Computer Based Classification of Carotid Arterial Disease: A Prospective Assessment

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SUMMARY A minicomputer based pattern recognition method has been used to prospectively classify the category of disease involvement of 105 carotid arteries. The system utilized spectral patterns obtained from a combined B-mode/pulsed Doppler unit. All decisions are based upon comparison of an unknown, averaged waveform with a series of vessels with known severity of disease. The variability in the computer decision as compared to arteriography is discussed.

DOPPLER ULTRASOUND TECHNIQUES are widely used in the evaluation of arteriosclerosis of the carotid bifurcation. The ability of the technique to detect minor lesions has been further enhanced by spectral analysis of the velocity-time waveform. The severity of disease may be estimated by a visual interpretation of the spectra which involves a qualitative assessment of the peak systolic frequency, late diastolic frequency and the amount of spectral broadening in the deceleration phase of systole.1 There have been reports in the literature describing the use of velocity parameters for the detection of disease of the carotid arteries.2-5 Rutherford et al.2 used a discriminant analysis of hand-measured waveform parameters to show that velocity waveform analysis was useful in the identification of normal and diseased arteries. We have developed similar techniques using computer selected waveform parameters which are used in a three step decision process to classify disease into four categories.5 This report describes these methods, our experience with the technique, and its performance with a set of prospectively analyzed patients.

Materials and Methods

The subjects in this study consisted of 11 presumed normal volunteers and 49 patients with suspected extracranial arterial disease. In the patient group, there were a total of 83 sides suitable for study. The remaining 15 sides were excluded from the analysis for the following reasons: (1) nine sides had occlusion of the internal carotid artery; (2) four had an endarterectomy; and (3) two were not recorded on tape for unknown reasons.

Biplanar contrast arteriography was performed at the discretion of the referring physician. The arteriograms were all read by an experienced radiologist who was unaware of the result of the noninvasive study. The arteriographic classification of disease was based on measurements of the diameter of the internal carotid artery made from the unsubtracted film. The use of unsubtracted films allowed small flecks of calcification within the vessel walls to be seen, thereby permitting an estimate of the position of the vessel wall to be made. The readings were made from both the anteroposterior and lateral projections. The degree of stenosis reported was derived from the minimum residual lumen diameter measured from one or other of the projections. The degree of stenosis was calculated from these measurements using the equation

\[
\text{\% stenosis} = 100 \times \left(1 - \frac{\text{diameter of diseased vessel lumen}}{\text{diameter of this vessel if normal}}\right)
\]

Neither the length nor the surface characteristics of the lesions were assessed in this study. While these would have an impact on the velocity pattern across the lesion, we had no way of either quantitating these factors or including them into our approach to the problem.

All of the sides were studied with a pulsed Doppler duplex scanning device. The scanhead contains piezoelectric crystals which operate at 5 MHz for both the B-
mode and pulsed Doppler system. The B-mode system permits the technician to view the anatomy of the carotid arteries in real-time. The position of the sample volume of the pulsed Doppler is indicated on the B-mode image by a dot with the path of the Doppler beam observed by a line through the sample volume dot. The angle of the sound beam and the position of the sample volume can be changed to any desired position during the examination.

For the purposes of this study, directional Doppler signals were obtained from the common carotid artery low in the neck and from the proximal internal carotid artery. In patients with detected stenoses, the recordings were made from the site of the maximal flow disturbance. This was judged either by a marked increase in peak velocity or the "rough" signal we have come to associate with turbulence. In practice, the site in the internal carotid artery with the highest frequency shift is usually recorded. At each examination site, the angle between the incident ultrasound beam and the longitudinal axis of the artery is directly measured from the B-mode image. These signals, together with a simultaneous recording of the ECG were recorded on audiotape for further analysis. The duration of recording is such that at least 25 consecutive cardiac cycles are recorded. This number of cycles is required in order to obtain at least 20 suitable heartbeats for the averaging which is done. These waveforms are processed by a real-time digital Fast Fourier Transform spectrum analyser (10 ms per spectrum) and stored on a computer disc with the ECG R wave as a time reference. The best 20 heartbeats are then selected as discussed in the next paragraph. Further details of the pattern recognition can be found in the work of Greene et al with the description here being provided for convenience and because it is more current.

