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# Velocity of ultrasound as an indicator of bubble content

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Hills BA, Kanani B, James PB. Velocity of ultrasound as an indicator of bubble content. Undersea Biomed Res 1983; 10(1):17–22.—The principle has been evaluated of detecting stationary tissue gas bubbles simply by measuring the velocity of ultrasound. Agar gel has been used to simulate tissue. At wavelengths appreciably larger than bubble diameter (at least 10:1) the ultrasound seems to "view" the gel-gas mix as though it were one medium, when the velocity of pulsed ultrasound is reduced approximately as predicted theoretically from the decreased modulus. The velocity of sound shows an appreciable (10%) decrease for only 0.65% of the gas phase as bubbles of 20–200 μm diameter and drops to about one-third of the bubble-free value for only 0.79% gas by volume—values well in excess of those theoretically predicted to elicit the symptoms of limb bends. These large changes in the velocity of sound can probably be measured with a much less expensive unit than the one used in this study and would seem to warrant further investigation as a very simple method for detecting bubbles in tissue—whether intravascular or extravascular.

bubble detection
decompression sickness
ultrasonic monitoring
velocity of ultrasound

It is particularly desirable to know when gas starts to separate from solution in the tissues of a diver, caisson worker, or aviator during decompression. Various noninvasive approaches have been used, including radiographs (1, 2), electrical conductance (3), and numerous applications of ultrasound. Ultrasonics would appear the most convenient to use under operational conditions, and some most practical Doppler units have been produced for detecting total venous bubbles as recorded when monitoring in the precordial position (4, 5). The Doppler principle is limited, however, to the detection of moving bubbles, yet in several categories of decompression sickness (6) the symptomatic bubbles probably lie in extravascular sites and are therefore stationary. Whatever the controversies between regarding intravascular or extravascular bubbles as the cause of each of the various categories (7) of decompression sickness, it is highly desirable to have a simple means of detecting the gas phase in both locations.

The early attempts to image total tissue gas consisted of studying the attenuation of a transmitted wave (8–10) or utilizing the "back-peak" method of looking at the reflections (11, 12). The early approaches produced rather unstable patterns from which it was difficult to decide what was happening in the tissue and which reflections referred to tissue boundaries. These instabilities have been largely overcome in recent developments (13, 14), but the apparatus now becomes too complex or too sensitive for routine use outside of the laboratory.

In searching for a very simple device to monitor total tissue gas—both extravascular and intravascular—there can be one property of ultrasonic transmission that may have escaped exploitation for this purpose. It is well established that the velocity of sound is equal to $\sqrt{E/\rho}$ where $\rho$ is the density of the medium and $E$ is its bulk modulus. If gas is now formed in the medium, it will have little effect on $\rho$, but a minute amount can cause a very large change in the overall value for $E$, since gas is so much more compressible than any solid, liquid, or tissue. The velocity of sound is then determined by effective material parameters (15). However, for the sound waves to react to the bubble-pervaded tissue as though it were one medium and not two, their wavelengths need to be large relative to the diameters of the individual bubbles (16)—probably at least 10:1. This requires rather lower frequencies than currently in vogue. We have therefore studied the velocity of ultrasound at 1.5 MHz in gels containing microbubbles of the order of 20–200 μm diameter—as found in vivo following decompression (17, 18). The frequencies also need to differ from the resonant values at which attenuation by the bubbles (19, 20) would greatly diminish the transmitted signal.

## METHODS

### Principle

When ultrasound is transmitted across tissue it can undergo many partial internal reflections at structural boundaries as well as at gas boundaries, so that interpretation of the peaks in the reflected sound returned to the transducer can become very difficult. The same disadvantages apply to sound transmitted from a "transmitting" transducer to a "receiving" transducer—with one exception. This exception is the unreflected sound that can easily be recognized as the first to reach the receiver and, thus, the first peak seen on the oscilloscope. Hence in our approach the principle has been adopted of simply placing the transmitting and receiving transducers a known distance apart and timing the arrival of the first sound emitted in the pulse irrespective of its attenuation by intervening tissue or gas boundaries. This enables the velocity of sound to be determined very easily.

The question then to be answered is whether this velocity will vary as predicted by $\sqrt{E/\rho}$ when microbubbles are present or whether the ultrasound will view the mixture as two phases, each with its own velocity of transmission. To answer this question, tissue has been simulated by agar solution in which microbubbles can be incorporated during gelation by adding tartaric acid and sodium bicarbonate, which react to liberate $CO_2$. The volume of this gas can then be varied by applying hydrostatic pressure to the whole system.

