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Improved Detection of Microbubble Signals Using Power M-Mode Doppler

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Background—Power motion-mode transcranial Doppler (TCD) (PMD) is a new, multigated technique that may simplify and enhance detection of embolus. We developed criteria for emboli detection using PMD. Then, we performed a blinded comparison of transcranial PMD with single-gate spectral TCD in TCD bubble study patients.

Methods—Patients with right-to-left shunt as detected with standard TCD were selected for this study. The international emboli criteria for spectral TCD were used. We defined novel PMD criteria for detecting emboli signature on PMD as follows: (1) signature at least 3 dB higher than the highest spontaneous PMD display of background blood flow; (2) embolic signature reflects motion in one direction at a minimum spatial extent of 7.5 mm and temporal extent of 30 ms; (3) embolus must traverse a prespecified depth. Each study was blindly assessed for microbubble signals (MBS) count on either modality.

Results—Thirty-six patients were included in the study. Mean age was 44.4 (SD 14.4), 50% were male, and median time from stroke onset to TCD bubble test was 12 days. Median MBS count in middle cerebral arteries (MCA) was 4 on both modalities. Spectral TCD MBS counts were highly correlated ($\rho=0.97$) with PMD MBS counts in MCA and similarly in anterior cerebral arteries (ACA) ($\rho=0.79$). When PMD microbubble counts in the ACA and MCA were summed, a clear 2-fold difference emerged between 2 modalities ($P<0.001$).

Conclusion—When compared with spectral TCD, PMD detects more MBS with higher counts by identifying ACA as well as MCA emboli. Pitfalls of overcounting emboli with PMD can be avoided by following such criteria. **(*Stroke*. 2004; 35:e14-e17.)**

Key Words: embolism ■ ultrasonography, Doppler, transcranial

Transcranial Doppler is gradually gaining acceptance as a monitoring tool to detect embolic signals often referred as microemboli signals (MES).[1] These MES correlate with true emboli in animal models.[2] MES are most frequently identified in the setting of large-vessel atherosclerotic disease such as carotid stenosis. [3]

In younger patients (<55 years), paradoxical embolization through cardiac right-to-left shunts has been proposed as etiology for ischemic stroke and transient ischemic attack (TIA).[4] A recent transesophageal echocardiography (TEE) study showed that patient with both patent foramen ovale (PFO) and atrial septal aneurysm (ASA) are at increased risk of recurrent stroke.[5] TCD detects right-to-left shunts via the "TCD bubble study," in which microbubble signals (MBS) are identified in the intracranial arteries several seconds after venous injection of a contrast agent or agitated saline. When performed with a validated protocol, this test has a sensitivity of >90% and specificity of 70% to 75% for identifying PFO when compared with TEE.[6] When both TCD bubble studies and TEE are used in all patients suspected to have PFO, PFO detection rate is higher than when using either method alone.[7]

A portable 2 MHz Power M-mode digital transcranial Doppler (TCD) system (PMD) has been recently introduced.[8] Transcranial PMD may enhance the detection of MBS during the TCD bubble study. We compared standard single-gate spectral TCD with multiple-gated PMD to detect MBS during TCD bubble studies.

Methods

Stroke and TIA patients from 2 academic stroke centers participated in the study. All patients had positive TCD bubble studies with right-to-left shunts on spectral TCD. In both centers, a technician and an expert neurosonologist performed the procedure.

Transcranial PMD (Spencer Technologies, Inc; PMD 100 mol/L) was used in all TCD bubble studies. This technology collects (1) 2-MHz spectral single-gate TCD information at a specific depth and (2) power M-mode information from 33 sample volumes placed at 2-mm intervals from 24 to 88 mm depth of insonation. The PMD display was configured with red or blue colors for directionality, and with brightness of colors to reflect Doppler signal intensity (Figure 1a). A 2-MHz pulsed-wave transducer was used to generate simultaneous M-mode and spectral TCD displays. The transcranial PMD equipment uses an emitting transducer surface 13 mm in diameter. The pulse repetition scale settings were 5 kHz, gain of 40 dB, and