Beat to beat variations are present in the velocity waveforms in patients with a normal sinus rhythm and in those with arrhythmias. To eliminate artifacts due to premature ventricular contractions, any waveform resulting from a heartbeat whose length differs from that of the previous by more than 110 milliseconds, or whose R-R interval is 33 percent greater than the previous R-R interval is rejected. These selection criteria reduce the chance of rejection of the waveform due to normal beat to beat variations, the specific values based on data from ten randomly selected subjects. The FFT spectra from 20 suitable heartbeats chosen by the computer in this manner are then subjected to an averaging routine to produce an ensemble averaged set of spectra as follows. The spectral record from each of the 20 cardiac cycles can be represented as the following function:

\[ E(f, t, n) \]

Where:

- \( E \) is Doppler amplitude at \( f, t, n \),
- \( f \) is frequency in 100 Hz increments from 3000 Hz reverse flow to 7000 Hz forward flow (\( f \) is proportional to flow velocity),
- \( t \) is time in 280, 2.5 ms increments since the ECG R wave, and
- \( n \) is the sequence number of the cardiac cycle.

For each valid value of \( "t" \), \( E(f, t, n) \) is averaged over the twenty cardiac cycles (all \( n \)) to produce the ensemble of averaged spectra denoted by \( E(f, t) \). The mode (frequency of maximum amplitude) for the flow component of the Doppler signal is computed for each of the 280 spectra comprising the heart cycle. The mode frequency was chosen as a measure of signal location because of its inherent resistance to low level wide-band "Johnson" noise that is invariably present. First moment calculations, also widely used, are in general more sensitive to this noise. It should be mentioned that in the absence of such noise, the first moment and mode frequencies are identical if the signal spectrum is symmetrical.

Having located the signal mode for a particular spectrum, the two "half-power" or 3 dB points (approximately 71% of maximum amplitude) are determined as well as the 9 dB points (approximately 40% of maximum amplitude). The frequencies of these four center points plus the mode are then used to represent the original 100 point spectrum. The averaged spectra are then discarded, resulting in reduction by a factor of 20 in the amount of computer disc space required to represent a given number of patient sides (fig. 1).

The compressed Doppler data are analyzed by a software system developed at the University of Washington to perform this pattern recognition work. The system computes selected waveform parameters from both the common and internal carotid arteries, selects a subcombination thereof, assigns weights to each, and then uses them to arrive at a decision as to the severity of disease. The waveform parameters from an unknown vessel are compared to those derived from groups of vessels whose severity of disease is known, until similarity is found with a particular group.

The basic parameters computed from the compressed contour data fall into three classes:

1. those involving spectral width (a measure of velocity distribution through the sample volume),
2. those reflecting time relationships (e.g., height of systolic pulse), and
3. those using frequency decomposition of the first moment waveform.

The latter process is accomplished by computing the first moment (frequency vs. time) waveform, and subsequently subjecting it to a windowed Discrete Fourier Transform (DFT) to extract its frequency components between 1 and 20 Hz. The spectral peaks of this mean frequency waveform are then (automatically) located, and their locations and amplitudes are used as candidate features.

The actual waveform parameters or features which are used are a subcombination of the extracted "raw" features. These processed features were selected by the computer as those which allowed classification of the known vessels (training set) with the highest degree of accuracy when compared with arteriography. The training set used at the time of the analysis of this data consisted of 93 sides (44 normals, 7 confirmed by
arteriography, 35 with disease in the 0–50% category, and 14 in the 50–99% group. The features thus derived fall into two classes; those that involve changes of velocity and those involving spectral width measurements made between the contour lines. The features used for each decision step are listed in Table I. The stepwise process goes through the following decisions: I. Normal or diseased, II. If diseased, decide greater or less than 50% stenosis, III. If less than 50% stenosis, decide greater or less than 20% stenosis.

The third decision step is defined at a 20% stenosis for the following reasons: (1) a natural minimum in the population distribution was observed in the training data at 20%; (2) there is currently insufficient data in the 0–10% range to be able to train a classifier, and (3) there is evidence that the interobserver agreement between radiologists is higher at 20% stenosis than at 10% stenosis.

