CEREBRAL EMBOLUS DETECTION USING DOPPLER ULTRASOUND

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Abstract – The majority of strokes are caused by emboli from distal sites blocking vessels in the brain. The discovery that emboli of various types can be detected using Doppler ultrasound as they are carried through the major cerebral arteries has led to a new field of study, which has considerable potential. The basic principle of detection is extremely simple: if an embolus backscatters more power than the surrounding blood in which it is moving, then the transient increase in power can be detected and measured. Questions that arise from this principle surround the circumstances under which such power increases can be detected, and whether the size and composition of the embolus can be inferred from such measurements.

The detectability of an embolus is determined by many factors including its size and composition, the ultrasound frequency, the size of the Doppler sample volume, the embolus trajectory and its interaction with the ultrasound beam. In general even relatively small gas bubbles will be detected, but some larger solid emboli may be missed. With regard to size and composition, several techniques have been suggested as being useful for characterising composition, and whilst in general considerable progress has been made in this direction there are still many challenges in distinguishing between large particulate emboli and small gaseous emboli.

1. Introduction

The standard TCD methodology for embolus detection consists of fixing a single element pulsed Doppler probe, with a frequency of around 2 MHz, over the temporal bone and adjusting its position, orientation, and sample volume depth to obtain a good signal from the blood flow in the ipsilateral   middle cerebral artery (MCA). Most frequently micro-embolic signals (MES) are 'detected' subjectively, although there have several attempts to automate the process [1,2]. Doppler audio signals from emboli are described as sounding like a 'snap', a 'chirp', or a 'moan' [3] and appearing on the Doppler sonogram as a short-duration unidirectional high-intensity signal within the Doppler flow spectrum, occurring at random within the cardiac cycle [4,5]. More objectively, they may be described as short-duration (usually between 8 and 80 ms) amplitude modulated sine waves that exceed the level of the background blood flow signal by between 3 dB and 60 dB [6]. An example of an MES that is approximately 10 dB higher than the background blood signal is shown in Fig. 1.
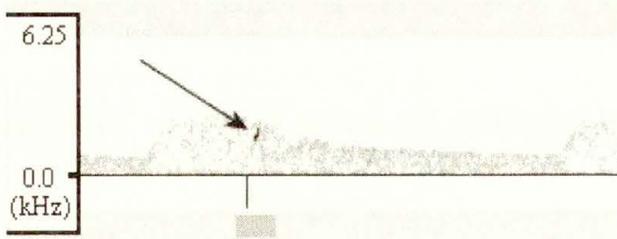
Fig. 1. Example of a sonogram of a Doppler signal recorded from the MCA of a patient in the recovery room following carotid endarterectomy. The MES appears as a region of increased Doppler power

2. Basic principles

The scattering of ultrasound by microemboli was first explored in detail by Lubbers and van den Berg [7], who calculated the scattering from gaseous microemboli, red blood cell aggregates (RCAs), and fat emboli flowing in blood. Their equations show that the backscatter cross-section (BSC) is a function of embolus size, ultrasound frequency, and the composition of both the embolus and its surrounding medium. It is not possible to measure the absolute power scattered by an embolus from within the body as the attenuation of the ultrasound by the tissue between the embolus and the transducer is unknown, and therefore it is necessary to compare the signal from the embolus with a known scatterer such as blood, if calibrated measurements are to be made. With this in mind, Moehring and Klepper [8] introduced the concept of 'embolus-to-blood ratio' (EBR), which they defined as:

$$EBR = \frac{\sigma_B + \sigma_E}{\sigma_B} = 1 + \frac{\sigma_E}{V\alpha} \qquad (1)$$