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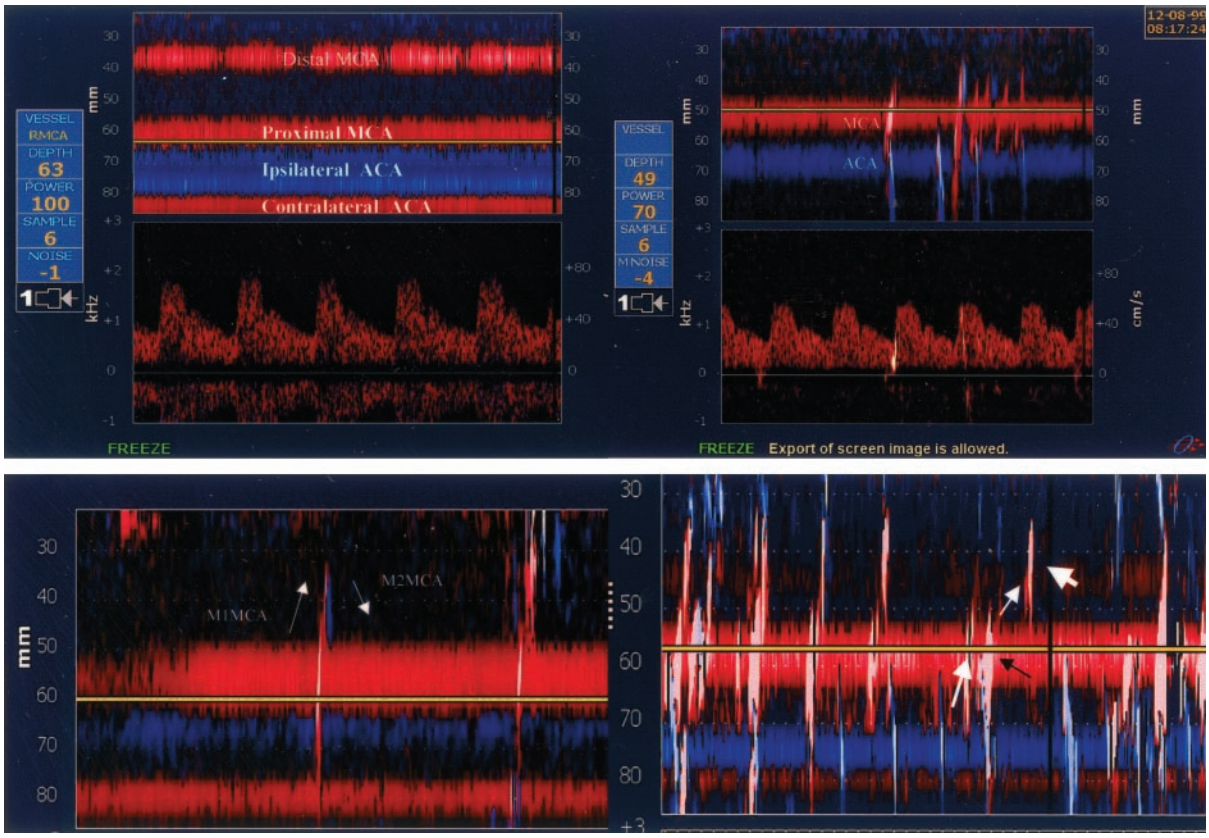

Figure 1. Panel TCD 100 mol/L displays. a, Power M-mode display of the middle cerebral artery at depths of 32 to 58 mm. This represents the entire signal through the ultrasound beam. The yellow line is the specific depth of 41 mm that can be chosen to display a single gate spectral waveform. b, Single-gate spectral TCD waveform at depth 49 mm showing 2 emboli simultaneously appearing in MCA and ACA on M-mode display but only MCA embolus seen on spectral TCD. Emboli counted when track has traversed proximal depth (ie, 50 to 60 mm MCA or 60 to 70 mm ACA) of high signal intensity. c, Patterns of embolic tracks on PMD, which can give an impression of 2 or 3 emboli where in reality only a single microbubble signal exists. d, Thin white arrow shows path of embolus traveling in and out of ultrasound beam. Emboli exits path of ultrasound beam and re-enters it distally. Based on criteria only signature at proximal depth with high intensity would be counted embolus (thin black arrow). The embolus track (thick white arrow) would not be counted.

minimum dynamic range of 80 dB. Algorithms for signal intensity measurement utilized power (in decibels) of the Fourier transform coefficients; acquisition and processing parameters included a 6-mm axial sample volume length, 128 points Hanning window data taper, 128 points fast Fourier transform (FFT) (16 ms), 50% FFT overlap, 2-MHz carrier frequency, 200-Hz high-pass filter (≈7 cm/s), and 1 minute recording time.