The features selected for use at each decision step differ. For decision step I the following features are used: a change in velocity feature, the height of the systolic peak, corrected for Doppler angle; the frequency of maximum amplitude within the DFT spectrum of the mean waveform; and a spectral broadening.

**Figure**  Example of an ensemble average waveform from the common carotid artery. The time axis extends from −100 msec to +600 msec relative to the R wave. The center contour line represents the mode with the other representing 3 and 9 dB above and below the mode frequency.
TABLE 1 The Spectral Parameters Used for Each Decision Step is the Angle Between the Incident Doppler Beam and the Longitudinal Axis of the Vessel. Ln is the Natural Logarithm. PCCA = Proximal Common Carotid. PICA = Proximal Internal Carotid.

<table>
<thead>
<tr>
<th>Decision</th>
<th>Definition</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal vs. diseased</td>
<td>(Decrease in velocity from systole to first zero slope point/cosine (6)</td>
<td>PCCA</td>
</tr>
<tr>
<td></td>
<td>Frequency of maximum amplitude in velocity waveform</td>
<td>PCCA</td>
</tr>
<tr>
<td></td>
<td>DFT between 3.9 and 11.7 Hz</td>
<td>PCCA</td>
</tr>
<tr>
<td></td>
<td>Ln (Upper 3 db spectral width at systole + 100 msec)/ (upper 3 db spectral width at systole)</td>
<td>PCCA</td>
</tr>
<tr>
<td>Greater vs. less than 50% stenosis</td>
<td>Ln lower 9 db spectral width 100 msec past systole/ cosine (6)</td>
<td>PICA</td>
</tr>
<tr>
<td></td>
<td>Lower 3 db spectral width 50 msec before R-wave</td>
<td>PICA</td>
</tr>
<tr>
<td></td>
<td>Lower 9 db spectral width 50 msec past systole/ cosine (6)</td>
<td>PICA</td>
</tr>
<tr>
<td>Greater vs. less than 20% stenosis</td>
<td>Decrease in mean frequency from systole to first zero slope point/cosine (0)^2</td>
<td>PCCA</td>
</tr>
<tr>
<td></td>
<td>Ln Upper 9 db frequency at systolic peak</td>
<td>PICA</td>
</tr>
<tr>
<td></td>
<td>Ln (upper 9 db spectral width at first zero slope point)^2</td>
<td>PCCA</td>
</tr>
<tr>
<td></td>
<td>Ln (upper 3 db spectral width at systole + 100 msec)</td>
<td>PICA</td>
</tr>
</tbody>
</table>

A feature measured between the upper 3 db frequency contour line and the mode of the spectrum. These features are all derived from the common carotid artery. Decision step II uses three spectral broadening features, all of which come solely from the internal carotid artery at selected times relative to peak systole. Decision step III uses four features, two being derived from the common carotid artery and two from the internal carotid artery. In each case the features derived from the vessel are a velocity mode and a spectral width feature. The above features are further defined in Table 1.

At each decision step, three choices were available with respect to the decision point: “More diseased” (if the discriminant score is positive); “Less diseased” (if the discriminant score is negative); and “Undecided” (if the discriminant score is near zero).

Results

Twenty-four “normal” internal carotid arteries were studied. Two of these had had carotid arteriograms which confirmed that these vessels were indeed normal. The remaining twenty-two sides must be regarded as “presumed” normal in that these were from eleven symptom free normotensive volunteers; all except one being less than 30 years of age. Eighty-one internal carotid arteries were classified as diseased by arteriography (mean age 62); ten having less than 20% diameter reduction, 39 a diameter reduction of 20–50%, and 32 a diameter reduction greater than 50%.

Table 2 is a crosstabulation comparing the arteriographic classification of disease with the classification by the computer. The vessels in which the computer provided an undecided decision are tabulated in Table 3. This table shows the decision point at which the computer was undecided compared with the degree of disease within the vessel by arteriography. Of the 24 normal arteries, a decision was reached in 21 (88%). Eighteen of these normals were correctly classified as normal (75%). Of the remainder, 2 were said to have stenoses less than 20% and one a stenosis of 20–50%.