Sound with a velocity $(v)$ of 1482 m/s in water at 20°C (16) should have a wavelength ($\lambda$) of about 1 mm ($10^3$ μm) at a frequenty of 1.5 MHz. This is about 50-fold in excess of the diameter of typical extravascular bubbles reported to be of the order of 20 μm (17), when a 1.5-MHz probe should be adequate for evaluating this approach. This would not apply to larger bubbles in the range 100–200 μm, but these tend to be fewer and intravascular (6).

### Apparatus

The basic unit was a pulse-echo diasonoscope (Type II, Smith Industries, London, U.K.) operating at a frequency of 1.5 MHz with oscilloscope display of the transmitted ultrasound. The transmitting and receiving transducers were aligned 6.58 cm apart within the gel in a container that was placed in a pressure chamber.

### Materials

The gel was made by dissolving agar in well-stirred warm water (30 mg/liter), adding about 0.5 g each of tartaric acid and sodium bicarbonate to generate very small bubbles, and then cooling without stirring. The bubbles were sampled for size by diluting the gel samples in water and determining the diameter of the released bubbles from their terminal velocities (21). Bubbles were found to lie in the range of 20–200 μm diameter and any gel having larger bubbles was discarded.

Bubble-free agar gel was also made as a control.

### Procedure

Transmission time was measured by the location of the first peak on the oscilloscope for pulses of ultrasound passing from one transducer to the other. Dividing this time into the fixed spacing of 6.58 cm then gave the velocity of sound *(v)*. This was measured first on the bubble-free gel and then on a gel with bubbles <200 μm in diameter at room pressure. The measurement was then repeated at different absolute pressures. These readings were taken within 5 s of compression in order to ensure that volume changes were due to the pressure alone as opposed to dissolving gas. On account of the effects of surface tension, Boyle's law was not invoked to estimate the relative volume of the bubbles in the gel, but the absolute volume was determined directly by extracting a sample and placing it in a dilatometer—a device for accurately measuring small changes in volume. The relationship between volume change and pressure can then be used to determine the absolute volume according to standard practice (22). Thus the velocity of sound in the gel can be determined for different known absolute volumes of microbubbles in the gel.

## RESULTS

The velocity of sound was found to be 1530 ± 100 m/s in bubble-free agar and to show no detectable change for a gas-phase fraction up to 0.0061 (0.61%). Above 0.0061 the velocity of sound was found to fall appreciably, the results for the whole range being shown in Fig. 1. This curve proved remarkably reproducible in 10 runs on different gels with readings lying within the limits of experimental error also shown in Fig. 1. Each gel differed in bubble size distribution but all bubbles were within the diameter range, 20–200 μm, averaging 45 ± 21 μm by direct microscopic estimation.

There was some attenuation with higher gas content, but the first peak still remained clearly distinguishable.

## DISCUSSION

The results indicate that the velocity of sound in a gel has a remarkably stable and reproducible dependence on total gas content in bubble form, the ultrasound appearing to "view" the gel-air mixture as though it were one phase. The wavelength of the ultrasound for the 1.5-MHz frequency used would be 1000 down to 374 μm—still well in excess of extravascular bubble diameters of about 20 μm (17, 18) found in tissue following decompression. The experimental curve of velocity vs. total bubble volume (Fig. 1) essentially follows the relationship derived theoretically by Wood (16). This may seem a little surprising, since the validity of that theoretical relationship has been claimed (19) to be limited to frequencies below the

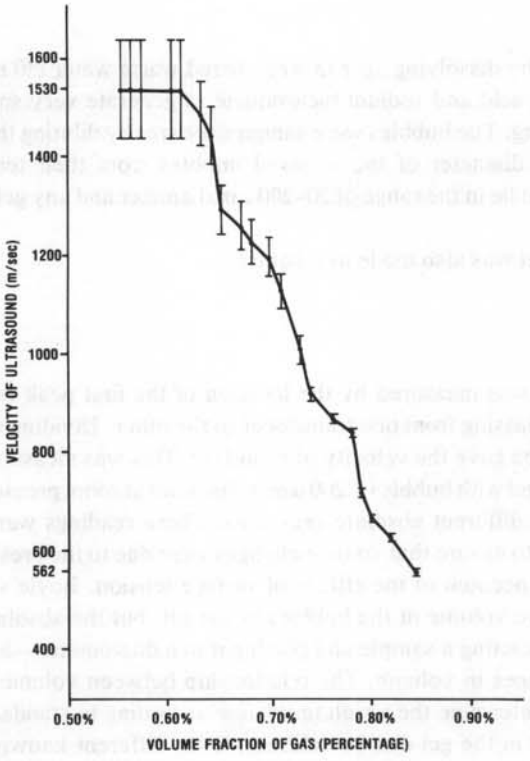


Fig. 1. Showing variation of velocity of ultrasound with the volume fraction of dispersed microbubbles of $CO_2$ in agar gel. Limits shown are the maximum estimated errors in the measurement technique.

