Developments in cardiac ultrasound

Sven Plein, Gordon J Williams

This article gives an overview of recent developments in cardiac ultrasound for the general hospital physician. It discusses contrast echocardiography, harmonic imaging, three-dimensional echocardiography, Doppler tissue imaging and perfusion imaging and give an outlook on future perspectives.

Cardiac ultrasound (echocardiography) is the most commonly used imaging modality in cardiology. In recent years a number of significant technical advances have been made that are now coming into clinical practise. It is important for the clinician, whether cardiologist or other specialist, to be aware of these developments and the new terminology, in order to utilize echocardiography to its full potential.

CONTRAST ECHOCARDIOGRAPHY

The basic principle of ultrasound imaging is the reflection of sound waves at borders of materials with different acoustic characteristics (i.e. density, absorption of sound waves, speed propagation). The reflected signal is detected and processed by the ultrasound receiver. In the heart the main acoustic border is that between blood and myocardium. Intravascular contrast agents for ultrasound imaging have been developed to enhance intracardiac contrast by adding a further acoustic border: contrast agent or blood and myocardium.

Early contrast agents used in ultrasound imaging were indonyacine green, saline or dextrose solutions that were manually agitated to create air bubbles in the solutions (Gramiak, 1968; McKay and Rubissow, 1978). Air bubbles produce ultrasonic contrast, because their acoustic characteristics differ significantly from both blood and myocardium. They have a large surface area, creating maximum backscatter of ultrasound waves.

The early contrast agents provided contrast only for a few seconds and the air bubbles were too large and unstable to cross the pulmonary vasculature. They were therefore used in the assessment of the right heart chambers and for detection of intracardiac shunts. If intravenously injected contrast bubbles appeared in the left-sided heart chambers, an intracardiac communication (atrial or ventricular septal defect) had to be present.

Since the 1980s, contrast agents have been produced by encapsulating gases in a stabilizing shell (Feinstein et al, 1984). These coated gas bubbles are very stable in the circulation and can be produced in a similar size to red blood cells. They flow unlimited in the blood stream and pass the pulmonary vasculature and can therefore be administered intravenously for imaging of the left heart. A variety of contrast agents have been produced in this way, using different gases and coating materials, resulting in different stability and persistence in the circulation (Cheng et al, 1998; Kaul, 1997).

A common clinical application of contrast echocardiography is bolus injection of contrast agents and imaging with conventional ultrasound. This allows enhancement of the cardiac cavities and is clinically useful in a number of situations:

- Enhancement of the left ventricular cavity and increased endocardial border definition in patients with suboptimal conventional images (*Figure 1*)
- Clarification of suspected left ventricular thrombus or mass
- Doppler imaging, where contrast agents increase the strength of the Doppler signal, resulting in a sharper definition of the Doppler envelope while the measured velocities are unaffected by the contrast agents (Terasawa et al, 1993).

Bolus injection and conventional imaging techniques do not allow assessment of contrast distribution in the myocardium. This is partly

Dr Sven Plein is Research Fellow and **Dr Gordon J Williams** is Consultant Cardiologist in Non-invasive Cardiology, Yorkshire Heart Centre, Leeds General Infirmary, Leeds LS1 3EX

Correspondence to: Dr GJ Williams

because of the strong contrast signal from the left ventricular cavity, which leads to a relative lack of visualization of myocardium. This phenomenon is called 'acoustic shadowing'. Another factor influencing the visualization of the myocardium is the complex interaction between contrast agents and the ultrasound waves during imaging. When coated contrast agents began to be used in echocardiography, it was observed by chance that the contrast bubbles were 'excited' by the ultrasound beam, leading to reverberation and destruction of the contrast bubbles. These observations have resulted in the development of specialized contrast imaging techniques such as harmonic imaging as well as techniques that allow imaging of contrast distribution in the myocardium (see 'myocardial perfusion imaging' below).

