Ultrasonic duplex scanning in the evaluation of carotid artery disease

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Ultrasonic Duplex Scanning in the Evaluation of Carotid Artery Disease

Proefschrift

Ter verkrijging van de graad van doctor in de geneeskunde aan de
Rijksuniversiteit Limburg te Maastricht, op gezag van de Rector
Magnificus Prof. Dr. H.C. Hemker, volgens besluit van het College
van Dekanen in het openbaar te verdedigen in de aula van de
universiteit op vrijdag 21 mei 1982 des namiddags te vier uur.

door

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geboren te 's Gravenhage

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K.W. Beach, Ph.D., M.D.

Technology is nothing more or less than tools whose proper use allows us to measure and understand what is observed. Observations, following in the wake of thoughtful hypotheses, are the foundation of science, and science must be the foundation of surgery.

D. Eugene Strandness, Jr.

*To my parents,
Liesbeth and Mark*

The studies underlying this thesis were performed at the Department of Surgery of the University of Washington, Seattle, Wa., U.S.A.

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Preface

Since transient ischemic attacks are recognized as precursors of stroke and cerebrovascular insufficiency is in large part related to arteriosclerotic disease located at the carotid bifurcation, carotid endarterectomy has become one of the most commonly employed vascular operations today.

Contrast arteriography remains the ultimate diagnostic procedure for patients being considered for carotid surgery. However, the patient discomfort and risk associated with contrast arteriography limits its use for routine screening and follow-up studies. Ideally, only patients who are candidates for carotid surgery should undergo contrast arteriography and accurate noninvasive tests should be used to select these patients.

Duplex scanning, as developed at the University of Washington, is a method with the potential to detect extracranial carotid artery disease at all stages of development. The Duplex concept, a combination of B-mode and pulsed Doppler ultrasound, provides advantages over either technique used independently. In addition to audible interpretation real-time spectral analysis can be used to evaluate the obtained Doppler signals from the common, internal and external carotid artery.

The main goal of the present study is the evaluation of the clinical value of Duplex scanning combined with spectral analysis. In chapter one the role of carotid artery disease in the pathogenesis of cerebral ischemia is reviewed. Chapter two provides a review of both invasive and noninvasive diagnostic approaches concerning extracranial carotid artery disease. Chapter three introduces basic hemodynamic principles of arterial stenosis. In chapter four the current status of ultrasonic techniques and the Duplex system are described.

Chapter five contains four clinical studies, concerning the accuracy of Duplex scanning combined with spectral analysis. In the first study the value of the velocity patterns from the common carotid artery as related to disease at the carotid bifurcation will be evaluated. In the second study the accuracy of Duplex scanning combined with spectral analysis as compared with contrast arteriography was evaluated. The third was a pilot study, performed to explore a means to improve the differentiation between normal and minimally diseased carotid arteries. In this study the velocity patterns of normal subjects breathing carbon dioxide were evaluated. The fourth study was carried out to evaluate a new algorithm, designed to estimate the degree of involvement in patients with high grade stenoses.

Chapter six contains four studies, concerning the role of Duplex scanning combined with spectral analysis in clinical practice. The first and second study evaluated the influence of the noninvasive test on the management of patients with suspected symptomatic and asymptomatic carotid disease. The third study evaluated the incidence of extracranial carotid artery disease in patients, who were candidates for coronary bypass surgery. The fourth study documented velocity pattern changes after carotid endarterectomy.

The studies of chapter five and six were the basis of the evaluation of the Duplex scanning combined with spectral analysis. The results of these studies were the consequence of the work done by many experts in the field of ultrasound at the University of Washington during the last ten years.

Chapter 1

The role of carotid artery disease in the pathogenesis of cerebral ischemia.

1.1. Anatomy

Familiarity with the anatomy of the intracranial and extracranial vasculature is essential to understand both hemodynamic changes and clinical neurological manifestations produced by extracranial carotid artery disease. The anatomical structures involved begin at the level of the aortic arch and extend to the terminations of the carotid and basilar arteries along with their potential collateral systems.

The intracranial circulation is supplied by four major extracranial vessels, consisting of the carotid and vertebral arteries on each side of the neck. On the right side, the common carotid and subclavian arteries originate from the innominate artery, the first branch of the aortic arch. The right vertebral artery begins a few centimeters beyond the origin of the right subclavian artery. The left common carotid artery is the second branch of the aortic arch and continues up into the neck as a separate trunk. The third and last major branch of the aortic arch is the left subclavian artery, which gives rise to the left vertebral artery. The right subclavian and left vertebral arteries occasionally arise directly from the aortic arch.

The course of the common carotid and vertebral arteries are similar bilaterally from the lower part of the neck upward to the circle of Willis. The common carotid arteries course upward in the neck to a point where they bifurcate into an internal and external carotid artery. The location of the bifurcation is not constant and may occur at any point within 5 cm of the angle of the mandible. At the bifurcation is a dilated, widened area called the carotid bulb. The bulb occurs at the terminal portion of the common carotid artery and the origin of the internal carotid artery. The dilatation of the bulb plays an important role in documenting extracranial carotid artery disease both by contrast arteriography and by direct noninvasive methods.

The external carotid artery soon divides into its superior thyroid, lingual, occipital, maxillary and temporal branches. The internal carotid artery pursues its upward course, through the petrous process of the temporal bone and the cavernous sinus. As it emerges upward out of the sinus, it gives off the ophthalmic artery, and soon thereafter the posterior communicating artery, which runs posteriorly to the posterior cerebral artery of the same side. Almost immediately it divides into the anterior and middle cerebral artery. The anterior cerebral arteries on the two sides are connected by the anterior communicating artery, which completes the circle of Willis anteriorly. The two posterior cerebral arteries complete the circle of Willis posteriorly. The size of each of these component arteries is highly variable and determines the adequacy of collateral circulation

from one side to the other, as well as between the vertebral and the carotid systems⁶⁴.

The most frequently described pathways of collateral circulation as a response to arteriosclerotic disease of the internal carotid artery are via the several external carotid to ophthalmic artery anastomoses¹⁰². Additional collaterals may develop intracranially between the anterior, middle and posterior cerebral arteries via their superficial branches.

1.2. Atherosclerosis of the carotid bifurcation.

Extracranial carotid artery disease is most frequently located at the carotid bifurcation, particularly at the origin of the internal carotid artery⁷⁵. Although the pathological findings in atherosclerotic lesions and the principles of collateralization in the carotid system are identical to those in other arteries, it is useful in the context of their clinical significance to describe them briefly.

Ulceration. The most widely accepted hypothesis for the pathogenesis of transient ischemic attacks resulting from involvement of structures in the internal carotid artery territory is the embolic theory^{62,166}.

The release of cholesterol, calcium, platelet aggregates and thrombi into the bloodstream from an ulcerated area within a plaque can lead to both transient and permanent neurological changes. Embolization is often difficult to prove, the best evidence found on occasion in patients with transient monocular blindness where the emboli may be seen in the retinal arteries¹²⁶. In an arteriographic study Eisenberg et al.⁵⁷ found demonstrable lesions (ulceration, stenosis, occlusion) in 89% of arteries in patients with hemispheric transient ischemic attacks. Amaurosis fugax, like the hemispheric transient ischemic attacks, is a warning sign of impending stroke or permanent retinal damage and should alert the physician to look for a treatable carotid lesion.

Stenosis. In many patients with hemispheric transient ischemic attacks contrast arteriography will demonstrate narrowing of the lumen at the origin of the internal carotid artery. This narrowing has been the basis for the hemodynamic theory of transient ischemic attacks. In general, stenoses can be divided in clinical terms into those that reduce total blood flow and those that do not¹⁵⁹. An increasing arterial stenosis does not reduce blood flow and distal pressure until a critical degree of stenosis is reached^{22,177}. In the carotid system flow reduction is not thought to occur until there is an internal diameter reduction of more than 50% of the vessel⁵¹. Whenever a flow or pressure reducing lesion is considered to be the cause of transient ischemic attacks, the stenosis should reduce the diameter by at least 50% in combination with an inadequate collateral system.

Occlusion. A total occlusion of the internal carotid artery is the most advanced lesion pathologically. A slowly developing occlusion may occur in the absence of manifest symptoms or signs of cerebral insufficiency⁵³. The explanation for asymptomatic occlusions is the development of available collateral pathways including the extracranial carotid arteries and intracranial communicating vessels^{28,102}. Knox et al.¹⁰² found in 45 patients with an unilateral occlusion of the internal carotid artery focal neurological symptoms in 26, the remaining 19 patients did not have any symptoms of cerebral insufficiency.

1.3. Clinical Considerations

The average age of patients with manifestations of cerebral ischemia is 60 years with twice as many men are affected as women ⁶².

Hypertension is found in about half of these patients, approximately 15% have diabetes mellitus. The clinical manifestations of an ischemic episode usually appear suddenly, and the full clinical picture develops within a matter of minutes or hours. Focal dysfunction in a territory of a cerebral artery lasting from a few minutes to 24 hours, returning to the preattack status is referred to as transient ischemic attack (TIA). Episodes of TIA are recognized as precursors of stroke since approximately 40% of affected patients are likely to have a cerebral infarct within the first five years after the initial event. This is more than 10 times the rate of expected stroke incidence for persons of the same age and sex in a general population ¹⁷². Furthermore, at least 75% of patients with completed stroke will give a history of previous transient ischemic attacks ¹¹⁵.

Data from the Joint Study Project ⁷⁵ indicated that 74% of patients with ischemic stroke syndromes have at least one significant stenotic lesion in the extracranial vasculature at a surgically accessible site. Since Thompson et al. ^{168,169} presented their long-term results, carotid endarterectomy has become accepted therapy for selected patients with cerebrovascular insufficiency. In general most authors in the recent literature will agree that carotid endarterectomy in symptomatic patients can be performed with a mortality rate of 1% to 2% ^{78,171,179}.

Medical treatment as a means to prevent stroke in patients with amaurosis fugax or focal transient ischemic attacks began with the introduction of effective antihypertensive therapy. The coincidence of the declining incidence of stroke ¹⁰⁸ with the introduction of effective antihypertensive therapy suggests that this treatment may be the most important cause of the decline ¹⁸. Anticoagulants were introduced in the 1950's. Despite all the clinical trials performed, Barnett ¹⁸ stated in the Robert Wartenberg Lecture: "From all those trials it cannot be concluded unequivocally that anticoagulants are helpful. Similarly, it cannot be concluded that anticoagulants have no place in TIA management." Platelet inhibiting drug therapy (aspirin) seems to have a potential place in the prevention of stroke as has been demonstrated in controlled trials ^{17,61}.

Although there is still disagreement as to what the treatment of choice should be in the prevention of stroke, the growing interest in this area has created a demand for both accurate invasive and noninvasive methods to detect carotid disease and assess its potential as a cause of symptoms.

Chapter 2

Diagnostic approaches.

2.1. Arteriography.

In 1937 Egar Moniz ¹²³ demonstrated the value of arteriography in the diagnosis of thrombosis of the internal carotid artery. This report, although primarily concerned with the arteriography of the intracerebral lesions, called attention to the association of hemiparesis and internal carotid thrombosis. Direct needle puncture of the common carotid artery and injection of contrast material became a standard technique in the diagnosis of carotid arterial disease.

In 1953 Seldinger introduced the arterial catheterization over a wire guide ¹⁵¹, this method permitted selective injection of all vessels of the aortic arch. Seldinger's technique gained wide acceptance and still is the preferred technique in most centers. It is a relatively simple method and permits visualization of all components of the intra and extra-cranial arterial circulation.

With the establishment of contrast arteriography follow-up studies by repeat contrast arteriograms were reported to assess progression of arterial occlusive disease of the carotid arteries. Javid et al. ⁹¹ reported a study of 93 patients who underwent repeated contrast arteriography with a mean follow-up period of 3 years. In 38% of these patients, there was no evidence of progression of arterial disease, in 62% marked progression was noted. The rate of progression in this study appeared to be related to hypertension, cerebral symptoms, and the degree of stenosis. Because contrast arteriography, like any invasive technique, presents a small but real risk with respect to morbidity and mortality ⁸⁰ the method is generally considered to be impractical to utilize on a repetitive basis in follow-up studies for quantifying progression of disease.

Complications due to cerebral contrast arteriography can be divided in major and minor complications. Hass et al. ⁷⁵ reported a mortality rate of 0.7% in a series of 4748 patients with cerebrovascular insufficiency, in which complete four vessel studies were made. The stroke rate in this study was 0.5%, minor complications occurred in 5.3%. In a multicenter retrospective study Swanson et al. ¹⁶⁴ reported 0.6% permanent neurological complications and 13% transient complications in 1328 patients undergoing cerebral arteriography. Wylie and Ehrenfeld ¹⁸³ reported a mortality rate of 0.4% and a stroke rate of 0.5% in a series of 800 patients undergoing four vessel studies using the Seldinger technique.

Neurological events related to extracranial carotid artery disease occur both in the presence of high grade lesions (hemodynamic theory) and minimal lesions (embolic theory). It is therefore important to review the reliability of arteriographic studies in detecting both minimal and severe lesions. In general most surgeons have found that arteriography underestimates the amount of disease found at the time of operation. For the coronary arteries this problem was

highlighted by Staiger et al.¹⁵⁴

In 203 coronary arteries in which the cross-sectional area was measured directly, post mortem arteriograms underestimated the extent of involvement in 47%. In a post-mortem study of 64 carotid bifurcations Croft et al.⁴⁷ found that the agreement between two observers on the x-ray appearances was 87.5% and between the agreed x-ray appearances and the macroscopic pathological findings 78.6%. This study shows nicely that even in post-mortem studies the disagreement about the actual diameter reduction at the level of the carotid bulb is considerable.

Hass et al.⁷⁵ concluded that in reading arteriograms, estimating the degree of stenosis of the internal carotid artery was more accurate when more than 50% of the diameter was involved. Edwards et al.⁵⁴ evaluated the accuracy of angiographic diagnosis of carotid artery ulcerations in 50 carotid arteries. In 34% of the cases there was disagreement between the surgical observations and the radiological findings. In a recent study by Chikos et al.⁴¹ the intraobserver and interobserver agreement reading 128 multiplanar selective arteriograms of the carotid arteries were evaluated. The intraobserver agreement for the internal carotid artery was 75% for a vessel with 0% stenosis, 90% for a vessel with a 50-99% diameter reduction, and 97% for a total occlusion when the same reader estimated the diameter reduction twice. The interobserver agreement (the probability that a second reader would agree with the first reader) for the internal carotid artery was 57% for a vessel with 0% stenosis, 85% for a vessel with a 50-99% diameter reduction, and 97% for a total occlusion. Overall it is obvious that there is considerable variability in reporting results of reading carotid arteriograms related to the number of radiologists involved and the number of times an individual radiologist evaluates the results.

The development of noninvasive methods of diagnosing extracranial arterial disease has highlighted the problem associated with reading arteriograms. Since contrast arteriography traditionally has been the method used for the diagnosis of extracranial arterial disease, it is generally accepted as the "gold standard" in evaluating the accuracy of the noninvasive tests. The previously described variability studies with regards to arteriography however have highlighted a serious problem, especially in patients with no or minimal disease. This variability is one of the reasons that total agreement between arteriography and noninvasive tests remains a problem to be considered.

Recent innovations in computer technology have permitted the development of digital subtraction arteriography as a new method in the diagnosis and management of patients with arterial disease¹⁷⁵. Preliminary results¹⁶² for the detection of extracranial carotid artery disease are promising.

Turnipseed et al.¹⁷⁶ reported that they found a close relation between intravenous digital subtraction and standard arteriography images of the carotid arteries. Intravenous digital subtraction arteriography will clearly find a role in the overall management of patients with extracranial carotid artery disease. The method does not require hospitalization, may be used for repetitive testing, and has less risk than conventional contrast arteriography.

However, digital subtraction arteriography must still be viewed as a potentially simpler method of obtaining views of the carotid artery. In that respect it will not

be a better "gold standard" than conventional studies. Furthermore, since venous arteriography is invasive, it will still pose risks. It is also unlikely that the method will be suitable for follow-up studies in order to document progression of disease. These research oriented follow-up studies should be preceded by accurate noninvasive tests.

2.2. Noninvasive methods.

2.2.1. Introduction.

Since stroke is the second most common cause of death due to vascular disease, a variety of noninvasive tests have been developed to evaluate arterial occlusive disease of the extracranial carotid arteries. Furthermore, the extracranial carotid system is an attractive system for noninvasive studies for the following reasons: (1) the disease is usually localized at the carotid bulb and the first few centimeters of the internal carotid artery; (2) the relatively superficial location of the extracranial carotid system makes it accessible to direct ultrasonic methods; and (3) more advanced lesions produce changes in pressure and flow, resulting in the development of collateral pathways which may be evaluated by indirect methods. The techniques used for noninvasive diagnosis are most readily separated into those which are termed indirect and those which are termed direct.

Techniques which are designated as indirect, test for hemodynamic changes at some point removed from the site of involvement. Since the ophthalmic artery is the first branch of the intracranial carotid artery, obstructive lesions at the carotid bifurcation may produce pressure and flow changes in the orbital branches of that artery and its periorbital ramifications. Supraorbital directional Doppler examinations^{13,38,116}, pulse-delay oculoplethysmography^{94,95}, and pressure oculoplethysmography^{55,68,70} are considered to be indirect methods. Indirect tests are the most common noninvasive techniques employed today.

