Computerized Detection of Cerebral Emboli and Discrimination From Artifact Using Doppler Ultrasound

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**Background and Purpose:** Transcranial Doppler ultrasound can detect circulating cerebral emboli. Monitoring of patients with potential embolic sources may allow identification of high-risk patients who can then be selected for prophylactic treatment. However, practical patient monitoring will require automated programs that can detect emboli and differentiate them from artifact.

**Methods:** A new off-line algorithm for the detection of emboli, which detects the characteristic relative power increase occurring with an embolus, was evaluated in both an animal model and in patients. (1) In a sheep model, solid embolic materials (thrombus, platelet aggregates, and atheroma) were introduced into the proximal carotid artery while the distal carotid artery or a major branch was insonated. The signals resulting from 77 emboli (mean size, 1.77 mm) were studied and compared with the Doppler signals resulting from artifact. (2) In patients, 100 embolic signals occurring in three patients were analyzed and compared with signals associated with artifact in the same patients.

**Results:** (1) In the sheep model, emboli resulted in a short-duration, high-intensity signal, but intensity increase alone did not distinguish between emboli and artifact. In contrast, the algorithm discriminated embolus from artifact with a sensitivity of 98.7% and a specificity of 98.0%. (2) In patient studies, embolic signals were differentiated from artifact with a sensitivity of 97.2% and a specificity of 97.0% by the algorithm.

**Conclusions:** Using such an algorithm, detection of cerebral emboli and discrimination from artifact are possible with a high sensitivity and specificity. Incorporation of such an algorithm into an on-line system should make prolonged patient monitoring practical. (Stroke. 1993;24:1667-1672.)

**Key Words** • cerebrovascular disorders • embolism • ultrasonics

Recently it has been suggested that circulating solid emboli can be detected in the human cerebral circulation using transcranial Doppler ultrasound. Experimental studies have demonstrated that in vivo and in vitro, solid emboli result in short-duration, high-intensity signals superimposed on the Doppler spectrum. Similar signals have been reported in patients with carotid stenosis, cardiac valvular disease, and recent stroke with atrial fibrillation. This technique may provide a very powerful new diagnostic test. Although detection of potential sources of emboli is possible in some patients, the ability to detect circulating cerebral emboli would represent a major advance in determining the cause of stroke in individual patients. In patients with stroke and more than one embolic source, such as atrial fibrillation and a unilateral carotid stenosis, recording from different sites would allow determination of which source is actively embolizing. Furthermore, the ability to detect asymptomatic circulating cerebral emboli might allow the selection of patients who are at highest risk of subsequent stroke and who would particularly benefit from preventative treatment. Recent trials have demonstrated that prevention of stroke is possible in patients with a variety of potential embolic sources, such as carotid stenosis and atrial fibrillation; however, a large number of individuals need to be treated to prevent each stroke. For example, 40 patients with atrial fibrillation need to be anticoagulated with warfarin for 1 year to prevent one stroke. The embolic signals reported so far have been clinically asymptomatic, but it is reasonable to assume that such events are markers of an embolic source with the potential to also produce larger symptomatic emboli.

Visually analyzing individual recordings is a time-consuming process. The optimum duration of recording for emboli is uncertain but is likely to be at least 30 minutes. In three patients who demonstrated such embolic signals, only one embolus every 38 minutes was noted in the middle cerebral artery above a symptomatic carotid stenosis. If the technique is to become clinically useful, some form of automated detection system is essential. An ideal detector should have a high sensitivity for embolic signals and be able to differentiate them from normal variations in intensity of signal due to blood flow alone and from artifact such as probe motion. It should be able to detect and save any relevant segments of recording, which may be reviewed later.
Early automatic detection devices detected a sudden increase in intensity of the returned signal; however, this does not differentiate artifact from embolus. Artifacts appear as bidirectional signals with maximum intensity at the lower frequencies and an increased intensity spread over a wide range of frequencies (Fig 1C and 1D). In contrast, emboli result in an increase in intensity that is focused on a small band of frequencies in the Doppler spectrum, resulting in a bell-shaped distribution (Fig 1B). In this study we have tested a new automated off-line embolus recognition algorithm (EME Ltd, Uberlingen, Germany). This is programmed to detect the characteristic bell-shaped increase in the relative power amplitude (RPA) occurring with an embolus, and it differentiates this characteristic power increase from that resulting from an artifact. The latter is achieved by detecting the usually symmetrically bidirectional low-frequency intensity increase typically produced by artifact. For each possible embolic signal an embolus probability score (in arbitrary units) is produced. A typical unidirectional embolic signal results in a positive embolus probability score; the higher the score, the more likely the signal is to represent an idealized embolic signal. However, the algorithm is designed to assign a low or negative score to the bidirectional intensity increase seen with artifact. We have determined the sensitivity and specificity of this algorithm in an animal model, using emboli of known material and size, and also in patients to determine if it detects the signals believed to represent solid cerebral emboli.