Ten arteries had stenoses less than 20% diameter reduction, seven (70%) of these were correctly identified by the computer, one was misclassified as having a 20–50% diameter reduction. The remaining two arteries were unable to be classified and were undecided.

Thirty-nine arteries had a 20–50% diameter reduction by arteriography. Nineteen (49%) of these were correctly identified, seven (18%) were predicted to be in the less than 20% group and 3 (8%) were overestimated and placed in the greater than 50% group. The remaining 10 arteries of the 20–50% subgroup were left undecided (25%).

Thirty-two arteries had a diameter reduction calculated on arteriography to be greater than 50%. Twenty-two (69%) of these were correctly identified, three underestimated as being in the 20–50% group while the remaining seven (22%) were undecided.

All of the diseased arteries were correctly identified by the computer and three of the 24 normal sides (12.5%) were classified as diseased.

Discussion

There are two reasons for developing methods of this type which address the issue of detecting carotid artery disease noninvasively. The first is related to clinical practice, the second to prospective clinical research studies.

While arteriography is relatively safe, there are categories of patients in whom an accurate method of screening could be of importance. These include those with asymptomatic bruits and nonspecific symptoms where the decision to perform the invasive procedure is not always clear. An accurate method of not only detecting disease but classifying it by degree of involvement could be very important.

Another critically important issue relates to the natu-

TABLE 2 Arteriographic Classification of Degree of Stenosis as Compared to That Made by Computer

<table>
<thead>
<tr>
<th>Arteriogram</th>
<th>Normal</th>
<th>20</th>
<th>20–50</th>
<th>50</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal*</td>
<td>18</td>
<td>2</td>
<td>1</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>7</td>
<td>1</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–50</td>
<td>7</td>
<td>19</td>
<td>3</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>3</td>
<td>22</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>16</td>
<td>24</td>
<td>25</td>
<td>83</td>
</tr>
</tbody>
</table>

*Only 2 of the 24 sides were normal by arteriography. The remainder were presumed normals.
ral history of carotid bifurcation disease and its relationship to the clinical practice. It is unlikely even with the introduction of digital subtraction arteriography that it will be reasonable to suggest its use for repetitive studies in large patient populations. Thus we badly need a technique which can be used in an objective manner to assess changes in the disease state as they occur.

In this regard, we want to eliminate the role of the observer in qualitatively assessing the velocity pattern as currently presented in the use of the Duplex scanner. Since the Doppler spectrum is extremely complex, the use of the computer and a pattern recognition approach appeared to be the logical way to proceed. This process involves identifications of potentially useful parameters and establishment of the decision steps.

Unfortunately, the classification of a particular carotid artery into a category of disease is based upon an imperfect gold standard: arteriography. In our own evaluation of the intra- and interobserver variability in this procedure, we have noted potentially serious problems. The ability of an angiographer to repeatedly estimate the percent stenosis to the nearest 5% from a single angiogram has been shown to be beyond the resolution of the method. Furthermore, classification of the degree of stenosis into five groups resulted in the same reader agreeing with himself on a second reading of the same film on only 73.8% of cases. Of equal concern is that two radiologists agree that a carotid bulb on an angiogram is normal or abnormal in only 56% of cases in one study. Therefore, the difficulty involved in the interpretation of carotid arteriograms presents a significant problem in the evaluation of the described technique.

