High-Resolution Emboli Detection and Differentiation by Characteristic Postembolic Spectral Patterns

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Background and Purpose—High-intensity transient signals (HITS) detected by transcranial Doppler ultrasonography correspond to microemboli in intracranial arteries. The purpose of this study was to develop new diagnostic criteria for the differentiation of these microembolic signals from artifact, based on a high-resolution analysis of Doppler power spectra in an in vitro model.

Methods—Two hundred seventy-six formed emboli, consisting of different biological and nonbiological materials and as air bubbles, were injected into a flow phantom with artificial blood vessels and perfused in a steady or a pulsatile way. Embolic passage was assessed with a modified 2.5-MHz pulsed Duplex machine and a commercial 2-MHz Doppler system. Embolic HITS were analyzed using internationally accepted criteria for the audiovisual characteristics of HITS. Doppler spectra changes associated with HITS were evaluated by means of a specially developed high-resolution analysis of Doppler raw data.

Results—Seventy-seven percent of all embolic events could be identified using conventional audiovisual criteria for embolic HITS. Analysis of Doppler spectra showed that all injected emboli generated high-amplitude signals with a minimum of at least 3 dB above background level. In addition, using high-resolution processing, specific changes in Doppler spectral patterns could be identified after all embolic HITS caused by solid particles. These postembolic spectral patterns were always characterized by a Doppler frequency shift decreasing in time and resembling the letter lambda (λ). Duration and appearance of the postembolic spectral patterns were mainly influenced by the size and velocity of the embolus. Similar phenomena could not be found in case of embolism by either small air bubbles or in case of provoked artifact registration. Using a commercial Doppler system specific, we documented postembolic spectral patterns in 47% of injected emboli.

Conclusions—In this study, highly specific changes in Doppler spectral patterns associated with microembolic HITS could be characterized, resulting in further criteria for the differentiation between microembolic signals and artifact in Doppler emboli detection. The sensitivity of the detection of these signals can be increased by high-resolution analysis of raw Doppler data. (Stroke. 1998;29:668-672.)

Key Words: diagnostic imaging ■ embolism ■ spectrum analysis ■ ultrasonography, Doppler

Cerebral microemboli presenting as high-intensity transient signals (HITS) were first described during transcranial Doppler monitoring of cardiac1,2 and carotid surgeries.3 Since these reports, the phenomenon of embolic HITS has been described in experimental settings,4,5 whereas the clinical relevance of cerebral microemboli is still controversial.6 One major problem of the current clinical application of Doppler embolus detection is the differentiation between true embolic signals and artifact. Moreover, it is difficult to differentiate true embolic signals from spontaneous speckling in the background signal. In this context, most common algorithms for embolus identification are based on the analysis of the internationally accepted basic audiovisual characteristics of HITS.7 Additionally, some centers use automated detection software including neuronal network expert systems8,9 or a multigate comparison of signals supposed to be of embolic origin.10 Although the differentiation between embolic HITS and artifact is principally feasible with these procedures, they are all subject to different methodological restrictions, and sometimes the underlying techniques still have to be verified.

The purpose of this study was to evaluate the specific influence of embolic material on Doppler power spectra to establish further criteria for embolus identification. This approach in emboli detection requires the development of a more fundamental analysis of Doppler raw data. Thus, a Doppler system with a very high time resolution and dynamic range was used, and Doppler raw data were analyzed with software tools that could reduce the influence of Doppler speckle interfering with embolic signals.

Subjects and Methods

Experiments were performed using an in vitro flow phantom. This phantom consisted of an electronically controlled pump system generating a steady or a pulsatile flow pattern. The pump was served by a 5-L reservoir filled with washed bovine erythrocytes or a blood...
analogue, consisting of a mix of 60/40% tyrode/glycerine solution and cellulose particles. Volumetric flow of steady flow patterns was 150 mL/min. Pulsatile flow was simulated with an arterial flow pattern, stroke volume was 8.5 mL, frequency was 60 pulses/min. A variable Windkessel was interposed in the circuit to control volumetric flow during diastole.

Doppler measurements were performed in a straight polyethylene tube with a diameter of 6 mm. Laminar flow in the tube was guaranteed by a tube segment 40 cm long without any mechanical devices, curves, or edges. The insonation area was located in a glass tank filled with castor oil for adaptation of acoustic properties and acoustic coupling. The system was degassed with a vacuum pump and an interposed air trap.