Methods

The same multifrequency transcranial pulsed Doppler ultrasound machine (TC2000, EME) with a 2-MHz probe was used for all studies. Signal analysis used a 128-point fast-Fourier transform. The Doppler signal was recorded onto an IBM-compatible microcomputer and analyzed off-line. Specifically designed software (EME) allowed individual time frames of the Fourier transform to be analyzed, and the maximum RPA in each successive time frame was recorded; this provides a measure of relative intensity. The increase in intensity associated with an embolus can then be calculated from the following equation: Intensity Increase=10 \log(\text{Peak RPA With Embolus}/\text{Mean RPA in Absence of Embolus}). Embolic signals were analyzed off-line using the embolus detection algorithm. This produces an embolus probability score in arbitrary units. A greater score represents a higher probability that the given signals result from an embolus. The maximum positive or negative score for each embolus or artifact was recorded.

Experimental Validation

A sheep model was used. This allows vessels similar in size to human cerebral vessels to be insonated. The sheep has a single carotid artery on each side that supplies the territories supplied by both the internal and external carotid arteries in the human. Animals were studied while under terminal anesthesia after a separate study of extracranial vascular grafting. A carotid angiogram was performed in all cases to confirm anatomy and patency of the carotid artery. A cannula was introduced into the proximal carotid artery in the neck and sutured in place. Heparinized saline (1000 U/L) was continuously infused through the indwelling carotid cannula. A constant infusion rate of 300 mL/h was used for all studies. Emboli were introduced into the saline infusion via a side arm, 30 cm upstream from the point at which the infusion entered the carotid cannula. This allowed visualization of the passage of an embolus as it passed through the transparent tube in the heparinized saline, and accidentally introduced air bubbles could be identified.

Two routes of insonation were used. The submandibular distal carotid artery was insonated at a depth of 26 mm with a sample volume of 9 mm at an angle of insonation of approximately 30 to 40 degrees. The transorbital route was also used to insonate a major branch of the carotid artery at a depth of 36 mm, with a sample volume of 9 mm at an angle of insonation of approximately 60 degrees.

Pathological embolic materials were studied. Thrombus was prepared by adding 1 mL (containing 10 NIH units) of human thrombin (Sigma Chemical Co, St Louis, Mo) to 10 mL fresh human blood. Platelet-rich aggregates were prepared by adding 1 mL of aged (48-h) human thrombin (Sigma) to 5 mL of platelet-rich plasma. Atheromatous material was obtained from fresh (less than 24-h) postmortem human aorta. Solid embolic material was cut under a dissecting microscope, using a graticule, into approximately cuboid pieces of determined dimensions. The maximum length of the longest edge (maximum dimension) was recorded for each embolus. The embolic material was then suspended in saline and injected immediately into the side arm of the constant infusion. Great care was taken to exclude air during introduction of emboli. Emboli were drawn up into a syringe filled with a saline/Tween solution. The syringe was then stood upright; emboli denser than saline fell to the bottom; air bubbles rose to the top of the syringe and were excluded.