Direct tests provide anatomical or hemodynamic information concerning the carotid artery itself. Phonoangiographic analysis^{52,94,101}, velocity waveform analysis^{122,134,135,148}, ultrasonic Doppler imaging^{87,88,138,153} and Duplex scanning^{11,12} are considered to be direct methods.

2.2.2. Indirect noninvasive test.

Supraorbital Doppler Examination.

The supraorbital directional Doppler examination, as initially described by Brockenbrough³⁸ and modified by Barnes et al.¹³ uses a direction sensing Doppler system to evaluate flow direction in the medial frontal or supraorbital arteries. Reversed flow in the frontal artery indicates extracranial collateral flow in the presence of a significant stenosis (flow reducing lesion). In the technique described by Barnes, compression of an external carotid branch may produce diminution, obliteration or reversal of flow in the medial frontal artery if this artery is the source of collateral flow to the brain. Low common carotid compression is also utilized to identify contralateral carotid or intracranial collateral flow. Although accurate when positive, this method alone is an

unsuitable diagnostic test for the patient with focal symptoms, since these are often due to emboli from ulcerations in plaques which are not large enough to produce a pressure gradient, and thus do not result in the development of collateral circulation ^{15,32,114}.

Pulse-delay Oculoplethysmography.

The method takes advantage of the fact that the ophthalmic artery is the first branch of the internal carotid artery. The system, developed by Kartchner and McRae ^{94,95} utilizes plastic corneal cups filled with water applied to the eyes with a negative pressure of 40-50 mm Hg. A pulse wave representing the volume change of ocular filling is generated for each eye and recorded on light sensitive paper. An electronic comparison is performed between the two waveforms, yielding a differential tracing which allows the examiner to compare the rate of ocular filling between the two eyes. In addition, photoplethysmographic clips are applied to each ear lobe to record the pulse arrival time from the external carotid artery in order to detect external carotid stenosis or occlusion. Bilateral internal carotid stenoses are detected by comparing the ocular with the ear pulse waveforms.

Kartchner and McRae ⁹⁶ presented data from their experience of 1287 patients evaluated by OPG combined with carotid phonoangiography (CPA), 295 of whom underwent arteriography. Of these 295 patients, 147 were noted to have arteriographic flow reducing lesions and 148 non-flow reducing lesions. Of the 147 "positive" arteriograms, 16 had a negative OPG for a false negative rate of 11%. Of the 148 "negative" arteriograms, 17 had a positive OPG for a false positive rate of 11%. In a clinical report, Blackshear et al. ²⁵ presented data from 191 patients evaluated by OPG-CPA at the vascular laboratory of the University of Washington. There were 106 sides available for comparison with arteriography. Results of the examination were negative in 47 of the 58 vessels that were either normal or had a stenosis of less than 50 percent diameter reduction, resulting in a false positive rate of 19%. All eight total occlusions of the internal carotid artery had positive tests. However, only 17 of 40 vessels with high grade lesions exhibited an ocular pulse delay, so the false negative rate was 58% for this category. These results as obtained by Blackshear indicated that the method is inadequate to screen patients suspected of having carotid artery disease. Keagy et al. ⁹⁷ reviewing 291 carotid arteries that were subjected to the pulse-delay OPG concluded, like Blackshear, that this method was inadequate to accurately screen patients.

Pressure Oculoplethysmography.

The technique of pressure oculoplethysmography, as developed by Gee et al. ^{68,69,70}, utilizes scleral eye cups placed lateral to the cornea and held in place with a negative pressure of 300 mm of mercury which obliterates ocular pulsations. There is a direct relationship between the degree of vacuum applied and the resulting intraocular pressure. If the intraocular pressure exceeds the ophthalmic artery pressure, the blood flow to the eye will stop and no pulsations will be recorded. The onset of the pulsations occurs when the systolic arterial

pressure exceeds the intraocular pressure, allowing the determination of the systolic arterial pressure in the ophthalmic artery.

Baker et al.¹⁰ reviewed their results for detecting carotid stenosis using the pressure OPG in 227 patients who underwent biplanar arteriography. Their overall accuracy in the correct identification of hemodynamically significant stenoses (more than 60% decrease in luminal diameter) was 93%. Eikelboom⁵⁶ presented data from the experience of 1200 OPG tests, from which 390 could be compared with contrast arteriography. In this material 106 patients had hemodynamically significant stenoses (stenosis of 65% or more). The sensitivity of the pressure OPG tests was 89% with a specificity of 84%.

Pressure oculoplethysmography seems to be an accurate method in detecting high grade lesions. There are basically two serious limitations of the method: (1) the method is not able to detect non-pressure/ flow reducing lesions which can be the cause of embolic focal neurological symptoms; and (2) the method is unable to differentiate between a high grade stenosis and a total occlusion, a distinction which is of clinical importance.

2.2.3. Direct noninvasive test.

Velocity Waveform Analysis

Most authors have used velocity waveform analysis as an indirect method, analyzing the tracings from the common carotid artery to estimate the involvement of disease in the internal carotid artery^{134,148}. More recently velocity waveform analysis is used as a direct method, analyzing the tracings from the carotid bifurcation⁹⁴.

Velocity wave form information from the extracranial carotid arteries can be obtained both by continuous wave and pulsed Doppler systems. Where continuous wave systems provide an analog output of one tracing, multigated pulsed Doppler systems have the potential to display a number of velocity tracings from several points across the artery simultaneously⁸⁵.

Planiol and Pourcelot¹³⁴ using a continuous wave device introduced the resistivity index (RI) of the common carotid artery as a means to predict extracranial carotid artery disease. This index is a ratio of peak systolic velocity and diastolic velocity, the RI is normally between 0.5 and 0.75. A RI greater than 0.75 is considered to be pathological. For total occlusions and stenoses with a diameter reduction of more than 90% the method seems to be accurate. A more complex method was introduced by Rutherford et al.¹⁴⁸. Using a continuous wave device, five hand measured parameters were obtained from the analog output of the velocity tracing of the common carotid artery. They found a 100% accuracy of separating normal from diseased carotid arteries, the discrimination between stenoses greater than and less than 50% diameter reduction was 82%. As will be discussed, this method has great potential particularly when a computer can be utilized to carry out the complex discriminant analysis which is required⁷³.

The use of multigated pulsed Doppler devices in obtaining simultaneous velocity tracings over the cross-section of the blood vessel have been reported by Keller et

al.⁹⁸ and more recently by Hoeks⁹⁴. Although the results from clinical studies are not yet available, this method will find a place in screening of patients with suspected extracranial carotid artery disease.

Carotid Phonoangiography (CPA)

This technique developed by Kartchner and McRae⁹⁴ for use in conjunction with the oculoplethysmograph utilizes a handheld microphone which is placed over the carotid artery in low, middle and high locations. A photographic display of the bruit in relation to the first and second heart sounds is produced. In addition, the bruits may be analyzed audibly by the examiner during the course of the study. In the study presented by Blackshear et al.²⁵ carotid phonoangiography either alone or in combination with pulse-delay oculoplethysmography was not of sufficient accuracy to recommend its use as part of a noninvasive evaluation of carotid artery occlusive disease.

Phonoangiographic Spectral Analysis (P.A.)

Quantification of the frequency spectrum of phonoangiographically recorded carotid bruits has been reported by Duncan et al.⁵² By Fast Fourier Transform (FFT) spectral analysis, they identified a single "break frequency" beyond which the intensity of all higher frequencies sharply declined. The diameter of the residual lumen (dp) within the stenotic vessel can be calculated from the equation $dp = U/f_0$, where U is the peak systolic velocity in the unoccluded portion of the artery and f_0 is the observed break frequency derived from the spectral analysis. The peak systolic velocity (U) is assumed to be a constant of 500 mm/sec. The commercial edition of the phonoangiograph was recently evaluated in the vascular laboratory at the University of Washington¹⁰⁴. One hundred and sixteen carotid bruits were analyzed, with biplanar contrast arteriography available for comparison in 43 instances. The diameter of the vessel at the site of the stenosis estimated by phonoangiography and contrast arteriography were compared and found to agree within 1 mm of each other in 85% of the cases. Phonoangiography provides an accurate method to estimate the residual lumen of the carotid arteries whenever a bruit is present. It is important to realize however, that only 13% of the patients in the vascular laboratory at the University of Washington were referred because of an asymptomatic bruit⁶⁰.

Continuous Wave Ultrasonic Arteriography

The combination of a position sensing arm and a continuous wave Doppler device with a storage oscilloscope permits visualization and identification of the major arteries in the neck and allows the examiner to interrogate the characteristics of flow from precise points along the carotid arteries^{109,138,153}. Clinical results using this method are reported by Weaver et al.¹⁷⁷. These authors noted that the method had no predictive value in detecting stenoses that fell in the 0-50% range. With 50-75% stenoses, the Doppler accuracy was 52%, increasing to 71% when 76-99% diameter reducing stenoses were present. The fact that the correlation between arteriography and ultrasonic imaging was poor in the group of patients with stenoses less than 50%, is a serious disadvantage of the method. Curry and

White⁴⁸ introduced the color coded ultrasonic arterial scanner (Echoflow), using a continuous wave Doppler device. The Doppler shifted signals scattered by the blood at peak velocity are detected by filters with varying frequency ranges, signals from each filter activated are color-coded. The color selected at any point, corresponds to the highest frequency filter passing a Doppler signal. Although the display differs from the continuous wave ultrasonic arteriograph, the principles of the method are basically the same. White and Curry¹⁷⁸ presented their results with the Echoflow in 424 carotid bifurcations. There was no differentiation between normal and minimally diseased internal carotid arteries. In the 75-99% diameter reduction range the Doppler accuracy was 80%.

Pulsed Doppler Ultrasonic Arteriograph

The pulsed Doppler ultrasonic arteriograph as initially developed by Hokanson et al.^{87,88,124,125,157}, consists of a transducer containing a 4 mm piezoelectric crystal mounted on a position sensing arm, a pulsed Doppler ultrasonic flow detector, and a storage oscilloscope. Whereas the continuous-wave Doppler velocity detector senses blood flow anywhere in the path of the ultrasound beam, the pulsed Doppler is able to sample from a small region in space at any desired distance from its transducer (see 4.1.3.).

Sumner et al.¹⁶³ reported the agreement between contrast arteriography and Hokanson's ultrasonic arteriography in 209 carotid arteries. Using a diameter reduction greater than 20% as criterion for a positive test, the sensitivity of the method was 81% and the specificity was 88%. Blackshear et al.²⁴ evaluated the results with this method in 66 carotid sides also studied by contrast arteriography. There were 8 arteriographic normal arteries, 9 with a diameter reduction less than 10%, 23 with a 10-49% diameter reduction, 22 with 50-99% diameter reduction, and 4 with total occlusions. With the pulsed system there was one false positive (12%). Audible changes in the Doppler signal compatible with turbulence were detected in 13 of the 22 vessels (59%) with a 10-49% diameter reduction, and in 20 of the 22 vessels with a 50-99% diameter reduction (91%). Three out of the four total occlusions were diagnosed correctly. Pulsed Doppler imaging, although far from perfect, represents a promising development in the field of noninvasive technology. It has the ability to detect not only total occlusions and high grade lesions but also, particularly in combination with spectrum analysis, lesser degrees of stenoses.

B-mode Imaging

Olinger¹³⁰ has made the first two-dimensional images of peripheral blood vessels using a pulsed echo system. Bernstein et al.¹²³ used ultrasonic imaging for detecting and following abdominal aortic aneurysms. Cooperberg et al.⁴⁴ reported the use of a B-mode scanner in detecting extracranial carotid artery disease. Out of 52 carotid bifurcations evaluated, they confirmed the arteriographic diagnosis in 44 (85%). They found false-negative results in the cases where the plaques were not calcified. Recently Hobson et al.⁸³ reported the accuracy of a B-mode imaging system with and without the additional use of a Hokanson ultrasonic arteriograph. The most dramatic difference between the B-

mode imaging system and the ultrasonic arteriograph was the poor accuracy of the B-mode echo system to predict total occlusions. Out of 17 arteriographic proven occlusions only 3 were identified correctly by the B-mode imaging system.

An important limitation of pulsed-echo systems as has been shown in the results presented by Hobson, is that a totally occluded internal carotid artery can appear to be patent from the B-mode ultrasound examination. This limitation was early appreciated by Hartley et al.⁷⁶ They showed a wide variation in the attenuation characteristics of plaques dependent on the presence or absence of calcium. In the case of soft, fatty plaques reflection is similar to that of blood, while calcified plaques showed an increase in intensity by a factor of 1000 over that of a normal vessel wall. Whenever an internal carotid artery is occluded without the presence of calcium, the occluded artery will not differ from a patent vessel on the B-mode image, hence the occlusion will not be identified. These findings motivated the development of the Duplex scanner which combines real-time B-mode imaging with pulsed Doppler ultrasound.

Ultrasonic Duplex Scanning.

The Duplex concept is based upon the ability to define the walls of the vessel within a two-dimensional image and uses the pulsed Doppler to evaluate the blood velocities within the artery visualized. This concept was integrated into the system described by Barber et al.^{11,12}. The first prototype available for clinical studies^{132,133} was used in the noninvasive laboratory at the University of Washington until January 1980. The accuracy of this method combined with spectral analysis in detecting extracranial carotid artery disease as compared with contrast arteriography was reported by Fell et al.⁵⁹. In this study 135 patients underwent contrast arteriography giving 270 carotid bifurcations available for comparison. The agreement between contrast arteriography and ultrasonic Duplex scanning combined with spectral analysis was: 35.5% (4/11) for a normal bifurcation; 45% (9/20) for a diameter reduction less than 10%; 58% (52/90) for a 10-49% diameter reduction; 81.5% (84/103) for a 50-99% diameter reduction; and 70% (32/46) for a total occlusion. In January 1980 the prototype scanner was replaced by a commercially available Duplex scanner*. The improvements made were in large part the results of previous experience and projected needs (see 4.3.).

* ATL Mark V Duplex Scanner.

Chapter 3

Hemodynamics of arterial stenosis.

Ultrasonic Doppler techniques utilize the Doppler effect to make an estimate of flow velocities¹⁴⁹. The velocity profiles are reflections of hemodynamic characteristics of the cardiovascular system. Changes in the velocity profiles will be more meaningful with the knowledge of basic principles of fluid dynamics. For that reason some of these hemodynamic principles will be introduced in this chapter.

Fluid energy. The driving force for flow in the circulation is not the difference in pressure but the difference in total fluid energy¹⁰. The total fluid energy (E) is expressed as the sum of the pressure energy (P), gravitational potential energy (pgh), and kinetic energy ($\frac{1}{2}pV^2$).

$$E = P + pgh + \frac{1}{2}pV^2$$

where p = the density of the fluid
g = the acceleration due to gravity
h = the depth
V = the velocity of the fluid.

The difference in total fluid energy between two points in the same streamline are expressed in the Bernoulli equation:

$$P_1 + pgh_1 + \frac{1}{2}pV_1^2 = P_2 + pgh_2 + \frac{1}{2}pV_2^2,$$

providing that the flow is steady and the system frictionless.

Energy losses. Because of friction in the human circulation, with resultant energy dissipation as heat, the Bernoulli equation requires modification with the addition to heat. There are two forms of energy losses due to blood flow: (1) inertial losses, due to changes in blood flow velocities or direction, and (2) viscous losses, as a result of blood viscosity.

Viscous energy losses are expressed by Poiseuille's law, which states that the pressure gradient along a tube (ΔP) is proportional to the mean velocity (V), the tube length (L) and the fluid viscosity (π) and inversely proportional to the second power of the tube radius (R):

$$\Delta P = V (8 L \pi / R^2).$$

From this equation has come the familiar relationship: pressure = flow x resistance, which is analogue to Ohm's law¹⁵⁹. It is important to realize that

Poiseuille's law applies only to the idealized conditions of steady (non pulsatile), laminar (non turbulent) flow of a Newtonian fluid (viscosity unaffected by velocity).

Laminar and turbulent flow. Reynolds¹⁴² was the first to precisely describe the conditions under which the transition from laminar to turbulent flow occurred. He demonstrated that at higher flow rates the fluid became more sensitive to disturbances, until a critical point was reached where laminar flow could not be maintained. It was observed that the point at which this transformation occurred was dependent upon the vessel diameter, the mean velocity, the density and viscosity of the fluid. These factors can be expressed as the dimensionless quantity called the Reynolds number:

$$Re = \frac{\bar{V} d_i \rho}{\eta}$$

where Re = Reynolds number
 $\bar{V}$ = the mean velocity of the flow
 d_i = the internal diameter of the artery
 ρ = the density of blood
 η = the viscosity of blood

At Reynolds numbers approaching 2000, a disturbance is necessary to institute turbulence in a smooth pipe. The larger the Reynolds number, the less disturbance is necessary to cause this turbulence¹⁸⁰. Although the use of Reynolds number helps to understand the circumstances in which turbulence can occur, it must be emphasized that the calculation of Reynolds number should be strictly applied only to conditions of steady flow.

Velocity profiles. Newtonian fluids under conditions of steady laminar flow develop parabolic velocity profiles. In the mammalian arteries however the profiles are seldom true parabolic. The fact that blood flow is pulsatile prevents the formation of a truly parabolic profile. The explanation for this is provided by McDonald¹¹⁸. Near the wall, blood moves more slowly than that of the center stream. Because of this the direction of flow near the wall is more sensitive to variations in the pressure gradient than the flow in the more central laminae. Consequently when flow reversal begins, it starts at the wall. During periods of the pulse cycle blood can reverse close to the wall, whilst it continues to flow in a forward direction at the center of the stream. As the pulse rate increases, there is no time for the development of a parabolic profile and the profile becomes flattened (plug flow).