where σ_E and σ_B are the BSCs of the embolus and flowing blood within the sample volume respectively; V is the volume of flowing blood within the sample volume; and α is the volume backscatter coefficient of blood. Equation (1) has been evaluated as a function of embolic diameter for emboli consisting of RCAs and of air, for a typical geometry found in TCD studies [9] and the results plotted in Fig. 2a and 2b to illustrate a number of points relevant to detection of emboli. First, gaseous emboli always backscatter more power than similarly sized solid emboli, but very small gaseous emboli may backscatter similar amounts of power to large solid emboli. Second, it is possible to detect gaseous emboli with diameters as small as about 2 microns, but solid emboli do not backscatter significantly greater power than the surrounding blood unless they have diameters of the order of 80 to 120 microns. Third, backscattered power does not rise monotonically with size.
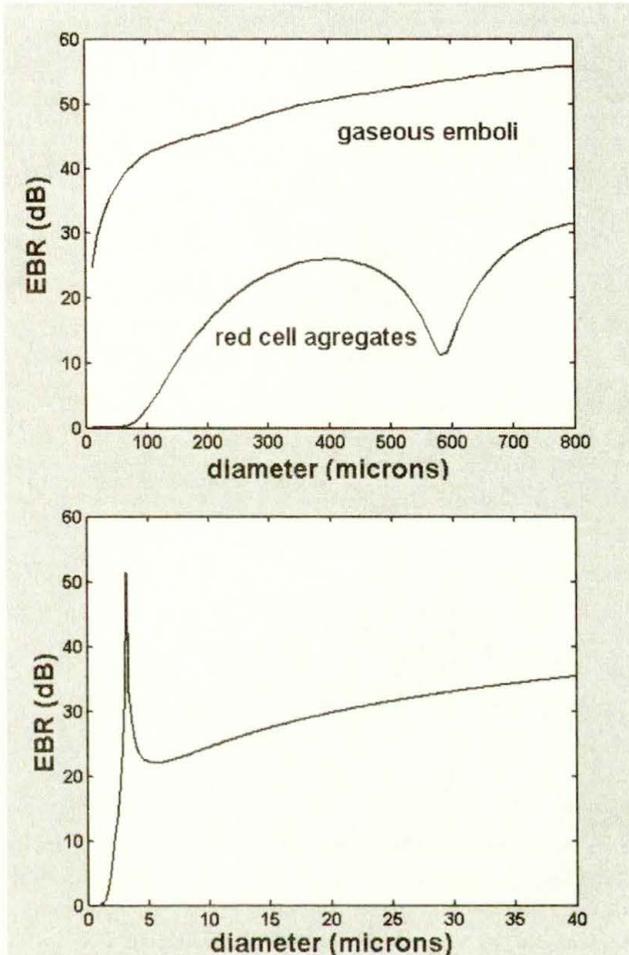
Fig. 2.a. EBR power ratios for air and RCA emboli plotted as a function of embolic diameter.
Fig. 2.b. Detail of EBR power ratios for small gaseous emboli.

3. Practical considerations

Ideally Doppler ultrasound studies would provide the clinician with information about embolus prevalence, composition and size, but there are difficulties both in making accurate measurements on MES and also in the interpretation of such measurements. In this section we discuss some of the practical difficulties of making measurements.

The first thing to note about Doppler embolic signals is that they are unlike typical Doppler signals from blood flow – in particular they exhibit very high dynamic ranges (a small solid embolus may exceed the background blood signal by only 6 dB, but a moment later a gaseous embolus may produce a signal 50 dB higher), and that they have very short durations (often of the order of 10 to 20 ms).

Fig. 3 shows typical values of the measured EBR (MEBR) and durations from 849 embolic signals recorded during 17 carotid endarterectomies [6].
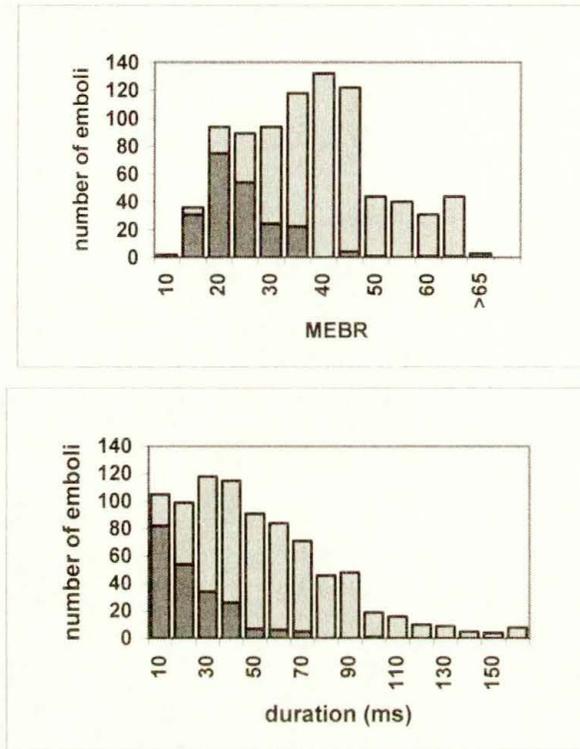

Fig. 3.a. Distribution of the MEBR values of 849 embolic signals recorded during 17 carotid endarterectomies. Dark shading indicates emboli detected during dissection, which can only be particulate in nature.