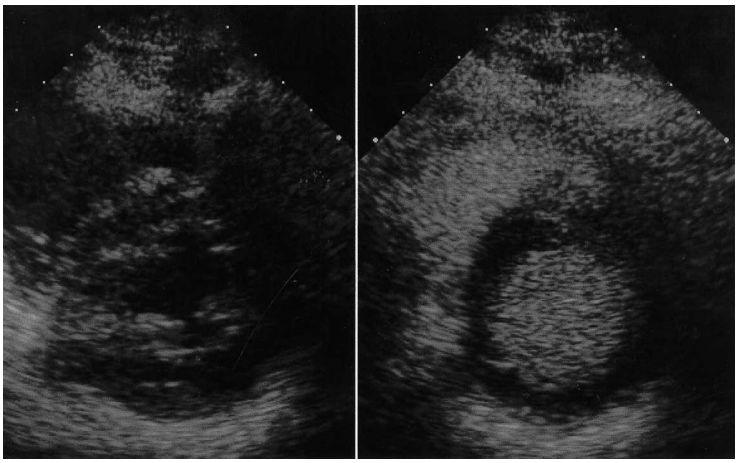

Figure 1. Short axis view of the left ventricle during a stress echocardiogram. The image on the left is taken without contrast and endocardial border detection is difficult. The image on the right is taken after an intravenous bolus injection of 1 ml of contrast (Optison®, Mallinckrodt, UK). The contrast material fills the left ventricular cavity and enhances endocardial border contrast.

CONTRAST HARMONIC IMAGING

As described above, contrast microbubbles interact with the ultrasound waves during imaging, being compressed and relaxing in sympathy (or linearly) with the ultrasound beam. All microbubbles have a specific resonance frequency that is determined by their size. If they are exposed to ultrasound waves of this frequency they oscillate in a non-linear fashion and return an ultrasound signal that contains not only the transmitted frequency ('fundamental' frequency), but also 'harmonics' of this frequency (Wei et al, 1997). If, for example, the transmitted frequency is 3 MHz, reflected frequencies are 3, 6, 9 and 12 MHz and so on. By coincidence, bubbles of the size used as contrast agents (around 3 μm) have a resonance frequency similar to the frequencies used in echocardiographic imaging of around 3 MHz.

This observation led to the development of ultrasound machines that transmit at one frequency and receive selectively at harmonics of that frequency. Other frequencies are filtered out, resulting in a strong signal from the resonating microbubbles. This technique is called harmonic imaging and is routinely used in conjunction with contrast imaging.

TISSUE HARMONIC IMAGING

When the harmonic imaging mode on ultrasound machines was used in imaging without contrast agents, it was again observed by chance that the image quality of the returning signal could be improved in harmonic compared with fundamental mode. This led to the development of tissue harmonic imaging.

Harmonic signals in tissue occur as a consequence of non-linear propagation of the ultrasound wave as it travels through tissue. The peaks of the ultrasound beam travel slightly faster than the troughs, resulting in a change in the shape of the ultrasound wave and the creation of harmonic signals (Thomas and Rubin, 1998).

These signals are used selectively for tissue harmonic imaging. The quality of these images is improved mainly for two reasons. First, the distortion of the ultrasound wave and hence the harmonic signal becomes stronger with increasing distance from the transmitter/receiver. As a consequence, there is almost no harmonic signal at the origin of the ultrasound wave, reducing artefacts from skin and ribs. Second, the interference from the side lobes of the echocardiogram, which are responsible for poor image quality in the far fields with conventional imaging, is reduced because the side lobes return a low harmonic signal. As a result of these factors, tissue harmonic imaging produces a much cleaner image compared with fundamental imaging, particularly in patients who are difficult to image because of obesity or lung disease. This has had a significant impact on routine echocardiographic imaging.

Most current ultrasound machines are equipped with both fundamental and harmonic imaging modes. *Figure 2* shows an example of images of the same patient acquired in fundamental and harmonic imaging modes.

