Automatic Classification of HITS Into Artifacts or Solid or Gaseous Emboli by a Wavelet Representation Combined With Dual-Gate TCD

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Background and Purpose—Transcranial Doppler (TCD) can detect high-intensity transient signals (HITS) in the cerebral circulation. HITS may correspond to artifacts or solid or gaseous emboli. The aim of this study was to develop an offline automated Doppler system allowing the classification of HITS.

Methods—We studied 600 HITS in vivo, including 200 artifacts from normal subjects, 200 solid emboli from patients with symptomatic internal carotid artery stenosis, and 200 gaseous emboli in stroke patients with patent foramen ovale. The study was 2-fold, each part involving 300 HITS (100 of each type). The first 300 HITS (learning set) were used to construct an automated classification algorithm. The remaining 300 HITS (validation set) were used to check the validity of this algorithm. To classify HITS, we combined dual-gate TCD with a wavelet representation and compared it with the current “gold standard,” the human experts.

Results—A combination of the peak frequency of HITS and the time delay makes it possible to separate artifacts from emboli. On the validation set, we achieved a sensitivity of 97%, a specificity of 98%, a positive predictive value (PPV) of 99%, and a negative predictive value (NPV) of 94%. To distinguish between solid and gaseous emboli, where positive refers now to the solid emboli, we used the peak frequency, the relative power, and the envelope symmetry of HITS. On the validation set, we achieved a sensitivity of 89%, a specificity of 86%, a conditional PPV of 89%, and a conditional NPV of 89%.

Conclusions—An automated wavelet representation combined with dual-gate TCD can reliably reject artifacts from emboli. From a clinical standpoint, however, this approach has only a fair accuracy in differentiating between solid and gaseous emboli. (Stroke. 2001;32:2803-2809.)

Key Words: HITS ■ solid/gaseous emboli ■ automated system ■ dual-gate TCD ■ wavelets

In recent years, the attention of physicians caring for stroke patients has been drawn to the ability of transcranial Doppler ultrasound (TCD) to detect high-intensity transient signals (HITS) said to be due to microemboli. There is increasing evidence that HITS do have clinical significance, but the value of HITS in determining patient care and the clinical usefulness of HITS detection are still under discussion. Additional information is needed about HITS, mainly on their nature: are they artifacts or solid or gaseous emboli?

Previous attempts at producing an automated system for classifying HITS into artifacts or emboli have failed to achieve the same level of sensitivity (embolus detection) and specificity (artifact rejection) as the human expert, considered the current “gold standard.” Without an automated embolic signal detection system that is as effective as the human expert in terms of sensitivity and specificity, embolus detection remains a time-consuming process, restricted to research studies and unsuitable for clinical practice. To separate artifacts from emboli, the best compromise is dual-gate TCD, which consists of tracing the embolus at 2 different depths in the same artery (time delay) (Figure 1). Lately, Cullinane et al have shown that the use of a frequency-filtering approach improves the differentiation of artifacts from emboli and that the performance of an online automated system is only slightly below the mean performance of that of a panel of human experts. Automated systems that can distinguish between solid and gaseous emboli are currently being developed.
In the present study, we describe the evaluation of a new automated system for the classification of HITS into artifacts or solid or gaseous emboli, based on HITS time-frequency distribution and dual-gate TCD. The rationale for our approach is based on increasing evidence that the fast Fourier transform (FFT), universally used in Doppler devices for spectral analysis of Doppler signals, has notable drawbacks, especially in terms of its poor time-frequency resolution and the large variation in the Doppler spectrum in clinical practice.24,25,28 Consequently, several authors have argued that new time-frequency techniques that avoid the limitations of FFT are needed, especially in the field of embolus detection and classification.24,28,29 In addition, recent pilot studies have suggested that wavelet approaches20,26,27 are particularly well suited to the analysis of short-duration transient signals, such as HITS, and that these new techniques are better than FFT in describing embolic signals. On the basis of our previous pilot study,27 we have tested one such new approach on a large number of HITS in 2 different clinical situations, while a series of artifacts was produced in normal subjects.