Microemboli consisted of polyethylene (n=198), cellulose (n=57), clotted blood (n=11), and air bubbles (n=10). Polyethylene balls had diameters of 0.8 mm to 1.0 mm (n=83), 1.35 mm (n=58), and 2.65 mm (n=57), with a SD of ±5%, clotted blood particles of 2 to 4 mm in size, and cellulose particles of about 2 mm. The size of the emboli was measured using an electronic caliper gauge. Air bubbles with volumes up to 1 mm³ were produced by manual injection with a micrometer syringe. One hundred ten emboli were injected under steady flow conditions, and 166 under pulsatile flow conditions. Solid emboli were injected through an injection port that was connected via a three-way tap to the circuit 120 cm upstream from the insonation area. Air bubble injection site was located only 40 cm upstream from the insonation area to avoid fractionating of the bubbles. Artificial HITS were actively produced by the observer by lightly tapping on the probe or its fixation.

Doppler measurements were performed with a commercially available Hewlett-Packard SONOS 1000 Duplex machine, equipped with a 2.5-MHz linear array transducer. Doppler probes were fixed to a specially developed tripod. The insonation depth was 60 mm with an insonation angle of 40°. Continuous correction of the insonation angle was done to provide corresponding velocity measurements. Sample volume was set to include the whole cross-sectional area of the tube. The dynamic range of the Doppler data was about 55 dB at lowest gain setting. Peak power of flow signal was set to 30% of maximum resolution on the ultrasound device (HP SONOS). In a dual display mode, B-mode information and Doppler spectra could be investigated instantaneously to correlate the passage of the embolus through the sample volume with the spectral Doppler data.

Emboli were identified on-line according to the conventional audiovisual criteria for embolic HITS with a minimum difference of at least 3 dB between the HITS and the background flow signal. Off-line evaluation of raw Doppler data was done using a specific software that allows high-resolution Doppler frequency spectrum analysis. Unprocessed data of 256 short-time Fast Fourier Transformations were stored on a data acquisition unit (486 DX2/66, 8 MB RAM, HD 2 Gbyte). An automated power spectral analysis was triggered by the trigger signal of the pulsatile pump. An averaging algorithm allowed the calculation of a representative spectral pattern based on corresponding segments of different pulse cycles, thus eliminating Doppler speckle (ensemble averaging, so-called “Bartlett procedure”13). This averaged pulse calculated from 10 to 20 different pulse cycles could be subtracted from single pulses that contained HITS. Thus, only the difference between the averaged flow signal and the flow pattern of the HITS-related pulses was displayed, so that HITS could be analyzed off-line with respect to subtle changes in Doppler spectrum. Using this procedure, all detected postembolic spectral changes were described in terms of intensity, duration, and Doppler frequency shift. For further statistical processing, data of polyethylene emboli of different sizes under pulsatile flow conditions were compared using an ANOVA (one-way) statistical analysis.

Under pulsatile flow conditions, Doppler recordings were performed simultaneously to registrations with the SONOS 1000 machine with two different MHz probes of a multigate transcranial Doppler device (DWL-Multidop X, maximum time resolution 64 short-time Fast Fourier Transformations). Doppler angle was 15°, two sample volumes of 8 mm were set into the center of the tube with a distance of 10 mm from sample volume to sample volume. For off-line evaluation, Doppler spectral patterns and unprocessed raw data were analyzed for both channels.

Results

Seventy-seven percent of all embolic events could be detected on-line according to the conventional audiovisual characteristics of HITS, and 23% did not create a sufficient audible signal. Referring to off-line analysis, all injected emboli generated a high-amplitude signal with a minimum of at least 3 dB above background level that could always be detected by both Doppler devices. In 29% of all events, the passage of emboli resulted in an excessive increase of signal intensity above the dynamic range of the Doppler system (HP SONOS 1000).