There are some disadvantages of tissue harmonic imaging. Resolution is lower than in fundamental imaging, as the harmonic signal from tissue is approximately 10 000 times weaker than the fundamental signal. The depth of harmonic

imaging is limited to approximately 10 cm. Beyond that depth, images are usually blended with fundamental images. Another potential problem is that axial distortion can make structures like the mitral valve leaflets appear unnaturally thickened.

ACOUSTIC QUANTIFICATION®, COLOUR KINESIS® AND DOPPLER TISSUE IMAGING

In addition to harmonic and contrast imaging, the manufacturers of ultrasound machines have developed other techniques to improve endocardial edge detection. These techniques vary between different manufacturers.

Acoustic quantification®

This technique uses a raw acoustic radio frequency signal with a band width of 120 dB to distinguish the endocardium–blood border. The measurement points are integrated on-line into the two-dimensional (2D) image and the endocardial border is automatically traced in a region of interest (Perez et al, 1992).

Colour kinesis®

Colour kinesis® is based on acoustic quantification. The endocardial border is detected every 40 ms and coded with a specific colour. The width of each colour shade correlates with the distance travelled by the endocardial border during the 40 ms. The colour overlay is superimposed on the 2D echocardiographic image and displayed in real time (Lang et al, 1996). This technique can help in the assessment of regional wall motion and is useful in stress echocardiography.

Doppler tissue imaging

Doppler tissue imaging is used to assess the velocities at which heart valves and myocardium move in the cardiac cycle (García-Fernández et al, 1998). It is based on the same principles as conventional colour Doppler imaging of blood flow and makes use of two main differences between the signal from blood and tissue. First, blood flow velocities in the ventricular cavities are relatively high and reach 100–150 cm/s. The myocardium and valves move at much lower velocities of up to 10 cm/s. Second, the amplitude of the Doppler signal from the myocardium and the valves is significantly higher than the blood velocity signal. For Doppler tissue imaging, the lower velocities and higher amplitudes are selected and the higher velocities and lower amplitudes caused by blood flow are filtered out. The Doppler tissue signals can then be superimposed on 2D or M-mode images and displayed in real time (*Figure 3*). In tissue Doppler imaging in M-mode, the high temporal resolution of M-mode allows the assessment of myocardial movements and intramyocardial velocity gradients.

In pulsed tissue Doppler imaging, short pulses of ultrasound are transmitted and the reflected signals detected after a set time delay. This allows the identification of velocities at specific regions of interest within the myocardium and a more accurate, at least semiquantitative detection of regional wall motion velocities.

The main clinical application for tissue Doppler imaging is in the assessment of ischaemic heart disease. Early changes in the process of this disease include abnormalities of regional diastolic function which can be assessed regionally and quantitatively by tissue Doppler imaging (García-Fernández et al, 1998).

Another clinical use for Doppler tissue imaging is the evaluation of depolarization. Early abnormal depolarization, as seen in Wolff–Parkinson–White syndrome, produces early velocity signals that can be detected with

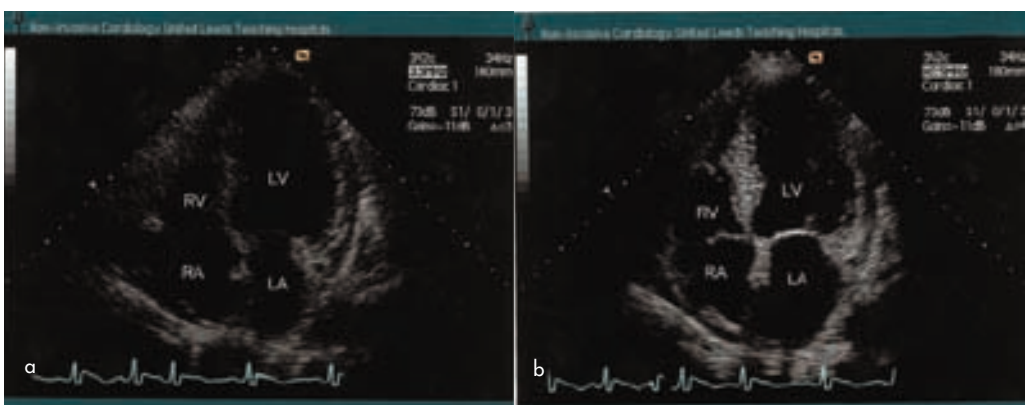

Figure 2. Apical 4-chamber view of a routine echocardiogram (a) with conventional, fundamental imaging and (b) with tissue harmonic imaging. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