Subjects and Methods

TCD Recording
All 5 neurology departments involved in this study used the same Doppler device and diagnostic criteria for embolic signal detection as described in this section. TCD signals were recorded with a Doppler device (Multi-Dop X 4, DWL). Each middle cerebral artery (MCA) was simultaneously insonated through the temporal window at 2 different depths (50 and 60 mm). Two 2-MHz pulsed probes (1 for each MCA) were fixed on a special headset connected to the Doppler machine. A setting guaranteeing optimal embolus discrimination from the background spectrum was used according to the criteria recommended in the International Consensus Group on Microembolus Detection.29 The parameters used were TCD-8 software for MDX (DWL), version 8.00K, a scale between −100 and +150 cm/s, a sample volume ranging from 5 to 8 mm in length, a 64-point FFT, an FFT length of 2 ms, an FFT overlap of 60%, and a high-pass filter set at 100 Hz. The separation between the 2 sample volumes was 5 mm (dual-gate TCD). We selected an intensity detection threshold of 9 dB for HITS after this criterion had been validated in each center according to the guidelines previously published,29 whereas a low gain was used to allow the HITS to be completely displayed within the dynamic range of the machine. The pulse repetition frequency was set at 6000 Hz. We wish to stress that we used recordings only of the raw Doppler signals, and not the FFT-transformed signals; in particular, we did not use the relative intensity calculated after the FFT transform.

Role of Human Experts
The experienced observer’s offline analysis of HITS was taken as a standard reference, because the human expert is currently the “gold standard” for embolus detection.13–24 In our study, the signals were reviewed by 2 observers, and for inclusion, both observers had to agree that the signal was a true embolic signal. The following definition for embolic signals was used: (1) typical visible, (2) short duration, (3) high-intensity signal, (4) within the Doppler spectrum, and (5) occurring at random within the cardiac cycle. In addition,6 the observers analyzed and assessed the time delay provided by the dual-gate Doppler to the signal of interest. For the differentiation between gaseous and solid emboli, the situation is different: because no expert can decide on the gaseous or solid nature of Doppler signals, we had to preselect patients to know the nature of embolic signals, solid emboli being obtained from high-grade symptomatic internal carotid artery (ICA) stenosis patients and gaseous emboli being collected during the diagnosis of a patent foramen ovale in stroke patients.

Patients and Subjects

Artifacts
Two hundred artifacts were recorded in 2 normal subjects (44±4 years old) who showed normal color Duplex flow imaging (CDFI) of their carotid arteries and MCAs. They did not have cardiac or cerebrovascular disease. In them, we performed a 6-minute series of provoked artifacts,16 including movement of the probe, coughing, sneezing, and head rotation.

Gaseous Emboli
Two hundred gaseous emboli were recorded in 4 patients admitted to our department (CHUV, Lausanne) for stroke associated with a
TABLE 1. Relative Power of Artifacts and Gaseous or Solid Emboli

<table>
<thead>
<tr>
<th></th>
<th>Artifacts, dB</th>
<th>Gaseous Emboli, dB</th>
<th>Solid Emboli, dB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>17.4</td>
<td>18.6</td>
<td>10.7</td>
</tr>
<tr>
<td>SD</td>
<td>7.9</td>
<td>4.4</td>
<td>4.8</td>
</tr>
<tr>
<td>Minimum value</td>
<td>2.3</td>
<td>5.3</td>
<td>3.8</td>
</tr>
<tr>
<td>Maximum value</td>
<td>34.1</td>
<td>29.8</td>
<td>25.9</td>
</tr>
</tbody>
</table>

Solid Emboli

A pure source of solid emboli was obtained from patients with high-grade symptomatic ICA stenosis without any other disclosed source of embolism. The emboli originating from ICA stenoses are all particulate by default, because no air is able to enter the arterial system.17,19,21,31–33 Two hundred solid emboli were recorded in 24 patients (67±9 years old) admitted to the 5 neurology departments for stroke attributed to a severe ICA stenosis (>70% lumen narrowing) diagnosed by both CDFI and MR angiography, in whom no coexisting cause of stroke was found after a complete diagnostic examination, including transesophageal echocardiography. All were taking aspirin at the time of contrast TCD, which was performed 1 month after the stroke to evaluate the size of the patent foramen ovale. The contrast used was 1 mL of air vigorously mixed with 9 mL of saline solution and rapidly injected into an antecubital vein via a 3-way stopcock immediately after contrast preparation.30

All patients had given informed consent.