Pulsatile flow. In spite of the fact that pulsatile flow seems less efficient than steady flow, the mammalian organism seems to function best under these circumstances¹⁰⁰. Although phenomena like energy losses and turbulence are much more complex in pulsatile flow than in the situation of steady flow, the basic principles stay the same.

Energy losses due to pulsatile flow has been estimated 10% in the descending aorta, 16% in the abdominal aorta, and 24% in the carotid artery as compared with steady flow⁶. These losses are largely a result of the acceleration of blood at certain points, the occurrence of disturbed flow patterns and the non-Newtonian character of blood¹¹².

Does turbulence occur in the normal pulsatile arterial system? The pulsatile nature of flow should encourage flow disturbances since at peak flow rates the critical Reynolds number (2000) is often exceeded. Attinger et al.⁵ were able to demonstrate that eddies, vortices, and turbulence may occur in the cardiovascular system, particularly during flow deceleration and at branch points. The energy losses associated with these flow instabilities appear to be insignificant with respect to average flow rates. For that reason Attinger preferred to refer to the appearance of eddies and vortices as "disturbed flow". The term disturbed flow, describes the intermediate state between laminar flow and fully developed turbulence.

In normal pulsatile flow the deceleration phase after peak systole is the most unstable phase of the pulse cycle. Whenever flow disturbances develop, they are first observed during the deceleration phase of systole¹¹¹.

Stenosis. As fluid passes from a tube of larger diameter through one of smaller diameter, it must accelerate to a higher velocity in the narrow segment to maintain the same total flow. With this acceleration of fluid, potential energy (pgh) is converted into kinetic energy ($\frac{1}{2}\rho V^2$) and a pressure drop occurs.

$$\Delta P = \frac{1}{2}\rho (V_1^2 - V_2^2).$$

At the distal end of the narrow segment there is a deceleration of velocities, where kinetic energy is converted into potential energy. This last conversion is not complete however, with a total pressure drop over the narrow segment as the result. The situation described above can only be calculated accurately for steady non-pulsatile flow, although the same principle applies to pulsatile flow.

Both experimental and clinical investigations indicated that it is necessary to have a marked stenosis of an artery before the blood flow is reduced. May et al.¹¹⁷ investigated the effect of short graded stenoses on the flow and pressure through iliac arteries of anaesthetized dogs. In their study it was necessary to constrict the luminal area by 80% before a significant decrease in arterial flow and pressure occurred. May pointed out that each organ system has its own characteristic critical stenosis.

Deweese et al.⁵¹ measured pressures proximal and distal to arteriosclerotic plaques in the internal carotid artery. They found that in the carotid system a stenosis of greater than 63% minimal lumen diameter, leaving a channel less than 1.0 mm in diameter, always produced a drop in pressure and flow. As a general rule a critical or "hemodynamically significant" stenosis of the internal carotid artery is considered to have a diameter reduction greater than 50%.

When blood flows through a stenosis the velocities of the bloodcells will increase in the stenosis. In the post-stenotic segment the movement of the red cells

adjacent to the wall are retarded as compared with those in centerstream and vortices will be present. With the increase of midstream velocities due to an increase of the stenosis, the movement of red cells adjacent to the wall are more retarded as compared with those in the centerstream and flow disturbance will be present.

Both changes in peak systolic velocities and eddies caused by flow disturbance, which occur with increasing stenoses, can be identified by pulsed Doppler techniques in combination with spectral analysis^{90,165}.

Bruits. It is presently considered that bruits can be created by periodic and uniformly oriented vortical eddies produced when a rapidly moving fluid stream encounters an obstacle⁴. Given a source of vortices, a rise in velocity of blood stream will increase the loudness of the murmur and raise its pitch. The spectra of the turbulent pressure fluctuations have been shown to be similar to those in vitro pipe turbulence¹⁰⁷. A method of arterial bruit analysis based on the analysis of turbulent flow allows estimation of the extent of arterial stenosis at the site of origin of the bruit⁵².

The characteristics of turbulent flow within a vessel are such, that the intensity of the sound produced declines as frequency increases beyond a single identifiable frequency (the break frequency).

This break frequency allows the evaluation of the residual lumen diameter from the equation:

$$dp = U/fo$$

where U = peak systolic velocity

fo = break frequency

dp = residual artery lumen

Kistler et al.¹⁰¹ found in 31 out of 33 arteriographic proven stenoses a residual diameter estimated by phonoangiography agreement within 0.5 mm. A study performed in the vascular laboratory of the University of Washington¹⁰⁴ has shown, that this form of bruit analysis first reported by Duncan et al.⁵², provides an accurate method to estimate the residual lumen of carotid arteries. It is important to recognize that 10% of the bruits heard with a stethoscope in the study by Knox et al.¹⁰⁴ could not be analyzed using this device.

Chapter 4

Current status of ultrasonic techniques

4.1. Basic Doppler and Echo systems

4.1.1. Introduction

The first clinically orientated application of Doppler ultrasound was by Satomura¹⁴⁹. Although red blood cells are weak reflectors (only 0.02% of the transmitted ultrasonic energy is reflected), they can be recognized by their motion. Many subsequent investigations have confirmed the utility of this method in providing useful data concerning flow patterns in the arterial and venous system.

The mechanism is based on the principle of the Doppler effect, which is a change in frequency of an acoustic or ultrasonic wave that results when the total path length between the transmitting and receiving transducer is changing. For convenience, the change in ultrasound frequency is referred to as "Doppler frequency", which can be expressed as in the following equation:

$$\Delta f = \frac{2f_0 v \cos \varnothing}{c},$$

where:

Δf = Doppler frequency (KHz)

f_0 = transmitting frequency (MHz)

v = velocity of red blood cells (cm/sec)

$\varnothing$ = angle between the Doppler beam and the axis of the vessel.

c = velocity of sound in soft tissue (cm/sec)

The equation shows that the angle between the Doppler beam and the axis of the vessel must be known to calculate the velocity of moving red blood cells. (see figure 1).

Figure 1.

Schematic cross section of ultrasound transducer whose sound beam intercepts a blood vessel at the angle $\varnothing$. The different values of velocity across the vessel are shown by the length of the velocity vectors.

When an ultrasonic Doppler instrument is used to detect the Doppler shift due to moving red blood cells, not just one frequency but many different frequencies are produced. The Doppler frequencies are spread in a "Doppler spectrum". The most important cause of different frequencies in the Doppler spectrum is the variation in velocities of red blood cells within the vessel¹³⁷. For example red blood cells close to the wall move, due to friction, more slowly than those centerstream. This is shown in figure 1, where each arrow represents a velocity vector whose length is proportional to the velocity.

Changes in the vessel wall will produce changes in the Doppler spectrum, which can be used to detect arteriosclerotic lesions^{26,27}. This will be discussed in detail later (see 4.1.3.).

The equipment used for the detection of velocity operates with either a continuous wave or pulsed Doppler system. Both are described in the following paragraphs.

4.1.2. Continuous wave Doppler device.

A continuous wave instrument usually has two piezoelectric crystals, one for transmission of ultrasound and one for reception of the backscattered signals. The velocities of all red blood cells within the ultrasonic range of the instrument will be detected (figure 2). The Doppler spectrum of the continuous wave instrument will for that reason be relatively broad.

Figure 2.
Schematic cross section of transducer and sound beam shape for a continuous wave Doppler system.
All velocities across the vessel are detected.

Early Doppler systems and many in use today are "non-directional", in other words there is no distinction made between targets moving away from the probe and those moving towards the probe. These systems can only be used to detect the presence or absence of flow and are frequently used in pressure measurements.

The ability to detect the direction of flow was a marked improvement in the Doppler instruments. At the University of Washington Nippa et al.¹²⁷ developed a phase rotated quadrature mode for bidirectional information. This system is based upon the introduction of a 90° phase shift in the detection process of the Doppler signals. Two channels are generated each having forward and reverse flow information. The phase relation between the two channels contains the directional

information. The quadrature method is applicable both for continuous wave and pulsed Doppler systems.

4.1.3. Pulsed Doppler device.

A pulsed Doppler instrument contains one piezoelectric crystal used both for transmission and reception of ultrasound²⁰. Short pulses of ultrasound are repeatedly transmitted into the tissue by the piezoelectric crystal. The pulses are spaced in order to permit one pulse to return before the next transmission.

At a selected time following transmission the signal from the piezoelectric crystal is gated for further processing into the Doppler signal^{7,8,9}. By selecting the time between transmission and gating one can choose the range or depth at which velocities are detected. The velocities detected by the device are an average of all velocities within a small region called "sample volume"⁹³. The size and shape of the sample volume depends on the duration of the transmitted burst, transducer bandwidth and receiver bandwidth⁸⁴. The depth at which the velocity is detected is controlled by the amount of delay in the range gate.

Since the pulsed Doppler device only measures velocities within its sample volume the Doppler spectrum will contain only partial information of velocities within a vessel (figure 3). With this system it is possible to place the sample volume in the centerstream of the vessel where most of the red blood cells have the same velocity, resulting in a narrow band of frequencies. When turbulence occurs the spectrum of frequencies will be broad. Moving the sample volume from centerstream closer to the wall will, even in normal vessels create broadening of the Doppler spectrum due to velocity gradients which are present near the wall.

Figure 3.

Schematic cross section of transducer and sample volume for a pulsed Doppler system. Only the velocities within the sample volume are detected.

The dual capacity (transmission and receiving) of the instrument forces a compromise in determining the best pulse repetition rate (PRF). Doppler shift frequencies above one-half of the pulse repetition rate in the forward direction appear in the reversed direction. For example with a PRF of 4 KHz, the maximum forward Doppler shift detected is 2 KHz. With Doppler shifts covering 4 KHz, the

first 2 KHz will appear in forward direction, the other 2 KHz will appear in the reverse direction. This phenomena is referred to as "aliasing" of the signal (figure 4).

Figure 4.
Directional aliasing at a PRF of 4 KHz.
Frequencies above 2 KHz appear in the reverse
direction.

Detection of disturbed flow in the arterial system has great potential as a means of identifying changes due to early atheromatous lesions. The hot film anemometer has proven a useful instrument in demonstrating disturbed and turbulent flow both in animals and model studies⁷¹. A sensitive noninvasive method which could be used to detect and possibly quantitate flow disturbances would be of great value.

The comparison of a pulsed Doppler ultrasonic velocimeter with a hot film anemometer in measuring disturbed flow in models has shown a good correlation between the two techniques¹⁶⁵. The visual manifestation of disturbed flow, as detected by a Doppler velocimeter, is an increase in the width of the spectrum of the back scattered signal. This is due to greater variation in velocities of blood cells within the "sample volume" of the pulsed Doppler device. Hutchinson et al.⁹⁰ demonstrated that disturbances downstream of graded stenoses caused a pattern of increased spectral width in the heart-cycle. This was found in the phase of flow deceleration with mild stenoses but occurred earlier in the pulse cycle as the degree of narrowing was increased. Thiele's and Hutchinson's studies have shown that pulsed Doppler instruments have the potential to detect early flow disturbances, they are the basis for estimating the degree of diameter reduction in extracranial carotid artery disease.

A major problem in pulsed Doppler operations is placing the sample volume at a desired anatomical site in a three dimensional arterial system. This problem can be solved by using multiple receiving gates set at different depths^{39,85}, or by using an imaging system to position the sample volume within the vessel of interest^{87,138}.

4.1.4. Pulse Echo Imaging.

Before the development of the Doppler method, ultrasonic imaging systems were introduced. These systems are based, like radar, on the time of flight of sound and the strength of the reflector. In the early systems, a stationary collimating transducer was used to send an ultrasound pulse into tissue. The reflections in time, from successively deeper tissue planes, were plotted on an oscilloscope with depth plotted horizontally and amplitude of the reflected wave plotted vertically. This amplitude versus depth plot was called amplitude or "A" mode.

An A-mode display can be converted to an intensity mode display by retaining the depth coordinate as dimension along a line and plotting the strength of reflection as intensity. The intensity can be either two level or providing a full range of scale. When properly adjusted, the level of gray can be used to identify tissue structures.

Moving structures can be followed in real time with both A-mode and intensity mode, which motion mode is referred to as "M" mode⁷⁹. A two dimensional image can be made by a similar system. The transducer is moved over the skin while the intensity mode line is moved over a display screen, painting a 2 dimensional image. Such a display is called a "B" mode image. In early systems, the B-mode probe was moved over the skin by hand. Now the ultrasonic transducers are moved mechanically or electronically over the image field producing a full field display in a fraction of a second, thus creating "real-time" imaging²⁰.

4.2. Analysis of the Doppler spectrum.

The analysis of the audible Doppler signals by an experienced technician has been successful in the detection of pathology in the arterial system¹⁵. In order to document the velocity information, a hardcopy of the audible Doppler signals should be available. In principle two methods of display are used to obtain a hardcopy of the audible signal: (1) zero-crossing frequency analysis; and (2) spectral analysis.

4.2.1. Zero-crossing frequency analysis.

The method is based on the electronic detection and marking of zero-crossing events of the Doppler signal. The electronic device may only count positive, negative, or both positive and negative crossings of the Doppler signal. The zero-crossing principle is traditionally used to obtain an analogue velocity tracing, displaying only the "mean" of the whole Doppler spectrum. The analog tracing gives the "averaged" velocity as an instantaneous function of time. The advantages of the method are its simplicity and the fact that the hardcopy can be obtained using a simple strip chart recorder. However several disadvantages should be known by the user of this method: (1) signals with a poor signal-to-noise ratio cannot be adequately recorded¹¹³; (2) since only the "mean" of the Doppler spectrum is displayed primarily artefacts may also be recorded and interpreted as pathological finding⁹² and; (3) since all information of the Doppler spectrum is reduced to one frequency, a certain amount of potential important information is

lost for further analysis¹³⁹. More information of the Doppler spectrum can be obtained when spectral analysis is used^{19,72}.

4.2.2. Spectral analysis.

Spectral analysis is the method of choice for processing the Doppler signals from peripheral arteries, since it retains all the Doppler information and allows the examiner to determine if potential artefacts are present. These artefacts can be the result of: (1) background noise; (2) high amplitude, low frequency signals arising from the arterial wall or probe movement; and (3) simultaneous recordings made from arteries or veins.

Spectral analysis may be accomplished by an off-line method. The Kay sonograph was originally such a method, it was reliable but time-consuming and directional Doppler information could not be displayed. Real-time spectral analysis is preferable and may be performed by multiple bandpass filter analysis^{110,184}, time compression analysis⁴², or fast Fourier transform analysis^{77,145}. Real-time spectral analysis is easily available and has found its place in many noninvasive laboratories^{26,43,72,139}.

Spectral analysis of continuous-wave Doppler signals can be used to determine a maximum frequency envelope, but an assessment of disturbed flow based on "spectral broadening" is not possible because the continuous-wave signal contains velocities from the entire flow profile. The wide range of velocities sampled with the system produces a broad frequency spectrum from both normal and diseased vessels. A pulsed Doppler system, as built in the Duplex scanner, samples flow from specific sites and avoids the disadvantages of the continuous wave instruments.

4.3. The Duplex concept.

4.3.1. Introduction.

Olinger¹³⁰ made the first two dimensional images of peripheral blood vessels, using a pulsed-echo system. An important limitation noted with such a system was, that a total occlusion of the internal carotid artery appeared to be patent from the B-mode images. A tissue study of atheromatous deposits, found within and along diseased arteries, by Hartly et al.⁷⁶ showed a wide variation in the absorption characteristics of plaques dependent on the absence or presence of calcification. These findings motivated the development of the Duplex scanner which combines real-time B-mode imaging with pulsed Doppler ultrasound. The Duplex concept is based upon the ability to define the walls of a vessel with a two dimensional image and utilizing pulsed Doppler ultrasound to evaluate the velocity characteristics of the flow within the visualized artery. These concepts were integrated into the Duplex Scanner II system described by Barber et al.^{11,12}, the first prototype available for clinical studies^{132,133} was used until January 1980. This device employs three 5 MHz ultrasonic transducers mounted on a rotating drum encased within a water-filled silastic boot used for generating a real-time B-mode image. Within the silastic boot, a single gate 5 MHz pulsed Doppler with a

quadrature output is mounted in the plane of the B-mode image. The beam path of the pulsed Doppler is represented on the image by an enhanced white line, while the point from which the flow is sampled is represented by a white dot. The clinical evaluation of this scanner was reported by Blackshear et al.²⁴ and Fell et al.⁵⁹.

Since the introduction of the method, the system had undergone continuous modification to improve not only on the ease of the study but the accuracy of the technique in predicting the presence or absence of carotid artery disease. In January 1980 the prototype system was replaced by a commercially available device. The improvements made then were in large part the results of previous experience and projected needs.

4.3.2. Instrumentation requirements.

A block diagram of the Mark V Duplex scanner system is shown in figure 5. The basic elements include: the scan head assembly, pulse echo electronics, scanhead controller, pulsed Doppler electronics, and associated display and recording instrumentation. Three fixed focus 5 MHz transducers imbedded in a rotating wheel generate a two dimensional image of soft tissue interfaces with 16 levels of grey. The sector angle of the B-mode image can be chosen at 45°, 60° or 90°. Routinely a 60° sector angle is used. The image rate is 30 frames per second. Since the image information is digitized the B-mode image can be "frozen", in which mode one of the three crystals is used as a pulsed Doppler. This permits the use of a pulse repetition frequency of 19.2 KHz which, given a certain depth, allows a Doppler frequency response up to 9.6 KHz before aliasing occurs (see 4.1.3.).