Fig. 3.b. Distribution of the durations of the signals from the same 849 emboli.

MES Dynamic Range

In general the instruments used for TCD work are relatively simple and cannot adequately cope with the large dynamic ranges involved, especially where gaseous emboli are present. Emboli with large BSCs cause overloading, particularly in the audio frequency stages of Doppler instrumentation and leads to several problems, which include the impossibility of estimating EBR, and the difficulty of distinguishing MES from artifact signals.

MES Duration

The short duration of embolic signals also poses some difficulties for measurements made using conventional FFT spectral analysis systems. Since some embolic events last less than 10 ms it is desirable to be able to make temporal measurements with a resolution of 2.5 ms or better, which implies a frequency resolution of only 400Hz. Since the Doppler frequencies involved are of the order of

only 2 kHz, this is clearly inadequate. To overcome this limitation we and other groups have used time-frequency analysis to achieve high temporal resolution measurements without sacrificing frequency resolution [10].

Measurement Limitations

The concept of EBR is extremely valuable, but is defined in terms of the BSCs of blood and emboli, which cannot be measured directly. In practice what is measured is the relative powers of the signals from the Doppler sample volume in the presence and absence of embolic events, which is therefore perhaps better called 'measured EBR' or MEBR to distinguish it from the more theoretical quantity. MEBR is influenced by many factors, but perhaps the most important are the size of the MCA, shape of the ultrasonic beam, the embolic trajectory through the artery, and the interaction of these parameters. Even if the free-field ultrasonic beam is sufficiently uniform to provide uniform insonation over a large sample volume, the shape of the skull, with its convoluted inner surface, leads to very non-uniform ultrasound fields within the brain [11,12]. Because of this, the amount of power backscattered by an embolus will be dependent on the particular trajectory it follows through the MCA. The power backscattered by the blood will depend on the ultrasonic beam shape and the diameter of the blood vessel, neither of which will be known, and the angle of insonation, which also may not be know. In a recent study from our laboratory, in which simulations were performed using ultrasound beam shapes measured through temporal bone, and likely geometrical configurations; the effects of embolus trajectory, likely insonation angles, and plausible vessel misalignments introduced uncertainties in MEBR values of up to 12dB [13].

4. Information from micro-embolic signals

Ideally embolus-monitoring systems would detect all micro-embolic events, and would be able to determine the size and composition of the causative embolus. Although much progress has been made in this direction, there remain many challenges.

Detection of Emboli

It will be clear from the previous section that there is a considerable degree of uncertainty in measurements on MES, and this must influence the sensitivity of event detection. Furthermore most embolus detection systems rely on subjective decisions made by an operator, and therefore in addition to variability due to physical factors, some intra-observer and inter-observer variability must be expected. Although there is a high probability that emboli with large BSCs (relative to BSC of the blood in the sample volume) will be detected, there is also a high probability that a significant percentage of emboli with small BSCs will be missed. Fortunately clinical experience suggests that quite large numbers of solid emboli which produce signals close to the detection threshold are necessary to cause any measurable damage to the brain, and thus whilst individual events may well be missed, the presence of embolisation will not.

Artifact Rejection

One of the difficulties of embolic event detection is that of distinguishing between signals due to true events, and those due to non-embolic events. There are many mechanisms that produce transient high intensity signals, many of which have similar characteristics to true MES. Any movement of the Doppler probe, either intentional or accidental, or of the underlying tissue such as that caused by head movement, speech, snoring or talking, can produce signals not dissimilar to MES.