Automated HITS Analysis

In signal processing, one often reconstructs a signal as a sum of certain elementary functions, called the basis functions. The aim is to represent a fairly complex signal as the sum of just a few basis functions, so as to retain the most relevant parts of the signals and reject superfluous details. Usually, a set of nonredundant basis functions is chosen a priori. Pursuit algorithms are an attempt to free ourselves from this a priori choice and proceed by selecting the elementary functions from redundant dictionaries of time-frequency atoms.34,35 These techniques are sufficiently flexible to build compact representations of complex signals, such as music recordings or biomedical signals.

Selection of HITS

From the recordings, 600 pairs of signals were selected by 2 human experts (the use of the dual-gate technique means that a pair of signals is associated with every HITS). Because of our experimental setup (see the section on patients), it is clear that the selection consisted only of eliminating artifacts from the recordings of patients with circulating emboli. We took care to include a wide variety of signals, ranging from noisy to high-intensity signals. In quantitative terms, the relative intensity (also known as the relative power), expressed in decibels (dB), ranged from 2 to 34 (Table 1). We used the classic definition of relative intensity as \(10 \log_{10} (\text{mean power of the embolus part of the signal}/\text{mean power of the part of the signal without embolus})\), rather than \(10 \log_{10} (\text{peak power of the embolus part of the signal}/\text{mean power of the part of the signal without embolus})\). The classic definition is more robust. Its use explains why we have observed HITS intensity of <9 dB (Table 1).

Distinction Between Artifacts and Emboli

To distinguish between artifacts and emboli, we used 2 features: the time delay and the peak frequency. It is widely accepted that the time delay provides useful information but is not absolutely reliable.16,22,23,33 From our extensive experience with TCD signals, we have learned that artifacts usually have lower frequencies than emboli, and we therefore decided to use a novel time-frequency method to calculate the time delay and the main frequency of the signal pairs. For this, we chose to use the matching pursuit performed on a dictionary of Gabor functions. Matching pursuit is related to the new famous wavelet transform34,35 and provides a remarkably compact time-frequency description of a signal. It has a better time-frequency compromise than FFT, ie, it produces a better joint estimate of time and frequency. Gabor functions or atoms are localized sinusoidal waveforms with a symmetrical Gaussian envelope. We found that 4 Gabor atoms were sufficient to represent a signal (Figure 2). To characterize the frequency of artifacts or emboli, we used the frequency of the first Gabor atom. This is a way of estimating what is called the main frequency or peak frequency, ie, the frequency when the signal reaches its peak. For each pair of

Figure 2. Signal of a gas bubble and its time-frequency representation obtained from its Gabor decomposition, whose 4 atoms appear in black. The first atom is fitted to the signal (gray in upper left rectangle). In the next 3 steps of the decomposition, the approximation error, or residual signal, of the previous step appears in gray.
signals, we then calculated the average peak frequency by averaging over the 2 channels.

**Distinction Between Gaseous and Solid Emboli**

The distinction between gaseous and solid emboli is more challenging. The criteria used in a preliminary study with a small data set, namely the instantaneous frequency variation index and envelope variation index, did not produce sufficiently good results. We then considered 3 new features: the peak frequency (as above), the relative power (as above), and the envelope symmetry index; in all 3 cases, the value used was the average of the 2 signals forming a pair. The envelope was obtained with a moving window in the time domain. To get the envelope symmetry index, we calculated the average difference between the positive and negative parts of the envelope and then divided this number by the difference between the positive and negative peaks.

