CAROTID ARTERIAL OCCLUSIVE DISEASE occurs most frequently in the carotid bifurcation, lending itself to easy detection by direct noninvasive ultrasonic techniques. Initially, bruit auscultation was the major physical finding that suggested carotid artery disease.1-3 Next, continuous-wave ultrasonic evaluation provided significantly more information.6-10 Finally, the duplex scanner, combining simultaneous real-time B-mode ultrasonic imaging with pulsed Doppler spectrum analysis represented a further advance.11-23 Blackshear and colleagues26 reported detection of 92% of all flow-limiting lesions (greater than 50%) in the internal carotid artery using the duplex scanner. Similar findings were reported by Fell and colleagues13 and Doorly and co-workers.23 However, these investigators, utilizing a subjective method of visually analyzing each Doppler velocity curve for spectral broadening, obtained less satisfactory results in detecting stenoses with less than 50% diameter reduction. In an effort to improve the detection of lesser degrees of disease, internal carotid artery to common carotid artery flow velocity (maximum and mean) ratios were examined.6-12,18,20 Use of these ratios improved the ability to detect hemodynamically insignificant lesions, but the data did not aid in quantitating the degree of stenosis.

Recently, Krause and colleagues26 applied power frequency spectrum analysis (PFSA) to carotid continuous-wave ultrasonic Doppler signals. The Doppler signals obtained during an 8-msec interval at peak systole were selected for further processing. Following frequency analysis, an amplitude versus frequency plot was obtained, and the bandwidth at 50% of peak amplitude (f_{50%}) was determined. By examining the bandwidth at 50% of peak amplitude, Krause and co-workers were able to identify correctly all degrees of internal carotid artery stenosis with 91% accuracy. In this report, PFSA analysis of pulsed Doppler data from the carotid bifurcation was compared with angiographic findings.

Materials and Methods

Power frequency spectrum analysis was performed on the carotid arterial pulsatile Doppler velocity signal from 115 patients and 10 healthy control subjects. Thirty-one patients (61 sites) subsequently underwent standard aortic arch and selective carotid arterial multiplanar angiography. Each diseased arterial site was recorded and measured, and the percentage of diameter reduction determined. All 10 control subjects were less than 30 years of age and assumed to be free of carotid occlusive disease. The PFSA results from these 61 angiographically documented carotid arteries and 20 normal carotid arteries form the basis of this report.

In contrast to the usual method of spectrum analysis, in which Doppler velocity frequencies are analyzed as a function of time, in PFSA the power (or amplitude) of the recorded signal is plotted as a function of frequency. In this study, an image of the arterial system was obtained via a 7.5 mHz or 10.0 mHz B-mode ultrasonic probe,* depending on the depth of the vessel beneath the skin. After locating the vessel, a pulse repetition frequency was chosen to position a 3.0-mHz Doppler signal in the center of the vessel lumen. Several representative tracings from each arterial location were recorded and a 20-msec segment of the Doppler signal at peak systole was sampled. Peak systole was chosen because (1) it is the instant at which turbulence begins, and (2) it is a reliable landmark that can be identified easily and quickly. The information available in the peak systolic segment is the basis for

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*Model No. DS-10, Disonics Corporation, Milpitas, California 95035.
power frequency spectrum analysis. Utilizing the output of a pre-programmed fast-Fourier transform, frequency is plotted on the X-axis, and the power (or amplitude) of the various frequencies is plotted on the Y-axis. In each sample, the frequency with the greatest amplitude receives a 100% power rating. Amplitudes of all other frequencies are then automatically calibrated in proportion. The equipment has software that computes the $f_{\text{peak}}$ bandwidth, $f_{\text{max}}$, and $f_{\text{mean}}$.

With the patient in the relaxed supine position, Doppler signals and power frequency spectra were obtained systematically from the common carotid artery traveling cephalad to the carotid bifurcation. Next, the course of the internal (ICA) and external (ECA) carotid arteries were located, followed, and analyzed, initially at the bifurcation and then 1-2 cm distal to the bifurcation. Each vessel was identified both on the basis of its anatomical location and its specific audio signal. Additional signals were analyzed where any change in the audio signal or ultrasonic image suggested possible pathology.

Each power frequency spectrogram was analyzed for peak frequency ($f_{\text{max}}$) and frequency bandwidth at 50% of maximum power ($f_{\text{peak}}$). A 50% frequency bandwidth was considered to represent a quantitative expression of spectral broadening. Both variables were compared with the corresponding angiographic findings.

Statistics

The unpaired t-test was used wherever applicable to determine statistical significance between two sets of measurements. Sensitivity was obtained by dividing true positive Doppler results by positive angiographic results. Similarly, specificity was calculated by dividing the true negative (normal) Doppler results by the negative (normal) angiographic results. Accuracy was determined by dividing the sum of true positive and negative Doppler results by the sum of positive and negative angiographic findings. The positive predictive value was obtained by dividing the true positive Doppler by the sum of true and false positive Doppler results. Negative predictive value was defined as true negative Doppler results divided by the sum of true negative and false negative results.