One hundred twenty emboli were studied (64 thrombi, 28 platelet aggregates, and 28 atheroma emboli). Seventy-nine were insonated via the distal carotid route and 31 by the transorbital route. The passage of 43 of the emboli was accompanied by a very intense signal, which led to receiver overload and a broad spread of spectral frequencies. This pattern is identical to that produced by electrical interference or very intense artifact (Fig 1), and therefore these were not included in the analysis. In clinical practice this is not a major problem because the signals commonly recorded in humans associated with solid emboli are less intense (see “Discussion”). Seventy-seven emboli (34 thrombus, 21 platelet, and 22 atheroma) resulted in signals that did not overload the receiver, and these were included in the subsequent analysis; mean±SD size was 1.77±1.38 mm.

We also studied 100 episodes of artifact produced by tapping the probe. The normal variations in intensity and embolus probability score in the absence of emboli or artifact were also studied by analyzing the frequency spectrum of 205 time frames free of abnormal signals, either artifact or embolic. For each of these frames the maximum RPA and the embolus probability score were recorded.

Human Studies

We studied three patients in whom multiple short-duration, high-intensity signals believed to represent
emboli had been recorded. In a 53-year-old woman with a symptomatic right carotid artery stenosis, multiple asymptomatic embolic signals were noted during recording from the ipsilateral middle cerebral artery 1 hour after successful carotid angioplasty. In two women (aged 52 and 28 years) with prosthetic mitral valves (Starr Edwards), multiple asymptomatic embolic signals were noted while recordings were made from the mid-
dle cerebral arteries. For all studies the probe was fixed in place by an elasticated strap, and the middle cerebral arteries were insonated via the transtemporal window at a depth of 45 to 50 mm. A total of 100 embolic signals recorded from the three patients were analyzed. In addition, the signals resulting from artifact were studied in the same patients. We studied 252 episodes of artifact produced by probe motion, caused either by tapping the probe lightly or by tapping nearby skin. Variations in intensity in the Doppler spectrum in the absence of artifact or emboli were also studied by analyzing 284 time frames from the three patients.

The data were treated as nonparametric because of the skewed nature of the distributions, and the Mann-Whitney U test was used to compare different groups. Significance was declared at the $P<.05$ level.

**Results**

**Experimental Validation**

Emboli resulted in a short-duration, high-intensity signal. The mean±SD intensity increase was higher with emboli (9.91±1.51 dB; range, 3.67 to 11.73) than with artifact (8.43±1.01 dB; range, 4.77 to 9.38; $P<.0001$). However, there was a great overlap between the intensity increase associated with artifact and embolus (Fig 2); therefore, intensity increase is not a useful parameter to distinguish between the two. In contrast, the embolus probability score differentiated between embolus and artifact. Mean±SD score was 79.39±32.95 units for emboli, and −7±16.77 units for artifact ($P<.0001$). The score with emboli was also significantly greater than that in the absence of emboli and artifact (1.02±2.53 units; $P<.0001$). The distribution of embolus scores for emboli, artifact, and in the absence of the two is shown in Fig 3. The algorithm differentiated emboli from artifact with a sensitivity of 98.9% and specificity of 98.8% using a cutoff of 30 units; increasing the cutoff to 40 increased the specificity to 100% at the expense of a sensitivity of 93.5%. It differentiated emboli from normal fluctuations in intensity in the absence of emboli or artifact with a specificity of 100%, using the cutoff of 30 units.

![Image](http://stroke.ahajournals.org/)

**Fig 2.** Experimental study in sheep model. Histogram showing distribution of relative intensity increases occurring with emboli (n=77), artifact (n=100), and during normal fluctuations in signal intensity occurring in the absence of embolus or artifact (n=205). The overlap between emboli and artifact means that this parameter cannot be used to distinguish the two.

**Fig 3.** Experimental study in sheep model. Distribution of embolus probability scores generated by the embolus detection algorithm for emboli (n=77), artifact (n=100), and during normal fluctuations in signal intensity occurring in the absence of embolic signals and artifact (n=205 time frames).