tissue Doppler imaging, provided a sufficiently high frame rate is used (Nakayama et al, 1998).

THREE-DIMENSIONAL ECHOCARDIOGRAPHY

Over the past decade, three-dimensional (3D) echocardiography has developed into a practical and useful new application of transthoracic and transoesophageal echocardiography (De Castro et al, 1998). This development has been made possible by the rapid advances in computer technology that have allowed extensive post-processing of echocardiographic data.

At present, 3D echocardiography relies on the reconstruction of multiple 2D images. The equipment used typically consists of a conventional echo machine, a motor device that moves a conventional 2D transducer (either transoesophageal or transthoracic) and a computer to control the motor device, image acquisition and display.

Image acquisition must ensure that the images can be related to one another in space and time for post-processing. Different techniques are used to achieve this, most of which rely on electrocardiographic and respiratory gating combined with sequential image acquisition in multiple planes. In sequential imaging, images are acquired in a linear, fan-like or rotational mode. In rotational image acquisition, for example, images can be acquired at steps of 2° rotation from 0° to 180°, so that after 90 image acquisitions a data set of the whole heart has been acquired. The computer then reconstructs this data set and displays a 3D image.

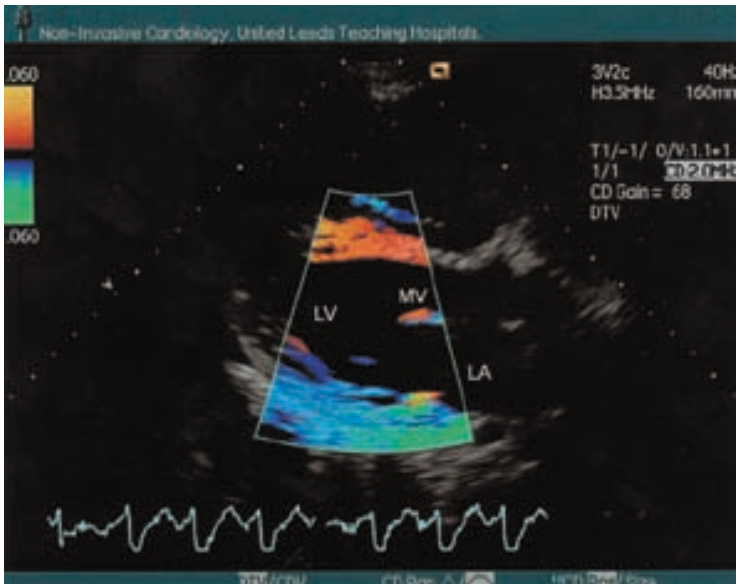

Figure 3. Doppler tissue images of a normal subject demonstrating movements of the mitral valve, the septum and the posterior left ventricular wall. LA = left atrium; LV = left ventricle; MV = mitral valve.

Post processing of these images allows the selection of regions of interest such as heart valves or chambers. These can then be examined in three dimensions and in any orientation desired (*Figure 4*). Images can be rotated and viewed from above or below. Special views such as 'surgical views' can be reconstructed.