**Data Analysis**

The 600 pairs of signals were divided into 2 sets of 300, each consisting of 100 artifacts, 100 gaseous emboli, and 100 solid emboli. The first data set was used in the elaboration of our classification model, and the second was used to test the adequacy of our model; this division of a data set into a learning set and a validation set is standard statistical practice. The goal of this double-set approach is to prevent overfitting of the model to a "small world," the learning set. As the term implies, "overfitting" of a model is a sure recipe for a disappointing performance outside the learning set. Another way of understanding this important point is to realize that the purpose of our model is to predict the nature of future events, ie, events never seen before, so a prediction model must be tested on new examples, in our case, the validation test. The values for the learning set are shown in Table 2, and those for the validation set in Table 3. The latter table shows that 98% of artifacts were recognized as artifacts, which means that the specificity is 98% (Table 4). The sensitivity is 194/200 = 97% (Table 4). The positive predictive value (PPV) is 194/196 = 99%, where positive refers to the emboli, and the negative predictive value (NPV) is 98/104 = 94% (Table 4).

**Distinction Between Gaseous and Solid Emboli**

In general, gaseous emboli tend to have a higher relative power and a higher frequency. We thus divided the plane defined by the peak frequency and the relative power into 3 regions. The high-frequency (>1600 Hz) or high-relative-power (>18 dB) region was associated with gaseous emboli, and the low-frequency (<1600 Hz) and low-relative-power (<14 dB) region was associated with solid emboli. The nature of points falling into the third region was decided as follows. If the envelope asymmetry was high (>2%), the corresponding point was classified as belonging to a gaseous embolus, whereas if the asymmetry was low (<1%), it was classified as belonging to a solid embolus; points with an
intermediate symmetry were classified as undefined. Again, the critical values (1600 Hz, 14 dB, 18 dB, 1%, and 2%) were chosen by human judgment over some reasonable range (see Figure 4 for peak frequency/relative power and <5% for envelope asymmetry) so as to achieve the best possible differentiation on the learning set before applying them in the validation set. On the validation set, as shown in Table 4, the sensitivity is 89% and the specificity 86%, where the sensitivity is the probability that a solid embolus is declared as such. Conditional on their being classified as emboli, the predictive value for solid emboli (PPV) is 89% and the predictive value for gaseous emboli (NPV) is 89% (for calculating these last 2 numbers, we regarded the outcome “undefined” as “gaseous”). The \( \kappa \) values for the entire table are 0.84 with 89% agreement (\( P<0.0001 \)), again on the validation set (Table 3). The results on the validation set, ie, on examples that were not used in building the model, are only slightly worse than those on the learning set (Table 2). This shows that the model is not overfitted to the examples of the learning set.

Table 2. Cross-Tabulation of HITS Classification Into Artifacts or Gaseous or Solid Emboli by the Automated Doppler System and Human Experts (Learning Set)

<table>
<thead>
<tr>
<th>Automated Doppler System</th>
<th>Human Experts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Artifacts</td>
</tr>
<tr>
<td>Artifacts</td>
<td>100</td>
</tr>
<tr>
<td>Gaseous emboli</td>
<td>0</td>
</tr>
<tr>
<td>Solid emboli</td>
<td>0</td>
</tr>
<tr>
<td>Undefined</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>

Agreement, 90%; expected agreement, 32.33%; \( \kappa \), 0.8522; SEM, 0.0396; \( P=0.0001 \).

Table 3. Cross-Tabulation of HITS Classification Into Artifacts or Gaseous or Solid Emboli by the Automated Doppler System and Human Experts (Validation Set)

<table>
<thead>
<tr>
<th>Automated Doppler System</th>
<th>Human Experts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Artifacts</td>
</tr>
<tr>
<td>Artifacts</td>
<td>98</td>
</tr>
<tr>
<td>Gaseous emboli</td>
<td>0</td>
</tr>
<tr>
<td>Solid emboli</td>
<td>2</td>
</tr>
<tr>
<td>Undefined</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>

Agreement, 89.33%; expected agreement, 33.0%; \( \kappa \), 0.8408; SEM, 0.0404; \( P=0.0001 \).

