Review article

Use of ultrasound in decompression research

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Abstract

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Techniques for ultrasonic assessment of decompression stress continue to evolve in concert with technological development. While aural Doppler remains a staple, imaging techniques are gaining in popularity. Current initiatives to increase the resolution of three-dimensional and dual-frequency imaging hold promise to expand our monitoring capabilities. An appreciation of the limitations and strengths of ultrasonic assessment is important to interpret existing work on decompression and to appropriately design new studies.

The formation of gas emboli (bubbles) in response to decompression was first observed in the eye of a snake by Robert Boyle almost 350 years ago. Forming in a variety of tissues, bubbles may be transient or persistent, varying with the exposure and the individual, and potentially capable of exhibiting both mechanical and biochemical effects. While the exact role bubbles play in the development of decompression sickness (DCS) remains to be determined, their formation is generally accepted as an indicator of decompression stress.

Ultrasound transducers emit sound waves (acoustic energy) when excited electrically. Sound waves transmitted through the body generate echoes when changes in density are encountered. Bubbles are easily identified because of the highly reflective nature of the liquid–gas interface. Echoes return to the transducer receiver and the acoustic energy is transformed back into electrical energy, processed, and presented aurally in the case of Doppler devices and visually with two-dimensional imaging devices.

Doppler

Doppler ultrasound is the principal tool for monitoring decompression stress outside of symptom development. Doppler was first used to detect bubbles circulating in blood more than 40 years ago.[1] The beginnings of formalised techniques to detect decompression-induced bubbles were reported in 1968.[2,3] A more quantitative categorical grading scale described by Spencer and Johanson in 1974 is still in use today (Table 1).[4]

Early measures were made with subjects remaining at rest. The Spencer and Johanson protocol was subsequently refined to include ‘at rest’ and ‘movement’ monitoring.[5] Movement promotes transient increases in identifiable bubble activity, potentially increasing the sensitivity of the monitoring. The most commonly employed movement was a deep knee bend.[6] Concerns over the aggressive physical effect and the difficulty in holding the transducer in position resulted in a range of alternatives being used. We currently employ seated, sequential limb motion as the movement case.[7] Upon the completion of ‘at rest’ measurement, subjects are asked to complete three cycles of movement with each limb. Each movement is supposed to involve every joint and contract every muscle in the limb during the approximately 1.5 sec flexion/extension cycle. Muscular effort is a combination of isometric and isotonic contractions. The technician listens for an audible change in the cardiac rate to confirm a satisfactory degree of effort. Monitoring continues for a minimum of 10 cardiac cycles or until the heart rate returns to approximately baseline before movement of the next limb is signaled. This approach to the movement case provides a moderate physical effort, makes it easier for the technician to conduct the monitoring, and provides additional information on regional origins of any bubbles.

The Kisman–Masurel method was developed after the

Table 1
Spencer scale of Doppler-detected bubbles[4]

Grade	Definition
0	No bubble signals
I	Occasional bubble signal; great majority of cardiac cycles signal-free
II	Many but less than half of the cardiac cycles contain bubble signals
III	All cardiac cycles contain bubble signals, but not obscuring signals of cardiac motion
IV	Bubble signals sounding continuously throughout systole and diastole and obscuring normal cardiac signals

Spencer scale to evaluate bubble signals on a 0–4 scale for each of three distinct parameters: frequency, percentage/duration and amplitude.[8] Frequency characterised the number of bubbles per cardiac period. Percentage/duration characterised the percentage of cardiac periods with specified bubble frequency at rest and following movement, respectively. Amplitude characterised the bubble sounds compared to normal background cardiac sounds. The parameter scores combine to yield a single 0-IV grade that includes '+' and '–' modifiers on non-zero values (note: there is no '+' associated with grade IV bubbles). Kisman–Masurel grades can be converted to equivalent Spencer grades but the reverse is not possible. The Kisman–Masurel scale provides a more sophisticated and subtle gradation of bubbles, but it requires more time to train and maintain the proficiency of technicians. While the Kisman-Masurel scale is favoured by some research groups, the Spencer scale is the most widely used.

Learning to record interpretable Doppler signals is relatively straightforward. The challenge comes in making the interpretation, and, even more so, in reliably interpreting the signals in real time. Sawatsky and Nishi reported on inter-rater reliability among a well-trained group of technicians.[9] They determined that good agreement could be achieved, particularly with Spencer grade III or IV bubbles, but that the training to get to this point can take months.

