac structures, estimation of cardiac dimensions, and image-guided blood flow measurements. At the higher levels of resolution, it is not only possible to record ventricular and valve function from the derived images but also to record tissue Doppler velocities and blood flow using myocardial contrast techniques. It is expected that the expanded research potential of these high-frequency systems will feed back into large animal and clinical research through the development of higher-frequency, higher-sensitivity IVUS catheters and expanded applications.<sup>28-30</sup>

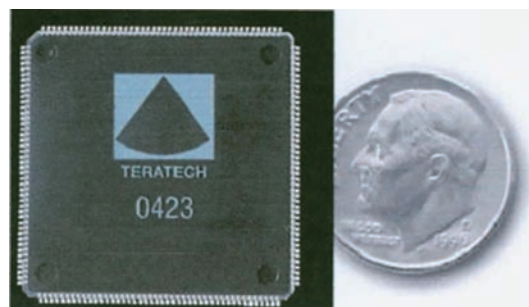
### Imaging Systems

Because ultrasound imaging applications are so widespread in medicine and the technique is safe and—beyond the cost of the instrument—inexpensive, it is expected that ultrasound imaging will become more widespread in the general medical community outside the dedicated

echocardiography laboratory. The ultimate goal is the development of a convenient portable or readily available ultrasonic equivalent of the stethoscope.

There are several limitations to more widespread use. There is no readily available equipment that can be carried in the physician's pocket/laboratory coat when he or she sees patients in the hospital or kept in the room where patients are examined. There is also a lack of education among the broader medical community in the recording technique and interpretation of echocardiographic images. In addition, there is the inherent difficulty of recording an echocardiogram in many patients. The first of these problems is being addressed by the increasing miniaturization and flexibility of recording devices.

**Figure 4.** Chip size for beam forming. (Courtesy of Terason, Teratech Corp, Burlington, MA.)



### Miniaturization

The original 2D dimensional imaging systems were comparable in size with household refrigerators. Although some of these systems had wheels and thus were moveable, they were hardly portable. Over time, the electronics for the imaging component of these systems have continued to shrink, but the advantage in size has been partially counterbalanced by the addition of new components, recording devices, and analysis capabilities. Recently, however, the increased power of ever smaller computer processing units has made it possible to put the basic functions of a 2D imaging system into a single chip (Figure 4) and to produce “hand-carried” instruments with the essential capabilities of the larger conventional full-function echocardiography machines. Despite their greater portability, these systems are still too large for physicians to routinely carry on rounds, from examining room to examining room, or from hospital to office.

One of the first steps in making these systems smaller is likely to be the elimination of the cord between the transducer and the display unit. The development of cordless transducers requires that the beam former be placed within the transducer housing, that there be an internal power source, and that a transmission circuit be used for communication with the display and the control unit. All of these components are available



**Figure 5.** Future advances in technology may result in a portable echocardiograph unit, shown here in an artistic rendering. [www.medreviews.com](http://www.medreviews.com)

or in evolution, and this step seems to be a more natural extension of current technology rather than a revolution.<sup>31</sup> Elimination of the cord, with continual miniaturization of the electronic components, should make it possible to have a small (palm-sized) monitor and control unit with a transducer the size of a large pen light either separate or attached by a thin power cord. This technology should ultimately result in a truly portable device that the physician could carry in his or her pocket (Figure 5).

As monitors become less expensive and echocardiographic instruments more flexible, it should also be possible to make imaging available in individual examining rooms through use of a central server, a beam former either centrally located or in the transducer, and a flexible monitor.

The transducers could then be placed on the wall along with the otoscope and the ophthalmoscope, and simple controls could be mounted in the examining table with a flexible monitor behind the patient. The main limitation would seem to be education and initial cost. Education would involve training physicians to record their own echocardiograms (at least for screening). To justify start-up costs—in this era of concern for health care expenses—money would need to be saved by reducing the number of more expensive tests or outcome would need to be improved. However, at least in cardiology, this seems a logical extension of current practice.