Results

A. Reproducibility

Ten carotid systems in control patients were re-studied by the same examiner approximately 30 minutes after the initial study was completed. A full examination was performed each time. Two measurements were taken from the internal carotid artery bilaterally in 5 control subjects. The initial examination yielded a mean of 210 ± 46 Hz (± standard deviation), while the mean of the second group of measurements was 200 ± 53 Hz ($p = \text{NS}, t = 0.6127$). Three internal carotid arteries provided identical $f_{\text{peak}}$ measurements during the second measurement, while 6 studies were within 50 Hz of the original $f_{\text{peak}}$ measurement. Only one study had a difference of 100 Hz between the two examinations. Finally, the percentage of mean difference ± 1 S.D. between the respective measurements was 2.7 ± 25.8%. The resolution of spectrum analyzer read-out was 50 Hz.

B. Clinical Studies

Sixty-one carotid arterial systems from 31 patients underwent pulsed Doppler power frequency analysis (PFSA) and multiplanar carotid angiography. One patient underwent only a unilateral angiogram after experiencing an allergic reaction to the dye. Angiographically, the internal carotid artery exhibited minor wall irregularities or stenoses of less than 10% in 9 cases, while 13 vessels were 10-24% stenotic and 13 vessels exhibited 25-49% diameter reductions. In 26 vessels, hemodynamically significant stenoses were documented: 8 vessels were 50-74% stenotic, 10 vessels were 75-99% stenotic, and 8 vessels were occluded (table 1).

Frequency bandwidth at 50% peak power ($f_{\text{peak}}$) and peak frequency ($f_{\text{max}}$) of each internal carotid artery velocity signal are compared with the angiographically determined percentages of diameter reduction in figures 1 and 2. A linear relationship was found for each analysis, with correlation coefficients of 0.920 and 0.889, respectively.

Receiver operator characteristic (ROC) curves were constructed to determine the optimal threshold $f_{\text{peak}}$ values to differentiate between the presence or absence of disease a various levels of disease severity. Diameter reductions of 10%, 25%, and 50%, were chosen as the levels of angiographically determined disease to be used as the cutoff between the presence or absence of disease. As seen in figure 3, the optimal 50% frequency bandwidths to differentiate 10%, 25%, or 50% stenoses were 350 Hz, 1200 Hz, and 1750 Hz, respectively. Utilizing an $f_{\text{peak}}$ value greater than 350 Hz to predict greater than 10% stenosis, the test was 97.7% sensitive, 97.5% specific, and 97.6% accurate (table 2). An $f_{\text{peak}}$ value greater than 1200 Hz predicted a 25% diameter reduction with 80.7% sensitivity, and an $f_{\text{peak}}$ value of greater than 1750 Hz predicted a 50% diameter reduction with 94.4% sensitivity.

These criteria were re-grouped to evaluate further the ability of range-gated pulse Doppler PFSA to predict the degree of carotid arterial disease. In this analysis, frequency bandwidths ($f_{\text{peak}}$) less than 1200 Hz were classified as less than 25% diameter reduction, $f_{\text{peak}}$ values of 1200-1750 Hz represented 25-49% stenosis, and values greater than 1750 Hz indicated great-

| Table 1 | Distribution of Internal Carotid Stenosis by Angiographic Measurements in 61 Vessels |
| --- | --- | --- | --- | --- | --- | --- |
| Percentage of stenosis | 10 | 10-24 | 25-49 | 50-74 | 75-99 | 100 |
| Number of vessels | 9 | 13 | 13 | 8 | 10 | 8 |
er than 50% diameter reduction. The absence of an ICA signal was interpreted as a total occlusion. Using this scheme, there were 70 correct interpretations among the 81 vessels examined, for an accuracy of 86.4% (table 3). Six stenoses were overestimated (false-positive). In addition, one severe (95%) ICA stenosis was misinterpreted as an ICA occlusion.

Similar techniques were used to obtain the optimal peak frequency ($f_{\text{max}}$) to differentiate 10%, 25%, and 50% stenosis. No acceptable value was found for 10% diameter reduction because there was significant overlap between the $f_{\text{max}}$ values from vessels with less than 10% stenosis and those from vessels with 10-49% stenosis. Peak frequencies ($f_{\text{max}}$) of 2500 Hz and 3000 Hz were best found to classify vessels into the categories of greater than 25% and 50% stenosis, respectively. To identify angiographic cases of 25% stenosis, the $f_{\text{max}}$ criteria of 2500 Hz was 77.4% sensitive, 91.1% specific, and 85.5% accurate. Utilizing an $f_{\text{max}}$ value of greater than 3000 Hz to predict 50% diameter reduction, the test was 88.9% sensitive, 91.4% specific, and 90.8% accurate (table 4).

By both ultrasonic imaging and Doppler spectrum analysis, nine internal carotid arteries were classified as occluded. Angiography verified the occlusion in eight. However, one vessel was found to have a high bifurcation with a 95% stenosis at the origin of the internal carotid artery. The highly stenotic lumen was never visualized, and, in addition, the Doppler sample volume could not be placed within the narrow flow stream. With the ultrasonic image alone and no Doppler, only five of the eight internal carotid artery occlusions would have been diagnosed. The ultrasonic image was entirely normal in one case and difficult to interpret in the other two, owing to nonhomogeneous plaques and acoustic shadowing.

