CAROTID ULTRASOUND

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This article provides an overview of carotid ultrasound. Much of diagnostic carotid ultrasound is focused on the detection of high-grade carotid stenosis amenable to surgical intervention. This goal is achieved when the basic principles of Doppler ultrasound are followed and integrated into the imaging protocol.

In the first section the results of the major clinical trials that have justified the value of carotid artery surgery are reviewed. The use of carotid ultrasound and the lessons learned from these studies are discussed. The second section covers the underlying principles, strengths, and weaknesses of the Doppler methodology in the context of evaluating the severity of carotid artery stenosis.

The next section reviews the use of gray-scale ultrasound imaging for evaluating carotid plaque. There is increasing evidence that the texture and elements within the carotid plaque can predict future cardiovascular outcomes. Although traditionally viewed in the context of surgical intervention, these new concepts in imaging may shift therapeutic options toward noninvasive therapies.

The fourth section focuses on the quantitative evaluation of the wall thickness of the common carotid artery. This intima-media-thickness measurement is gaining increasing popularity as a technique for evaluating the effects of exposure to atherosclerotic risk factors in the general population.

In the final section, new methodologies that may add to the diagnostic value of carotid ultrasound are reviewed. This includes the use of three-dimensional imaging for evaluating rare pathologies. In addition, the use of contrast-enhanced techniques is reviewed. Two aspects of contrast-enhanced imaging are covered: (1) following the intravenous administration of ultrasound contrast agents and (2) using new ultrasound pulse sequences.

CAROTID STENOSIS: WHAT IS SIGNIFICANT?

Started in the late 1980s and conducted throughout the 1990s, two major carotid endarterectomy trials have shown that surgical intervention for significant carotid artery stenosis offers benefits to the patient. These endarterectomy trials have not only given data on the value of the surgical intervention but have also standardized the technique for evaluating the severity of carotid artery stenosis on angiography. This gold standard method of evaluating carotid artery stenosis on angiography serves as the common denominator against which the results of carotid artery Doppler ultrasound must be compared.

Carotid Endarterectomy Trials

Two large trials have been conducted in symptomatic patients: (1) the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and (2) the European Carotid Sur-
gery Trial (ECST). Both studies enrolled patients in the late 1980s and published their preliminary results in the early 1990s. The NASCET showed definite value for operative intervention for patients with stenosis of 70% diameter narrowing or more. The differences between the medically treated population and the surgically treated patients were so dramatic that an alert was generated in 1990 on the recommendations of the data safety monitoring board. The results of NASCET clearly indicated a benefit for surgical intervention when the degree of stenosis in the proximal internal carotid artery was 70% or greater. This benefit was also a function of disease severity: the more severe the stenosis, the greater the benefit of surgical intervention (Fig. 1). For example, the absolute risk reduction for stroke or death at 2 years with surgical intervention increased from 12 ± 4.8% for stenoses between 70% and 79% to 18 ± 6.2% for stenoses between 80% and 89% and then to 26 ± 8.1% for stenoses between 90% and 99%

The NASCET study used a nontraditional method to grade the severity of internal carotid artery stenosis seen on a carotid arteriogram. This technique for grading carotid stenosis is shown in Figure 2. In essence, the degree of residual lumen seen at the stenosis is compared with the lumen of the internal carotid artery more distally.

Results from the ECST, although also showing a benefit for surgical intervention in those patients with a greater than a 70% diameter narrowing of the carotid artery, differed significantly from the NASCET results. The method used to grade stenosis severity in the ECST study was different than the method adopted by NASCET. The ECST method of measuring stenosis severity is consistent with the traditional approach of comparing the residual lumen at the lesion to an overall subjective guess of the true lumen of the artery at the level of the lesion in the carotid artery (Fig. 3). Because of this difference in measurement of the degree of carotid artery stenosis, the benefit of surgical intervention for greater than 70% diameter stenosis in the ECST translates to a benefit for a

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**Figure 1.** The results of the two major trials, North American Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST). On the left are plotted the absolute risk reduction for a combined outcome of stroke or death as a function of the severity of carotid stenosis. The more severe the stenosis, the more significant the reduction in stroke/death with surgery as compared with medical therapy. The surgical complication rates for each level of intervention are shown on the right of the figure. In each group of five: First bar = NASCET ≥ 70% (at 2 y); second bar = ECST ≥ 60% (at 3 y); third bar = NASCET 50–69% (at 5 y); fourth bar = NASCET < 50%; fifth bar = ECST < 40% (at 3 y).
degree of stenosis of 50% or more by NASCET measurements.\textsuperscript{31}

The first publication from the NASCET study showed an advantage for identifying patients who have high-grade lesions of at least 70% diameter stenosis and then performing a surgical intervention.\textsuperscript{31} The same report showed the lack of any benefit for surgery on lesions of 30% diameter narrowing or less.\textsuperscript{31} This left an unanswered question: at what degree of stenosis should surgery be performed? The final results of the NASCET study showed that a net benefit to the patient can be shown for surgery of a carotid stenosis causing between 50% and 69% diameter narrowing.\textsuperscript{3} These data, published in 1998, unfortunately include all of the outcome results into the broad category of 50% to 69% diameter stenosis. The data do not present evidence of any better advantage of surgery for a more severe stenosis (e.g., between 60% and 69% as compared with the group with a stenosis between 50% and 59%). An aggregate of the results from both the ECST and NASCET is shown in Figure 1. To compare the results of the NASCET with the ECST studies, the angiographic measurements of ECST have been translated to the standard method of grading stenosis severity used by NASCET.\textsuperscript{29} These estimates of disease severity show a definite benefit for surgical intervention for stenoses of 50% diameter narrowing or more. These benefits take into consideration the surgical complication rates that count towards the overall morbidity to the patient. There is an early disadvantage for performing carotid surgery, more dramatic in the first 30 days of the perioperative period. Following this, the long-term benefits to the patient show up as a prolonged time interval with lessened risk of future carotid strokes.