Discussion

Because there is increasing evidence that time-frequency techniques other than FFT are necessary to classify HITS into artifacts or solid or gaseous emboli, we evaluated a new offline automated system based on a very general approach, the matching pursuit, the usefulness of which was suggested in our pilot study.\(^{27}\) With only 4 characteristic features—peak frequency, time delay, relative power, and envelope symmetry index (Figure 5)—the classification model presented above is fairly efficient. Our results show a high level of agreement between the human experts, still considered the gold standard,\(^{13-24}\) and the automated classification of HITS into artifacts or solid or gaseous emboli (\( \kappa \) value >0.8, \( P<0.0001 \)).

To distinguish between artifacts and emboli, our automated system uses only 2 characteristic features, the peak frequency and the time delay (Figure 5), and achieved an excellent correct classification rate of 98% compared with human experts. With a sensitivity of 97% and a specificity of 98% for emboli, the level of artifact elimination obtained is on the
order of that required if automated analysis is to replace the trained human observer in the detection of embolic signals. To distinguish between gaseous and solid emboli, our automated system uses 3 features: the peak frequency, the relative power, and the symmetry of the signal envelope (Figure 5). Given the large variability of TCD signals, it is clear that a combination of features is necessary, and this is all the more true for the distinction between gaseous and solid emboli. From a statistical perspective, however, excessive multiplication of features should be resisted, because it leads to overfitting. In this initial attempt at building an offline automated system for the classification of HITS into solid and gaseous emboli, we achieved correct classification rates of 87% for solid emboli and 83% for gaseous emboli in the validation set. To discriminate solid emboli from gaseous emboli, we obtained a sensitivity of 89% and a specificity of 86% for solid emboli. Although these results are promising, this performance in discriminating between solid and gaseous emboli can still be improved, but it seems evident that this latter task is more difficult than the separation of emboli from artifacts.

To distinguish between gaseous and solid emboli, we introduced a novel feature, envelope symmetry. One may ask why the envelope of weak gaseous emboli should be less symmetrical than that of strong solid emboli (“weak” and “strong” refer to the intensity of the embolic signals). We offer the following explanation for this empirical observation, an example of which is shown in Figure 1. The attenuation of the incident and reflected ultrasound waves through the tissues is a complex process. If attenuation is strong, the operator will try to compensate for it by increasing the acoustic pressure, and if this is not small relative to the nondisturbed pressure of the medium, nonlinear propagation will occur, resulting in distortion of the pulsed waveforms, including envelope asymmetry. This distortion is likely to occur with weak emboli, whether gaseous or solid. Fortunately, gaseous emboli have a higher relative power than solid emboli, and overlap in relative power is therefore seen only between weak gaseous signals and strong solid signals, hence the relevance of the envelope symmetry in this overlap region.

In conclusion, our study shows that an automated system combining a time-frequency technique and dual-gate TCD and using only 4 features can classify HITS into artifacts or solid or gaseous emboli. It also demonstrates that the solid/gas classification is more challenging than the embolus/artifact classification.

References
16. Droste DW, Hagedoorn G, Notzold A, Siemens HJ, Sievers HH, Kaps M. Bigated transcranial Doppler for the detection of clinically silent circu-

Table 4. Key Values of the Algorithm to Classify HITS Into Artifacts or Solid or Gaseous Emboli

<table>
<thead>
<tr>
<th></th>
<th>Sensibility</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artifact vs emboli</td>
<td>97</td>
<td>98</td>
<td>99</td>
<td>94</td>
</tr>
<tr>
<td>Solid vs gaseous</td>
<td>89</td>
<td>86</td>
<td>89</td>
<td>89</td>
</tr>
</tbody>
</table>

Figure 5. Decision tree with the key parameters to classify HITS into artifacts or solid or gaseous emboli (peak frequency in Hz; time delay in ms; relative power in dB; envelope asymmetry in %). For emboli with envelope asymmetry between 1% and 2%, see text (Results).


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