The most common method of rejecting artifacts is still subjective assessment of a candidate signal by comparing it with a set of standard criteria. One commonly used set is that published as a result of a consensus meeting [3]. Another approach to artifact rejection is to use more than one Doppler sample volume in an attempt to track the movement of an embolus through the circulation [14-16]. The method consists of placing two or more sample volumes at different positions along the arterial tree, and monitoring the signal from each gate for transient increases in power. If such transients are due to an embolus, then since it is flowing with the blood, it will enter the distal sample volume (SV1) before it enters the proximal sample volume (SV2), and therefore the resulting increase in power from SV1 will occur before that from SV2. The time difference will be given by the velocity of embolus propagation divided by the distance between the leading edges of the two sample volumes (very approximately). If, on the other hand, the transient increase in power is not due to an embolus, it is likely that either the increase in power will occur only in one sample volume or in both simultaneously. This technique has been shown to be quite reliable for MES with relatively high MEBR, but is less useful for MES with low MEBR which is when it is most difficult to distinguish MES from artifacts using standard criteria.

Embolic Composition

It is important to know the nature of any embolus for several reasons, but most importantly because solid emboli are believed to be more hazardous than small gaseous emboli. Even if emboli of different types produced similarly sized MES this would be important, but it is particularly so since small gaseous emboli produce similar signals to large solid emboli.

Power Based Methods

The most obvious characteristic of MES that can be used to discriminate between solid and gaseous emboli is the EBR. Reference to figures 2a and 2b shows that if EBR exceeds about 30 dB then the embolus is likely to be gas, whilst if EBR is less than 20 dB the embolus is likely to be solid. For values in between there is a region of uncertainty, but in itself this is probably not of too great a concern, it is more a question of how to estimate EBR directly or indirectly with sufficient accuracy to use this property for classifying emboli. Some of the difficulties of making accurate measurements of EBR and associated quantities have been described in section III and earlier in this section, where it has been seen there are considerable uncertainties. If it were not for these uncertainties it is likely that methods based on power estimation would be adequate for distinguishing between solid and gaseous

emboli in most circumstances.

Dual Frequency Methods

Another method of attempting to distinguish between solid and gaseous emboli is to compare the MEBR values at two different frequencies [8,17]. Evaluating the Lubbers and van den Berg model [7] for gaseous emboli with diameters greater than their resonant frequency, and up to the diameter at which they generate so much backscattered power that they cannot be confused with solid emboli, suggests that the EBR at 2.0 MHz is consistently greater than the EBR at 2.5 MHz by between 4 and 5 dB (Fig. 4a). A similar calculation for RCAs shows that the difference between the EBR at 2.0 MHz and 2.5 MHz fluctuates wildly (Fig. 4b).
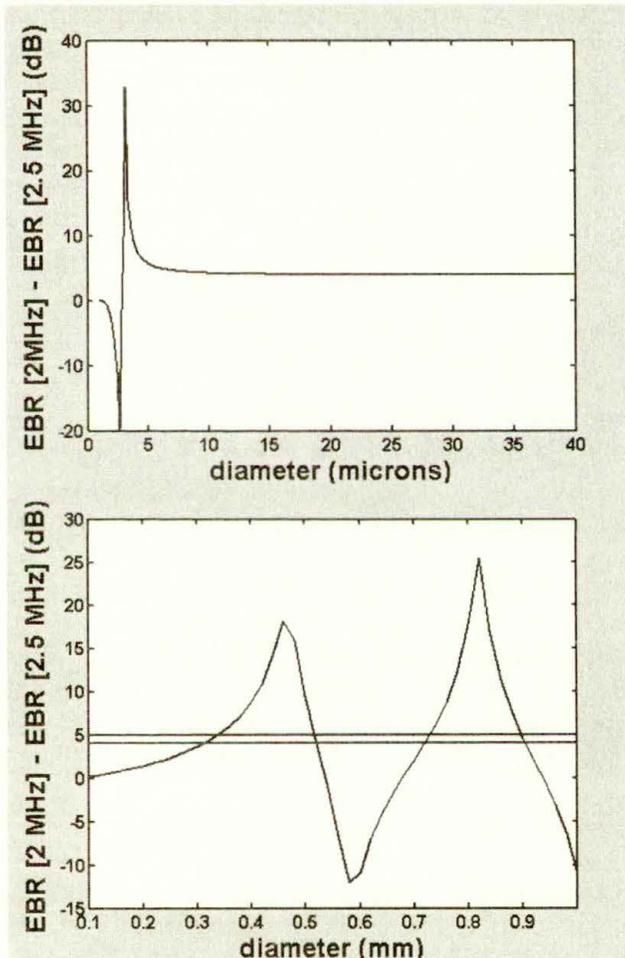

Fig. 4.a. Difference between EBR at 2 MHz and 2.5 MHz for gas.
Fig. 4.b. Difference between EBR at 2 MHz and 2.5 MHz for RCAs. The upper and lower limits for EBR differences for the majority of important gas bubble sizes are superimposed (i.e. between 4 and 5 dB).

