A Comparison of Four Methods for Distinguishing Doppler Signals From Gaseous and Particulate Emboli

Julia L. Smith, BSc; David H. Evans, PhD; Peter R.F. Bell, MD; A. Ross Naylor, MD

Background and Purpose—Many reports in the medical literature have proposed methods of differentiating between gaseous and particulate emboli detected with the use of transcranial Doppler ultrasound. The purpose of this study was to compare the previously published methods with our own sample volume length (SVL) parameter to assess the accuracy of each method in classifying emboli.

Methods—A pure source of gaseous and particulate emboli was obtained from in vitro and in vivo studies, respectively, and recorded onto digital audiotape for off-line analysis. In total, 100 gaseous emboli and 215 particulate emboli were analyzed to measure four embolic parameters, namely, embolic duration, embolic velocity, relative signal intensity increase (measured embolic power [MEP]), and SVL of the embolic signal (=Duration×Velocity). Receiver operator characteristic analysis was used to assess the optimum threshold for each parameter to differentiate between particulate and gaseous emboli, and levels of sensitivity and specificity were calculated.

Results—Embolic duration and velocity produced the poorest levels of sensitivity and specificity compared with the MEP and SVL parameters. The optimum thresholds for embolic duration and velocity were 35 ms and 1 m/s, respectively, which produced a sensitivity (specificity) of 85.1% (87%) and 87% (67%), respectively. The optimum MEP and SVL thresholds were 30 dB and 12.8 mm, respectively, which produced a sensitivity (specificity) of 86.5% (95%) and 93% (97%), respectively. The SVL and MEP parameters were compared statistically (χ²) at chosen specificity values of 90%, 95%, 97%, 99%, and 100%, which showed that the SVL sensitivities were statistically greater than MEP sensitivities (P<0.01).

Conclusions—SVL is the best parameter for differentiating between gaseous and particulate emboli but needs to be calculated with the use of a high-temporal-resolution spectral analyzer to measure embolic duration and velocity. (Stroke. 1998;29:1133-1138.)

Key Words: embolism • receiver operator characteristics • ultrasonography, Doppler

During CEA and cardiac surgery, both air and particulate emboli can be detected with the use of TCD. The clinical significance of each type of embolus is relatively unknown because it has been very difficult to distinguish between gaseous and particulate matter. However, there is circumstantial evidence that particulate emboli are potentially far more damaging than gaseous emboli, and therefore simply counting the number of emboli during each surgical procedure does not necessarily correlate with their clinical significance. A recent study showed that persistent embolization during the dissection phase of CEA, when all emboli are particulate by default, was associated with a significant decline in cognitive function, while emboli detected during the early recovery phase were associated with an increased risk of perioperative thrombosis and cerebral infarction. This study also showed that presumed air emboli rarely cause significant morbidity.

Many studies have been published in scientific and clinical journals concerning the differentiation between solid and gaseous matter. Essentially there are two different embolic parameters that previous researchers have used when attempting to classify or size emboli: (1) embolic signal duration and (2) the ratio of embolic signal amplitude to background blood signal amplitude (ratio of embolus to blood [MEP]). In addition, embolic velocity has also been found to correlate with the MEP. In 1991 and 1992, Russell et al²–⁴ published various works concerning the composition and size of emboli. A series of experiments was performed by injecting emboli of known compositions and sizes into rabbits. Doppler recordings were made from the descending aorta, which has a diameter similar to that of the human middle cerebral artery. All 125 injected emboli were detected with TCD and produced MEP values greater than 15 dB, with air and fat emboli producing higher MEP values than platelet or atheromatous emboli. A positive correlation was found between MEP and embolic size for platelets, blood clots, and atheroma. Markus and Brown⁵ also performed an in vitro study using different compositions of solid emboli injected into a flow rig model with intervening skull bone between the TCD transducer and the tubing. A positive correlation was found between MEP
and embolic size; for emboli of the same composition, a positive correlation was also found between embolic size and embolic signal duration. A similar correlation was found when different sizes and compositions of emboli were injected into an in vivo sheep model.\(^\text{6}\) Grosset et al\(^\text{7}\) investigated the difference between the embolic signal characteristics from cardiac and carotid origins using TCD and found that embolic signals of cardiac origin produced greater MEP values than those of carotid origin, concluding that emboli of cardiac origin were either greater in size or of different composition than carotid emboli. It was also noted that the embolic signals with higher MEP values had significantly longer embolic signal durations. Georgiadis et al\(^\text{8}\) injected various compositions and sizes of emboli into an in vitro flow model and found a positive correlation between MEP and embolic size, with MEP values being comparable to those seen in vivo. Droste et al\(^\text{9}\) found a distinct inverse relationship between embolic velocity and embolic signal duration in both in vivo and in vitro studies for all sizes and compositions of emboli. The reason given for this relationship was that the product of velocity and duration is equal to the length of the sample volume, which was assumed constant for all embolic signals. A slight positive correlation was also found between embolic velocity and MEP in vivo but was not corroborated in vitro. Bunegin et al\(^\text{10}\) described a method for estimating the volume of air in the middle cerebral artery using TCD. This was achieved by injecting controlled volumes of air (0.5 to 40 \(\mu\)L) into the carotid arteries of monkeys. A linear correlation was found between MEP and air volume; however, all the embolic signals produced amplitude saturation of the TCD system, and therefore Bunegin et al actually correlated the duration of the saturated embolic signal with the volume of air.