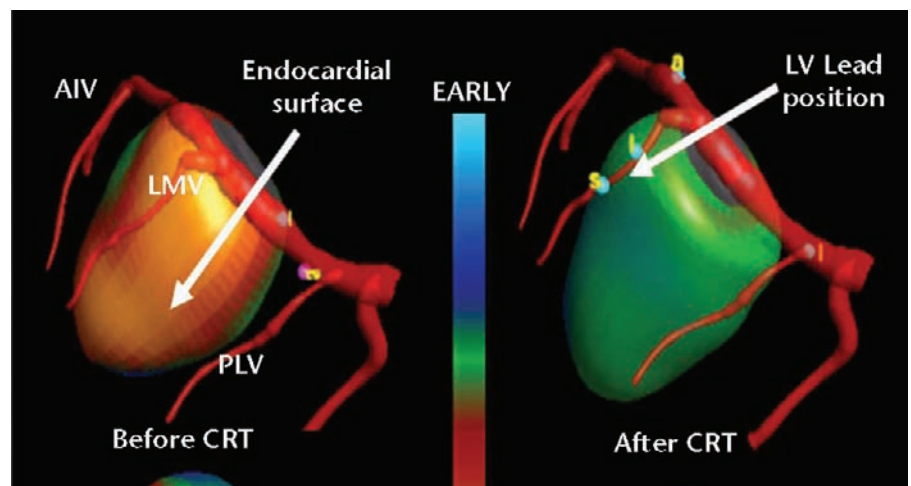
#### *Integration of Imaging Techniques—Fusion Imaging*

Another area of future interest is the integration of imaging techniques or “fusion imaging.” An example of fusion imaging is the combination of radiographic and 3D echocardiographic images for catheter localization and function analysis during pacing and electrode placement for cardiac resynchronization. In this

approach, the cardiac venous system is first outlined using contrast radiography, and the targets for catheter placement defined. Areas of dyssynchrony are then defined by 3D echocardiographic imaging, and the 2 data sets combined using fixed internal references (Figure 6). During the procedure, it could then be possible to optimize catheter placement by observing the changes that occur in the pattern of contraction on the 3D images following pacing at different locations. Combining datasets offers the possibility of optimizing the strengths of various techniques (eg, real time access to data or spatial resolution), while limiting potentially harmful effects such as radiation exposure.

#### *Combination With Electromagnetic/ Ultrasound Heating for Tissue Characterization*

Tissue characterization by ultrasound has been an area of interest for decades, but to date, there have been limited practical applications of this technique beyond the gross recognition of different tissue types. An area of potential longer-term interest for



**Figure 6.** Fusion of contrast radiographic image of the cardiac venous system and a 3D echocardiographic recording of the left ventricle with color-coded superimposition of graded cardiac function. (Illustration courtesy of Francois Tournoux, MD.) AIV, anterior interventricular vein; LMV, lateral marginal vein; PLV, posterior left ventricular; CRT, cardiac resynchronization therapy; LV, left ventricular. [www.medreviews.com](http://www.medreviews.com)



tissue characterization is thermoacoustics. Thermoacoustics describes the sound waves that are produced when electromagnetic or high-intensity ultrasound waves are absorbed by tissue. The absorption of electromagnetic/ultrasound energy produces local heating, which in turn leads to tissue expansion that causes pressure waves that are in essence sound waves. The amount of heating required is small ( $< 1^{\circ}\text{C}$ ). The stimulating waves can be anywhere in the electromagnetic spectrum with absorption dependent on the water content of tissue. Because different absorption leads to different heating and, thus, pressure wave production, the water content of tissue and tissue type can theoretically be determined in this manner. Preliminary studies in noncardiac and excised vascular tissue have demonstrated the feasibility of this approach, although its clinical application in cardiac and vascular tissue remains to be explored.<sup>32</sup>

## Conclusion

The core components of the echocardiographic examination are rela-

tively mature. However, advances in imaging capability, resolution, and portability/accessibility should greatly increase its diagnostic potential and future clinical and research applications. ■

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## Main Points

- Tracking speckle/features of the myocardium in 3-dimensional (3D) dimensions greatly enhances the computational requirements but should overcome the errors produced by translation and rotation of the ventricle, making the technique more robust and providing a 3D map of local myocardial function (tissue velocity, strain, and strain rate) at multiple points within the left ventricle.
- Better display formats in real-time 3-dimensional imaging that permit target definition and image quality to be assessed in multiple planes during recording—such as C-scan imaging and real-time cropping—should improve the operator's ability to appropriately align individual sampling beams within the volume relative to selected targets to optimize imaging of the structure(s) of interest.
- Automated border detection algorithms have been studied and gradually improved for decades, and although still imperfect, they offer the promise of more rapid function and real-time volume analysis when combined with 3D data.
- The potential of targeted drug delivery is great and the future realization of even a few of these applications could have enormous clinical potential.
- New imaging approaches will likely be developed to facilitate the imaging of small vessels and the limited concentration of contrast agents that may occur with molecular targeting.
- Fusion imaging, such as the combination of radiographic and 3D echocardiographic images for catheter localization and function analysis during pacing and electrode placement for cardiac resynchronization, is another area of interest.

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