Consensus on Microembolus Detection by TCD

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International Consensus Group on Microembolus Detection

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Abstract—Transcranial Doppler ultrasound is capable of detecting microembolic material, both gaseous and solid, within the intracranial cerebral arteries. To avoid discrediting this promising and exciting new technique, experts in this field met in January 1997 in Frankfurt, Germany, to discuss the limitations and problems of embolus detection and to determine guidelines for its proper use in clinical practice, as well as in scientific investigations. In particular, the authors suggest that studies report the following parameters: (1) ultrasound device, (2) transducer type and size, (3) insonated artery, (4) insonation depth, (5) algorithms for signal intensity measurement, (6) scale settings, (7) detection threshold, (8) axial extension of sample volume, (9) fast Fourier transform (FFT) size (number of points used), (10) FFT length (time), (11) FFT overlap, (12) transmitted ultrasound frequency, (13) high-pass filter settings, and (14) recording time. There was agreement that no current system of automatic embolus detection has the required sensitivity and specificity for clinical use. **(*Stroke*. 1998;29:725-729.)**

Key Words: embolism ■ ultrasonography, Doppler

Transcranial Doppler ultrasound (TCD) is capable of detecting microembolic material, both gaseous and solid, within the intracranial cerebral arteries. Although these microemboli are clinically silent, they may be clinically important by indicating an increased risk of stroke.

The following potential advances in the treatment of patients with cerebrovascular disease have been suggested by pioneers in this field but have not yet been proven unequivocally. In asymptomatic patients, this technique may identify those with an active embolic source, ie, microembolus detection would allow for preclinical identification of a subgroup of patients at high risk for stroke. In symptomatic patients, after an index event, microembolus detection might be able to pinpoint those individuals at high risk for recurrent stroke.[1] Furthermore, this technique could help to identify the site of the embolizing lesion, particularly in patients with competing sources of embolism.

The ultrasound-based detection of microembolism might also serve as a surrogate marker in interventional trials. In patients with a first-ever ischemic event and a high-grade carotid artery stenosis, the prevalence of a recurrent stroke is low (approximately 7% per annum).[2] However, in symptomatic internal carotid artery stenosis the prevalence of clinically silent embolic signals in recordings of 20 minutes to 4 hours is much higher (approximately 21% to 100%).[3–5] Microembolus detection might reduce the observation time and the number of patients needed to perform interventional trials but first requires validation as a meaningful prognostic parameter.

To avoid discrediting this promising and exciting new technique, this work discusses the limitations and problems of embolus detection and sets out guidelines for its proper use in clinical practice, as well as in scientific investigations. A further aim is to help both the clinician and the scientific community to evaluate the clinical usefulness and reliability of microembolus detection in clinical settings and trials. Recommendations are based on presently available data and may be updated in following years as more information becomes available.

Technical Background and Physics of Embolus Detection

The detection of microemboli is based on the measurement of the backscatter (not specular reflection) from the emboli, and at present no reliable conclusion as to the composition and the size of an embolus can be drawn from the echo of the embolus.[6] The backscatter of the ultrasound from normal flowing blood (including transient erythrocyte aggregates) is usually lower than the backscatter from solid emboli. The latter, however, is usually much lower than the backscatter from gaseous emboli of similar size.

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The most important technical parameters affecting the detectability of microembolic signals are (1) the relationship between the backscattered power from emboli and that from the blood (relative intensity increase), (2) the detection threshold, (3) the size of the sample volume, (4) the fast Fourier transform (FFT) frequency resolution, (5) the FFT temporal resolution, (6) the FFT temporal overlap, (7) the dynamic range of the instrumentation, (8) the transmitted ultrasound frequency, (9) filter settings, and (10) the recording time.

The setting of the ultrasound instrumentation strongly influences the detectability of microembolic signals.[7] It is essential to maintain several parameters constant throughout and between recordings and to synchronize settings in multicenter studies and in serial repetitive investigations. We strongly recommend that both clinical and research material are accompanied by a summary of technical parameters (see "Appendix" for suggested list).

Relative Intensity Increase

A useful parameter is the relative intensity increase, which is the ratio of the acoustic power backscattered from the embolus to that of the moving blood surrounding the embolus.[8] The relative intensity increase is affected by the transmitted ultrasound frequency and other technical parameters and depends strongly on embolus size and composition and the volume amount of blood in the Doppler sample volume.