The recently published results from the NASCET and ECST trials have somewhat calmed the confusion that arose in the mid
1990s with the publication of results from the asymptomatic carotid artery surgery trials. The Asymptomatic Carotid Artery Surgery Trial (ACAS) showed a distinct advantage for surgical intervention for patients who had at least a 60% stenosis. After the results of this trial were published in 1995, a confusing situation existed. A surgical intervention seemed indicated in symptomatic patients with lesions of at least 70% diameter stenosis whereas asymptomatic patients seemed to benefit from surgical intervention at lower degrees of stenosis (60%). An important factor that affects the interpretation of the results for symptomatic and asymptomatic patients is the lower overall required complication rate on the side of the asymptomatic study, which accepted up to 3% surgical complication rates, whereas the North American trial accepted up to 6% complication rates for enrollment.

There is a benefit for surgical intervention in symptomatic patients who have at least a 50% diameter stenosis. This benefit is dependent on a low surgical complication rate. For asymptomatic patients, it seems that surgical intervention can be done for carotid stenosis of 60% or more. The NASCET and ACAS studies have had an impact on carotid ultrasound in two ways: (1) defining a new way of grading stenosis severity and (2) giving attention to quality assurance issues needed to minimize errors on carotid ultrasound.

Gold Standard Method of Grading the Severity of Carotid Stenosis

The NASCET and the ACAS studies introduced a standard method of grading the severity of carotid stenosis. In essence, the point of maximal lumen diameter narrowing as seen on multiple projections of the carotid angiogram is compared with the lumen of the artery in a more cranial location (see Fig. 2). This creates an internal self reference for grading the severity of the stenosis. It translates poorly in estimating the amount of plaque burden that might be present at the level of the proximal internal carotid artery. This region, the carotid sinus, is typically associated with a local dilatation of the outer wall of the internal carotid artery. Plaque shows a tendency to deposit into this area of slow flow.

An angiogram, which may seem to show no stenosis whatsoever, may miss a large plaque burden (Fig. 4). In addition, the implication is that the carotid arteriogram has been performed on multiple projections. As compared with a traditional selective arteriogram taken in the lateral and anterior projections, an oblique view better delineates the severity of the stenosis in 10% of cases. Data published on the value of rotational angiography showed that traditional biplane carotid angiography underestimates the severity of stenosis in 7 (28%) of 25 cases.

Despite these limitations of methodology of grading carotid stenosis by angiography, however, this remains a gold standard against which the performance of carotid ultrasound and Doppler velocity measurements has to be measured. This holds despite an interobserver variability in the range of ±7% for grading stenosis severity on preselected arteriographic images of the carotid arteries.

Diagnostic Performance of Carotid Ultrasound in the NASCET and ACAS Studies

Results of the diagnostic accuracy of carotid ultrasound in the centers participating in the NASCET study published in 1995 showed that the sensitivity and specificity of carotid ultrasound were 68% and 67%, respectively. This observation generated a great controversy. A full discussion of the possible reasons for the poor diagnostic performance of carotid ultrasound in NASCET is beyond the scope of this article. Certain methodologic issues that likely played a role include the following: variations in patient selection, in imaging device performance, and in the imaging protocols. The effect of imaging device is certain, at least based on the experience derived from ACAS. In ACAS, the specificity of carotid ultrasound was above 95% and gave consistent values once a standard protocol had been adopted. To qualify, however, centers had to show evidence of correlation between Doppler measurements and carotid arteriography. Between-center variations were dramatic. The possibility that differences in imaging devices or imaging protocols could also have had an effect on diagnostic performance has been supported by other published data. Data from our laboratory, where we compare readings on different ultrasound imaging devices, show great consistency between estimates of stenosis severity made by different sonographers and dif-
Figure 4. A, Gray-scale image of the carotid artery bifurcation shows a large plaque burden sitting in the proximal internal carotid artery. B, The corresponding Doppler waveform shows increased peak systolic velocity consistent with a 50% diameter stenosis. C, The arteriogram shows a plaque. The residual lumen at the level of the lesion, however, is the same as the diameter of the internal carotid artery. The arteriogram is interpreted as not showing a significant stenosis (0%) despite a large plaque burden.

 different ultrasound devices as long as a consistent imaging protocol is followed.