The common thread that has hindered all of the above studies in their analysis of TCD-detected emboli is that of an inadequate dynamic range and poor time resolution of conventional spectral analyzers. To overcome these two limitations, TCD systems need to have a dynamic range of at least 60 dB and a spectral analyzer with a time resolution of at least 1 ms. Although TCD manufacturers have begun to address the problem of dynamic range, the inadequate time resolution, inherent with FFT spectral analyzers, still remains. One alternative to an FFT is the Wigner distribution function, which is simply an alternative processing algorithm with the advantage of a high time resolution (0.08 ms) without the disadvantage of sacrificing frequency resolution.\(^\text{11}\) The Wigner analyzer is able to measure embolic duration and velocity far more accurately than conventional FFT analyzers, enabling the SVL, which is the product of duration and velocity, to be calculated with up to 250 times greater accuracy. The SVL has been proposed as a parameter to characterize emboli, the underlying hypothesis being that air reflects more of the incident ultrasound and will therefore be detected over a greater SVL than particulate emboli. Although this is effectively an alternative method of measuring the MEP, it was thought to be better because of its ability to smooth out any local “hot spots” that may be present in the amplitude of the embolic signal as a result of distortion and attenuation of the ultrasound beam by the skull and intervening tissues. The SVL parameter was shown to be a good predictor of embolic composition but has not previously been compared with the more conventional methods described above.

The aim of this study was to calculate the SVL measurements of a known group of both air and particulate embolic signals and to compare this method with three other embolic parameters, namely embolic velocity, embolic duration, and MEP.

**Materials and Methods**

A pure source of particulate emboli was obtained during the dissection phase of routine CEA surgery when no air was able to enter the arterial system. This procedure was performed in the standard manner with the use of normotensive, normocarbic general anesthesia, systemic heparinization (5000 IU IV), and carotid sinus nerve blockade (1 mL 1% lidocaine). One hundred sixteen patients underwent continuous intraoperative TCD monitoring of middle cerebral artery blood flow velocity during CEA. The TCD system used was a Scimed PcpDop 842 that had been modified to increase the effective dynamic range to 60 dB.\(^\text{11}\) Nineteen patients (16.4%) had evidence of more than one embolus during the initial dissection phase of the operation before cross-clamping. All Doppler signals were recorded onto digital audiotape for off-line analysis. Unfortunately, one of the Doppler channels was not functioning during two of the 19 patient recordings in which there was evidence of particulate emboli, and therefore these were excluded from this study since they could not be analyzed. In total, 215 particulate embolic signals were detected in 17 patients during dissection.

A pure source of gaseous bubbles was acquired in vitro with the use of a pulsatile flow rig model. Silicon tubing was used except at the insonation site, where a 30-cm length of 3-mm internal diameter heat-shrunk tubing was inserted to provide a more realistic model of arterial wall. Fresh human whole blood was used as the flow medium in the flow rig and was left to circulate for 2 to 3 hours to expel any small air bubbles before the experiment was started. Once the Doppler signal was free of any inadvertently introduced air, controlled volumes of air (1 \(\mu\)L) were introduced through a rubber-sealed side port with a 50-\(\mu\)L Hamilton syringe and repeating dispenser that delivered 2% of the syringe capacity at the press of a button. The emboli were injected at a distance of 20 cm proximal to the insonation site, a distance similar to that between the carotid bifurcation and the middle cerebral artery. Our aim was to generate a “worse case scenario” by analyzing the smallest volume of air possible to inject (1 \(\mu\)L), since larger volumes generate larger MEP and SVL values, thus increasing the separation between air and particulate data. The angle of insonation of the transducer with respect to the axial direction of flow was set to 0°. One hundred air emboli were injected into the system, and the backscattered Doppler signal was recorded onto digital audiotape for off-line analysis. The duration of each embolic signal was measured with the Wigner analyzer in its fine-resolution mode to the nearest 80 \(\mu\)s. The embolic signal duration was defined as the period of time that the amplitude of the backscattered signal was 10 dB or greater than the background blood signal. The Wigner analyzer displays the instantaneous mean velocity, and the mean embolic velocity was defined as the point at which there is maximum deviation (within the
embolic signal duration) from the mean blood velocity (outside the embolic duration). The ratio of embolus to blood (MEP) was calculated for each embolic signal in this study with the use of the Wigner analyzer in its fine-resolution mode. The backscattered power of the background Doppler blood signal was measured over one complete cardiac cycle immediately preceding the cardiac cycle containing the embolic signal. This background signal was also taken as the reference when the 10-dB threshold limit for calculating embolic duration was defined. The peak value of the instantaneous power within the embolic signal was then taken as the embolic signal power. The MEP was then calculated as follows:

\[
\text{MEP} = 10 \log_{10} \left( \frac{\text{Peak Embolic Backscattered Power}}{\text{Mean Blood Backscattered Power}} \right)
\]

Finally, the SVL of each embolic signal was calculated from the product of embolic duration and velocity.

**Statistical Analysis**

Our data were not normally distributed, and accordingly all the results in the text and figures refer to median values and their IQRs. Nonparametric (Mann-Whitney) tests were used. Significance was assumed at a value of \( P < 0.05 \).

**Results**

Figure 1 shows scatterplots of the four embolic parameters for each embolic composition. The median (IQR) embolic velocity for particulate emboli was 0.72 m/s (0.58 to 0.85)
Figure 2. ROC curves plotted for each of the four embolic parameters used to attempt to classify emboli. The best performance is achieved by the SVL curve. EBR indicates embolic-to-blood ratio.

and for gaseous emboli was 1.10 m/s (0.90 to 1.32) ($P<0.001$). The median (IQR) embolic duration for particulate emboli was 14.32 ms (5.76 to 27.52) and for gaseous emboli was 48.72 ms (39.12 to 65.04) ($P<0.001$). The median (IQR) MEP for particulate emboli was 19.9 dB (16.3 to 24.9) and for gaseous emboli was 36.8 dB (34.5 to 39.4) ($P<0.001$). The median (IQR) SVL for particulate emboli was 4.1 mm (1.8 to 6.9) and for gaseous emboli was 20.0 mm (16.4 to 24.8) ($P<0.001$). It is not clear from these results which parameter is the best to differentiate particulate from gaseous emboli since there is a significant difference between the two types of emboli for all four parameters. All four scatterplots in Figure 1 show an obvious overlap of the two data groups, and therefore any arbitrary threshold could be chosen that does not necessarily provide optimum specificity and sensitivity.

To choose the optimum threshold for each embolic parameter, an ROC curve was plotted. This was achieved by plotting a graph of sensitivity against the false-positive rate for a series of different threshold values. Four ROC curves were generated, one for each embolic parameter (SVL, MEP, duration, and velocity) and plotted on the graph shown in Figure 2. The ROC curve that produces the best performance of separating particulate from gaseous emboli is the one that is the highest and lies furthest to the left of the ROC space. Figure 2 shows that the SVL ROC curve performs best, and therefore this embolic parameter will correctly classify a higher percentage of emboli than the other three parameters.

To test whether the SVL parameter was statistically different from the MEP parameter, a series of $\chi^2$ tests was performed at chosen specificity values of 90%, 95%, 97%, 99%, and 100%. At each specificity value the sensitivity values for SVL and MEP were statistically different ($P<0.05$), and when we used the additive property of the $\chi^2$ test by combining the results of all five tests, even greater statistical significance was achieved ($P<0.001$).

Defining the optimum SVL threshold to predict embolic composition is dependent on a variety of factors. The ROC curve shows that an SVL threshold that identifies all particulate emboli correctly (ie, 100% sensitivity) would result in a poor specificity of only 34%. However, an SVL threshold that always identified gaseous emboli correctly (100% specificity) would produce a relatively good sensitivity of 87.4%. The best threshold for this study is one that correctly identifies the highest number of particulate and gaseous emboli combined, which occurs when the combined sensitivity and specificity are greatest. This can be deduced from the ROC curve by selecting the point closest to the top left corner of the ROC space.

The Table shows some of the possible combinations of sensitivity and specificity for different threshold values that can be achieved with each of the four embolic parameters used to attempt to classify emboli. The optimum SVL threshold that yields the highest combined sensitivity and specificity for defining gaseous and particulate matter was 12.8 mm, which yielded a sensitivity of 93% and a specificity of 97%. The optimum MEP threshold was 30 dB, which yielded a sensitivity of 86.5% and a specificity of 95%.

### Discussion

The aim of this study was to compare three existing embolic signal parameters (MEP, embolic duration, and embolic velocity) with the more recently defined SVL parameter without the restrictions of temporal resolution and amplitude saturated embolic signals to find the optimum method of classifying emboli.