The relative intensity increase of the embolic signal is presently measured in different ways. Different types of signal analysis are used in the different devices and can additionally be modified by the user. The relative intensity increase of the embolic signal is usually measured in decibels. In frequency domain–based analysis, for instance, the peak intensity, or its mean within a defined time frame and frequency range, can be used. Similarly, the intensity of the background signal may be expressed as a mean value or a median value over variable time periods and frequency ranges (eg, at a location similar to that of the embolus in the preceding cardiac cycle, or comprising time frames preceding the embolus, or the whole sweep including signal-free areas of the screen). Thus, for a given embolic signal, different decibel values of relative intensity increase can be calculated with the use of different background and embolic signal intensity measurements. The user should be aware of which technique is used in the automated embolus detection systems he or she is working with; this should be specified. In the same way, manual techniques of calculating signal intensity should always be specified.[9]

Some intensity calculations of the embolic signal and the background depend on the frequency scale setting (pulse repetition frequency), as more or less spectrum-free area is included. Thus, the scale setting should also be indicated and kept constant.

Detection Threshold

At present, the various manufacturers and investigators use greatly different parameters and criteria for identifying a short-lasting ultrasound event as microembolic in nature. Particularly, greatly different decibel thresholds ranging from 3 to 9 dB have been recommended for discriminating microembolic signals from the general background noise and from

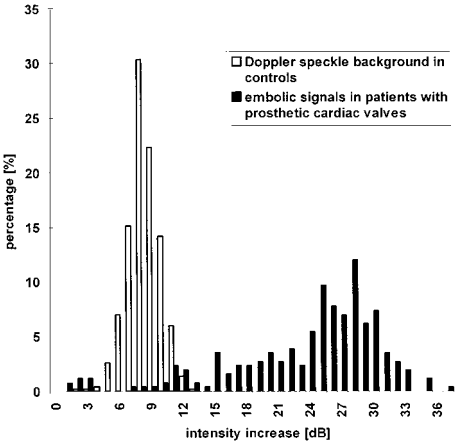

Figure 1. The relative intensity increases of the Doppler speckle background (n=501 events) in the absence of embolic signals or artifacts in 12 control subjects and of embolic signals (n=267) in 10 patients with prosthetic heart valves, both given as percentages.[14]

spontaneous, specklelike intensity fluctuations of the physiological Doppler flow signals.[3,5,10] Fig 1 illustrates the intensity distributions of the Doppler speckle background and of embolic signals. An intensity detection threshold of ≥12 dB was chosen in this study (Fig 1). The parameters were as follows: This threshold was found for the device Multidop X (DWL) including a 2-MHz monitoring probe with a diameter of 1.7 cm, the middle cerebral artery at an insonation depth from 48 to 58 mm, the software TCD-8 for MDX, version 8.00 K (this algorithm uses the whole screen as a background), a scale between 32 −100 and +150 cm/s (corresponding to a pulse repetition frequency of 6500 Hz), a sample volume of 5 mm, a 64-point FFT, an FFT length of 2 ms, and an FFT overlap of 60%; high-pass filter was set at 100 Hz.[7] The situation is even more complicated because different algorithms are used to calculate the background noise and the intensity of the presumed microembolic signal as such. These technical aspects may have contributed to the striking discrepancy in the prevalence of microembolic signals described in the literature in various types of stroke or stroke-prone patients.[4,5,11–13]

There are two possible ways of determining the detection threshold of microemboli in decibels for a given device: either defining the range of spontaneous intensity fluctuations within the Doppler signals of normal controls or defining fluctuations on a case-by-case basis during emboli-free periods.[5,14] It is not yet clear whether thresholds defined in a middle cerebral artery can be used for other intracranial arteries or for poststenotic middle cerebral artery flow spectra. To the best of our present knowledge, calibration of individual machines by either normal controls or by intrapatient analysis of the background signal is equally valid. Each device should be individually calibrated, and the approach used should be clearly indicated. A higher detection threshold results in lower sensitivity but higher specificity and higher intercenter agreement.[15]

Sample Volume

The beam width defines the cross-section of the sample volume at the insonation depth. For a given probe, the beam width varies with insonation depth. Unfortunately, the beam

can be severely distorted by the human skull in an unpredictable manner, and the best the investigator can do is to ensure that the "undistorted" beam has an adequate diameter to cover the whole of the middle cerebral artery at the depth of insonation in a fairly uniform (±3 dB) manner.

By contrast, the axial length of the sample volume can easily be manipulated by the investigator. The axial length of the sample volume strongly influences measurements of relative intensity increase. At present there is no good evidence for an ideal axial length, but most investigators use a value for sample volume length ≥3 and ≤10 mm.