ULTRASOUND EVALUATION OF THE SEVERITY OF CAROTID ARTERY STENOSIS

Principles of Velocity Estimation Using Doppler Ultrasound

With carotid ultrasound, a sound pulse of carrier frequency somewhere between 3 and 5 MHz is transmitted into the patient's soft tissues. The returning echoes from blood moving in the carotid artery give information on the relative motion of blood with respect to the direction of this ultrasound beam. The angle between the ultrasound beam and the direction of blood flow is kept at 60 degrees or less. The sonographer then estimates the direction of blood flow and applies an appropriate angle correction. This frequency shift information is transformed to the velocity of moving blood.

The first manuscript to describe a systematic way of using the Doppler frequency shift to estimate the severity of internal carotid artery stenosis was published in 1979. This article is commonly quoted and is the source of the figure relating stenosis severity in the carotid artery to Doppler frequency shift (Fig. 5). At a point of maximal narrowing in the carotid artery, the velocity of moving blood
increases because of the restriction of the lumen of the artery. As the degree of stenosis increases, the velocity of blood and the measurable Doppler frequency shift increase. At higher grades of carotid stenosis, because of the overall increased resistance to blood flow, the amount of blood being delivered into the diseased carotid artery decreases.

Compensatory flow typically develops in collateral branches either from the ipsilateral external carotid artery, vertebral artery, or from the contralateral arteries. This decrease in the amount of blood being delivered into the diseased artery causes the association between the Doppler velocity to start decreasing as a function of disease severity. The positive association, increasing blood flow velocity with increasing stenosis severity, is maintained until the stenosis is critically severe (somewhere near to 90% or 95%). This leads to a paradoxical situation: it is possible to have, for the same Doppler velocity, two different degrees of stenosis. These critical stenoses can be detected by noting alteration of the Doppler waveform distal to the lesion or by observing the size of the narrowed lumen on a color Doppler or power Doppler image. From a practical point of view, however, color Doppler flow imaging facilitates the evaluation of these high-grade stenoses.

There are, however, certain elements of an imaging protocol that improve the reliability of Doppler velocity for grading the severity of carotid artery stenosis. The first element is the capability of identifying the location of the point of maximal narrowing. At this point, two physical phenomena should be observed. First, this is the point of highest blood flow velocity. This site corresponds to the location where blood has the highest amount of kinetic energy. In addition, because the zone of blood flow is severely restricted, all red cells at the stenosis move at the same velocity. This translates into what is called plug flow. A Doppler velocity spectrum (Fig. 6) acquired at this point shows cohesive motion of the red cells and a relatively clear spectral window (Fig. 6A; see also Color Plate...
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Estimating the severity of carotid stenosis is focused on locating this point. An additional physical phenomenon comes into play just distal to the point of maximal narrowing: the presence of a velocity jet. The red cells that have acquired increased kinetic energy at the stenosis then dissipate this energy over a short distance but maintain some cohesive pattern of blood flow called the velocity jet.

**The Velocity Jet**

As indicated previously, the point of maximal narrowing in the carotid artery causes a zone of increased velocity where blood flow is very cohesive. Red cells move at the same velocity, a phenomenon referred to as **plug flow**. Detecting this point is the basic goal of any sonographer trying to estimate the severity of a carotid stenosis. As such, the sonographer must keep in mind certain basic principles. Distal to the stenosis, the zone of increased velocity translates into a jet of increased velocity, the so-called **velocity jet**. Within this jet, which tends to diverge relatively quickly, the peak velocity of red blood cells tends to decrease relatively slowly over a distance of 1 to 2 cm (Fig. 6B; see also Color Plate V, Fig. 39). For a distance of 1 to 2 cm, it is possible to get a relatively accurate Doppler tracing of the velocity increase caused by a stenosis. The measurement obtained downstream tends to underestimate the peak velocity of blood and tends to underestimate the severity of the lesion located more proximally. Knowledge of the hemodynamic behavior of a carotid stenosis is especially important in cases where there is extensive carotid calcification. The point of maximal narrowing might be masked within a zone of calcification that cannot be penetrated by the ultrasound beam. Evidence of a high-grade stenosis is seen distally and manifests as a zone of increased velocity and alterations in the overall Doppler tracing.

The appearance of the Doppler waveform downstream to the stenosis shows both broadening and reversal of blood flow (Fig. 6C; see also Color Plate V, Fig. 40). The broadening of the Doppler envelope is caused by
divergence of the red cells from the velocity jet and a change in the direction of red cells as they slow down at the sides of the velocity jet. More to the side of the velocity jet, a zone of vorticeal blood flow is established. Red cells in this zone are reversing their direction and show up on the Doppler waveform as a region with negative velocity with respect to the main component of forward blood flow. At a point 1 to 2 cm downstream to the stenosis proper, a zone of turbulence is established. Here, the bulk flow velocity of the red cells is still high despite the widening of the velocity jet. The velocity of moving blood can then reach the critical Reynolds' number. The Reynolds' number is strongly dependent on the overall diameter of the artery and on velocity and viscosity of the fluid that is moving at a given velocity. Above a given Reynolds' number, blood flow becomes turbulent or disorganized. This zone of transition with a high enough Reynolds' number is likely to occur at a distance of between 1 and 2 cm from the point of maximal narrowing (Fig. 6D; see also Color Plate V, Fig. 41).