Intensity of embolic HITS was positively correlated to emboli size and strongly influenced by the acoustical properties of the detected material. Depending on the acoustical impedance, small air bubbles generated high-amplitude signals compared with the relatively low intensity of large polyethylene particles. HITS had a mean duration of 40 ms with a SD of 6 ms (steady flow conditions). Mean velocity of the emboli passing the Doppler beam, defined as Doppler frequency shift at maximum amplitude of HITS, was 32.4 cm/s (±3.7 cm/s) under pulsatile flow conditions and 38.9 cm/s (±11.2 cm/s) under pulsatile flow conditions. Embolus velocity was significantly influenced by embolus size (ANOVA: F ratio=8.9, P<.001; see Table). Post hoc group analysis revealed significant differences in velocity between faster small emboli (0.8 to 1.0 mm) and slower large emboli (2.65 mm).

Off-line evaluation of postembolic spectral patterns using the high-resolution Doppler raw data recordings (HP SONOS 1000) showed characteristic postembolic spectral patterns following solid emboli in all registrations for all experimental conditions (steady versus pulsatile flow; biological versus nonbiological material). These spectral patterns were characterized by a Doppler frequency shift decreasing in time and resembling the letter lambda, they will therefore be described as λ-signs13 in the following part of this manuscript (see λ-sign in Figure 1 for the HP-SONOS machine, in Figure 2 for the DWL-machine). All injected air bubbles produced strong HITS but were never followed by λ-signs even in those cases when signal intensity was much higher than in solid particles followed by strong postembolic spectral changes. Large clusters of air bubbles (only caused by degassing of the system) resulted in detection of postembolic spectral changes resembling a λ-sign. λ-Signs were never detected after artificial HITS that were not of embolic origin, produced by mechanical irritation of the Doppler probe.
In spectral Doppler, postembolic patterns occurred after appearance of a short-lasting very weak signal or no signal at all, 10 to 20 ms after the last spectrum of a HITS. Initially, the intensity of these signals was clearly above the level of the background flow pattern, then rapidly decreased with time. In 60% of all λ-signs, the velocity of the signal finally passed zero to a reverse flow direction. In the remaining 40%, the spectral patterns did not pass the baseline. Duration of λ-signs following the initiation of a HITS period was always longer than the preceding HITS. The mean duration of all detected λ-signs was 230 ms (±54 ms) under steady flow conditions and 169 ms (±53 ms) under pulsatile flow conditions. For polyethylene emboli under pulsatile flow conditions, duration of λ-signs was significantly influenced by embolus size (ANOVA: F ratio=5.3, P<.01; see Table). Post hoc group analysis revealed significant differences between steeper λ-signs of small emboli (0.8 to 1.0 mm in size) and flatter λ-signs of large emboli (2.65 mm in size). Furthermore, the slope of the λ-signs showed a strong and highly significant positive linear correlation to the initial velocity of the embolus (for polyethylene emboli with a size between 0.8 and 1 mm under pulsatile flow conditions r=.88, P<.001, scatter plot shown in Fig 3).

Registrations with the dual display mode showed exact coincidence of the embolus passage through the sample volume in B-mode and HITS in spectral Doppler. Postembolic spectral signals occurred clearly after the passage of the embolus and sometimes were even detected at a time period when the embolic particle had left the display on the screen. The DWL machine was less sensitive for the detection of these specific spectral patterns associated with microembolic HITS. Nevertheless, postembolic spectral changes resembling the λ-sign could be detected in 46% of all injections under pulsatile flow conditions. These signals showed again a clear distinction to the preceding HITS due to reflection by the embolus particle and could always be seen in both channels of the multigate probes and in the raw data sets as well. The duration of postembolic signals in spectral Doppler and Doppler raw data display was identical (Figure 2).

**Discussion**

The purpose of this study was to evaluate the influence of embolic material on Doppler power spectra to develop new diagnostic criteria for the differentiation of HITS due to the passage of microemboli from artifact. Our results demonstrate that embolic HITS are followed by characteristic postembolic spectral patterns with a Doppler frequency shift decreasing in detected λ-signs was 248 cm/s² (±67 cm/s²) under steady flow conditions and 356 cm/s² (±154 cm/s²) under pulsatile flow conditions. For polyethylene emboli under pulsatile flow conditions, this slope was again significantly influenced by embolus size (ANOVA: F ratio=7.3, P<.001; see Table). Post hoc group analysis revealed significant differences between steeper λ-signs of small emboli (0.8 to 1.0 mm in size) and flatter λ-signs of large emboli (2.65 mm in size). Furthermore, the slope of the λ-signs showed a strong and highly significant positive linear correlation to the initial velocity of the embolus (for polyethylene emboli with a size between 0.8 and 1 mm under pulsatile flow conditions r=.88, P<.001, scatter plot shown in Fig 3).