**Human Studies**

We analyzed 100 presumed embolic signals; 10 occurred in the patient with carotid stenosis and 71 and 19, respectively, in the two patients with prosthetic cardiac valves. The recording period in each patient was 20 minutes. All fulfilled the criteria for emboli as short-duration, high-intensity signals as previously described.12

The mean±SD intensity increase associated with an embolic signal was 9.00±0.88 dB and with artifact was 8.27±1.84 dB ($P=.0058$). However, the distribution of values for emboli and artifact again overlapped (Fig 4), making intensity increase alone unable to distinguish between the two. The mean embolus probability score was 93.8±53.22 units for embolic signals, −10.63±17.40 units for artifact, and 2.98±2.91 units in the absence of emboli or artifact. The embolus probability score was significantly higher for embolic signals than for artifact ($P<.0001$) or for signals in the absence of embolus or
artifact (P<.0001). Taking a cutoff of 30 units or above to indicate an embolus, the algorithm provided a sensitivity of 97.2% and a specificity of 97.0% in the discrimination between artifact and embolus. The specificity could be increased to 98.4%, at the cost of a lower sensitivity of 92%, by increasing the cutoff point to 40 units. The distributions of embolus probability scores for the different samples are shown in Fig 5.

Discussion

Our results demonstrate that it is possible to automatically discriminate Doppler ultrasound signals associated with emboli from artifact and from normal fluctuations in the blood velocity display. We used an algorithm programmed to detect the characteristics of the bell-shaped frequency distribution associated with emboli and to differentiate it from the bidirectional frequency distribution associated with artifact. This algorithm uses the differing characteristics of the relative power increase occurring with emboli and artifact. In the sheep model, in which emboli of known characteristics were studied, a sensitivity and specificity of more than 98% were obtained. A similar specificity and sensitivity, both more than 97%, were obtained by analyzing presumed embolic signals recorded from three patients with embolic sources. In contrast, our results demonstrate that detection devices based on detecting a sudden increase in intensity alone will detect emboli but will not distinguish artifact from embolic signals.

The one situation in which this embolus detection algorithm will not work is in which intense signals occurring with emboli lead to receiver overload and a broad spread of frequencies. This occurred in our animal model with some emboli, but these were the larger emboli. There is a positive relation between intensity and embolus size,13 and the asymptomatic embolic signals recorded in patients that are presumably due to smaller emboli only very rarely result in receiver overload. Therefore, this should not present a major problem in human emboli recordings in detecting smaller emboli if a low gain setting is used. Development of Doppler receivers with a wider dynamic range and the incorporation of an automatic gain control could completely overcome this limitation. Accidental air introduction could also result in receiver overload because even small air bubbles, because of their low acoustic impedance, result in intense Doppler signals.13 For this reason great care was taken to prevent introduction of air with the emboli; furthermore, we have found a highly significant correlation between embolus size and intensity in this in vivo model for all three solid embolic materials studied, which would be unlikely if air contamination occurred.14

Our results demonstrate that highly specific and sensitive computerized detection of cerebral emboli is possible in an off-line system. Because of the inability to insonate the cerebral circulation in the sheep via the transtemporal route, insonation was performed via the distal carotid and transorbital routes. For this, low settings of power and gain were used compared with human middle cerebral artery recordings. However, we found similar sensitivity and specificity results in patients in whom recordings were made from the middle

FIG 4. Recordings in patients. Histogram showing distribution of relative intensity increases occurring with embolic signals (n=100), artifact (n=252), and during normal fluctuations in signal intensity occurring in the absence of embolus or artifact (n=284). The overlap between emboli and artifact means that this parameter cannot be used to distinguish the two.

FIG 5. Recordings in patients. Distribution of embolus probability scores generated by the embolus detection algorithm for embolic signals (n=100), artifact (n=252), and during normal fluctuations in signal intensity occurring in the absence of embolic signals and artifact (n=284 time frames).
cerebral artery. The emboli studied in our sheep model were larger than those presumed to cause asymptomatic embolic signals in patients. However, the algorithm also detected asymptomatic embolic signals in patients with prosthetic cardiac valves and in a patient after carotid angioplasty. It is possible that its sensitivity may not be as good in detecting embolic signals in patients with other embolic sources if such signals were less intense in these patients, but this remains to be determined. The incorporation of this algorithm into an on-line system should enable prolonged monitoring to become a practical option in the management of patients with cerebrovascular disease. Detection of asymptomatic emboli may allow identification of the source of cerebral embolism and allow high-risk patients to be identified. This method also has potential for assessing the effectiveness of preventive treatments.

References

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