The direction of the velocity jet indicates the direction of moving blood and is a useful index for the proper angle correction of the Doppler frequency shifts into estimates of the velocity of blood flow. Although limited by sample rates and artifacts, the color Doppler image offers a good estimate of the direction of blood flow. This can be achieved by sampling from multiple longitudinal projections, until on one projection a velocity jet of sufficient length can be identified and used to measure the direction of blood flow. This strategy is especially useful in cases of hypoechoic lesions that are not identified on grayscale imaging alone.

Estimation of the velocity of blood flow with Doppler measurements still requires that the relative angle between the direction of blood flow and the ultrasound beam be kept at 60 degrees or less. There are two reasons for following this recommendation: (1) above 60 degrees, errors engendered by the person performing the angle correction increase dramatically; and (2) artifacts associated with the detection of velocity signals taken closer to 90 degrees to the direction of motion are significant.

Adherence to this principle is helpful when evaluating a carotid stenosis that is eccentric and located in a carotid artery with an atypical course. For example, in the case of an artery that is directed upward, sampling from upstream (right to left, with the aorta to the right of the image) may lead to large angles between the direction of blood flow and the Doppler ultrasound beam. The best strategy is to direct the Doppler ultrasound beam into the direction of estimated red cell flow as is shown in Figure 7 (left to right, the right still being the location of the aorta) (see also Color Plate VI, Fig. 42). This permits one to achieve a lower angle between the ultrasound beam and the direction of blood flow and mini-

Figure 7. A, This color Doppler image shows a plaque with hypoechoic elements. Blood flow is directed upwards (toward the top of the image). (See also Color Plate VI, Fig. 42.) B, Sampling with the Doppler sample gate is directed from right to left (into the lesion) to keep the angle between the Doppler beam and the direction of blood flow at less than 60°.
mizes the error engendered by the operation of angle correcting between the direction of blood flow and the direction of the ultrasound beam.

The ability to obtain accurate velocity estimates may also be affected by the algorithm used for angle correction in the ultrasound device, especially for linear array transducers. A deficient algorithm for estimating the angle between the ultrasound beam and the direction of flowing blood leads to overestimation of blood velocity. This artificial spectral broadening effect may have led to poor or inconsistent performance of some ultrasound machines in different clinical studies. This may also be one of the reasons why the performance of Doppler ultrasound in the NASCET study showed poor accuracy.

The Subtotally Occluded Carotid

The NASCET and ECST studies showed that the risk of stroke is directly linked to the severity of carotid stenosis. Although the major pathologic mechanism for stroke is an actual atheroembolic event, the likelihood of artheroembolism is positively associated to the degree of stenosis. As such, the more severe the stenotic artery, the more likely the patient is to experience a stroke over the next few months and years. This leads to the development of an interesting scenario where continued restriction of flow of the carotid artery leads to the point where the artery is subtotally occluded. Volume blood flow is directed away from the diseased carotid to other collaterals, as mentioned previously. In this situation, absolute blood flow and velocities in the artery decrease dramatically. It seems, however, that the lesion’s potential for causing stroke is maintained.

Because the velocity of moving red cells is decreased dramatically in these situations, it is possible that the Doppler measurements might fail to detect slowly moving blood in the still open vessel. This has significant impact on the patient because operative intervention in this subtotally occluded artery decreases the risk of subsequent stroke. Ignoring the subtotally occluded carotid artery and letting it occlude leads to a persistent risk of stroke of approximately 5% per year.

Because of the limitation of the Doppler technique that might fail to detect very slow blood flow velocities, it is almost routine clinical practice to recommend some form of ancillary diagnostic testing to supplement carotid ultrasound in patients who have internal carotid arteries that appear totally occluded. Diagnostic testing with MR angiography, CT angiography, or carotid arteriography are all useful in the evaluation of these lesions. The traditional carotid angiogram with the prolonged infusion of contrast while filming still remains a gold standard. The character and residual lumen of the distal internal carotid artery seems, however, more easily evaluated with the cross-sectional imaging modalities, such as CT. There is a suggestion, based on some published data, that color Doppler imaging has improved the diagnostic accuracy of carotid ultrasound to the point that testing with other modalities might no longer be necessary.

Velocity Parameters

Various velocity parameters have been used for estimating the severity of carotid stenosis. Typically, the peak-systolic velocity is measured at the point of maximal narrowing in the carotid artery. Another single parameter that may be used is the end-diastolic velocity. Both measurements are made by placing a cursor or using automatic edge detection to identify the top of an appropriately acquired Doppler spectrum. The end-diastolic velocity came into vogue mainly because of the inherent limitation of some ultrasound devices. At points of maximal stenosis, some ultrasound devices were not capable of processing the high-frequency shift information contained in the returning echoes from the Doppler ultrasound beam. This led to a paradoxical situation where the highest velocities close to peak systole were folded (or aliased) into the spectrum below it. This led to ambiguities in terms of obtaining an actual peak-systolic velocity. In such cases, the severity of the carotid stenosis can still be estimated by using the end-diastolic velocity. The end-diastolic velocity, by virtue of being much lower than peak-systolic values, is less likely to alias and can be more consistently obtained.