At first sight this appears to provide a valuable way of distinguishing between solid and gaseous emboli, but in reality the majority of solid microemboli probably have diameters of less than 0.3 mm, simply because patients show few ill effects unless they have a very large number of embolic events. For emboli in this size range it is necessary to be able to estimate the difference in MEBR at 2 MHz and at 2.5 MHz to within 0.5 dB to 5 dB (depending on the size of the embolus) to separate the two types of emboli. In order to do this it is necessary to match the shapes of the ultrasound beams at the two frequencies to the same precision, which is extremely difficult once the ultrasound beam has passed through the skull.

Sub-harmonic and Ultra-harmonic Emissions

Gas bubbles behave in a non-linear manner when at, or near resonance, whilst solid particle scatter in a linear manner irrespective of frequency, and it is possible that this property could be used to classify emboli. Palanchon and colleagues have been exploring this property *in-vitro* using low ultrasound frequencies (130 kHz and 250 kHz) and have shown that scattering takes place at the second and third harmonic frequencies when bubbles sizes are approaching resonance, and at even higher harmonic frequencies when their sizes are very close to resonance [18]. They have also shown that by using properties of sub-harmonics, ultra-harmonics, and harmonics, bubbles around the resonance size, and around twice the resonance size can be detected from the surrounding medium [19]. Whilst this technique has obvious attractions, it remains to be seen if it can be made to work *in-vivo*.

Partial Gas Pressure Manipulation

There has long been a controversy over whether the very high numbers of microemboli detected in patients with artificial heart valves are solid or gaseous. One school of thought has it that they cannot be solid otherwise the patient would show significant clinical effects, whilst the opposite school maintains that even if gas bubbles were generated in the heart, they would dissolve before reaching the brain. To some extent this controversy has been resolved by studying the effect of oxygen ventilation and of hyperbaria on these patients [20,21]. The result of oxygen ventilation is to dramatically decrease the number of MES, whilst the effect of hyperbaria is to increase the counts, implying that at least a significant proportion the emboli are gaseous. Whilst techniques like these cannot help to classify individual emboli, where there is a chronic source of emboli it can provide useful information.

Embolic Size

An ultimate goal of embolus detection work would be to estimate the size of each embolus. To date there has been little progress towards this goal. The most obvious quantity to measure with sizing in mind would be MEBR, but there are two difficulties with this. The first is that for solid emboli (for example RCAs) EBR does not increase monotonically with power, and therefore any one value of MEBR could correspond to two or three embolus sizes, the second is that the variation in EBR with size is not large compared with the errors in estimating MEBR. One technique

that has shown some promise *in-vitro* is to make use of more that one transmitted frequency. The principle behind this is that since the pattern of variation of EBR with diameter is frequency dependent, it should be possible to combine independent information from measurements made at different frequencies [22,23]. Even *in-vitro* however, beam refraction causes considerable difficulties, and at present the *in-vivo* problem is far from being solved.

5. Summary and conclusions

It is relatively easy to detect both solid and gaseous microemboli traveling in the major cerebral arteries, but great care is needed in the interpretation of the resulting MES. Most emboli can be classified as 'gaseous' or 'probably solid' solely on the grounds of the amount of Doppler power they backscatter, but there is an overlap between the size of the signals from small gaseous and large solid emboli. Solid emboli are likely to be more dangerous than gaseous emboli, but unfortunately they are the most difficult to detect. Power measurements on emboli have a high degree of variability associated with them due to unknown factors such as the shape of the ultrasound field inside the brain, the size of the artery, and the vessel/ultrasound beam configuration. Work is continuing on new techniques for characterizing and sizing emboli, and on automating their detection.

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