An appropriate temporal window was identified prior to the procedure with a standard handheld technique. Probe fixation using Marc 500 head frame (Spencer Technologies) was used for monitoring. One proximal middle cerebral artery (MCA) segment was insonated and, where possible, ipsilateral anterior cerebral artery (ACA) for PMD display. The insonation depth for spectrogram recording was between 45 to 65 mm for the unilateral MCA. Intravenous access was obtained in the antecubital fossa with an 18- or 20-gauge needle. Agitated saline (9 mL normal saline mixed with 1 mL air) was used as a contrast agent and rapidly injected intravenously. Monitoring started just prior to agitated saline injection and continued for 1 minute after bolus. The MBS were monitored simultaneously on the spectrogram and PMD display. Positive bubble studies were identified if at least 1 MBS was identified by spectral TCD. The test was repeated with Valsalva maneuver if the frequency of MBS was <3. The Valsalva maneuver was performed for 5 seconds starting at 5 seconds after the beginning of contrast injection.[9]

The spectral and PMD TCD bubble studies were each assessed independently and blind to patient information by expert neurosonographer. The spectral TCD MBS counting was based on established criteria for embolus detection using consensus conference recommendations[10] (Table).

The PMD display embolus counting was based on stringent "embolic signature" criteria (Table).

Where the number of emboli was impossible to count because a shower or curtain of emboli appeared after saline bubble injection, the number of emboli was set at 50. Demographics of study population and MBS counts were compared using descriptive statistics. Simple linear regression was used to compare modalities.

Results

Thirty-six patients were included in the study. The mean age was 44.4 (SD 14.4), 50% were male, and the median time from stroke or TIA onset to TCD bubble test was 12 days (interquartile range [IQR], 5 to 30). Twenty-two patients had bilateral insonation and 14 unilateral insonation.

TCD bubble studies were performed at rest (by hemisphere, n=58). The median MBS count on spectral TCD was 4 (IQR, 0 to 12). The median MBS count on PMD in the MCA only was 4 (IQR, 0 to 10). The median MBS count in PMD in the ACA was 1 (IQR, 0 to 5). Spectral TCD MBS counts were highly correlated (ρ=0.97) with PMD microbubble signals counts in the MCA and similarly in the ACA

Criteria for Counting Emboli Signal on Spectral and PMD TCD

Spectral TCD Criteria	Novel PMD TCD Criteria
1. Transient, lasting <300 ms	1. "Embolic signature" visible at least 3 dB higher than the highest spontaneous PMD display of background blood flow signal.
2. At least 3 dB higher signal intensity than that of the highest background blood flow signal.	2. "Embolic signature" reflects motion in one direction at a minimum spatial extent of 7.5 mm and a minimum temporal extent of 30 ms. An MCA embolic signature is required to move toward the probe, with a positively sloped track. An ACA embolic signature moves away from the probe, with a negatively sloped track (Figure 1b).
3. Unidirectional	3. The "embolic signature" must traverse a specific depth determined by the highest intensity of the insonated artery in order to avoid repeated counting of the same embolus. For this study we chose the depth defined by the optimal spectrogram waveform (Figure 1b).
4. Accompanied by snap, chip, or moan on the audible output.	

(ρ=0.79). No significant differences in MBS counts were observed between 2 modalities for individual arteries (Figure 2). When PMD microbubble counts in the ACA and MCA were summed, a clear 2-fold difference emerged between the 2 modalities (P<0.001).

TCD bubble studies were performed with Valsalva maneuver (by hemisphere, n=36). The median MBS count on spectral TCD was 20 (IQR, 2.5 to 50). The median MBS count on PMD in the MCA was 21 (IQR, 3.5 to 50). The median MBS count on PMD in the ACA was 4.5 (IQR, 0 to 14.5). Microbubble signal counts after Valsalva maneuver were similarly highly correlated between modalities in the ACA and MCA and no significant differences were observed between the modalities for individual arteries. Summating microbubble counts in the ACA and MCA on PMD resulted in a 2-fold increase in counts compared with spectral TCD (P<0.001).