Reliance on a single peak-systolic or end-diastolic value for estimating a stenosis seems somewhat simplistic and many clinicians believe that this approach does not take into consideration changes in cardiac output and other sources of interindividual variations in blood flow velocities. Using the velocity of
blood in the common carotid artery, specifically a point of 2 to 4 cm from the bifurcation, it is possible to obtain a ratio of the velocity in the internal carotid artery to that in the common carotid artery. The estimated peak-systolic velocity ratio tends to have, in the same patient, slightly more error than the simple peak-systolic velocity measurement. There are two velocity ratios based on end-diastolic velocities: (1) the end-diastolic velocity in the internal carotid artery divided by the common carotid artery end-diastolic velocity or (2) the peak-systolic velocity in the internal carotid artery divided by end-diastolic velocity in the common carotid artery. These two parameters can be used for estimating the severity of carotid artery stenosis. Consideration should, however, be given to normal fluctuations in the Doppler velocities or velocity patterns in the common carotid artery. For example, the common carotid artery velocities are typically higher by 10 to 20 cm near the origin (so-called low common carotid) and decrease when nearing the level of the carotid bifurcation. Near the flow divider, the zone dividing the external from the internal carotid artery, blood flow patterns are perturbed by the presence of the bifurcation. The direction of blood flow is altered and preferentially directed toward the inner wall of the internal carotid artery. Blood flow patterns tend to be relatively consistent and close to laminar pattern approximately 3 cm from the level of the carotid bifurcation. A consistent estimate of common carotid artery peak-systolic (or diastolic) velocity is made at this point in the absence of any lesion or plaque formation.

Various values have been used for estimating the stenosis severity on carotid arteriography. The values published in the 1980s compared the results of carotid ultrasound with arteriographic measurements made using a traditional method (see Fig. 3) of grading. With the adoption of NASCET and the ACAS studies, it became necessary to recalibrate the system of velocity estimates made by Doppler ultrasound to match the new method of estimating the severity of internal carotid artery disease on arteriography (see Fig. 2).

**Velocity Cut-Points for Detecting Significant Stenosis of the Internal Carotid Artery**

Many papers have compared various Doppler velocity values for distinguishing stenosis severity above or below a certain cut-point for 70% (NASCET) or 60% (ACAS) stenosis. Some of these papers are shown in Table 1 and Table 2. With the recently published results of the NASCET study it becomes necessary to detect patients who have carotid artery lesions causing a stenosis of 50% or more. The cut-points published in the papers shown in Table 1 share a common characteristic: the cut-point is selected on the basis of optimizing sensitivity, specificity, or overall accuracy. Implicit to this approach of using Doppler ultrasound is the fact that some form of correlative imaging is performed. In addition, the sonographer being asked to make a very specific decision and to determine whether a patient has a

<table>
<thead>
<tr>
<th>Author</th>
<th>Parameters</th>
<th>Accuracy</th>
</tr>
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<tr>
<td>Hunink et al</td>
<td>ICA peak-systolic velocity ≥ 230 cm/s</td>
<td>sens 0.80, spec 0.90</td>
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<tr>
<td>Moneta et al</td>
<td>ICA/CCA peak-systolic velocity ratio ≥ 4</td>
<td>sens 0.91, spec 0.87</td>
</tr>
<tr>
<td>Faught et al</td>
<td>ICA peak-systolic velocity ≥ 130 cm/s and ICA end-diastolic velocity of ≥ 100 cm/s</td>
<td>sens 0.81, spec 0.98</td>
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<tr>
<td>Neale et al</td>
<td>ICA peak-systolic velocity ≥ 270 cm/s and ICA end-diastolic ≥ 110 cm/s</td>
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<td>Hood et al</td>
<td>ICA peak-systolic velocity ≥ 130 cm/s and ICA end-diastolic ≥ 100 cm/s</td>
<td>sens 0.87, spec 0.97</td>
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<tr>
<td>Carpenter et al</td>
<td>ICA peak-systolic velocity ≥ 210 cm/s or ICA/CCA velocity ratio ≥ 3</td>
<td>sens 0.94, spec 0.77</td>
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<td>Chen et al</td>
<td>ICA peak-systolic velocity ≥ 125 cm/s and ICA end-diastolic velocity ≥ 135 cm/s</td>
<td>sens 0.76, spec 0.93</td>
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ICA = internal carotid artery; CCA = common carotid artery.
Table 2. DOPPLER VELOCITY CUT-POINTS FOR DETERMINING 60% OR GREATER STENOSIS OF THE INTERNAL CAROTID ARTERY

<table>
<thead>
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<th>Author</th>
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<td>Moneta et al</td>
<td>ICA peak-systolic velocity ≥ 260 cm/s and ICA end-diastolic velocity ≥ 70 cm/s</td>
<td>sens 0.84, spec 0.94</td>
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<td>Carpenter et al</td>
<td>ICA peak-systolic velocity ≥ 170 cm/s</td>
<td>sens 0.98, spec 0.87</td>
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<td>Fillinger et al</td>
<td>ICA/CCA peak-systolic velocity ratio ≥ 2.6</td>
<td>sens 0.93, spec 0.97</td>
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<td></td>
<td>ICA peak-systolic velocity ≥ 200 cm/s</td>
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<td>ICA peak-systolic velocity ≥ 190 cm/s</td>
<td>sens 0.87, spec 1</td>
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<td></td>
<td>ICA/CCA peak systolic velocity ratio ≥ 3.3</td>
<td>sens 0.95, spec 0.90</td>
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<tr>
<td>Jackson et al</td>
<td>ICA peak-systolic velocity ≥ 245 cm/s and ICA end-diastolic velocity ≥ 65 cm/s</td>
<td>sens 0.89, spec 0.92</td>
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ICA = internal carotid artery; CCA = common carotid artery; Sens = sensitivity; spec = specificity.