Frequency Resolution and Temporal Resolution

The frequency resolution of an FFT is given by the reciprocal of the temporal resolution; therefore, it is impossible to simultaneously obtain both high temporal and high frequency resolution, and some form of compromise is necessary.[16] Embolic signals may vary considerably in duration but are generally in the range of 10 to 100 ms. To obtain a reasonable temporal resolution, the data segment analyzed should therefore not usually exceed 5 to 10 ms and should preferably be less. When these data lengths are used, the spectral resolution of the FFT is 100 to 200 Hz. It should be noted that for a given sampling rate (which is determined by the maximum Doppler shift to be analyzed), the greater the number of points used for the FFT, the poorer will be the temporal resolution; therefore, an FFT resolution of 64, 128, or 256 frequency bins (or "points") is preferred at present. For short (time) embolic events, the lower the FFT frequency resolution, the stronger the event will appear in the display since the percentage of the input data samples representing the embolic event is higher. From this fact one might expect that the lower the FFT resolution, the better it would be for emboli detection. Newer frequency estimation techniques such as the Wigner transform are not subject to the same limitations as the FFT and may find a place in the analysis of embolic signals in the future.[17]

Temporal Overlap

A temporal overlap of adjacent FFT time frames is essential to avoid gaps in the continuous frequency analysis, which would allow emboli to escape registration. In practice, this could lead to the phenomenon that individual embolic signals may be audible from the analog signal but are not visible in the FFT display on the screen. An FFT overlap of at least 50% is essential; smaller overlaps (eg, 10%) risk the danger of missing individual microembolic signals.[5] This parameter should be indicated by the manufacturer for different instrumental setups. The importance of FFT overlap is illustrated in Fig 2. It will vary with equipment settings, particularly sweep speed. (A faster sweep results in greater overlap).

Dynamic Range

Gaseous or large solid emboli can produce echoes of such high intensity that overload occurs. This prevents assessment of both the relative intensity increase of the echoes and the velocity of the embolus.[18] It also makes a visual discrimination of artifacts from microembolic signals difficult. The devices presently marketed have dynamic ranges on the order of 30 dB. Manufacturers are encouraged to increase this dynamic range in future products. In clinical practice, we advise investigators to minimize the background signal by using a low power and low gain to allow the strong embolic signal to be completely displayed within the dynamic range of the instrument.[7]

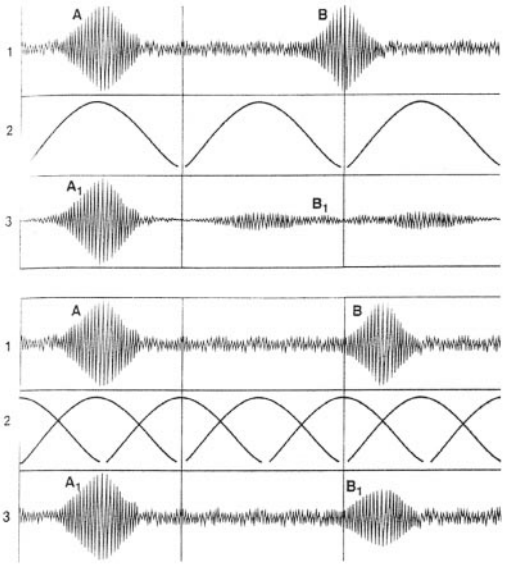

Figure 2. The importance of overlap. In each tracing, the upper tracing (1) illustrates the ultrasound signal before signal processing, the middle tracing (2) illustrates the time window, and the lower tracing (3) represents the ultrasound signal after time windowing. Top, In the absence of overlap, embolic signals may not be displayed on the spectral processor. An embolic signal (A) (an increase in amplitude on the upper tracing) that is sampled during the middle of a time window (tracing 2) is displayed as signal A1. However, a similar signal (B) arriving between the two windows is not detected. Bottom, With higher degrees of overlap no signals will be missed, but the position of the signal during the time window may affect the intensity of the spectral signal. An embolic signal sampled during the middle of the time window (A) is detected as a higher-intensity signal (A1) than a similar signal (B) sampled midway between the two time windows (B1).[24]

Transmitted Ultrasound Frequency

The characteristics of the embolic signal and the background signal vary with the transmitted ultrasound frequency. The most frequently used frequency is 2 MHz. Other frequencies are currently under investigation. The sensitivity is lower with much higher frequencies (eg, 4 or 5 MHz).[19]

Filter Setting

High-pass filters suppress low frequencies originating from arterial wall oscillations. The level of this filter should be reported and kept constant. The same applies to the low-pass filter.