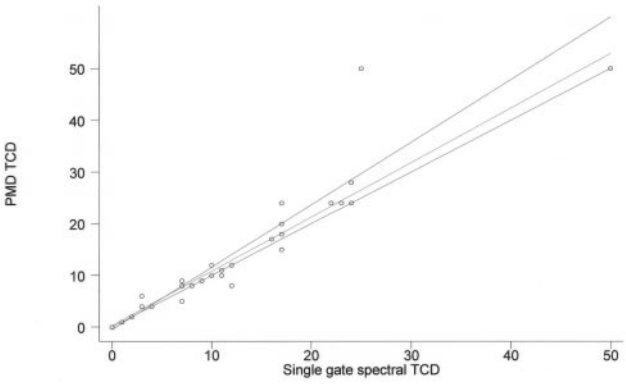

Figure 2. Relationship between PMD microbubble signal counts and single gated spectral TCD counts in the MCA (middle line). The line can be compared with the line of unity (bottom line). The PMD insonation of the MCA shows a slope >1, indicating a trend to increased detection of microbubbles by PMD. This was a nonsignificant difference until cases of curtain or shower of emboli were removed (top line). The arbitrary assignment of curtain or shower of emboli conservatively biased the relationship between the 2 modalities.

Post-hoc analysis of the relationship between MBS counts using transcranial PMD compared with spectral TCD showed that studies in which a curtain or shower of emboli were seen were influential data points. Arbitrarily these studies were assigned a value of 50 microbubbles. In both the resting and post-Valsalva maneuver studies, PMD increased the number of curtain/shower of emboli findings by 1 study. Exclusion of 4 cases with this finding on spectral TCD revealed a significant increase in microbubble detection using transcranial PMD in the MCA (P=0.0003). The same finding was observed in the post-Valsalva maneuver studies (P=0.0019) (Figure 2).

Discussion

Paradoxical embolism via cardiac right-to-left shunt is a recognized mechanism of ischemia in young patients with cryptogenic stroke or TIA.[4] Spectral TCD enhanced by a contrast agent and Valsalva maneuver is a widely used screening test to detect these shunts. Emboli detection has been improved by using dual-gate, reference-gate, and multifrequency Doppler, which help distinguish artifact from real emboli.[11,12] In this study we showed that when compared with spectral TCD, the transcranial PMD detected more microbubble signals, thereby improving the diagnostic accuracy of PMD in detecting cardiac right-to-left shunt.

The reason for the increased yield of MBS counts with transcranial PMD is increased sampling due to the simultaneous insonation of both MCA and ACA, allowing detection of emboli traveling in either artery. This effect persists after Valsalva maneuver. Post-hoc analysis demonstrated that transcranial PMD also shows improved microbubble detection when only the MCA counts were assessed. A single gate placed at the carotid siphon level may have been an alternative way of achieving a complete capture of these emboli.

Despite the advance of power M-mode technology in TCD, there are potential pitfalls with overdetection of emboli. These include: (1) overcounting at branching points (Figure 1c) for vessels such as the MCA at (45 mm) and ACA at (70 mm) where emboli may change direction; (2) overcounting at locations where emboli may go out of and back into plane of ultrasound beam (Figure 1d); and (3) double-counting emboli that briefly arrest and then resume anterograde travel. Using prespecified depths where little branching occurs and good signal intensity (in beam) is present mitigates these drawbacks.

This improved yield from transcranial PMD for embolus detection needs to be confirmed when applied to other clinical situations. Emboli detection has not been established in clinical practice as yet, although considerable research is in development assessing whether total emboli counts stratify risk in such diseases as asymptomatic carotid stenosis,[13] carotid endarterectomy,[14] and coronary artery bypass sur-

gery.[15] Therefore, it is likely that methods to improve absolute embolus counts will have future clinical application.

In conclusion, when compared with single-gate spectral TCD, multigated power M-mode TCD detected more microbubble signals. The difference in the 2 methods is modest and largely due to the detection of ACA emboli not easily possible with single-gate spectral TCD. Transcranial PMD may improve embolus counting and enhance applications where the frequency of emboli is important. Stringent power M-mode embolic signature criteria must be used to avoid overcounting of emboli with this new technology.

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