Two previous studies have shown that embolic signal duration correlates well with MEP and therefore can be used to determine embolic size or composition. For this reason it was decided to test the measurement of embolic duration as a parameter to help determine embolic composition, but in this study, despite improved temporal resolution, it was not
the best parameter to classify emboli. The effect that embolic velocity had on signal duration was minimized in the previous in vitro studies because the mean velocity of the flow medium was kept constant and emboli were injected at the same site, causing them to travel in similar axial planes at similar velocities. It is likely that the variation in embolic velocity observed in the in vitro studies was extremely small compared with the wider range observed during surgical procedures, when blood flow velocities can change significantly. For example, if an embolus travelling at 1.0 m/s has a signal duration of 100 ms, then a similarly sized embolus travelling at 0.5 m/s would take 200 ms to traverse the sample volume, no longer producing a correlation between embolic duration and MEP. Furthermore, it is probable that any small deviations in the relationship between signal duration and MEP were masked because of the poor temporal resolution (10 to 20 ms) used in the previous studies.

Droste and colleagues were able to demonstrate a significant positive linear correlation between embolic velocity and MEP. This was a result of finding a significant inverse relationship between embolic velocity and embolic duration due to a relatively constant sample volume length for all embolic signals studied. Our study has shown that the measured SVL of embolic signals is not constant for all compositions and sizes of emboli. However, the experiments of Droste et al were performed using a relatively small size range (105 to 150 μm) of emboli all having the same composition, which would not be expected to produce any appreciable variation in the SVL measurement. If a much larger size range of emboli or different compositions of similarly sized emboli had been used, there would not have been such a significant correlation between embolic velocity and MEP. Consequently, our study showed that embolic velocity performs poorly as a predictor of embolic composition, yielding the lowest combined sensitivity and specificity of all four parameters studied.

The MEP method performed relatively well in this study, with the effective dynamic range of the TCD system increased to 60 dB. If the dynamic range was kept at 20 dB, then all the air bubbles detected in vitro would have been amplitude saturated, resulting in a much larger overlap in MEP values between the particulate and gaseous emboli, yielding a very poor sensitivity and specificity for classifying emboli. Despite increasing the dynamic range to 60 dB, the SVL parameter was statistically more accurate for classifying emboli than the MEP parameter. The optimum thresholds for MEP and SVL were 30 dB and 12.8 mm, respectively. It is interesting to note that the 30-dB optimum MEP threshold defined from the ROC curve agrees exactly with the optimum embolus-to-blood ratio threshold determined theoretically. One possible reason for the SVL parameter performing better than the MEP parameter is that the SVL measurement is able to “smooth out” any aberrant peak values of intensity within the signal duration. This is in contrast to the MEP measurement, which is derived from a single peak intensity within the embolic duration and which may result in overestimation or underestimation of the MEP value for some embolic signals.

Ideally, both gaseous and particulate emboli would be obtained from the same source, either in vivo or in vitro. Unfortunately, when we tried to inject small particles of platelet thrombus into the flow rig through the rubber-sealed side port, small volumes of air were also introduced, which no longer provided a pure source of particulate data. Alternatively, a pure source of in vivo generated gaseous bubbles is desirable. This would not be possible if we used the same patient group in which the particulate emboli were detected because of the presence of atherosclerotic disease in the arteries of these vascular patients. Although there are clinical situations in which pure gaseous emboli could be detected (ie, hyperbaric decompression, cerebral arteriography in young patients, testing for patent foramen ovale), it is unlikely that the size range of these emboli would match with those detected in vivo during CEA, thus providing no better model than in vitro generated gas bubbles. To simulate more closely the type of gaseous emboli detected during carotid endarterectomy, an injection of gas bubbles into the carotid artery would be required; however, because it has not been conclusively proven that air emboli are asymptomatic, this would be both unethical and potentially dangerous. Although this report has used both in vitro and in vivo data, we believe that this is valid for a comparison study of the four parameters, which were all computed using the same data set. Use of a different data set may lead to differing degrees of overlap between the results of gaseous and particulate emboli but would be unlikely to change their ranking in terms of performance. The type of particulate material (ie, atheroma, platelets, or thrombus) detected in vivo is likely to be different for different patient groups (ie, carotid versus cardiac patients). The variability in MEP measurements due to unknown particulate composition has previously been investigated by Markus and colleagues, who found that there was no significant difference between thrombus and atheroma, while the mean MEP values of thrombi and atheroma were greater than that of platelets. The range of mean MEP values of all three types of particulate emboli was slightly less than 3 dB, which is unlikely to produce a significant effect on the threshold values presented in this study because of unknown particle composition but, more importantly, is unlikely to affect the ranking of the four parameters.

In conclusion, this study has shown that measuring the SVL of embolic signals and defining a threshold of 12.8 mm is the best of the four embolic parameters tested for classifying emboli. The SVL is calculated as the product of embolic duration and velocity, which are measured with the use of the high-temporal-resolution Wigner analyzer.

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