Common sites for Doppler monitoring include the pulmonary artery, subclavian vein and carotid artery. Less common sites include the femoral vein and inferior vena cava. Precordial monitoring of the pulmonary artery is probably the single best monitoring choice. It provides a single sampling site of all blood returning from the body en route to the lungs. Developments in transducer technology have made it easier to reliably capture pulmonary artery signals in subjects with a reasonable range of anatomical variation. The precordial site is also the only one that is truly compatible with the Spencer or Kisman–Masurel grading scales. Grades III and IV are determined by the interaction between bubble signals and background heart sounds. Heart sounds cannot be discerned at most other monitoring sites. The limitation of focusing on a single site is that some transient bubbles that might be identified at other sites could be missed.

Doppler bubble detectors can employ continuous wave (CW) or pulsed wave (PW) technology. CW systems use two or more transducers, one transmitting and one or more receiving. All moving particles in the beam are detected. Key advantages of CW systems are simplicity and relatively low cost. PW systems use a single transducer that alternates between transmitting and receiving modes, allowing calibration so that only signals originating from a target depth are registered. PW systems require more complicated electronics and are more expensive than CW. Calibration for individual subjects can be effective, but this may not be feasible if a unit must be used to scan multiple subjects sequentially.

Two-dimensional echocardiography

Two-dimensional echocardiography combines ultrasound imaging and Doppler flow detection technology to provide a visual display of scans. 'Gain' controls adjust the amplification of returning echoes to optimise the image, balancing sensitivity and visual clutter. Originally, transducers transmitted and received the same frequency. More recently, transducers have been developed to transmit one frequency and receive a higher harmonic frequency. The transmitted frequency is the fundamental or first harmonic; the received frequency is an integer multiple of the fundamental frequency. For example, a device might transmit a 2 MHz fundamental frequency and receive a 4 MHz second harmonic frequency. Such 'harmonic processing' improves image resolution and is generally employed as a standard when available.

Two-dimensional transducers are available to conduct transoesophageal echocardiographic (TEE) or transthoracic echocardiographic (TTE) scans. The resolution of TEE is generally greater than TTE, but practical issues of placing and leaving a probe in the oesophagus make TTE a more attractive alternative for the prolonged or repeated measurement expected for decompression research and thus the focus of this discussion.

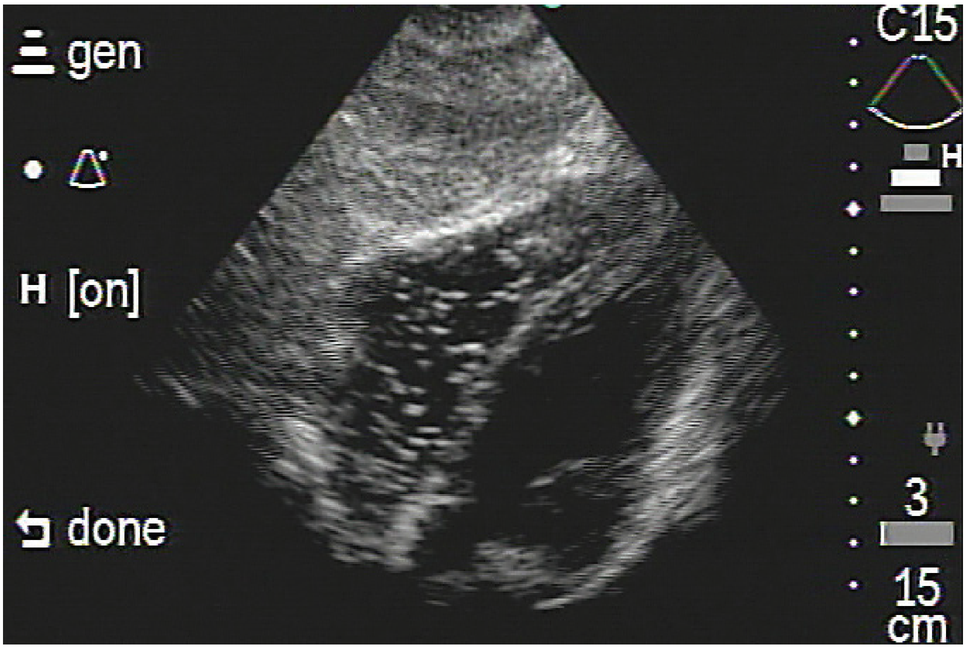
TTE imaging can provide a cross-sectional view of multiple heart chambers and major vessels (Figure 1). Apical or subcostal long axis views can allow good visualisation of the right atrium and ventricle to monitor the blood volume prior to it entering the pulmonary artery. In this way, TTE can serve as a tool similar to Doppler. Visual grading systems have been developed to conceptually match the Spencer scale for Doppler signals. The highest degree of quantification is found in the Eftedal and Brubakk scale (Table 2).[10,11] When developed, it was expected that grades 0–4 would apply to human subjects; grade 5 had been observed only in animal subjects at the time. Boussuges et al described a dual-use scale to reconcile Doppler and two-dimensional image scoring (Table 3).[12] The scale paralleled the established 0–IV Spencer range.