Table 3. ESTIMATED INTERNAL CAROTID ARTERY STENOSIS SEVERITY BASED ON PEAK-SYSTOLIC VELOCITY IN THE INTERNAL CAROTID ARTERY

<table>
<thead>
<tr>
<th>Peak-Systolic Velocity (cm/s)</th>
<th>Estimated % ICA Stenosis</th>
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<th>Higher 95% Confidence Interval</th>
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ICA = internal carotid artery.

stenosis above or below 70% (or 60%). This implies the ability of distinguishing a 69% (59%) stenosis from a 70% (60%) stenosis. The Doppler technology is imperfect and shows enough variation in measurement that this approach may lead to errors in identifying potential surgical candidates.

Velocity cut-points have been very useful in analyses of the overall cost effectiveness of carotid artery Doppler ultrasound. Papers looking at the contribution of MR angiography to carotid ultrasound show a definite benefit in the noninvasive strategies as compared with carotid arteriography for symptomatic patients. If the accuracy of carotid ultrasound reaches 90% or more, the additional use of MR imaging for asymptomatic patients or carotid arteriography for symptomatic patients may no longer be necessary.

Cut-points may be selected to optimize further the diagnostic yield of carotid Doppler ultrasound. Whereas this type of analysis may be useful to the researcher, the epidemiologist, or the health policy maker, it is difficult for physician interpreters to use this information effectively when evaluating a given patient. Because of this limitation, we have adopted an alternate methodology of grading the severity of internal carotid artery stenosis by Doppler ultrasound.

Grading the Severity of Internal Carotid Artery Stenosis

Going back to the originally described association between Doppler frequency shifts and severity of internal carotid artery stenosis, it seems reasonable to believe that the degree of stenosis can be directly estimated from the Doppler velocity. In essence, a given velocity corresponds to a certain degree of stenosis (see Fig. 5) with the addition of an error caused by sonographer, device, and patient variability. The resultant estimate of the degree of stenosis includes a certain range. For example, Figure 8 shows a simple regression curve with the relationship between percent stenosis as measured using the NASCET method and peak-systolic velocity measured by Doppler ultrasound. A peak-systolic velocity of 155 cm per second corresponds to a 50% diameter stenosis. This estimate, however, can vary between 43% and 58% (95% confidence intervals [Table 3]). It is possible, given a certain Doppler velocity, to give an estimated range of the severity of an internal carotid artery stenosis. The same principle can be applied to regression curves compar-
ing end-diastolic velocities or the peak-systolic velocity ratios with the degree of carotid artery stenosis (Tables 4 and 5). The physician interpreter of the carotid ultrasound study is no longer asked to make a definite decision for a stenosis being above or below a certain value (e.g., 70%). Instead, the Doppler velocity is used to estimate the degree of stenosis and the errors that are inherent to the use of Doppler technique are taken into consideration when reporting the final value.

A potential limitation of this approach arises with a subtotal occlusion or a very high-grade lesion. In these situations, the Doppler velocity range actually decreases. The strategy adopted in our laboratory and

Table 4. ESTIMATED INTERNAL CAROTID ARTERY STENOSIS SEVERITY BASED ON END-DIASTOLIC VELOCITY IN THE INTERNAL CAROTID ARTERY

<table>
<thead>
<tr>
<th>End-diastolic Velocity (cm/s)</th>
<th>Estimated % ICA Stenosis</th>
<th>Lower 95% Confidence Interval</th>
<th>Higher 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>49</td>
<td>48</td>
<td>50</td>
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<tr>
<td>200</td>
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<td>82</td>
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</tr>
</tbody>
</table>

ICA = internal carotid artery.

Table 5. ESTIMATED INTERNAL CAROTID ARTERY STENOSIS SEVERITY BASED ON THE RATIO OF THE INTERNAL TO COMMON CAROTID ARTERY PEAK-SYSTOLIC VELOCITIES

<table>
<thead>
<tr>
<th>End-diastolic Velocity (cm/s)</th>
<th>Estimated % ICA Stenosis</th>
<th>Lower 95% Confidence Interval</th>
<th>Higher 95% Confidence Interval</th>
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<tr>
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</table>

ICA = internal carotid artery.
Figure 9. A, The Doppler signals sampled in the internal carotid artery show low-amplitude signals. This suggests the possibility of a high-grade lesion. B, The corresponding color Doppler image shows a small lumen (red) and reciprocating (red and blue) signals in the proximal internal carotid artery (vessel at the bottom). (See also Color Plate VI, Fig. 43.) C, The corresponding arteriogram shows a greater than 95% stenosis of the internal carotid artery.

other laboratories is to look for evidence of a high-grade lesion with color Doppler imaging. A very narrowed restricted lumen on the color flow image is an indicator that the degree of stenosis has gone beyond the level of a direct association between velocity and stenosis and is actually in the zone of paradoxically decreased blood flow velocities (Fig. 9; see also Color Plate VI, Fig. 43).