Recording Time

The optimal recording time depends on the study population, specifically, on the rate of embolic events. The preferred recording time for patients with carotid stenosis or atrial fibrillation is at least 1 hour, but the time may need to be shortened in acute stroke patients.[20] A 30-minute recording time may suffice in patients with mechanical heart valves. Pilot work suggests that embolization shows marked variation over

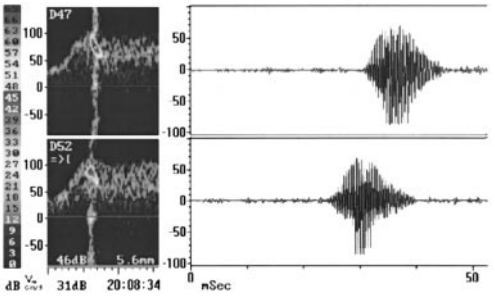

Figure 3. Example of bigated transcranial Doppler ultrasound. An embolic signal was detected at a depth of 52 mm, with a relative intensity increase of 31 dB, and a second time at a depth of 47 mm. The background intensity increase (entire screen) was 46 dB. The software also detected the velocity of the embolic signal (80 cm/s). The time lag in occurrence of the two signals is visible as a pre–fast Fourier transform signal on the right side. There is a lag of 7 ms between the peaks of the two signals. This difference indicates that the embolus has moved 5.6 mm from the first to the second sample volume [(7 ms)*(800 mm/1000 ms)=5.6 mm]. The expected preset difference was 5 mm.[25]

time, and the optimal number of occasions on which recordings need to be repeated remains to be determined.

Artifact Rejection

Discrimination of true embolic signals from artifacts, eg, signals produced by probe displacement, is of crucial importance. Bidirectional signals, ie, signals above and below the baseline, are frequently artifacts. However, embolic signals may also occasionally produce bidirectional signals, particularly if gaseous in nature or with inadequate instrumentation settings. Investigators new in this field are encouraged to purposely produce artifact signals to become familiar with their characteristics. The multigated technique (see below), which uses sampling from several depths of the same artery, reveals the movement of the embolus, whereas an artifact affects all channels simultaneously (Fig 3). The TCD devices currently available are not yet able to automatically discriminate artifacts from microemboli.

Safety

Prolonged ultrasound insonation raises the question of safety. It is incumbent on manufacturers of ultrasound equipment to ensure that their equipment follows the guidelines published from time to time by various national and international ultrasound organizations. It is incumbent on the user to regularly examine the safety literature, to be aware of the potential risks of prolonged ultrasound exposure, and to keep ultrasound exposures as low as possible consistent with obtaining necessary clinical data. It is recommended that all manufacturers implement the American Institute of Ultrasound in Medicine/National Electrical Manufacturers Association Output Display Standard and, where relevant, display the TIC (cranial bone thermal index) so that users are made aware of possible heating effects at the cranial bone surface.

Documentation

The presently most widely used documentation system is the recording of the pre-FFT audio signal (raw data) on digital audiotapes.[21] This allows the data to be subjected to quality control and the reevaluation of regions of interest. It also allows for off-line analysis. For scientific purposes, observer bias can be avoided by a blinded analysis of the audiotapes by different observers.

Quality Control

It is important to ensure reproducibility both between and within centers in the identification of embolic signals. For interobserver studies it is important to guarantee that observers select the same embolic signals. A statistical method that determines this is required (eg, probability of specific agreement, rather than counting the total number of emboli recorded by each observer).[15] Exchange and analysis of data among centers are encouraged.

For multicenter studies, the use of identical devices and a standardized, identical setting of the equipment are strongly recommended.

Automatic Embolus Detection

Embolus detection is very time consuming and laborious. The use of a trained neural network and the multigated technique are attempts toward automatic embolus detection.[3,14,22,23] The multigated Doppler technique traces the moving embolus in different depths of the same artery and takes the time delay of its appearance as the crucial criterion. There is agreement that both techniques have potential. However, no current system has the required sensitivity and specificity for clinical use.

Conclusion

Embolus detection with the use of TCD is a promising technique with the potential to enter routine clinical practice and to guide additional diagnostic and therapeutic decisions. However, the investigator must be aware of the technical problems, limitations, and pitfalls of this method to ensure its reliability and validity.

Appendix

In particular, we suggest that studies report the following parameters:

1. Ultrasound device
2. Transducer type and size
3. Insonated artery
4. Insonation depth
5. Algorithms for signal intensity measurement
6. Scale settings
7. Detection threshold
8. Axial extension of sample volume
9. FFT size (number of points used)
10. FFT length (time)
11. FFT overlap
12. Transmitted ultrasound frequency
13. High-pass filter settings
14. Recording time

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