In carrying out the data acquisition and signal processing for application of the pattern recognition program, there are several important considerations. Because beat to beat variations may be seen in the waveforms from a single site, the spectra from twenty suitable cardiac cycles were averaged to produce an ensemble averaged spectrum upon which the analysis was performed. Averaging will reinforce those characteristics of the waveform which are constant cycle to cycle relative to the R wave but the time variant characteristics will be lost in the cardiac cycle. From the entire set of raw features which are derived from both the common and internal carotid arteries, a subset was computer selected for classifying unknown subjects as normal or diseased. The four features used to make this particular decision (see table 1) happen to all use data from the common carotid only. This is interesting since there is no bias in the selection of which features will be used in making any of the three decisions. Detection of changes in velocity patterns proximal to the site at which the problems exists is not new. Rittenhouse et al. has shown that changing the peripheral resistance will markedly affect the velocity patterns recorded from a proximal artery. Archie showed that a normalized velocity index derived from the common carotid artery can be used to identify internal carotid disease. Similarly, Rutherford, et al. noted changes in the velocity waveform of the common carotid artery which paralleled the severity of disease in the internal carotid artery. Some of the waveform parameters recorded using a zero-crossing detector were more discriminating than others, and by weighing these particular variables this group of investigators was able to grade the severity of disease in the internal carotid artery with a high degree of accuracy.

The disease categories selected by Rutherford et al. were normal, less than 50% stenosis, greater than 50% stenosis and total occlusion of the internal carotid artery. We have chosen an additional subdivision of the less than 50% group; namely those greater or less than 20% stenosis. This subdivision was chosen because of our desire to gradate disease and in addition the variability of reading the arteriograms is low at this point. Despite this further subdivision, 18/21 normal sides were correctly classified and all sides harboring disease were correctly identified (table 2).

The subsequent decision steps all require the quantifying of spectral broadening during the deceleration phase of systole, scaled for the Doppler angle. This is in keeping with our day to day clinically derived interpretation of the spectra, which relies on a visual estimation of spectral width during the deceleration phase of systole to identify disease less than a 50% diameter reduction. More severe disease is readily detected by the associated increase in the systolic and diastolic frequencies at the site of disease. It is noticeable that the spectral broadening features vary in time relative to the R wave and are measured between different contour lines above or below the spectral mode (table 1). This is necessary as spectral broadening does not occur symmetrically about the spectral mode.

An "undecided" category has been allowed at each decision step if the classification score fails to exceed a preselected threshold. We feel that this approach is more realistic than forcing decisions. It recognizes that there is overlap between the features of the different disease categories and also recognizes that the radiologists have difficulty in estimating the degree of stenosis to within 15%.

A review of the sides which remained undecided showed that their tendency, with few exceptions, was to lie close to the borderlines of the arteriographic estimate of the diseased groups (table 4). These sides were in each case correctly classified by the previous decision step, thus all of those undecided about the
TABLE 4 Severity of Disease for Those Arteries in Which the Computer was Undecided. PN is Presumed Normal.

<table>
<thead>
<tr>
<th>Decision point</th>
<th>Arteriogram</th>
<th>20</th>
<th>20-50</th>
<th>50</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diseased vs. normal</td>
<td>PN PN</td>
<td>10</td>
<td>20</td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>Greater or less than 20%</td>
<td>PN PN</td>
<td>15</td>
<td>20</td>
<td>20</td>
<td>11</td>
</tr>
<tr>
<td>Greater or less than 50%</td>
<td>PN PN</td>
<td>40</td>
<td>60</td>
<td>65</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>3</td>
<td>2</td>
<td>10</td>
<td>7</td>
</tr>
</tbody>
</table>

*Only 2 of the 24 sides were normal by arteriography. The remainder were presumed normals.

greater or less than 20% decision were correctly classified as having stenoses less than 50%.

All of the decisions are based on the comparison of an unknown waveform with a series of waveforms from a group of vessels whose severity of disease is known. The vessels whose disease state is known comprise the "training set" which ideally should be composed of a representative selection of waveforms in each category. At present the training set consists of 93 sides which are not evenly distributed throughout the spectrum of disease. Developing a representative training set is one of our major goals which unfortunately is likely to take considerable time as only 22% of new patients studied in our laboratory undergo subsequent arteriography.

This report is in many respects preliminary but does appear to hold promise. Further gradations of the degree of stenosis will be tested as the size of the training set increases. While it may never be possible to fine-tune the program for minimal changes of ± 20%, this may not be necessary for clinical applications or even long term followup. If we can show that the computer classification remains stable (in the absence of change in the disease state), it may well be feasible to use this pattern recognition approach to quantitatively document changes without having to resort to arteriography.

References

Computer based classification of carotid arterial disease: a prospective assessment.
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