Figure 5.
Block diagram of Mark V Duplex scanner. The basic elements includes: scanhead assembly, pulse echo electronics, scanhead controller, pulsed Doppler electronics, and associated display and recording instrumentation.

The B-mode image is displayed on an oscilloscope screen. The position of the Doppler beam is indicated by a white line superimposed on the B-mode images in order to be able to measure the angle between the axis of the vessel of interest and the Doppler beam. A small dot represents the position of the sample volume along the Doppler beam. Both Doppler angle and sample volume depth are adjustable by controls on the scan head. Hardcopy of the Doppler signals from a normal common carotid artery from different angles demonstrates nicely that whenever comparison is made between studies, the angle between the Doppler beam and the axis of the vessel should be known (see 5.2.1.). The differences between the signals at 45°-60°-90° can be explained by the Doppler equation, where the Doppler frequency changes with the cosine of the angle between the Doppler beam and the axis of the vessel (see 4.1.1.).

Two different scan heads are commercially available, the medium focus scan head and the short focus scan head. The medium focus scan head has a designation CCC, operating at 5 MHz, 9.5 mm crystal diameter and a 40 mm focal point. The short focus scan head has a designation CBB, operating at 5 MHz, 6 mm crystal diameter and a 20 mm focal point³.

The pulsed Doppler sample volume can be defined as the region in space in which the detection of the movement of the blood cells occurs^{9,93}. The use of a pulsed system allows this sample volume to be positioned at any desired depth from the transducer.

Since the width of the ultrasound beam (W) varies as a function of range, the sample volume is likewise range dependent. The beam widths at different ranges from the two scan heads are shown in figure 6 and 7. These plots were obtained using a hemispherical point reflector¹⁰³. Results from such studies have been shown to provide beamwidths similar to those obtained with moving scatterers in water tank studies^{93,136}. The pulse echo techniques were employed as they are easier to perform. The beamwidth of the medium focal scan head is narrowest from 35 to 45 mm in its focal range, whereas that of the short focus scan head is narrowest from 20 to 30 mm. Therefore the short focus scan head is appropriate for studies of vessels which lie less than 30 mm from the transducer, and the medium focus scan head is more appropriate for vessels lying further than 30 mm from the scan head. The arteries in the neck lie within 30 mm of the skin surface in the majority of human subjects. Therefore, the short focus scan head should on theoretical basis, be used for all subjects of normal build. Since this study was performed¹⁰³, the short focus scan head has been used routinely in the vascular laboratory at the University of Washington.

Additionally, the size of the sample volume, relative to the size of the vessel being studied, will have a considerable effect on the velocities which are recorded. If the sample volume is large relative to the vessel diameter, then a greater distribution of velocities will be detected. This results in an increase of the spectral width. The use of pulse echo techniques have allowed the calculation of the relative sizes of the sample volumes of the 2 scan heads. The beam widths for the medium and short focus scan heads are 5.5 mm. and 2.0 mm respectively at the 20 dB level at a range of 25 mm (figure 6 and 7). The corresponding range measurements for the five cycle gated burst is 2.3 mm for both scan heads. The sample volumes for the

short and medium focus scan heads are calculated to be 3 mm^3 and 24 mm^3 respectively. This calculation is based upon the 20 dB beam width measurements, a sample and hold window of one micro second and an oblate spheroid used as the geometrical model. It is apparent that the medium focus scan head will sample a much greater volume and potentially a greater range of velocities than the short focus scan head. This will be demonstrated by the results of the clinical studies (chapter 5).

Medium Focus

Figure 6.
The beam plots for the medium focus scanhead. These were generated from a 2.4 diameter stainless steel hemisphere. The width of the the beam W (mm) is shown for the ranges R (cm).

Short Focus

Figure 7.
The beam plots for the short focus scanhead. These were generated from a 2.4 diameter steel hemisphere. The width of the beam W (mm) is shown for the ranges R (cm).

4.3.3. Output and recording systems.

The quadrature outputs of the pulsed Doppler signal are sent to a Fast Fourier Transform spectrum analyzer. The initial work with the Duplex scanner utilized a time compressing method (Honeyell model SAI-51C spectrum analyzer). More recently a Fast Fourier Transform (FFT) has been used (Honeywell research prototype FFT Spectral Analyzer). This digital device operates on-line and provides a full scale frequency display of 10 KHz (amplitude versus frequency).

The maximum frequency range of the spectrum analyzer is 12.8 KHz, constructed from 128 frequency bins spaced at 100 Hz. Of the 12.8 KHz only 10 KHz is displayed, 7 KHz reserved for forward flow and 3 KHz reserved for reversed flow. The FFT analyzer samples the two quadrature channels at a 12.8 KHz range and provides spectra at a rate of 400 per second. Since each spectrum is composed of 25% new data and 75% old data, every fourth spectrum is independent from a statistical viewpoint. This method is appropriate, where the input signal is not stationary but continually varying with time. A hardcopy of the output of the spectral analysis is obtained on light-sensitive paper, where frequency is displayed versus time with the amplitudes as levels of grey.

Before the display of the signal, the signal is "normalized" in order to improve the signal-to-noise ratio. The principle of normalizing is based on increasing the highest amplitude of each analysis to a reference level with the same scaling factor applied to all other amplitudes (figure 8).

Normalizing

Figure 8.
The principle of "normalizing" is based on the increase of the highest amplitude to a reference level. Amplitude is displayed on the vertical, and frequency on the horizontal axis.

Following normalizing only a certain amount of the signal is displayed, according to the "dynamic range" of the Doppler signal. A dynamic range of only 15 dB is chosen (figure 9), whenever a large dynamic range is chosen (60 dB) the chance exists that not only the desired Doppler signal but also noise will be displayed.

Dynamic Range

Figure 9.
The "dynamic range" is measured from the reference level. For centerstream information a dynamic range of 15 dB was chosen. Amplitude is displayed on the vertical, and frequency on the horizontal axis.

Although disturbed flow associated with high grade stenosis can be readily distinguished from normal flow by audible means¹³⁹, flow disturbances resulting from lesser degrees of narrowing require more sensitive methods such as spectral analysis. The real-time FFT spectrum analyzer helps the technician performing the study to determine the frequency, direction and characteristics of the obtained signals. The quadrature outputs from the pulsed Doppler together with the corresponding B-mode images are fed to a Sony V02600 video tape recorder for permanent recording and analysis.

4.3.4. Patient examination method.

The study is performed with the patient supine and the head supported to eliminate lateral movement. A water-soluble acoustic gel is used to couple the sound from the scan head to the skin surface. Blood vessels are identified by their characteristic B-mode images with prominent wall echos separated by a dark, sonolucent lumen (see figure 10). Calcified plaques are recognized as bright

Figure 10.
B-mode image of a normal common carotid (A), carotid bulb (B), and internal carotid artery (C). The white line represents the direction of the pulsed Doppler system. The white dot represents the position of the Doppler sample volume.

intraluminal echoes and regions of posterior acoustic shadowing (see figure 11). The operator places the sample volume of the pulsed Doppler in the centerstream

Figure 11.
B-mode image of a stenotic proximal internal carotid artery. A is the common carotid, B the internal carotid artery. Note the calcified plaque with the posterior acoustic shadowing in the proximal internal carotid artery.

of the vessel and measures the angle of the Doppler beam relative to the axis of the vessel of interest. A Doppler angle of approximately 60 degrees provides a favorable return signal for further processing.

The Doppler sample volume is placed near the centerstream of the vessel in order to avoid detection of velocities and eddies close to the wall. These eddies would cause an increase of the spectral width even in normal arterial vessels. In order to obtain the most representative signal the operator monitors the amplitude versus frequency output from the FFT on an oscilloscope, the audible signal from the speaker and the screen of the real-time spectrum analyzer.

The examination begins low in the neck with the identification of the common carotid artery. Moving distally, the carotid bulb can be recognized by a typical audible signal. By scanning in various planes the bifurcation can often be visualized with the external carotid artery usually anteromedial to the internal carotid artery (see figure 12). The differentiation between the internal and external carotid artery is made by characteristic Doppler signals, noted as the sample volume moved through the scan plane. Flow in the common and internal carotid artery is normally quasi-steady and always well above zero during the entire pulse cycle due to the low resistance of the cerebrovascular bed. Flow in the external carotid artery, supplying a vascular bed with a relative high peripheral resistance (the face), either goes to zero or reverses in diastole. This difference in the characteristics of the velocity signals makes it possible to differentiate accurately between the internal and external carotid artery.

Figure 12.

B-mode image of a normal carotid bifurcation. A is the common carotid, B the external carotid, and C the internal carotid artery. Note the jugular vein above the common carotid artery.

When the common, internal and external carotid artery are localized, signals from the common carotid artery, the proximal internal carotid artery, the distal internal carotid artery and the external carotid artery are recorded on videotape for documentation and further analysis. The whole study of both carotid sides takes approximately 30 minutes in the hands of an experienced technician.

After the study is completed the quadrature information from the pulsed Doppler is analyzed using a Fast Fourier Transform spectrum analyzer and recorded on light sensitive paper. The hard copy displays frequency on the vertical axis versus time on the horizontal axis with the amplitudes expressed as levels of grey. Eight levels of grey are chosen for displaying the different amplitudes for routine studies. The frequency range is 10 KHz, where 7 KHz is reserved for forward flow and 3 KHz for reversed flow.

A normal Doppler spectrum consists of systolic peak frequency up to 4 KHz and a narrow band of frequencies during systole, resulting in a clear region beneath the systolic peak (window). With minimal stenosis spectral changes occur as spectral broadening during the deceleration phase of systole. Further stenosis generally results in increased spectral broadening until the entire window beneath the systolic peak is filled, followed by an increase in peak systolic and diastolic frequencies⁹⁰.

For the validation studies five categories of diameter reduction were used (see figure 13). The radiologists classified the biplanar contrast arteriograms with regard to the degree of involvement at the level of the bulb. They expressed the diameter reduction as a percentage of the estimated normal wall diameter to the nearest five percent (see figure 13). The unsubtracted arteriograms were used because the presence of calcification in the outer layers of the vessel wall in the region of the stenosis facilitated the estimation of the normal wall diameter. The radiologists reporting the diameter reductions were unaware of the results of the noninvasive tests, the technicians performing the noninvasive studies were unaware of the results of the contrast arteriograms.

Figure 13.
Arteriographic classification of the proximal internal carotid artery.

The spectral changes used to define each category include:

(A) normal: systolic peak frequency up to 4 KHz without spectral broadening; (B) 5-15% diameter reduction: systolic peak frequency up to 4 KHz, spectral broadening in the deceleration phase of systole; (C) 16-49% diameter reduction: systolic peak frequency up to 4 KHz, spectral broadening throughout systole; (D) 50-99% diameter reduction: systolic peak frequency above 4 KHz, spectral broadening throughout systole, increased frequencies in diastole; and (E) occlusion: no signal in the internal carotid artery, flow to zero during diastole in the common carotid artery.

It should be noted that in contrast to previous publications from our laboratory^{59,61}, the arteriographic classification has been changed. In the new classification the "B" category has changed from diameter reduction less than 10% to 5-15% diameter reduction. The "C" category changed from 10-49% to 16-49% diameter reduction. There are two reasons for the new classification. In the first place from a clinical point of view a cutpoint at 15% diameter reduction seems to be more practical¹⁶⁶. Secondly, experience with the computer controlled pattern recognition program, as developed at the University of Washington, also demonstrates a cutpoint at 15% diameter reduction. Introducing the new classification makes it possible to compare the spectral analysis hardcopy results with the pattern recognition computer results.

Chapter 5

Accuracy of Duplex scanning.

5.1. Introduction.

The accuracy of the Mark V Duplex scanner combined with spectral analysis as compared with contrast arteriography will be presented and discussed in this chapter. Four separate studies form the basis of the data for this evaluation. The first study was performed after the results with the Periperal Vascular Scanner III were analyzed⁵⁹. It became obvious that the accuracy of predicting a total occlusion of the internal carotid artery by the noninvasive test could be improved by paying more attention to the velocity pattern of the common carotid artery. In order to assess in an objective fashion the value of the velocity pattern of the common carotid artery as related to disease at the carotid bifurcation, the velocity patterns of 156 patients who had undergone contrast arteriography were reviewed.

In the second study the accuracy of the Mark V Duplex scanner in combination with spectral analysis was evaluated. Multiplanar contrast arteriograms of 246 carotid sides were available for comparison. The purpose of this study was to review the accuracy of the noninvasive method and its potential applications for clinical research studies.

The spectral changes observed with early disease are often minimal and therefore difficult to separate from velocity patterns in normal carotid arteries. In order to "unmask" lesser degrees of stenoses, we considered to increase the blood flow to the brain by giving patients with minimal disease carbon dioxide. However, before applying this method to patients, it was necessary to evaluate the changes in normal subjects. The third study of this chapter was designed to evaluate the velocity pattern changes that occur when there is an increase of total cerebral blood flow in normal subjects.

The fourth study concerned the evaluation of a parameter for accurate classification of severe carotid disease. The study was performed in order to estimate the degree of involvement in patients with stenoses within the 50-99% diameter reduction category.

5.2. The role of common carotid artery velocity patterns in the evaluation of carotid bifurcation disease.

5.2.1. Introduction.

Over the past three years the application of a prototype Duplex scanner has been evaluated^{24, 59, 161}. With the development of the Fast Fourier Transform spectrum analyzer, which could be used to accept the directional signals from the pulsed Doppler, it became apparent that the velocity patterns recorded from the

common carotid artery could be of additional use in detecting high grade stenoses or total occlusions of the internal carotid artery.

Fell et al.⁵⁹ found in their study, using the periperal vascular Duplex scanner III, an agreement between contrast arteriography and the noninvasive test for the total occlusion category of 70%. Of the 46 arteriographic occluded internal carotid arteries only 32 were predicted correctly by the Duplex scanner. Since the differentiation between a high grade stenosis and a total occlusion of the internal carotid artery is of great clinical importance, inaccurately classifying total occlusions was of great concern.

A study of the velocity patterns of the common carotid artery using the Duplex scanner was performed by Bodily et al.³¹. They observed flow to zero during late systole or diastole in 33 of the 34 sides with internal carotid occlusion. It should be stressed however that, whenever flow to zero is used to characterize the velocity pattern of the common carotid artery, the angle between the Doppler beam and the axis of the vessel should be optimal. In order to demonstrate the changes in the velocity patterns that occur with different Doppler angles, hardcopy of the velocity pattern from the common carotid artery were recorded over a range of 45 degrees to 90 degrees in steps of 15 degrees. (see figure 14-17). In our studies we routinely establish a Doppler angle of 60 degrees to obtain a favorable return signal for further processing.

Figure 14.
Hardcopy of the velocity pattern of a normal common carotid artery. The angle between the Doppler beam and axis of the artery was 45°. Note the frequencies above zero during diastole.

Figure 15.
Hardcopy of the velocity pattern of a normal common carotid artery. The angle between the Doppler beam and the axis of the artery was 60°. The frequencies during diastole remain above zero.

Figure 16.
Hardcopy of the velocity pattern of a normal common carotid artery. The angle between the Doppler beam and the axis of the artery was 75°. Peak systolic frequencies are decreased, the frequencies during diastole reach the zero line.

Figure 17.
Hardcopy of the velocity pattern of a normal common carotid artery. The angle between the Doppler beam and the axis of the vessel was 90°. The velocity pattern has lost all characteristics of a common carotid artery.

Flow in the common carotid artery is normally quasi-steady and always well above zero during the entire pulse cycle due to the low resistance of the cerebrovascular bed^{120, 122, 148}. At the bifurcation, flow is separated to supply two vascular beds each with different peripheral resistance. The internal carotid artery supplies a low resistance vascular bed, allowing marked forward flow during diastole resulting in a flow above zero at all times in the pulse cycle. The velocity pattern of the common carotid artery is dominated by the low resistance of the ipsilateral hemisphere giving a flow pattern which is similar to that observed in the internal carotid artery. This latter velocity pattern can be influenced by changes in peripheral resistance^{147, 136}, and central hemodynamic changes¹⁴⁸.

Significant occlusive disease of the internal carotid artery which increases the resistance to flow, may be detected by changes in the common carotid artery velocities patterns^{31, 134}. A total occlusion of the internal carotid artery produces a flow pattern in the common carotid artery resembling that in the external carotid artery; i.e. the flow will go to zero during diastole and even reverse in some instances. Thus, when no velocity signal is found in the region of the internal carotid artery and a total occlusion of the internal carotid artery is considered, the diagnosis can be confirmed by the finding of flow to zero in the common carotid artery.

Flow to zero in diastole with reversal of flow during late systole can also occur in the velocity pattern of a common carotid artery of patients with aortic valve disease¹⁴⁶. In this case, it is expected to be found bilaterally.

To assess in an objective fashion the frequency of flow to zero, as related to

disease in the carotid bifurcation, the velocity patterns of the common carotid artery of 156 patients who had undergone biplanar contrast arteriography were reviewed. Data was obtained with both the prototype PV III Duplex scanner and the Mark V Duplex scanner.