resonant value for the bubbles, which might have exceeded the 1.5-MHz range used in this study.

The attenuation of the first peak, representing the first ultrasound in each pulse to reach the receiving transducer, may be due to bubble resonance or several other factors, such as diffraction of the sound. Some of this—especially the larger bubbles—may not regard the gel-air mix as one phase but as two, with consequent partial reflexion. It is a little surprising that this phenomenon has not been reported as a source of distortion in studies of ultrasonic imaging of tissue gas. Variable attenuation presents no problem, however, since there is ample signal to locate the first peak, whose actual magnitude is of no importance in the determination of bubble content by this method.

The interesting feature of the results is that, although the velocity of sound may not change for percentage bubble volumes up to 0.61%, it then falls precipitously, reaching about one-third of its original value at 0.85%. This finding would thus seem to offer considerable potential as a basis for designing a very simple device for monitoring tissue gas. The sensitivity of the velocity of sound to bubble content would seem to be so great that it should be very easy to detect a 2:1 reduction in the velocity of sound with a much simpler and less-expensive apparatus than used in this study. According to the results in Fig. 1, it takes only 0.79% of bubble volume to cause this reduction and only 0.65% to be detectable by this means, for agar, at least. This compares favorably with the tissue bubble volume predicted for a case of limb bends where a "weak" diver with a minimum bends depth (23) of 33 ft (1 atm) on air ($F_{N_2} = 0.8$) would precipitate a gas volume of $1 \times 0.8 \times 0.0125 \times 100\% = 1.0\%$, for a nitrogen solubility of

0.0125/atm at body temperature (6), assuming no residual supersaturation. Thus it should be possible to detect the formation of tissue gas by the decrease in the velocity of sound before it reaches the proportion at which it would elicit symptoms of decompression sickness. However, it must be pointed out that the above results refer to agar gel only and that the same dramatic decrease need not necessarily occur in tissue.

This preliminary study would thus indicate that the concept of detecting tissue gas by monitoring the velocity of sound is worthwhile developing as a very simple bubble detector for further evaluation in vivo. It has the particular advantage of detecting all tissue gas, whether stationary or moving, and could form the basis for an inexpensive device sufficiently robust for routine use offshore. One very practical advantage is that by simply measuring the velocity of sound, the device is not locating the gas and, therefore, not so hypersensitive to tissue movement as found with most imaging techniques.

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Hills BA, Kanani B, James PB. Vélocité des ultrasons comme indicateur du contenu en bulles. Undersea Biomed Res 1983; 10(1):17–22.—Le principe de la détection des bulles de gaz tissulaires immobiles par la simple mesure de la vélocité des ultrasons a été évalué. Le gel d'agar fut employé pour simuler le tissu. Quand la vélocité des ultrasons pulsés est réduite approximativement comme le prévoit théoriquement le modulus, en utilisant des longueurs d'ondes appréciablement plus grandes que le diamètre des bulles (≥ 10:1), les ultrasons semblent "voir" le mélange gel/gas comme un milieu homogène. On constate que la vélocité des ultrasons montre une diminution appréciable (10%) quand seulement 0,65% de la phase gazeuse existe sous forme de bulles de 20 à 200 μm de diamètre; celle-ci tombe à environ un-tiers de la valeur obtenue en l'absence de bulles quand seulement 0,79% du gaz par volume se trouve sous forme de bulles. Ces valeurs sont nettement supérieures à celles qui sont prévues théoriquement pour provoquer les symptômes de douleur aux extremités du corps suite à la décompression. Ces variations importantes de la vélocité des sons peuvent probablement être mesurées avec un appareil beaucoup moins cher que celui utilisé dans cette etude; elles semblent mériter d'autres investigations dans le future comme méthode très simple de la détection de bulles tissulaires, soit intravasculaires, soit extravasculaires.

vélocité
ultrasons
bulles

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