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time and resembling the letter lambda. These postembolic changes of Doppler spectra, which will be called the \( \lambda \)-sign,\(^{13} \) could be detected after the passage of all injected solid particles consisting of different biological and nonbiological materials. In the case of air embolism, \( \lambda \)-signs could only be detected following the larger bubbles caused by degassing the system, whereas \( \lambda \)-signs were never seen following HITS due to artifact registration.

These results indicate that the \( \lambda \)-sign is highly specific for embolic HITS, especially for those caused by solid particles. Thus, the detection of specific postembolic spectral patterns may represent an important addition to the widely accepted consensus criteria for the identification of microembolic signals caused by different thrombotic material. These criteria include the evaluation of intensity, duration, appearance, and acoustic characteristics of HITS.\(^7\) When they were used in the present study, embolic events could only be identified in 77%, while specific postembolic spectral patterns were documented following all embolic HITS. These results suggest that the analysis of postembolic spectral patterns could also increase the sensitivity of embolus detection, especially for those HITS that only create a weak audible signal. As the sensitivity for the detection of \( \lambda \)-signs dropped to 47% in a commercial Doppler system designed for emboli detection, a high-resolution analysis of background-subtracted Doppler raw data is necessary for application of spectral analysis in embolus detection.

Until now, no specific postembolic spectral patterns have been described. However, a review of the current literature concerning emboli detection in patients revealed examples of spectral changes resembling the \( \lambda \)-sign, randomly shown in the presented figures.\(^{14,15} \) The reproducible appearance of this phenomenon, which had not been considered in these studies, could be evaluated first in our laboratory under the optimized conditions of an in vitro flow phantom. Moreover, the development of a specific algorithm for emboli detection even allowed the detection of characteristic spectral changes due to the embolic passage of material, usually causing HITS of lower intensity. Therefore, the implementation of this technique to commercially available Doppler devices should allow one to use this phenomenon in clinical studies to differentiate embolic HITS from high-intensity artifact as well as from background Doppler speckle.

We assume that postembolic changes in Doppler spectra early after the passage of emboli can be explained by Doppler reflection phenomena caused by postembolic flow disturbances. Ultrasound studies on different flow conditions demonstrated that Doppler power increases significantly with the onset of flow distortion,\(^{16,17} \) a finding that could explain the higher intensity in the first third of the \( \lambda \)-sign compared with the background flow signal. However, technical factors concerning beam geometry may play a major role in the generation of this phenomenon. The linear decline of spectral patterns of the postembolic signal frequently passing zero to a reverse flow direction (as well as the strong correlation between the initial embolus velocity and the slope of the signal) could not be explained by mere turbulence effects. For further explanation of the \( \lambda \)-sign, the physical interactions between postembolic Doppler spectral patterns, and technical settings of the Doppler device, flow conditions and properties of the emboli have to be investigated using mathematical models and flow simulation studies.

Other technical methods to increase the specificity of embolus identification are based on automated detection software that includes neuronal network expert systems or a bigate comparison of signals supposed to be of embolic origin. Neuronal network systems compare actual HITS to formerly identified “real” embolic signals.\(^9\) Embolus detection with these systems is limited by the possibility of systematic errors caused by an insufficient identification of reference signals. The validity of reference signal identification could be improved by the analysis of postembolic spectral patterns. Bigated Doppler devices evaluate the time delay between the occurrence of HITS in two spatially separate Doppler sample volumes using the coincidence method.\(^10\) If this method is not applicable for methodological reasons (eg, in case of a short middle cerebral artery) analysis of postembolic spectral patterns for embolus identification could still be done using only one sample volume. An in vivo study comparing the specificity and sensitivity of embolus detection using high-resolution spectral analysis versus the bigate procedure and conventional criteria is currently in progress.

In conclusion, the present study has shown that the analysis of Doppler power spectra can provide specific information for the detection of cerebral microemboli, which can be used as additional criteria for embolus identification with ultrasound. For clinical application of these results, transcranial Doppler systems have to include a high-resolution raw data analysis in clinical settings to evaluate specific postembolic changes of Doppler spectra in vivo.

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References
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