5.2.2. Results.

The velocity waveform from a common carotid artery without disease in the internal carotid artery is shown in figure 18. Flow is well above zero at all points in the pulse cycle. The velocity waveform from a common carotid artery with a total occlusion of the internal carotid artery is shown in figure 19. Flow goes to zero during diastole with flow reversal during late systole.

Figure 18.
Hardcopy of the velocity pattern of a common carotid artery without disease in the internal carotid artery. Note the frequencies above zero during diastole.

Figure 19.
Hardcopy of the velocity pattern of a common carotid artery with an occlusion of the internal carotid artery. Note the frequencies reaching zero during diastole.

The distribution of the degree of involvement of the internal carotid artery as classified by the velocity patterns and confirmed by contrast arteriography is shown in Table I. A total occlusion of the internal carotid artery was found in 18% (56/312), a 50-99% diameter reduction in 37% (116/312), a 16-49% diameter reduction in 34% (107/312), a 5-15% diameter reduction in 8% (23/312), and a normal internal carotid artery in 3% (10/312).

Table I.

Arteriographically estimated percent diameter reduction of the internal carotid artery and flow to zero in the common carotid artery.

Internal Carotid Artery		Common Carotid Artery		
Category	Sides	Unilateral Flow to Zero (Sides)	Bilateral Flow to Zero (Sides)	Total Sides With Flow to Zero
A. Normal	10	0	0	0
B. 5-15%	23	0	3	3
C. 16-49%	107	0	9	9
D. 50-99%	116	15	11	26
E. Occlusion	56	39	13	52
Total	312	44	36	90

As noted in Table I, flow to zero was found in the common carotid artery in 90 of the 312 sides (29%). The highest percentage was found in cases of total occlusion of the internal carotid artery, 52 of 56 (93%). Of these 52 sides, flow to zero was found unilaterally in 39 and bilaterally in 13 sides. The 13 sides with bilateral flow to zero were found in eight patients; five patients had bilateral occlusions of the internal carotid artery (10 sides), and three patients had a contralateral 50-99% diameter reduction (3 sides).

With a 50-99% diameter reduction of the proximal internal carotid artery (D category), flow went to zero in 22% (26/116). In those cases with stenoses of less than 50% diameter reduction (B and C category) flow went to zero on twelve sides, in each instance flow to zero was found bilaterally.

Further breakdown of the 50-99% diameter reduction group is shown in Table II. The Table shows three groups of internal carotid arteries: (1) total occlusions, (2) tight stenoses, with a diameter reduction of 90-99%, and (3) stenoses with diameter reductions less than 90% and normal internal carotid arteries. In the tight stenosis group (90-99% diameter reduction) flow to zero was found in 52% (11/21). In nine cases the finding was unilateral, in two cases it was a bilateral finding. In one of these two cases the contralateral carotid artery was occluded, in the second case, there was a diameter reduction of less than 90% in the contralateral internal carotid artery.

Table II.
Arteriographically estimated percent diameter reduction of the internal carotid artery and flow to zero in the common carotid artery.

Internal Carotid Artery		Common Carotid Artery		
Category	Sides	Unilateral Flow To Zero (Sides)	Bilateral Flow To Zero (Sides)	Total Sides With Flow To Zero
1. Occlusion	56	39	13	52
2. Tight Stenosis (90-99% Diameter Reduction)	21	9	2	11
3. Stenosis Less than 90% Diameter Reduction	235	6	21	27
Total	312	44	36	90

If the total occlusion and tight stenosis groups (Table II) are excluded from the analysis, flow to zero in the common carotid artery was found in 11% (27 sides). Of these 27 sides it were noted to be bilateral in 21 instances (78%).

5.2.3. Discussion.

Flow to zero in late systole or during diastole in the common carotid artery can occur as a reflection of central hemodynamic changes¹⁴⁶ or as a reflection of increased peripheral resistance due to atherosclerotic changes in the internal carotid artery³¹.

In the present data the finding of flow to zero was observed in 93% (52/56) of the cases of an internal carotid artery occlusion. In these instances the phenomenon can be explained as a result of increased peripheral resistance. An increased resistance however can also occur when there is a tight stenosis of the proximal internal carotid artery. In the present study, flow to zero in the common carotid artery with a tight stenosis in the internal carotid artery was found in 52% (11/21). In this situation, in contrast to a total occlusion, a high velocity signal should be found in the region of the stenosis, which is usually at the level of the proximal internal carotid artery.

The finding of this high velocity signal is very important, since the clinical consequences of the diagnosis of a tight stenosis are different from that of a total occlusion. A very tight stenosis of the proximal internal carotid artery in a patient with focal neurological symptoms is considered amenable to carotid endarterectomy, whereas the patient with a total occlusion is not considered to be candidate for this procedure. This stresses the importance of searching for velocity signals of the internal carotid despite the finding of unilateral flow to zero in the common carotid artery.

Whenever flow to zero is found bilaterally in the common carotid artery during the study, the technician should realize that this may be secondary to bilateral peripheral resistance changes or to central hemodynamic changes. For example, aortic valve insufficiency will cause bilateral flow to zero in diastole with reversal of flow during late systole. Under these circumstances, the characteristics of the velocity signals from the internal carotid artery are used to distinguish a central cause from bilateral internal carotid artery pathology. In the present data this is demonstrated by the fact that the finding of flow to zero in the common carotid artery with minimal disease in the internal carotid artery (category B and C) was bilateral in all instances, suggesting that the finding was due to central pathology.

Flow to zero in the common carotid artery was not found in combination with a total occlusion of the proximal internal carotid artery in four sides. The reason for this finding is not clear, an explanation could be that due to the excellent collateral system via the external carotid artery the peripheral resistance was not markedly increased.

Bilateral flow to zero was found in the common carotid artery with an occlusion of the internal carotid artery in 13 sides, the bilateral finding was explained in ten sides by a bilateral occlusion of the internal carotid artery and in one case the contralateral internal carotid artery was found to have a tight stenosis (90-99% diameter reduction). In the remaining two sides there was no peripheral resistance change to explain the finding.

In conclusion, there is evidence from the data in this study that there are three groups of patients with flow to zero in the common carotid artery: (1) patients

with bilateral flow to zero in the common carotid artery not related to occlusive disease of the internal carotid artery; (2) patients with flow to zero in the common carotid artery with tight stenoses (90-99% diameter reduction) of the internal carotid artery; and (3) patients with flow to zero in the common carotid artery with total occlusions of the internal carotid artery.

Obtaining the velocity patterns of the common carotid artery should be a part of the total noninvasive study. The technician, performing the study, should understand the reasons for changes occurring in the velocity pattern of the common carotid artery. As will be demonstrated in section 5.3., the appreciation of the characteristics of the velocity pattern of the common carotid artery has considerably improved the accuracy of the Duplex scanner combined with spectral analysis in predicting high grade lesions and total occlusions of the internal carotid artery.

5.3. The accuracy of ultrasonic Duplex scanning as compared with contrast arteriography

5.3.1. Introduction.

During the past decade, a variety of indirect noninvasive tests have been developed to assess carotid bifurcation arteriosclerosis. The most commonly used included periorbital Doppler^{13, 32, 114} and plethysmographic methods^{56, 68, 94} which are theoretically capable of detecting those lesions which produce a reduction in pressure and flow. However, these methods cannot distinguish between a high grade stenosis and a total occlusion of the internal carotid artery. Furthermore they cannot differentiate between normal and minimal disease (non pressure or flow reducing lesions). It is now known that disease of the carotid bifurcation which may produce transient ischemic attacks and strokes can vary from minimal lesions to total occlusion¹⁶⁶. It is, therefore, necessary to utilize methods of noninvasive testing which can identify both normal vessels and those with the entire spectrum of involvement.

The approach taken at the University of Washington has been to develop an ultrasonic system which not only permits imaging of the bifurcation, but also attempts to identify flow changes at that level which occur secondary to the presence of atherosclerosis. This has led to the development of the ultrasonic Duplex scanner which permits such studies to be made^{132, 133}. Most recently the results of the prototype PV III Duplex scanner were reported by Fell et al.⁵⁹. In this study 135 patients underwent contrast arteriography, giving 270 carotid bifurcations available for comparison. The agreement between contrast arteriography and ultrasonic Duplex scanning combined with spectral analysis of this study is shown in Table III. For a normal bifurcation the agreement was 35.5% (4/11), for a diameter reduction less than 10% the agreement was 45% (9/20), for a 10-49% diameter reduction the agreement was 58% (52/90), for a 50-99% diameter reduction the agreement was 81.5% (84/103), and for a total occlusion 70% (32/46). This study demonstrates that, although far from perfect, the method of Duplex scanning combined with spectral analysis has the potential

to predict the extent of involvement present, varying from plaques not producing diameter reductions to those with a total occlusion of the internal carotid artery. In January 1980, the PV III Duplex scanner was replaced by the commercially available Mark V Duplex scanner. The improvements made were in large part the results of experience gained with the prototype PV III scanner. The accuracy of the Mark V Duplex scanner is the subject of this section.

Table III
Correlation of PV III Duplex results and arteriographic results for the internal carotid artery.

Duplex (PV III)						
Arteriography	0%	<10%	10-49%	50-99%	100%	
0%	4	3	4			11
<10%	3	9	8			20
10-49%	4	12	52	20	2	90
50-99%		3	10	84	6	103
100%			2	12	32	46
	11	27	76	116	40	270

5.3.2. Methods and Materials.

The Mark V Duplex scanner used for this study is described in section 4.3. The system combines real-time B-mode imaging (see 4.1.4.) with a pulsed Doppler device (see 4.1.3.). The B-mode images are used to identify the carotid arteries and to visualize calcified plaques. When the B-mode image is "frozen" (see figure 20), one of the crystals is used as a pulsed Doppler. This permits the use of a pulse repetition frequency of 19.2 KHz, which allows a Doppler frequency response up to 9.6 KHz before aliasing occurs (see 4.1.3.).

In addition to the audible interpretation, the quadrature outputs of the Doppler are sent to an on-line spectrum analyzer employing a digital fast Fourier transform analysis. The spectrum analyzer (Honeywell prototype FFT Spectrum Analyzer) provides 400 spectra per second with a frequency display range of 10 KHz, 7 KHz are reserved for forward and 3 KHz for reverse velocity components (see 4.3.3.). The characteristics of the Doppler spectrum have been described previously (see 4.3.4.). Hardcopy output of the spectral analysis is obtained on light sensitive paper, where frequencies are displayed vertically as a function of time with the amplitudes of the backscattered signal expressed in levels of gray (see 4.3.4.).

Figure 20.
B-mode image of a normal common carotid (A) and internal carotid artery (B). With the B-mode image "frozen", one of the crystals is used as a pulsed Doppler. The white dot is the location of the sample volume of the Doppler system.

From January 1980 till November 1980 the medium focus scanhead was used, in this period 500 patients were referred to the laboratory for a noninvasive evaluation of their carotid arteries. Of these 500 patients 85 (169 sides) underwent multiplanar contrast arteriography. Between November 1980 and May 1981 250 patients were evaluated using the short focus scan head. Of these 250 patients 39 (77 sides) underwent multiplanar contrast arteriography.

The main difference between the two scan heads is, that the medium focus scan head employs 9.5 mm. diameter transducers focused at 4 cm while the short focus scan head employs 6 mm. diameter transducers focused at 2 cm. (see 4.3.2.). Calculations of the sample volume size for the medium focus scan head using 20 dB measurements and assuming an oblate spheroid model at a range of 2 cm. is 24 mm^3 , the sample volume size for the short focus scan head using the same measurements at a range of 2 cm is 3 mm^3 (see 4.3.2.).

The radiologists reading the multiplanar contrast arteriograms were unaware of the results of the noninvasive study. The extent of disease of the proximal internal carotid was expressed as a percent diameter reduction of the normal wall diameter at the level of the stenosis (see 4.3.4.).

The arteriographic criteria and velocity pattern characteristics used to categorize the extent of internal carotid artery disease are shown in table IV. It should be noted that in contrast to previous reports from the same institution, the B category

Table IV.

Arteriographic and spectral analysis criteria for the classification of the internal carotid artery.

Categories of Internal Carotid Artery		
Category	Arteriographic Criteria	Velocity Pattern Criteria
A.	Normal (0% diameter reduction)	Systolic peak frequency up to 4 KHz, no spectral broadening.
B.	5-15% diameter reduction	Systolic peak frequency up to 4 KHz, spectral broadening in deceleration phase of systole.
C.	16-49% diameter reduction	Systolic peak frequency up to 4 KHz, spectral broadening throughout systole.
D.	50-99% diameter reduction	Systolic peak frequency above 4 KHz, spectral broadening throughout systole, increased frequencies in diastole.
E.	Occlusion (100% diameter reduction)	No signal, flow to zero during diastole in common carotid artery.

contains 5-15% diameter reductions. One of the reasons for the new classification, as has been described previously (see 4.3.4.), was that the computer pattern recognition program employs a 5-15% diameter reduction group⁷³.

Although the main emphasis in predicting extracranial carotid artery disease has been focused on the internal carotid artery, there are situations in which predicting the extent of external carotid artery disease can be of clinical importance. Thus it is important to have a classification scheme for the external carotid artery as well. For clinical purposes it is only necessary to differentiate between a normal external carotid artery, a non hemodynamic significant stenosis, a hemodynamic significant stenosis and a total occlusion. The arteriographic criteria and velocity pattern characteristics used to categorize the extent of external carotid artery disease are shown in table V.

Table V.
Arteriographic and spectral analysis criteria for the classification of the external carotid artery.

Categories of External Carotid Artery		
Category	Arteriographic Criteria	Velocity Pattern Criteria
1.	Normal.	Systolic peak frequency up to 4 KHz, no spectral broadening.
2.	5-49% reduction.	Systolic peak frequency up to 4 KHz, spectral broadening in systole.
3.	50-99% diameter reduction.	Systolic peak frequency above 4 KHz, marked spectral broadening.
4.	Occlusion.	No signal.

5.3.3. Results.

Internal carotid artery. Hardcopy output of the spectrum analyzer from the 5 categories of the internal carotid artery are shown in figure 21-25. Note that the velocity waveform displayed in the total occlusion category is a common carotid artery waveform with flow to zero during diastole (see 5.2.3.).

Figure 21.
Hardcopy of a normal internal carotid artery signal. Frequency is displayed on the vertical and time on the horizontal axis, with the amplitude as level of grey. There is no spectral broadening during systole. (clean area beneath the systolic peak).

Figure 22.
Hardcopy of a 5-15% diameter reduction of the internal carotid artery. There is spectral broadening in the deceleration phase of systole.

Figure 23.
Hardcopy of a 16-49% diameter reduction of the internal carotid artery. There is spectral broadening throughout the entire pulse cycle.

Figure 24.
Hardcopy of a 50-99% diameter reduction of the internal carotid artery. There is marked increase in peak systolic and diastolic frequencies, associated with spectral broadening.

Figure 25.
Hardcopy of a common carotid artery signal
with a total occlusion of the internal carotid
artery. Note the flow to zero during diastole.

The results of the ultrasonic Duplex scanner compared to the results of multiplanar contrast arteriography for the internal carotid artery using the medium focus scan head are shown in Table VI. Regarding the contrast arteriographic data as "gold standard", 7% (12/169) of the internal carotid arteries

Table VI.
Correlation of Duplex results and arteriographic results for the internal carotid artery, using the medium focus scanhead.

Arteriography	Medium Focus Scanhead Duplex					
	0%	5-15%	16-49%	50-99%	100%	
0%	1	6	4	1		12
5-15%	1	19	15	2		37
16-49%	2	10	24	5		41
50-99%		1	2	61	1	65
100%				1	13	14
	4	36	45	70	14	169

were classified as normal (0% diameter reduction), 22% (37/169) had a 5-15% diameter reduction, 24% (41/169) had a 16-49% diameter reduction, 39% (65/169) had a 50-99% diameter reduction, and 8% (14/169) had a total occlusion (100% diameter reduction).

Out of the twelve arteriographic normal carotid arteries, there was only agreement with the Duplex data in one, hence eleven sides were called diseased. In the 5-15% diameter reduction category there was agreement in 51% (19/37), one side was undercalled and 17 sides were overcalled. In the 16-49% diameter reduction category the agreement was 59% (24/41), twelve sides were undercalled and five sides were overcalled by the Duplex method. In the 50-99% diameter reduction category the agreement between the arteriographic data and Duplex data was 94% (61/65), three sides were undercalled and one side was overcalled by the Duplex method. In the total occlusion category (100% diameter reduction) the agreement with the Duplex data was 93% (13/14), one side was undercalled.

The distribution of internal carotid artery disease as classified by contrast arteriography and studied with the short focus scan head is shown in table VII. Regarding the contrast arteriographic data as "gold standard", 10% (8/77) were classified as normal (0% diameter reduction), 17% (13/77) were classified as a 5-15% diameter reduction, 30% (23/77) were classified as a 16-49% diameter reduction, 36% (28/77) were classified as a 50-99% diameter reduction, and 7% (5/77) were classified as total occlusion (100% diameter reduction).

Table VII.
Correlation of Duplex results and arteriographic results for the internal carotid artery, using the short focus scanhead.