The Eftedal and Brubakk scale provided more objective criteria for grading than the scale of Boussuges et al. This

Table 2
Two-dimensional echocardiographic imaging scale[10,11]

Grade	Definition
0	No observable bubbles
1	Occasional bubbles
2	At least one bubble every four cardiac cycles
3	At least one bubble every cardiac cycle
4	At least one bubble·cm^{-2} in every image
5	'White-out', single bubble cannot be discriminated

Figure 1
A two-dimensional long axis view of the four chambers of the heart (transducer positioned subcostally). Visible structures include nearly complete chamber margins (wall and septum) of both atria and ventricles, and both mitral and tricuspid valves. The valves are better seen in motion. The image is inverted, with the atria at the bottom. A substantial number of bubble signals are evident on the right side of the heart (appearing on the left side by convention). No bubble signals appear in the left heart.



is important in order to facilitate inter-rater reliability. The inclusion of a sixth grade in the Eftedal and Brubakk scale was also a positive step, recognising the capacity of two-dimensional echo to be more sensitive to differences at high bubble concentrations than aural Doppler. The magnitude of the jump between the definitions of grade 4 and grade 5 scores, however, was larger than necessary. Scale references are provided on the displays of most two-dimensional imaging systems to facilitate rapid density estimates. It is reasonable for a trained technician to differentiate an intermediate state between the top two Eftedal and Brubakk scores.

A new grading scale, described in Table 4, employs objective criteria and accommodates the capability of two-dimensional imaging systems to differentiate between high bubble loads. The grading for this proposed scale is based on the peak group of 10–30 consecutive cardiac cycles for resting measures and the peak group of 10 consecutive cardiac cycles following movement. 'New' bubbles are specified since fractional cardiac ejection may leave some bubbles within the ventricle for multiple cardiac cycles. Views should

Table 3
Dual-use Doppler and two-dimensional echocardiographic imaging scale[12]

Grade	Definition
0	Complete lack of bubble signal (two-dimensional echo [2D] and pulsed wave Doppler [PW])
1	Occasional bubbles, the great majority of cardiac periods are free of bubbles (2D & PW)
2	Flow of bubbles (2D), many but less than half of the cardiac periods contain bubble signals singularly or in groups (PW)
3	Flow of bubbles (2D), majority of the cardiac periods contain bubble signals singularly or in groups (PW)
4	Bubbles fill cardiac chambers (2D), all the cardiac periods contain bubble signals in groups (PW)

Table 4
Proposed new two-dimensional echocardiographic imaging scale (see text for more detailed explanation)

Grade	Definition
0	No observable bubbles
I	Occasional bubbles
II	At least one new bubble every four cardiac cycles
III	At least one new bubble every cardiac cycle
IV	At least one bubble·cm^{-2} in every image
V	At least two bubbles·cm^{-2} in every image
VI	At least 80% of visible lumen obscured by bubble cloud; single bubbles cannot be discriminated

be optimised so that the maximum cross-sectional lumen is visible in the image field and reference structures are clearly discernible. The target for visualising reference structures for the apical/subcostal views include: > 80% of ventricular margins (septum and wall), mitral valve, and > 25% of atrial lumen area. The proposed scale is directly comparable to the Spencer Doppler scale only for grades 0 and I bubble signals. The new scale could be applied, however, to Doppler signals through grade III. The scale would allow greater differentiation of high bubble loads than is possible with the Spencer scale. The need for the additional increment will grow as the resolution of imaging systems continues to improve. The use of Roman numerals is preferred to remind users that the grade categories are non-linear and that scores cannot be averaged.

One of the ways that two-dimensional imaging surpasses Doppler technology for decompression studies is in the ability to directly monitor the left side of the heart. Left ventricular gas emboli (LVGE) are in a position to be distributed systemically and are implicated as causative agents in neurological DCS. While the absolute risk of DCS is not known, the conservative approach during altitude decompression research trials is to establish the presence of LVGE, regardless of symptom status, as a test-termination criterion. Researchers at the Brooks Air Force base in New Mexico may have been the first to use TTE to simultaneously monitor gas phase on the right side of the heart (RVGE) and LVGE during decompression studies. They used a powerful clinical-standard TTE machine positioned outside the chamber with a transducer introduced to the chamber through a wall penetrator and deployed by either a robotic arm or an inside technician. In our laboratory, we use Doppler equipment to monitor RVGE and portable TTE devices that reside within the chamber for use by inside technicians to monitor for LVGE during altitude decompression studies. We have observed LVGE in two cases out of more than 700 person-exposures monitored. Both subjects were immediately compressed to ground level and remained asymptomatic.