**Discussion**

Pulse Doppler frequency shift spectrum analysis was recently introduced as another noninvasive modality for the detection of carotid arterial occlusive disease. This method was described by Blackshear and colleagues, who accurately predicted the presence of 50% diameter reduction in the internal carotid artery with 92% sensitivity. However, the identification of lesser degrees of stenosis was not as accurate, a finding confirmed by Fell et al, Dooley et al, and Russell et al. Several attempts to improve the accuracy of detecting carotid arterial stenoses of less than 50% have been reported. Measurements of peak frequency and of several ratios of internal to common carotid artery velocity have improved the accuracy of detecting hemodynamically significant le-
sions. For lesser degrees of stenosis, Rittgers et al calculated the systolic window of carotid artery CW Doppler velocity tracings as a quantitative measure of spectral broadening. These investigators successfully detected all stenoses greater than 40% and correctly identified all normal vessels (less than 20%). At the 25% diameter reduction level, their data were 90% sensitive, 98% specific, and 95% accurate.

Sheldon and coworkers utilized the ratio of maximum to mean frequency at peak systole from Power Frequency Spectrum Analysis data to quantitate spectral broadening. Among the parameters examined, the distal ICA systolic window provided the best sensitivity for detecting moderate to severe stenoses (greater than 40%) with a specificity greater than 85%.

Recently, Krause and colleagues reported their preliminary experience with continuous-wave Doppler PFSA to detect carotid arterial occlusive disease. Frequency bandwidths at 50% peak power (f50%) were identified as an index of disease severity. For hemodynamically significant lesions (greater than or equal to 50% stenosis), the test was 100% sensitive, although its specificity was only 45%. Utilizing greater than 11% diameter reduction as the cutoff between the presence or absence of internal carotid artery disease, the sensitivity remained high (92%) and the specificity increased to 83%. At this level, the peak frequency (fmax) was 79% sensitive, but 100% specific.

The results of the present study support the PFSA technique in the evaluation of pulsed Doppler frequency shifts in the carotid arterial system. The measurement of peak frequency is sensitive to hemodynamically significant stenoses (greater than 50%), but its sensitivity, specificity, and overall accuracy begin to drop off in the detection of less severe disease. As seen in figure 2, this decline in fmax accuracy is due to an increased overlap between the values obtained from the vessels with lesser stenoses and normals.

The frequency bandwidth at 50% of peak power (f50%) eliminates some of the limitations of peak frequency measurements. In the lesser disease categories (less than 50% stenotic), PFSA f50% is most useful and can be considered a quantitative index of spectral broadening. The f50% value at peak systole increased in proportion to increasing vessel diameter reduction. As seen in figure 1, there was little overlap between f50% values from various categories of disease severity, particularly with less than 50% stenosis. As diameter reduction approached 50%, the peak frequency of the Doppler curve gradually increased in a linear fashion, as noted in figure 2. However, the highest peak frequency recordable with the equipment used in this study was 5000 Hz. Stenoses greater than 75% produce peak frequencies higher than 5000 Hz (fig. 2), but fmax values greater than 5000 Hz could not be recorded. On the other hand, this drawback has been remedied in the latest modification of the instrument.

In addition to its capability to detect hemodynamically insignificant stenoses, f50% determination can readily detect severe stenoses. As seen in Table 2, f50% identified stenoses greater than 50% with sensitivity of 94%, specificity of 93%, and accuracy of 93%. This compares favorably with peak frequency measurements. Using an fmax value of 3000 Hz to differentiate 50% diameter reduction, the fmax measurement was 89% sensitive, 91% specific, and 91% accurate.

One of the major advantages of the duplex scanner is its ability simultaneously to image the vessel and visualize the sampling site of the Doppler velocity sensor. This technique aids substantially in the reliable detection of vessel occlusions. All 8 internal carotid artery occlusions in this study were easily detected utilizing both ultrasonic imaging and pulse Doppler PFSA.
However, three of these vessels would not have been definitely diagnosed as occluded had the ultrasonic imager been used alone; consequently, both imaging and frequency analysis are necessary to predict accurately the total vessel occlusion. However, a very tight stenosis was misdiagnosed as occluded in the present study. The patient had a 95% internal carotid artery stenosis, but the lumen could not be visualized nor was flow detected with the pulsed Doppler system. Two explanations for this error are possible: (1) the very tight stenosis became occluded soon after angiography prior to the noninvasive evaluation; or (2) the Doppler sample volume missed the narrow jet of blood squinting through an extremely tight stenosis. The recent introduction of a variable sample volume pulsed Doppler should remedy this deficiency.

Our data support the quantitative index of the $f_{50\%}$ analysis from a range-gated pulsed Doppler. It not only detected hemodynamically significant stenoses but also correlated linearly with the degree of hemodynamically insignificant stenoses. On the other hand, peak frequency ($f_{\text{peak}}$) values greater than 3.0 kHz were useful to confirm $f_{50\%}$ indices of hemodynamically significant stenoses.

### References

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