Short Focus Scanhead Duplex						
Arteriography	0%	5-15%	16-49%	50-99%	100%	
0%	4	4				8
5-15%	1	9	3			13
16-49%		4	16	3		23
50-99%		1	2	25		28
100%					5	5
	5	18	21	28	5	77

Out of the eight arteriographic normal internal carotid arteries, four were classified as normal by the Duplex method, hence four were overcalled. In the 5-15% diameter group the agreement between arteriographic and Duplex data was 69% (9/13), one side was undercalled and three sides were overcalled. In the 16-49% diameter reduction group the agreement was 70% (16/23), four sides were

undercalled and three sides were overcalled by the Duplex method. In the 50-99% diameter reduction group the agreement was 89% (25/28), three sides were undercalled. In the total occlusion category (100% diameter reduction) the agreement was 100% (5/5) between the arteriographic and Duplex data.

External Carotid Artery. Hardcopy output of a normal external carotid artery is shown in figure 26. Note the flow to zero in late systole reflecting the relatively high resistance peripheral vascular bed supplied by this artery.

Figure 26.
Hardcopy of a normal external carotid artery signal. Note the flow to zero during diastole.

The results of the ultrasonic Duplex study compared to the results of multiplanar contrast arteriography for the external carotid artery using the medium focus scan head are shown in table VIII. Regarding the contrast arteriographic data as "gold standard", 48% (81/168) of the external carotid arteries were classified as normal (0% diameter reduction), 38% (64/168) were classified having a 5-49% diameter reduction, 12% (19/168) were classified having a 50-99% diameter reduction and 2% (4/168) were classified having a total occlusion (100% diameter reduction).

Out of the 81 arteriographic normal external carotid arteries, agreement with the Duplex data was found in 25% (20/81). In the 5-49% diameter reduction category the agreement with the Duplex data was found in 67% (42/64). In the 50-99% diameter reduction category the agreement was 84% (16/19), and in the total occlusion category (100% diameter reduction) the agreement was 50% (2/4).

Table VIII.
Correlation of Duplex results and arteriographic results for the external carotid artery, using the medium focus scanhead.

Arteriography	Medium Focus Scanhead Duplex				
	0%	5-49%	50-99%	100%	
0%	20	57	4		81
5-49%	9	42	13		64
50-99%		3	16		19
100%		1	1	2	24
	29	103	34	2	168

The results of the ultrasonic Duplex Scanner compared to the results of multiplanar contrast arteriography for the external carotid artery using the short focus scan head are shown in table IX. Regarding the contrast arteriographic data as "gold standard", 47% (36/76) of the external carotid arteries were classified as normal (0% diameter reduction), 42% (32/76) were classified having a 5-49% diameter reduction, 8% (6/76) were classified have a 50-99% diameter reduction, and 3% (2/76) were classified having a total occlusion (100% diameter reduction).

Table IX.
Correlation of Duplex results and arteriographic results for the external carotid artery, using the short focus scanhead.

Arteriography	Short Focus Scanhead Duplex				
	0%	5-49%	50-99%	100%	
0%	6	29	1		36
5-49%	3	21	8		32
50-99%		1	4	1	6
100%			1	1	2
	9	51	14	2	76

Out of the 36 arteriographic normal external carotid arteries, agreement with the Duplex data was found in 17% (6/36). In the 5-49% diameter reduction category the agreement between the arteriographic and Duplex data was 66% (21/32). In the 50-99% diameter reduction category the agreement was 67% (4/6), in the total occlusion category (100% diameter reduction) one out of two was classified correctly.

5.3.4. Discussion.

Noninvasive methods such as pulsed Doppler and spectral analysis allow the use of parameters such as peak frequency and spectral width to categorize carotid artery disease. It is essential, however, to realize the potential and limitation of the methods in order to properly interpret the acquired data. For instances information about the angle between the Doppler beam and axis of the vessel is important, since it affects the recorded frequency shift which is used in classifying the degree of stenosis (see 5.2.1.). Given the availability of the B-mode image, it is used to measure the angle of the sound beam to the long axis of the vessel. With the present scan head, it is relatively easy to utilize an angle close to 60 degrees even in the distal internal carotid artery.

Since spectral width is used as one of the parameters to classify severity of disease, it is essential to place the sample volume in the centerstream of the vessel.

Approaching the wall there will be velocity gradients even in normal vessels. The increase in the range of frequencies, produced by these gradients, will be recorded as spectral broadening. The short focus scan head provides a sample volume at its focus range which is a factor of 8 smaller than with the medium focus transducer (see 4.3.2.). The smaller sample volume has a theoretical advantage in these patients where spectral broadening is used to differentiate between normal arteries and those with minimal disease.

Internal carotid artery. There were 169 internal carotid arteries evaluated using the medium focus scan head. Twelve of these were called normal by contrast arteriography. Of these twelve normal sides only one was classified normal by Duplex scanning. One of the explanations for this poor agreement could be the fact that arteriography is not an ideal "gold standard" for classifying normal carotid arteries.

Because the arteriograms in this study were reported independently by two radiologists, we had the opportunity of evaluating the agreement between two radiologists in reporting varying degrees of stenoses as defined by the categories previously mentioned for the internal carotid artery⁴¹. The likelihood of two radiologists agreeing that a carotid bifurcation is normal, was only 56.8%. When the same observer reviewed the films on two separate occasions, agreement occurred 74.8% of the time. This raises the question of what is the optimum method for identifying normal carotid arteries as the standard for comparison against noninvasive methods.

There are several possible methods available for defining the extent of stenosis from the arteriogram. In this study, the method used the unsubtracted arteriogram because the presence of calcification in the outer layers of the vessel

wall in the region of the stenosis greatly facilitates the estimation of the normal vessel diameter. We have expressed the degree of stenosis as the percent diameter reduction of the normal wall diameter at the level of the stenosis. Other authors have measured the minimal transverse diameter and have compared this to the diameter of the internal carotid artery beyond the region involved in the disease process^{57, 129}. This measurement technique is mainly used by institutions where indirect noninvasive studies are performed to estimate the extent of extracranial carotid artery disease. For a direct noninvasive test this measurement technique may well miss or underestimate lesions of the carotid bulb. Obviously, the difficulties involved in the interpretation of carotid arteriograms^{41, 47, 54} present a serious problem in the evaluation of the accuracy of noninvasive methods.

The second feature of note is the fact that there is a relatively small number of normal internal carotid arteries available for evaluation. It should be noted that with few exceptions, the decision to perform arteriography was not the responsibility of the personnel performing the noninvasive study. The results of the Duplex scan were simply reported to the referring physician without any recommendation as to the subsequent management of the patient. This issue will be addressed in chapter 6.

With the medium focus scan head only one of the twelve arteriographically normal carotid sides was called normal by the Duplex method. Identification of spectral broadening (six out of the twelve normal internal carotid arteries were classified as a 5-15% diameter reduction) in normals might be caused by variations in the position and size of the sample volume. With the smaller sample volume of the short focus scan head the agreement between arteriography and Duplex method for normal carotid arteries was 50% (4/8), which is an indication that with a smaller sample volume normals may be identified more accurately.

The disagreement in the four arteriographically normal internal arteries which were classified as 16-49% diameter reduction, using the medium focus scanhead, was of some concern. With the short focus scanhead no normals were classified as having a 16-49% diameter reduction. This again suggests that a smaller sample volume provides a "cleaner" signal (less spectral broadening) from normal carotid arteries.

The most serious disagreement in the group of 12 arteriographically normal internal carotid arteries, using the medium focus scanhead, was found in a patient where a 50-99% diameter reduction was predicted. The arteriograms of this patient demonstrated a kink of the internal carotid artery, which was not recognized during the study (figure 27). The hardcopy of the spectrum of the internal carotid artery demonstrated systolic peak frequencies above 4 KHz with spectral broadening during systole. The high peak frequencies were caused by the steep (not noticed) angle between the Doppler beam and the axis of the vessel. The spectral broadening was presumably caused by an incorrect position of the sample volume. Since this error occurred more attention has been devoted to the identification of kinked arteries.

The agreement between arteriographic and Duplex data in the 5-15% diameter reduction category using the medium focus scanhead was 51% (19/37), 17 sides

were overcalled by the Duplex data. Of these 17 sides, 15 were classified as 16-49% diameter reduction. The sample volume size of medium focus scanhead can be a reasonable explanation for the increased spectral broadening in these cases. More serious are the two sides which were classified as 50-99% diameter reduction. An explanation for these two errors was not found when both the spectra and the arteriograms were reviewed.

The agreement between arteriographic and Duplex data in the 5-15% diameter reduction category using the short focus scanhead was 69% (9/13), which is better than the agreement using the medium focus scanhead (51%). Only three sides were overcalled, all were found in the 16-49% diameter reduction category.

Combining the normals with the 5-15% diameter reduction category the agreement between arteriographic and Duplex data is 55% (27/49) for the medium focus and 86% (18/21) for the short focus scanhead. This demonstrates that the short focus scanhead, providing a smaller volume, appears to be better for defining those patients with normal or minimally diseased carotid arteries (category A and B).

In the 16-49% diameter reduction category the agreement between arteriographic and Duplex data using the medium focus scanhead was 59% (24/41). For the short focus scanhead this agreement was 70% (16/23), again higher than for the medium focus scanhead. Using the short focus scanhead three carotid sides were overcalled by the Duplex method. A review of the spectra demonstrated systolic peak frequencies above 4 KHz in each instance. The results in all groups with a diameter reduction less than 50% (category A, B and C) were better using the short focus scanhead, making this scanhead more applicable for detecting and differentiating normal and minimally diseased internal carotid arteries.

In the 50-99% diameter reduction category, the agreement between the two methods was 94% (61/65) using the medium focus scanhead. In one case an arteriographic 50-99% diameter reduction was called a total occlusion. Compared with early results of the Duplex method (table I) the accuracy in predicting a 50-99% diameter reduction has improved, which in part is a reflection of the appreciation of the characteristics of the common carotid artery (see 5.2.). Using the short focus scanhead the agreement between the arteriographic and Duplex data was 89%, in no instance overcalled the Duplex method the arteriographic diameter reduction. This is reassuring since differentiating between a high-grade stenosis and a total occlusion is of great clinical importance.

In the total occlusion category the agreement between the two methods was 93% (13/14) using the medium focus scanhead and 100% (5/5) using the short focus scanhead. Only on one occasion was a arteriographic proven total occlusion undercalled by the Duplex method. The overall agreement in predicting a total occlusion combining the data from the medium and short focus scanhead was 95% (18/19), demonstrating that the Duplex concept is able to identify a total occlusion accurately. The fact that Duplex scanning in combination with spectral analysis is able to differentiate accurately between high grade lesions and total occlusions of the internal carotid artery makes this method superior to all indirect noninvasive methods currently in use.

External carotid artery. The distribution of disease in the external carotid artery is different from that found in the internal carotid artery. Forty eight percent of the external carotid arteries (117/224) were normal by arteriography, this was only 8% (20/246) for the internal carotid arteries. An arteriographic 50-99% diameter reduction was found in 10% (25/224) of the external carotid arteries and in 38% (93/246) of the internal carotid arteries.

The clinical information desired for the external carotid artery is to differentiate between low-grade and high-grade lesions. For the latter it is important to differentiate between high grade stenoses and total occlusions. Combining the normal and 5-49% diameter reduction category the agreement between the arteriographic and Duplex data using the medium focus scanhead was 88% (128/145). Using the short focus scanhead the agreement was 86% (59/68), demonstrating that there is no difference using the two different scanheads. For the 50-99% reduction category the agreement between the two diagnostic methods using the medium focus scanhead was 84% (16/19). Using the short focus scanhead the agreement was 67% (4/6), combining the medium and short focus scanhead data the agreement was 80% (20/25). These percentages demonstrate that the Duplex method does differentiate between non-hemodynamic and hemodynamic diameter reduction reasonably well.

For the occlusion category the numbers are small, the overall agreement between the arteriographic and Duplex data combining the medium and short focus scanheads studies was 50% (3/6).

The reason that there is no marked difference between the medium and short focus scanhead is in the fact that the sample volume size of both systems is relatively large compared with the diameter of the external carotid artery.

Difficult studies.

Most problems are found in those cases where the anatomy of the extracranial carotid system is difficult to delineate. Kinking of the internal carotid artery, when not identified, creates a situation in which the technician can be misled due to a steep angle between the Doppler beam and the axis of the vessel (figure 27).

Another problem can arise when the first branch of the external carotid artery (superior thyroid artery) is incorrectly identified as the proximal internal carotid artery. The Doppler spectrum from this small artery will show high systolic peak frequencies with marked spectral broadening. This problem can be anticipated by consequently identifying the proximal internal carotid artery just distal to the carotid bulb.

Figure 27.

Contrast arteriogram of a kinked internal carotid artery. Due to a steep angle, which was not noticed during the noninvasive study, the velocity pattern was classified as 50-99% diameter reduction.

There are situations in which the external carotid artery velocity patterns are difficult to differentiate from the internal carotid artery velocity signals. This can occur with a total occlusion of the internal carotid artery where the external carotid artery functions as a collateral for the ipsilateral hemisphere. Due to the

Figure 28.

Hardcopy of an external carotid artery signal in a patient with a total occlusion of the internal carotid artery. Note the high frequencies during diastole.

low resistance of the intracerebral vascular bed, flow remains well above zero during diastole in the external carotid artery (see figure 28). One should be aware of this situation when velocity signals from only one artery can be identified above the carotid bifurcation.

A typical velocity signal can be obtained when the sample volume of the Doppler system is placed within the stenosis. Turbulence normally occurs just distal to the stenosis. In the stenosis itself high systolic frequencies will be found due to a velocity increase. The signal from the stenosis itself will be without spectral broadening (see figure 29). Whenever this type of signal is noted, the sample volume should be moved more distally to obtain the expected marked spectral broadening which is typical for a high grade stenosis.

Figure 29.
Hardcopy of an internal carotid artery signal. The sample volume is localized within a high-grade stenosis. Note the high systolic and diastolic frequencies and the absence of spectral broadening.

A difficult situation can occur when a patient with an occlusion of the common carotid artery is studied. The occlusion is diagnosed whenever no velocity signal can be obtained in the region of the common carotid artery. One should be aware of the fact, that in this situation the homolateral external carotid artery can by reversal of flow, supply blood to the internal carotid artery ²⁸. Figures 30-32 show how important the directional flow information is in such a study. Figure 30 shows the Doppler spectrum from the bulb, with velocities both in the forward and

reverse direction. Blood flow to the external carotid artery is due to collateral filling in the reversed direction (figure 31), with flow in the internal carotid artery in the forward direction (figure 32). This study shows that common carotid artery occlusion is not invariably associated with thrombosis of the internal carotid artery. Furthermore, the study demonstrates that whenever an occlusion of the common carotid artery is found, velocity signals in the internal and external carotid artery can be detected.

Figure 30.
Hardcopy of a signal from the carotid bulb in a patient with an occlusion of the common carotid artery. There are frequencies present both in the forward and reverse direction.

Figure 31.
Harcopy of a signal from the external carotid artery of the same patient. The flow in this artery is in the reverse direction due to collateral blood supply.

Figure 32.
Hardcopy of a signal from the internal carotid artery of the same patient. The flow in this artery is in the forward direction.

Conclusions.

The presented data has demonstrated that in the hands of experienced technicians, following a standard protocol, Duplex scanning combined with spectral analysis is an accurate method in predicting noninvasively the extent of internal carotid artery disease. For identifying normal and minimal diseased internal carotid arteries (5-15% diameter reduction and 16-49% diameter reduction category) the short focus scanhead improves the accuracy of the method significantly. For identifying hemodynamically significant diameter reductions (50-99% diameter reduction and 100% diameter reduction category) of the internal carotid artery, there is no significant difference in the accuracy using the medium or short focus scanhead. The capability to differentiate between a high grade stenosis and a total occlusion makes the method superior to any indirect noninvasive test.

The accuracy of the Duplex concept justifies the use of this method as a screening device for patients with suspected carotid artery disease. Furthermore, the method has the potential to document progression of arterial disease when it is used in follow-up studies.

5.4. Effect of carbon dioxide on flow patterns in normal extracranial arteries.

5.4.1. Introduction.

The results of the Duplex scanner studies in identifying normal carotid arteries and differentiating them from minimal diseased carotid arteries should still improve. The problems we encounter concerning this issue are complex. In the first place the number of normal arteriogrammed carotid arteries remains small as a result of the influence of our test on the management of referring physicians (see 6.2.3.). Secondly, we have to realize that arteriography, especially in identifying normals, is not an ideal gold standard ⁴¹.