The future of ultrasonic assessment

THREE-DIMENSIONAL ECHOCARDIOGRAPHIC IMAGING

One of the limitations of two-dimensional imaging is that bubbles passing above or below the focal plane may be missed during scanning. Identification requires bubble targets to pass close to or through the plane. Three-dimensional echocardiographic imaging has the potential to improve current capability. Current systems can capture 60° x 15° sections that are indexed to the cardiac cycle. A gated scan can capture four cardiac cycles and accumulate a 60° x 60° wedge that can be stored electronically and then manipulated for subsequent study. The volume can be progressively sliced in any plane to capture target structures. The resolution of the current systems is lower than that achieved with two-dimensional settings, but the potential for future improvements is promising.

DUAL-FREQUENCY ULTRASOUND

Another limitation of ultrasonic assessment of bubbles is the focus on intravascular locations. The ability to monitor extravascular locations could provide additional information. Dual-frequency ultrasound was proposed to overcome this limitation more than 20 years ago.[13] The approach requires two transducers: one employing a pump frequency to stimulate existing bubbles to vibrate, and a second employing an image frequency to capture the vibrating bubbles.[14] Frequency sweeping, discussed 30 years ago, could provide size information.[15] The resonance frequency of a bubble is inversely proportional to its diameter. Sweeping through a frequency range could provide the size information not available with current Doppler, two-dimensional or three-dimensional technologies. Practically technical problems are still being overcome but these techniques may ultimately provide reliable measures of the presence and sizes of bubbles in extravascular locations not in close proximity to bony structures.

Limitations and uses of ultrasound measures

The role that bubbles play in the development of clinical DCS is not clear. Bubbles can be found much more often than DCS following decompression. The interpretation of bubble data is generally based on relatively little DCS.[6,16] The highest incidence of DCS is seen with altitude studies. A review of altitude DCS cases noted that the absence of VGE was highly correlated with an absence of DCS symptoms, with a negative predictive value of 0.98.[17] Conversely the presence of Spencer grade III and IV VGE had a positive predictive value for DCS of only 0.39.[17] The data are more limited for diving decompression but the observed relationship is similar. The absence of bubbles is more strongly associated with decompression safety than the presence of even high grade bubbles is associated with DCS. It is important to appreciate, however, that this observation may be partially confounded by the limitations of our monitoring capability.

The chief limitation is that standard monitoring is limited to a small number of intravascular sites. It is possible that the presence of bubbles in unmonitored vascular or extravascular locations may be important. Instrument resolution is also an issue. While various authors have speculated on the size of decompression-induced bubbles that may be identified, there is little to validate these estimates or to document the size range of decompression-induced bubbles. At the small size extreme, the reflectivity of a 2.0–5.0 µm second-generation, stabilised gas microsphere may be quite different from that of a spontaneously arising decompression-induced bubble. It is possible that the latter bubbles are far less visible. The monitoring schedule may also be problematic. Inter-measurement intervals of 15–60 min are reported.

Much can be missed during the unmonitored interval, particularly with less frequent sampling. Variations in monitoring protocols can also have an influence. The specifics employed to generate a movement case vary substantially in the magnitude and duration of physical effort and motion.[7,18] Some investigators choose to report at-rest data only.[11,18] At-rest monitoring is expected to underestimate grades achieved following movement. Finally, the large inter-individual variability in bubble formation can adversely affect the outcome of any but the largest studies.

Advancement in technology and methodology may ultimately strengthen the measurable relationship between observable bubbles and DCS. Even without that achievement, bubble data will remain attractive to those institutions uncomfortable with experimental studies that carry a clear expectation of generating some DCS. While bubble data cannot currently be used to determine absolute decompression stress, they can be used to estimate relative stress. Repeated measures designs with subjects as their own controls can be used to address a number of questions while restricting exposures to those with less risk of DCS.

Conclusions

Techniques for ultrasonic assessment of decompression stress continue to evolve. While aural Doppler remains a staple, imaging techniques are gaining in popularity. Current initiatives to increase the resolution of three-dimensional and dual-frequency imaging hold promise to expand our monitoring capabilities. An appreciation of the limitations and strengths of ultrasonic assessment is important to interpret existing work and to design appropriate studies.

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