Clinical indications for 3D echo include imaging of valvular heart disease, in particular preop-

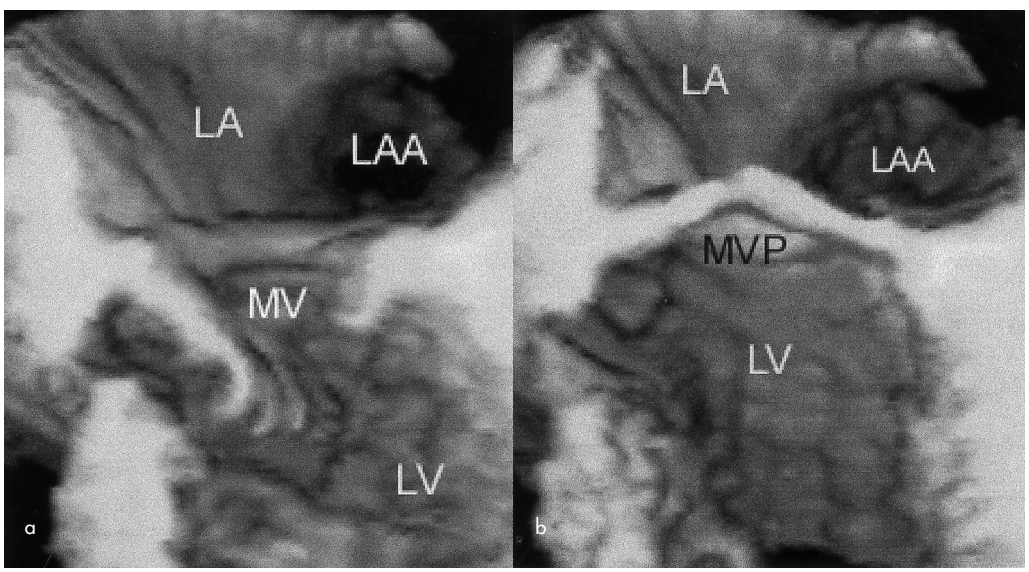

Figure 4. Three-dimensional echocardiographic images of the left ventricle and the mitral valve in (a) diastole and (b) systole. The mitral valve can be seen to prolaps into the left atrium in systole. MV(P) = (prolapsing) mitral valve; LA = left atrium; LAA = left atrial appendige; LV = left ventricle.

erative assessment of valvular anatomy, imaging of congenital heart disease (Salustri et al, 1995), cardiac masses (Kupferwasser et al, 1994) and 3D assessment of valvular flow jets (Delabayas et al, 1995).

The most common practical problems with 3D image acquisition at present are movement artefacts during image acquisition and finding suitable acquisition windows in transthoracic imaging (see 'Future perspectives' below).

STRESS ECHOCARDIOGRAPHY

Improvements in general ultrasound imaging, as described above, have had a major impact on stress echocardiography, which in the past often suffered from poor image quality and hence difficult image interpretation. Today, with the use of contrast agents, harmonic imaging, colour kinesis or tissue Doppler if indicated, good quality ultrasound images can be acquired from the vast majority of patients, making stress echocardiography a reliable diagnostic tool in cardiology (Yvorchuk et al, 1996).

In principle, images are acquired from standard views at rest and after physical or pharmacological stress. Systolic myocardial thickening and wall motion in predefined segments of the ventricle are assessed and compared before and after stress. Flow-limiting coronary stenoses cause wall motion and wall-thickening abnormalities in the affected myocardial segments.

In pharmacological stress echocardiography, images can be acquired at inotropic and chronotropic doses of agents such as dobutamine or arbutamine. Myocardial contractility increases with low doses of these agents in areas of viable but chronically downregulated (so-called 'hibernating') myocardium. With high doses, contractility decreases in these areas as well as in those supplied by stenotic coronary arteries. Other pharmacological agents used in stress echocardiography are the vasodilators dipyridamole and atropine.

At present, interpretation of stress echocardiographic images is visual and qualitative. Using tissue Doppler imaging, sample volumes can be placed in the myocardial segments and their movement plotted over the cardiac cycle at rest and with stress. This technique may bring quantitative methodology to stress echocardiography.