Other limitations of this grading approach are the tendency for velocity measurements to overestimate the degree of stenosis in cases (1) of contralateral high-grade stenosis, (2) of recent endarterectomy, and (3) following stent placement.

CAROTID ARTERY PLAQUE CHARACTERIZATION

Limitations of Gray-Scale Imaging

Studies performed in the early 1980s showed clearly that gray-scale evaluation of the carotid bifurcation was in and of itself not sufficient to diagnose high-grade carotid lesions. In fact, as the severity of disease increases, gray-scale evaluation is rendered less reliable. A possible explanation is the failure of gray-scale imaging to detect hypoechoic carotid plaque, because its echogenicity is similar to that of red blood cells.
For smaller plaques, however, and with optimal image quality, gray-scale image evaluation has the potential to detect vulnerable carotid plaque, which is at risk for causing subsequent stroke. This is because there may be an association between carotid plaque composition and stroke that is similar to the association between coronary artery plaque and myocardial infarction.

**Pathophysiology: Model of Vulnerable Plaque**

Pathologic correlation and arteriographic evaluation of the coronary arteries suggest that acute myocardial infarction relates to acute rupture of coronary artery plaques. This model proposes that thrombus formation develops in the region of plaque rupture, and this leads to subsequent occlusion of the coronary artery.* 19, 22 The vulnerable plaque is believed to be composed primarily of lipid-rich material that is surrounded by a cap of fibrous material. This lipid-rich plaque is susceptible to mechanical forces that are associated with local blood flow dynamics. The presence of high metalloproteinase activity at the leading edge of the plaque (where the shear stress rate is greatest) may be responsible for the propensity of plaque rupture at this site.

In the carotid circulation, the equivalent of lipid-rich plaque is hypoechoic plaque. Although data remain sparse, hypoechoic plaque has been shown to be associated with subsequent stroke. As such, the hypothesis that plaque rupture contributes to cerebrovascular disease is being increasingly accepted.

Unfortunately, the literature on carotid plaque evaluation is based primarily on review of surgically extracted specimens. As such, only larger plaques associated with greater than 50% stenosis have been investigated. Hypoechoic areas visible within subsequently removed carotid plaque have been reported as areas of intraplaque hemorrhage. From the ultrasound perspective, it is not possible to distinguish lipid-rich material from intraplaque hemorrhage. Both result in low-intensity echoes when imaged by gray scale. At pathology, these plaques have a heterogeneous composition with mixtures of lipid, thrombus, and fibrous material.

**Plaque Echogenicity**

The signal intensity of returning echoes can be used to characterize plaque echogenicity. High-intensity or hyperechoic signals are comparable with those detected from fascial layers, or the adventitial layer of the artery, whereas isoechoic signal intensities are comparable with those arising from the muscles of the neck. Both hyperechoic and isoechoic material presumably represent fibrous constituents of plaque material.

It is important to differentiate hyperechoic and isoechoic echoes from hypoechoic echoes within plaque. By definition, the echogenicity of hypoechoic plaque is similar to that of blood. Areas of plaque that are relatively hypoechoic may represent lipid-rich material, hemorrhage, or possibly smooth muscle proliferation. An example of a vulnerable-appearing, homogeneously hypoechoic plaque is illustrated in Figure 10. Note there is a rim of increased echogenicity at its periphery, which possibly corresponds to the caplike envelope of fibrous material that surrounds the lipid constituents.

**Plaque Texture**

Plaque texture is established on the basis of its echogenic constituents. In Figure 10, for
example, the plaque is homogeneous, although close inspection reveals varying echogenicity. From the perspective of classification, an almost totally hypoechoic plaque or one that is centrally hypoechoic with a rim of increased echogenicity is classified as a homogeneous hypoechoic plaque. A plaque that is homogeneously echogenic is classified as a homogeneously hyperdense plaque (Fig. 11).

Most plaque, however, is heterogeneous and contains both hyperechoic and hypoechoic elements (Fig. 12). By definition, if greater than 50% of the plaque elements are hyperechoic, it is classified as a heterogeneous hyperechoic plaque. In contrast, if more than 50% of the plaque elements are hypoechoic, it is classified as a heterogeneous hypoechoic plaque.

**Plaque Surface Characteristics**

Although plaque echogenicity may potentially be able to predict subsequent events, the surface characteristics of plaque may have a more immediate impact on a patient who presents with acute neurologic symptoms. This is because of the relationship between the extent of surface irregularity and the presence of transient ischemic attack symptoms. In one angiographic report of symptomatic patients, ulcerated plaque was an important prognostic indicator of cerebrovascular events.

The most severe plaque contour abnormality is associated with ulceration. By definition, an ulcer consists of an intraplaque defect or excavation that is greater than 2 x 2 mm. Unfortunately, with respect to plaque detection the literature indicates low sensitivity and specificity for both ultrasound and arteriography. Color flow and power Doppler imaging may improve sonographic detection of ulcerated lesions by showing areas of flow reversal within the plaque matrix. Contrast-enhanced imaging (see later) may also be useful for detecting ulcerated plaque.