The change in equipment, i.e. the short focus scan head improved the accuracy of normal and minimal diseased internal carotid arteries considerably (see 5.3.). With this short focus scan head still 50% of the normal internal carotid arteries were classified as a 5-15% diameter reduction. Since it is well known that lesser degrees of stenoses may be "unmasked" by increasing flow rates across the lesion, we considered to increase the blood flow to the brain in patients with minimal carotid disease. However, before applying this method to patients it was necessary to evaluate the velocity pattern changes due to an increase in total blood flow of normal subjects. As a pilot study we gave five normal subjects carbon dioxide. For the purpose of the present study velocity pattern recordings were made from the centerstream of three sites in each carotid system using the Duplex scanner: (1) low common carotid artery; (2) proximal internal carotid artery; and (3) proximal external carotid artery. Since velocity changes in diastole are closely related to changes in total blood flow ¹⁴⁴, the following hand measured parameters were used to document changes in flow in the carotid arteries:

- (1) velocity (cm/sec) in diastole of the common carotid artery (500 mseconds after peak systole)
- (2) velocity (cm/sec) in diastole of the internal carotid artery (500 mseconds after peak systole)
- (3) velocity (cm/sec) in diastole of the external carotid artery (500 mseconds after peak systole)

The velocity signal, the incident angle of the sound beam and ECG signal were simultaneously recorded on a four channel audiotape recorder. The output of the audiotape was first analyzed with the fast Fourier Transform spectrum analyzer configured to output 100 bins of frequency information every 2.5 msecond in digital format which together with the ECG timing signal was read to disk. The information recorded on disk was then subjected to a computer program designed to measure specified parameters of the velocity waveform⁷³. The spectra of twenty heart beats were averaged to form an ensemble waveform. The frequency with the highest amplitude (termed "the mode") of this averaged spectrum was computed. Contour lines calculated 9 dB above and below the mode were plotted thus allowing measurements of the spectral width to be made at any desired point of the pulse cycle. The following waveform parameters were used for the analysis:

- (1) velocity in peak systole at upper 9 dB line in the common carotid artery
- (2) velocity in peak systole at upper 9 dB line in the internal carotid artery
- (3) spectral width between 9 dB lines in the deceleration phase of systole in the common carotid artery.
- (4) spectral width between 9 dB lines in the deceleration phase of systole in the internal carotid artery.

Five healthy volunteers were used for this study. After 15 minutes of rest in the supine position, baseline heart rate and blood pressure were recorded. The carotid arteries were studied with the Duplex scanner and the subject breathing room air. The volunteer then started to breathe a mixture of 6.8% carbon dioxide and 93.2% oxygen. This mixture was chosen as it has been shown to increase the total cerebral blood flow by approximately 75%^{99, 152}. After two minutes and while continuing to breathe the gas mixture, heart rate and blood pressure were again recorded. The two minute interval was chosen, as it has been shown that the response to carbon dioxide is maximal after twenty seconds and after two minutes remains stable⁹⁹. Ten sides in five subjects were available for evaluation both prior to and while breathing carbon dioxide.

5.4.2. Results.

There were no significant changes found in the pulse rate or blood pressure during breathing 6.8 percent carbon dioxide. Examples of the hardcopy of the spectral analysis prior to and during breathing carbon dioxide are shown in figures 33 to

Figure 33.
Pulsed Doppler spectrum from a normal
common carotid artery prior to breathing
carbon dioxide.

Figure 34.
Pulsed Doppler spectrum from the same
common carotid artery during breathing
carbon dioxide.

Figure 35.
Pulsed Doppler spectrum from a normal
internal carotid artery prior to breathing
carbon dioxide.

Figure 36.
Pulsed Doppler spectrum from the same
internal carotid artery during breathing carbon
dioxide.

36. There was an increase in diastolic frequencies both in the common carotid artery (figure 34) and the internal carotid artery (figure 36) under the influence of breathing carbon dioxide. The velocity in diastole (500 mseconds after peak systole) prior to and during breathing carbon dioxide for the common, internal and external carotid artery are shown in table X. The mean velocity in diastole of both sides of the five subjects increased by 106% in the common carotid artery. The difference from side to side in one subject and the difference between subjects however should be noted. The mean velocity in diastole of both sides in the internal carotid artery of the five subjects increased by 96%. Again a marked spread was noted between the sides within one subject and between the subjects. The mean velocity in diastole of both sides of the five subjects increased by 21% in the external carotid artery. On one side we were unable to obtain a satisfactory hardcopy of the velocity pattern of the external carotid artery.

Table X.

Velocity (cm/sec) prior to and during breathing carbon dioxide in diastole (500 msec after peak systole) from the common, internal and external carotid artery.

		Common Carotid Artery			Internal Carotid Artery			External Carotid Artery		
		Prior (cm/sec)	During (cm/sec)	% Change	Prior (cm/sec)	During (cm/sec)	% Change	Prior (cm/sec)	During (cm/sec)	% Change
No. I:	R	15	33	120	30	57	90	24	35	45
	L	25	46	84	23	46	100	24	24	-0-
No. II:	R	24	49	104	30	46	53	16	17	6
	L	32	50	56	21	42	100	27	38	40
No III:	R	17	39	120	17	41	141	16	23	43
	L	17	43	153	27	49	81	8	7	-12
No. IV:	R	24	55	129	21	48	128	18	-	-
	L	36	63	75	29	61	110	20	22	10
No. V:	R	15	38	153	23	41	78	20	20	-0-
	L	23	37	60	23	42	82	17	27	58
Mean ($\pm$ SD)		22 ($\pm$ 7)	45 ($\pm$ 9)	106%	24 ($\pm$ 4)	47 ($\pm$ 6)	96%	19 ($\pm$ 5)	23 ($\pm$ 9)	21%

Examples of the computer hardcopy of the averaged spectrum prior to and during breathing carbon dioxide are shown in figure 37 to 40. Under the influence of carbon dioxide the frequencies in diastole in the common carotid artery (figure 38)

Figure 37. Computer hardcopy output of an averaged spectrum from a normal common carotid artery prior to breathing carbon dioxide.

Figure 38. Computer hardcopy output of the same common carotid artery during breathing carbon dioxide.

Figure 39.
Computer hardcopy output of an averaged spectrum from a normal internal carotid artery prior to breathing carbon dioxide.

Figure 40.
Computer hardcopy output of the same internal carotid artery during breathing carbon dioxide.

and the internal carotid artery (figure 40) are markedly increased. The velocity at peak systole measured at the upper 9 dB line of the common carotid artery and internal carotid artery are shown in table XI. The mean common carotid peak

Table XI.
Velocity (cm/sec) prior to and during breathing carbon dioxide at peak systole from the common and internal carotid artery.

Subject		Common Carotid Artery			Internal Carotid Artery		
		Prior	During	% Change	prior	During	% Change
No. I:	R	84	110	30	84	131	55
	L	118	123	4	84	138	64
No. II:	R	139	155	11	69	123	78
	L	139	152	9	84	113	33
No. III:	R	144	138	-4	76	110	44
	L	144	130	-9	109	113	3
No. IV:	R	164	166	1	91	110	20
	L	191	210	10	82	130	59
No. V:	R	69	69	-0-	53	90	67
	L	84	104	23	46	70	53
Mean		127	135	7%	77	112	47%
(±SD)		(±38)	(±38)		(±18)	(±20)	

systolic velocity of both side of the five subjects increased by 7% during breathing carbon dioxide. The mean internal carotid peak systolic velocity of both sides of the five subjects increased by 47% during breathing carbon dioxide. The spectral widths between the 9 dB lines in the deceleration phase of systole in the common carotid artery are shown in table XII. The mean spectral width of the both sides of the five subjects increased by 51%. The spectral widths between the 9 dB lines in

Table XII.

Spectral width (KHz) between the 9 dB lines in the deceleration phase of systole from the common carotid artery.

Subject		Common Carotid Artery		
		Prior	During	% Change
No. I:	R	0.23	0.43	87
	L	0.29	0.36	24
No. II:	R	0.35	0.54	54
	L	0.39	0.70	79
No. III:	R	0.56	0.79	41
	L	0.55	0.71	29
No. IV:	R	0.69	0.53	-23
	L	0.77	0.93	20
No. V:	R	0.16	0.25	56
	L	0.17	0.42	147
Mean ($\pm$ SD)		0.41 ($\pm$ 0.21)	0.56 ($\pm$ 0.21)	51%

Table XIII.

Spectral width (KHz) between the 9 dB lines in the deceleration phase of systole from the internal carotid artery.

Subject		Internal Carotid Artery		
		Prior	During	% Change
No. I:	R	0.55	0.94	70
	L	0.56	0.67	20
No. II:	R	0.29	0.51	75
	L	0.46	1.06	130
No. III:	R	0.68	0.82	20
	L	0.85	0.81	-4
No. IV:	R	0.36	0.73	102
	L	0.69	1.07	55
No. V:	R	0.13	0.32	146
	L	0.18	0.35	94
Mean ($\pm$ SD)		0.47 ($\pm$ 0.23)	0.72 ($\pm$ 0.26)	70%

the deceleration phase of systole in the internal carotid artery are shown in table XIII. The mean spectral width of both sides of the five subjects increased by 70% breathing 6.8% carbon dioxide.

5.4.3. Discussion.

Doppler devices have been used to evaluate changes in blood flow of the extracranial carotid arteries induced by breathing varying concentrations of carbon dioxide ^{121,144}. Inhalation of carbon dioxide produces a marked increase in the otherwise constant cerebral blood flow ^{63, 128, 131, 152}.

Risberg and Smith ¹⁴⁴, in a comparative study between continuous wave Doppler and Xenon inhalation, demonstrated that velocity changes during diastole are reliable indices of the increase in total cerebral blood flow. In the present study the mean peak velocity in diastole (500 mseconds after peak systole) of the common carotid artery and internal carotid artery increased approximately 100%, an increase which correlated well with the increase in total blood flow induced by breathing 6.8% carbon dioxide. However, the variations noted between individuals were not inconsiderable. These variations can be explained by errors in the measurements or by true physiological differences that occur between different normal subjects and between the two sides of the same subject.

The breathing of carbon dioxide should not have a significant effect on the peripheral resistance of the vascular bed supplied by the external carotid artery. The present findings confirmed this expectation, the mean velocity in diastole of the external carotid artery only increased by 21% during carbon dioxide inhalation. Again however, there was a marked variation between the five subjects.

A major change in the velocity patterns induced by breathing carbon dioxide was the increase in spectral width. In vessels in which laminar flow is present, the velocities of red blood cells within the sample volume of the pulsed Doppler device are relatively similar. Spectral analysis of the velocities within such a sample will show a narrow band of frequencies ⁶⁶. With disappearances of laminar flow the movement of red blood cells in the sample volume becomes more random, this will be reflected as a greater variation in frequencies, i.e. an increase in spectral width. In this study, when spectral width was measured in the deceleration phase of systole in the common and internal carotid artery, a 51% increase was observed in the common carotid artery after breathing carbon dioxide while in the internal carotid artery an increase of 70% was observed. The observed change in the spectral width is assumed to be related to the change in the flow pattern across the bifurcation that occurred secondary to the marked increase in flow.

Previous studies have used both qualitative and quantitative changes in spectral width to grade the degree of stenosis in the internal carotid artery. With disease at the carotid bulb, there is an initial increase in spectral width occurring first during the deceleration phase of systole, which comes to occupy the entire pulse cycle as the stenosis approaches a 50% reduction in diameter. For stenoses of less than 50% increases in peak systolic velocity are minimal with most emphasis placed upon the time of onset of spectral broadening. However, the spectral changes

observed with early disease are often minimal and difficult to precisely classify. Thus, the separation of patients with minimal lesions from those who are considered arteriographically normal is a problem. The present study shows quite clearly that the increase in cerebral blood flow dramatically altered the velocity pattern in normal internal carotid arteries. While this type of provocative test is simple to perform, further studies will be required in patients with minimal extracranial arterial disease to determine if it is useful in increasing the sensitivity of the method in detecting minor degrees of stenoses.

5.5. Algorithm for categorization of high grade stenoses.

5.5.1. Introduction.

The accuracy of predicting a 50-99% diameter reduction, using Duplex scanning combined with spectral analysis, is sufficient enough to justify the method as a screening device for patients with suspected extracranial carotid artery disease. However, for the purpose of documenting progression of disease, the 50-99% diameter reduction group is too broad. In order to estimate the degree of involvement within this category we evaluated an algorithm utilizing information from both the common and internal carotid artery.

In recent years, a great deal of effort has gone into the development of noninvasive algorithms to predict extracranial carotid artery disease. Planiol and Pourcelot^{134, 135}, using a continuous wave device, introduced the resistivity index (R.I.) measured from the velocity waveform of the common carotid artery to predict high grade stenoses and total occlusions of the internal carotid artery (see 2.2.3.). Rutherford et al.¹⁴⁸, using a continuous wave device, introduced five hand measured parameters from the velocity waveform of the common carotid artery to predict extracranial carotid artery disease (see 2.2.3.). Archie¹, using a similar Doppler device, introduced a "normalized" algorithm measured from the velocity waveform of the common carotid artery to predict severe internal carotid artery disease. All three methods were based on the hypothesis that disease in the internal carotid artery can be predicted by changes in the velocity waveform of the common carotid artery.

Blackshear et al.²⁷ introduced the ratio of the mean peak internal carotid artery velocity to the mean peak common carotid artery velocity to predict severe internal carotid artery disease. This ratio was below 0.8 in all normals and above 1.5 in all 21 high-grade stenoses of the internal carotid artery. The ratio did not provide a means to estimate the degree of stenosis within high-grade lesions.

It is a well known fact that systolic peak velocities rise with increasing stenosis, while previous experience (see 5.2. and 5.4.) has demonstrated that diastolic velocities of the common carotid artery are sensitive to changes in the peripheral resistance³⁵. Therefore we choose the ratio of peak systolic velocity in the internal carotid artery to the late diastolic velocity, as measured 500 mseconds after peak systole in the common carotid artery to estimate the severity of disease.

A retrospective analysis of 86 common and internal carotid arteries which had been studied with the Duplex scanner was the basis for this study. All of these

vessels had been assessed with multiplanar contrast arteriography. The diameter reduction of the internal carotid artery was expressed as has been described previously (see 4.3.4.). A group of 30 normal subjects were studied using the Duplex scanner combined with spectral analysis in an identical fashion to the diseased subjects. These subjects were "persumed" normals in that they had not undergone confirmatory arteriography. Their ages ranged from 29 to 32 years.

5.5.2. Results.

The range of velocities found in each group is shown in table XIV. The velocity ranges in the common carotid artery (late diastolic velocity) found in each group from normal to stenosis greater than 90% diameter reduction are wide, but the values tend to fall with increasing disease in the internal carotid artery. The range of peak systolic velocities in the internal carotid artery is also wide in each group, but the values tend to rise with increasing disease in the internal carotid artery.

Table XIV.
Late diastolic velocity and peak systolic velocity ranges in the common carotid and internal carotid artery (cm/sec).

Carotid Lesion	Common Carotid (Diastole)	Internal Carotid (Systole)
Normal	48-53	30-114
10-60% Stenosis	22.4-53.9	39-220
65-90% Stenosis	7.9-23.1	123-282
Greater than 90% Stenosis	7.2-15.4	154-325

The variation of the ratio VICA (Velocity Internal Carotid Artery) to VCCA (Velocity Common Carotid Artery) with severity of disease is shown in figure 41.

Figure 41.
VICA systole / VCCA diastole ratio in the 86 vessels plotted against the percentage diameter reduction.

The ratio increases exponentially as the severity of disease increases. The scattergram shows that it is impossible to distinguish disease states less than 60% using the VICA to VCCA ratio but for stenoses greater than 60% it is possible by selecting particular values of the ratio to gradate the severity of disease (table XV). If the value of 7.5 is selected as defining disease greater than 60% diameter reduction than 2/42 (5%) of the sides are wrongly classified giving an accuracy of 95%. Selecting of a value of 11.0 as defining disease greater than 65% diameter reduction results in 1/36 (3%) of sides being wrongly classified, remaining an accuracy of 97%. Selecting a value of 18.0 allows all diseased vessels with 90% diameter reduction or more to be correctly classified.

Table XV.
Accuracy of VICA/VCCA ratio in predicting disease as compared with contrast arteriography.

	Category	Number of Sides	Accuracy	Ratio
60-99%	Stenosis	42	95%	7.5
65-99%	Stenosis	36	97%	11.0
90-99%	Stenosis	10	100%	18.0

The values of the VICA to VCCA ratio for the normals are shown in figure 42. All were equal to or below 3 with a range from 1.3 to 3. These did not overlap with the values seen in those with diameter reduction greater than 60%

Figure 42.
VICA systole / VCCA diastole ratio for the normals.

The values of the VICA to VCCA ratio for each category of disease have a small range, which for the diseased categories above 60% diameter reduction do not overlap. There is considerable overlap in values of the VICA to VCCA ratio for all states of disease less than 60% diameter reduction.

5.5.3. Discussion.

If constant flow rates are to be maintained through a increasing stenosis the velocity of flow through the stenosis must increase (see chapter 3). The velocity of flow is proportioned to the cross-sectional area of the arterial lumen at the site of measurement. Studies of steady flow in bifurcating tubes have shown that the mean flow velocity in the branch bears a constant relationship to the velocity in the parent tubes. While the flow velocity is influenced by the cross-sectional area of the vessel, the compliance of the vessel wall and the peripheral resistance also have an effect ¹¹⁸. The ratio of velocity in the internal carotid artery to the velocity in the common carotid artery will cancel the effects of the compliance of the vessel wall. However, the problem associated with the differing peripheral resistance perfused by the internal and external carotid artery remains. In a previous report ³⁵ we implied that changes in the peripheral resistance of the vascular bed of the brain find their reflections in the velocity pattern of the common carotid artery. Since only 20% of the blood flow in the common carotid artery will supply the external carotid artery, changes in the velocity waveform of the common carotid artery will be in large a reflection of disease in the internal carotid.

Ideally, any velocity ratio, in order to be sensitive to increasing disease, should consist of a numerator which increases with severity of disease and a denominator which decreases with increasing disease. Such a ratio will tend towards infinity with increasing severity of disease. The ratio of peak systolic velocity in the internal carotid artery to the diastolic velocity in the common carotid artery appears to fit this definition.