MYOCARDIAL PERFUSION IMAGING

The assessment of myocardial perfusion with echocardiography is still undergoing clinical evaluation and is not currently an established technique, but the initial results are encouraging. As the intravascular rheology of ultrasonic contrast microbubbles is similar to that of red blood cells, they remain entirely within the intravascular space and can provide unique information about the myocardial microcirculation (Skyba et al, 1996). Clinically, this can be used to obtain information about microvascular integrity following an ischaemic episode. In the so-called 'no-reflow' phenomenon, for example, myocardium remains underperfused as a result of microvascular damage after an occluded coronary artery is recanalized.

As described above, imaging of myocardial perfusion is complicated by acoustic shadowing and contrast microbubble destruction with conventional imaging techniques. A number of additional techniques have been developed to allow imaging of the myocardial distribution of contrast agents:

Intermittent or transient response imaging

The extent of microbubble destruction is proportional to the power ('mechanical index') of the transmitted ultrasound signal and the duration of microbubble exposure to ultrasound. The destruction of microbubbles can hence be limited by reducing the power of the transmitted ultrasound signal or by reducing the time the bubbles are exposed to ultrasound. In intermittent imaging, ultrasound is transmitted only once every few (4–8) cardiac cycles. The pause in transmission allows microbubbles to redistribute in the myocardium (Porter and Xie, 1995).

Amplitude mapping (power Doppler® and power harmonic imaging®)

Amplitude mapped images are generated by coding the colour Doppler map to the strength (power) of the returning ultrasound signal rather than its frequency as in conventional Doppler imaging. This technique can also be used in contrast echocardiography because the destruction of microbubbles creates a high-amplitude signal as the bubble disintegrates. This signal can be detected by a Doppler processor and displayed as an amplitude-mapped signal (Tiemann et al, 1997).

Power harmonic imaging uses only the harmonic components of this returning signal for image reconstruction, similar to harmonic imaging as described above.

Pulse inversion imaging®

In pulse inversion imaging, the standard ultrasound pulse is followed immediately by a second pulse of inverted polarity. The two

returning signals are detected separately, superimposed in the ultrasound processor and the resulting image is displayed. All linear interactions, as in tissue, return two mirror images and are therefore cancelled out in image reconstruction. The non-linear components of the signal returning from oscillating microbubbles, however, result in differences between the two images and the combined image displays these differences. An unwanted consequence of pulse inversion imaging is that the frame rate is reduced, as two ultrasound pulses are sent for each imaging frame.

FUTURE PERSPECTIVES

Myocardial perfusion imaging is currently being evaluated in clinical studies that will establish its role and potential shortcomings in clinical practice and compared with nuclear isotope perfusion studies.

Three-dimensional echocardiography is developing further with advancing computer technology and will become faster with improved image quality. Currently multi-plane transducers are being developed that allow imaging of the whole heart in one cardiac cycle ('real-time 3D imaging'). This would reduce imaging time dramatically and eliminate the movement artefacts in image acquisition.

Coronary flow reserve can potentially be assessed with cardiac ultrasound, using contrast echocardiography (Caiati et al, 1999).

Uses of ultrasound agents outside cardiology include the possibility of drug delivery in microbubbles. Microbubbles containing drugs could be injected intravenously and then be destroyed by ultrasound waves at a very specific target site, e.g. a tumour, releasing the drug.

Conflict of interest: none.

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KEY POINTS

- A number of new developments in echocardiography are becoming available in routine clinical use.
- Contrast agents improve image quality in patients with suboptimal conventional images and increase diagnostic yield in stress echocardiography.
- Harmonic imaging improves image quality in contrast echocardiography and in tissue harmonic imaging.
- Tissue Doppler provides information about regional myocardial wall motion and can aid early diagnosis of ischaemic heart disease.
- Stress echocardiography has become a reliable diagnostic tool in cardiology as a result of improvements in image quality.
- Three dimensional echocardiography is a valuable tool for imaging of cardiac structures in three dimensions and in any projection required.
- Myocardial perfusion imaging is a promising new development, which is currently being evaluated.