**COMMON CAROTID INTIMAL–MEDIAL THICKNESS**

Although carotid ultrasound imaging is used primarily to detect and to characterize focal lesions, it may also have an important role evaluating diffuse changes that involve the arterial wall. This is based on reports from the late 1980s that indicate diffuse thickening of the intima and medial layers of the aorta and carotid arteries are associated with atherosclerosis.

**Definition**

The combined thickness of the intimal and medial layers of the common carotid artery
Figure 13. Ultrasound obtained at the level of the distal common carotid artery shows the location in which intimal-medial thickness (IMT) measurements are obtained on the far wall. (Courtesy of Carotid IMT.)

(known as the intimal-medial thickness [IMT] can be measured accurately with high-resolution gray-scale imaging. This thickness is defined as the distance between the interface of the lumen and intima to the interface between the media and the adventitia (Fig. 13). The IMT is analyzed by determining either its mean thickness, or its maximal thickness over a defined length of vessel.

Methodology

The IMT measurements are taken at the level of the straight segment of the common carotid artery, just proximal to the bulb. At this level, flow patterns are believed to be relatively laminar. To optimize resolution, IMT measurements should be done with a transducer that is at least 5 and preferably 7 MHz or higher. Precise measurements can be obtained by using sophisticated software to assist analysis of either human-drawn lines or those obtained by automated edge detectors (Fig. 14).

To determine the IMT value, a sequence of point measurements are made along the arterial wall. The range and distribution of these measurements is quite small, and in older adult individuals fluctuates between 0.6 and 1 mm. IMT measurements have been shown to be useful for evaluating cardiovascular disease in both symptomatic and asymptomatic individuals.

Symptomatic Disease

Population studies done on white and Asian patients suggest that the IMT value correlates with a variety of cardiovascular pathologies, including stroke, myocardial infarction, and peripheral arterial disease. The fact that a large IMT measurement is present in an individual who already has symptomatic cardiovascular disease is, however, of limited utility. More important is to consider asymptomatic individuals, and to determine whether or not IMT measurements can be used in this group to predict future cardiovascular events.

Asymptomatic Disease

The IMT measurements are considered a marker of subclinical cardiovascular disease. This suggests that IMT is useful potentially as a noninvasive method to determine the atherosclerotic burden of an asymptomatic population. The question that remains to be answered and continues to be debated, however, is whether or not this measurement is
superior to currently used tests that determine risk factors for atherosclerosis.

Recent investigations suggest that IMT measurements can be used to stratify asymptomatic patients into high-risk groups.\(^{11,15,66}\) In a study with a 6-year follow-up, those individuals placed in the highest 20% group had a threefold risk of having a subsequent myocardial infarction or stroke.\(^{15,66}\)

In addition, IMT measurements have been used to look for regression of atherosclerosis following medical therapies.\(^4\) Whether these measurements can be applied to an individual patient, as opposed to a group of patients, however, remains open to question. Despite these reservations, one recently published report proposed that IMT measurements were superior to coronary artery calcification scores, and that IMT was the single best measurement for identifying high-risk patients.\(^{38}\)

NEW ULTRASOUND TECHNOLOGIES FOR CAROTID IMAGING

Dimensional Imaging

Ultrasound imaging devices are now capable of rendering three-dimensional reconstruction of acquired images.\(^{5,90}\) During the last two decades, sophisticated spatial encoding methods have been developed to define carotid artery lesions better.\(^{69,75}\) An example is illustrated in Figure 15 (see also Color Plate VI, Fig. 44), which shows focal disruption of the common carotid artery following carotid endarterectomy. The three-dimensional display has improved conspicuity, and defines better the extent of pathology. This display method can also be used to advantage for depicting complex tortuosity of carotid arteries and their branches.

Contrast-Enhanced Imaging

Contrast-enhanced imaging can be done either following injection of ultrasound contrast agents or by altering the sensitivity of the ultrasound machine to detect signals generated by moving blood. Imaging carotid arteries following injection of ultrasound contrast agents can increase Doppler detection of blood flow signals, and can be advantageous for evaluating patients with difficult anatomy. In addition, because contrast agents improve the conspicuity of luminal interfaces, this approach may be used to improve visualization and characterization of plaque, and to analyze directly residual arterial lumen.\(^{24,26}\) Administering intravascular ultrasound contrast, however, requires venous injection and adds cost to the examination.
An alternative method to improve visualization of moving blood is based on a digital encoding scheme that increases ultrasound delivery, and also increases the signal intensity of returning echoes that are reflected from moving blood cells. Because contrast-enhanced imaging seems to be superior for delineating the surface between blood and the arterial wall, this technique has the potential to map more accurately the contour of the artery, and to analyze plaque surface characteristics, including ulceration (Fig. 16; see also Color Plate VI, Fig. 45). This approach also offers a more accurate rendition of sharp bends, turns, and kinks within the arterial lumen. Relative to using injected contrast agents, digitally encoded image enhancement is simpler to use, and adds minimal cost to the study.

SUMMARY

This article provides an overview of basic diagnostic carotid ultrasound applications, and emphasizes practical aspects of this examination. Areas currently being investigated include carotid plaque characterization and applications relative to IMT measurements. Contrast-enhanced ultrasound imaging also offers promise to improve plaque characterization, which in turn may link these evaluations to outcome studies.
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