The present study has demonstrated the feasibility of using a ratio to grade disease states greater than 60% diameter reduction. It is not entirely unexpected to find that we were unable to distinguish normals from diseased subjects with diameter reductions less than 60% using this velocity ratio. Markedly decreased diastolic flow in the common carotid artery is not seen until more severe disease states are reached. The ratio is, therefore, reliant on increasing velocities at peak systole in the internal carotid artery to produce discriminatory changes in the normal to 60% diameter reduction group. These changes in peak systolic velocity are not seen until diameter reductions of 50% or more are present.

When correlating the ratio of velocities with arteriography, it must be expected that there are errors in the classification of disease based on arteriography. Previous described work ⁴¹ has shown that the intraobserver agreement for the classification of carotid disease into five categories was 83%. The interobserver agreement for the same categories was 75%. It is important to bear this variation in mind when interpreting any comparative study. The arteriograms in this series were read by one radiologist; therefore, we do not have to consider the interobserver agreement which is lower than the intraobserver agreement.

While we have used a Duplex scanner to obtain our data, it is possible to use other Doppler devices providing these incorporate a method of measuring the angle of the incident Doppler beam to the long axis of the vessel. A potential problem may arise in cases where the internal carotid artery is kinked and the incident Doppler beam approaches the longitudinal axis of the vessel (see 5.3.3.).

In conclusion, the algorithm seems to be useful in further gradating the degree of stenosis in the 60-99% diameter reduction range. It allows the use of a 90-99% diameter reduction group with an accuracy of 100 percent.

Chapter 6

The role of Duplex scanning in clinical practice.

6.1. Introduction.

Noninvasive techniques used in the detection of extracranial carotid artery disease should provide a means of screening patients to select those who should undergo contrast arteriography. Such a noninvasive technique should be able to identify both normal vessels and those with the entire spectrum of disease involvement with an acceptable accuracy. The accuracy of the Duplex concept, as presented in section 5.3., justifies the use of this method as a screenings device. Combining the normals with the 5-15% diameter reduction category, the agreement between arteriographic and Duplex data is 86% for the short focus scanhead. In the 50-99% diameter reduction category, using the medium focus scanhead, the agreement is 94%. For total occlusions the agreement was 95%, combining the data from the medium and short focus scanhead.

In addition to the screenings role, Duplex scanning combined with spectral analysis can be used to obtain answers about the prevalence and significance of extracranial carotid artery disease in certain patients populations. An unanswered question relative to the role of noninvasive testing is for example, its impact on the subsequent decision making process by referring physicians. In order to answer this question data of all new referrals in a certain period of time were reviewed. The incidence of extracranial carotid artery disease in patients with asymptomatic bruits and their clinical significance will be presented and discussed in the second study of this chapter. The third study concerns the incidence of extracranial carotid artery disease in patients who are candidates for coronary bypass surgery. The role of a noninvasive test in screening these patients for carotid disease will be discussed. In the last study of this chapter patients were studied prior to and after carotid endarterectomy in order to document velocity pattern changes in the carotid system. The relevance of flow disturbances due to this surgical procedure will be discussed. The four studies in this chapter represent the kind of work performed in a noninvasive vascular laboratory.

6.2. The influence of ultrasonic Duplex scanning on the management of patients with suspected carotid disease.

6.2.1. Introduction.

A major unanswered question relative to the role of noninvasive testing for carotid artery disease is its impact on the subsequent decision making process by the referring physician. Ideally, only patients who are potential candidates for carotid surgery should undergo contrast arteriography. The role of the noninvasive test is to select those patients who are candidates for carotid surgery

and avoid contrast arteriography in those who are not^{21,158,160}. While noninvasive testing is often considered to be unnecessary for patients with focal neurological symptoms, there remains a large group of patients with vague neurological symptoms or asymptomatic bruits, in which the outcome of an accurate noninvasive test could be of value to the referring physician.

The referral base for the present study was from a variety of sources both within and outside the University of Washington. The reports sent back to the referring physician contained only the results of the study without any recommendations concerning further diagnostic tests or treatment. In order to assess the impact of the Duplex studies on the management of these patients with possible carotid artery disease, the data of all new referrals between January 1980 and December 1980 were reviewed.

In that period of time 410 patients with neurological symptoms were referred to the vascular laboratory for an ultrasonic evaluation of the extracranial carotid arteries. The patients were grouped according to the reason of referral: (1) patients with focal neurological symptoms (n=263); and (2) patients with nonfocal neurological symptoms (n=147). The patients with focal symptoms were subdivided into those with focal symptoms lasting less than 24 hours (n=156), and those with focal symptoms lasting longer than 24 hours (n=107).

The reports, sent to the referring physicians, contained the results of the study expressed in diameter reductions without any further recommendations. At the end of the year the noninvasive data were reviewed and the number of patients in each group that underwent contrast arteriography and subsequent carotid surgery documented.

6.2.2. Results

The distribution of carotid artery disease on the appropriate side as estimated by the Duplex scanner in the group of patients with focal neurological symptoms lasting less than 24 hours is shown in table XVI. Using the previously described 5 categories 4 patients were found to have a normal internal carotid artery (category A). A 5-15% diameter reduction (category B) was found in 64 patients, a 16-49% diameter reduction (category C) was found in 37 patients, a 50-99% diameter reduction in 44 patients, and a total occlusion (category E) in 7 patients. Of the patients with a reported 50-99% diameter reduction of the internal carotid artery (category D), 77% (34/44) underwent contrast arteriography. This was statistically significantly different (X^2 , $p < 0.005$) from the percentages of patients with lesser degrees of disease (25/105) who underwent arteriography. The percentage of patients with a reported total occlusion of the internal carotid artery (category E) who underwent contrast arteriography was 43% (3/7).

The percentage of patients who underwent subsequently carotid surgery was 0% for category A, 21% (3/14) for category B, 20% (2/10) for category C, 88% (30/34) for category D and 0% for category E. Again the highest percentage was found in the 50-99% diameter reduction group.

The distribution of carotid disease in patients with focal neurological symptoms lasting longer than 24 hours is shown in table XVII. A normal internal carotid artery was found in one patient, a 5-15% diameter reduction (category B) in 45

Table XVI

Duplex categories, number of arteriograms and number of operations in patients with focal neurological symptoms lasting less than 24 hours.

Focal Neurological Symptoms (Less than 24 hours)				
	Duplex	Arteriogram		Surgery
Category	Number	Number	Percentage of Total	Number
A	4	1	25%	0
B	64	14	22%	3
C	37	10	27%	2
D	44	34	77%	30
E	7	3	43%	0
Total	156	62	40%	35

Table XVII.

Duplex categories, number of arteriograms and number of operations in patients with focal symptoms lasting longer than 24 hours.

Focal Neurological Symptoms (Longer than 24 hours)				
	Duplex	Arteriogram		Surgery
Category	Number	Number	Percentage of Total	Number
A	1	0	0%	0
B	45	5	11%	0
C	34	3	9%	2
D	17	8	47%	4
E	10	1	10%	0
Total	107	17	16%	6

patients. A 16-49% diameter reduction (Category C) was found in 34 patients, a 50-99% diameter reduction (Category D) in 17 patients, and a total occlusion (Category E) in 10 patients. Of the patients with a 50-99% diameter reduction 47% (8/17) underwent contrast arteriography. This was statistically significantly different (X^2 , $p < 0.005$) from the percentages of patients with lesser degrees of disease (8/80) who underwent contrast arteriography. Of the 10 patients with a

reported total occlusion of the related internal carotid artery one underwent arteriography (10%). The percentage of patients who underwent subsequently carotid surgery was 0% for category A, 0% for category B, 67% (2/3) for category C, 50% (4/8) for category D, and 0% for category E.

The distribution of carotid disease in the group of patients with nonfocal symptoms is shown in tabel XVIII. The side reported in the table is the one with

Table XVIII.

Duplex categories, number of arteriograms and number of operations in patients with nonfocal neurological symptoms.

Nonfocal Neurological Symptoms				
	Duplex	Arteriogram		Surgery
Category	Number	Number	Percentage of Total	Number
A	0	0	0%	0
B	48	0	0%	0
C	70	5	7%	2
D	25	13	52%	9
E	4	2	50%	0
Total	147	20	14%	11

the most marked disease. A normal internal carotid artery was not found in this group of patients, a 5-15% diameter reduction (category B) was found in 48 patients. A 16-49% diameter reduction (category C) was found in 70 patients, a 50-99% diameter reduction (category D) was found in 25 patients, and a total occlusion (category E) in 4 patients. Of the patients with a 50-99% diameter reduction 52% (13/25) underwent contrast arteriography. That was statistically significantly different (X^2 , $p < 0.005$) from the percentages of patients with lesser degrees of disease (5/118) who underwent contrast arteriography. Of the patients with a reported total occlusion 50% (2/4) underwent contrast arteriography. Table XIX shows in a tabulation the distribution of carotid disease on both sides in the group of patients with nonfocal symptoms. The two patients with an occlusion (category E) who underwent contrast arteriography, were found to have a 50-99% diameter reduction (category D) on the contralateral side, which was probably the reason for the arteriography. Of the patients with at least one 50-99% diameter reduction 75% (15/20) underwent contrast arteriography.

A total of eleven patients underwent carotid surgery in this group; nine of these patients had at least one high grade stenosis (50-99% diameter reduction) of the internal carotid artery. Of these nine patients five had a bilateral high grade stenosis and two had a high grade stenosis with a contralateral total occlusion of the internal carotid artery.

Table XIX.

Duplex categories of the right and left internal carotid artery in patients with nonfocal neurological symptoms. The right side is displayed on the horizontal and the left side on the vertical axis. The numbers in parentheses are the number of patients who underwent arteriography.

Non focal Neurological Symptoms

Left Side	Right Side					
	A	B	C	D	E	
A		2				2
B	3	43	17	2 (1)		65
C		15	38 (5)	5 (2)		58
D		6 (2)	4 (2)	8 (6)	1 (1)	19
E			1	2 (1)		3
	3	66	40	17	1	147

6.2.3. Discussion.

The question of the clinical role that noninvasive tests play in the management of patients with suspected carotid disease needs to be answered separately for each group of patients. The role of the noninvasive test in a patient with transient focal neurological symptoms will be different from that in a patient with vague nonfocal neurological symptoms or in a patient with an asymptomatic bruit. This was clearly reflected in the numbers of patients who underwent contrast arteriography in the different groups. As might be expected patients with transient focal symptoms were more likely to have arteriography than patients in the other groups.

However, a surprising finding was that even though patients were classified as having focal symptoms by the referring physician, there remained a considerable number who did not have arteriography. For the overall group of 263 patients with focal symptoms, 70% did not have a contrast study. The reasoning behind this approach is unknown, but it would appear that patients with high grade stenoses (category D) were given special consideration with regard to further study. This is reflected in the fact that 69% of patients in this category did undergo arteriography. When the symptoms are broken down by duration, in those with

episodes lasting less than 24 hours the number of arteriograms performed was greatest (40%). For categories B and C, this was 22 and 27%, the highest for any of the other groups. This would be consistent with current ideas relative to this problem which is usually given highest priority with regards to both diagnosis and management¹⁸.

For patients in the group with focal symptoms lasting less than 24 hours, there was a significant difference (X^2 , $p < 0.005$) between the number of patients who underwent surgery in the D category (30/34) and categories B and C. The finding of a high grade stenosis by arteriography was clearly of importance in the decision to carry out surgical treatment^{29, 169}. Of the four patients in the D category who did not undergo surgery, the Duplex study reported a high grade stenosis which was not confirmed by contrast arteriography in two cases. In two cases the general condition of the patient was considered to be a contra- indication for surgery.

The most perplexing group of patients from a clinical standpoint are those with nonfocal symptoms, especially when the clinical picture is vague which is often the case^{62, 65, 119}. In this group, the results were not surprising since if the symptoms are due to extracranial arterial disease, they are often thought to be due to a reduction in cerebral blood flow and not to emboli. In this group 52% with either a high grade stenosis or occlusion did have arteriography with only 4% of those with lesser degrees of disease having contrast studies. Of the eleven patients who underwent carotid surgery, nine patients had at least one high grade lesion. The presence of bilaterally significant disease (7/9) seems to have played a role in the decision to proceed with surgical treatment.

It is clearly not possible to draw any firm conclusions concerning the subsequent workup of patients referred to a noninvasive laboratory. However, it is clear that in general physicians (rightly or wrongly) consider the finding of a high grade stenosis of great clinical importance for each of the patient subgroups.

It could well be argued that the studies might have an adverse impact on subsequent management. For example, patients with focal symptoms lasting less than 24 hours are in general considered candidates for arteriography regardless of the results of any noninvasive tests. Yet in this patient subgroup 60% did not have what many consider to be the definitive study. While many of these patients may not have had the so-called classic symptoms if examined by a single neurologist experienced in the field, this was the basis for referral. It should be noted that it is our own policy to require contrast arteriography in all patients with typical transient ischemic attacks or amaurosis fugax (focal symptoms lasting less than 24 hours) regardless the result of the Duplex test.

Regardless of the ultimate answers to many of the questions posed, it is clear that the results of the Duplex test reported to the physician did influence his or her decision to proceed with arteriography. Furthermore, it is also evident that the finding of a high grade stenosis on the arteriogram resulted in a greater number of patients undergoing carotid surgery. Only subsequent follow-up studies will provide the answers to many remaining questions concerning the correct approach in the evaluation and treatment of patients with suspected carotid disease.

6.3. The impact of Duplex scanning on the evaluation of patients with asymptomatic bruits.

6.3.1. Introduction.

The finding of a bruit in the neck has been the standard clinical method for the detection of unsuspected disease at the carotid bifurcation. On the other hand is the presence of a bruit in the neck an aspecific finding. The incidence of neck bruits in 1,000 presumed normal subjects from age 4 to age 94 performed by Hammond and Eisinger⁷⁴ was 31%. The incidence of neck bruits varied with age; in 87% of the subjects under 5 years of age a bruit was found, with advancing age the frequency decreased so that by the age of 60 only 12% had audible bruits. In a group of 70 medical students who were free from obvious disease Rennie et al.¹⁴⁰ found neck bruits in 40% of the cases. If the neck bruits are found with this frequency even in normal subjects, what relevance could this have to the overall problem of carotid artery disease?

Clearly the finding of a bruit is inadequate to predict either its origin or the extent of narrowing of the involved vessel. More information about the extent of carotid disease in patients with neck bruits can be obtained by arteriography or noninvasive studies.

There are several arteriographic studies that have examined the extent of carotid disease in patients with asymptomatic bruits. David et al.⁴⁹ in a series of 417 patients undergoing arteriography reviewed their finding in patients with asymptomatic bruits. The internal carotid artery was normal in 14% while 47% had a stenosis which reduced the diameter by 50% or more. Ziegler et al.¹⁸⁵ demonstrated that carotid disease can be present without an associated neck bruit. These authors found in a study of 199 patients who underwent arteriography that 73% had a stenosis without the presence of a bruit. Out of 208 asymptomatic bruits Riles et al.¹⁴³ found arteriographically proven high grade stenoses (60-99% diameter reduction) in 61% of the cases. It is difficult to extrapolate the exact incidence of high grade lesions in patients with asymptomatic bruits from arteriographic studies. These patients were for one reason or the other already selected for an invasive procedure.

Noninvasive tests are used frequently to evaluate the extent of extracranial carotid artery disease in patients with an asymptomatic bruit. Out of the 750 patients evaluated by the Duplex scanner between January 1978 and January 1980, 100 patients (13%) were referred to the vascular laboratory because of an asymptomatic bruit⁶⁰. Kartchner and McRae⁹⁶ using pulse-delay OPG (see 2.2.2.) found 21% (273/1287) positive tests in patients with asymptomatic bruits. Gee et al.⁶⁹ using pressure-OPG (see 2.2.2.) found a positive test in 36% (42/116) of the patients screened because of an asymptomatic bruit. Out of the 165 asymptomatic bruits of the 100 patients in the study of Fell et al.⁶⁰, 37% (61/165) were found to have a 50-99% diameter reduction. In 6% (9/165) an asymptomatic bruit was found in combination with a total occlusion of the internal carotid artery.

One other noninvasive test should be mentioned, although not commonly used yet for screening patients with asymptomatic bruits. Duncan et al.⁵² reported the use

of phonoangiographic spectral analysis (see 2.2.3.). This method has been evaluated at the University of Washington¹⁰⁴. A good correlation between phonoangiography and contrast arteriography was found in all 43 documented stenoses of the internal carotid artery. This method, which accurately quantified the residual diameter of the internal carotid artery, seems to be valuable for follow-up studies to document disease progression.

In the present study are reported the results in 95 patients referred to our laboratory between January 1980 and May 1981 because of an asymptomatic bruit in the region of the carotid arteries. All patients had at least an unilateral bruit originating in the mid-cervical region, radiating to the base of the skull. All patients were free of symptoms related to extracranial carotid artery disease.

6.3.2. Results.

Of the 95 patients unilateral bruits were found in 48 patients and bilateral bruits in 47 patients. A total of 142 carotid sides with a bruit were available for evaluation. The distribution of disease as estimated by the Duplex scanner combined with spectral analysis is shown in figure 43. Out of the 142 carotid sides 2% (3/142) were found to be normal (category A). Spectral broadening in the deceleration phase of systole, consistent with a 5-15% diameter reduction (category B), was found in 30% (42/142). Spectral broadening throughout systole, consistent with a 16-49% diameter reduction (category C), was found in 37% (53/142). Peak systolic frequencies above 4 KHz with spectral broadening throughout systole and increased diastolic frequencies, consistent with a 50-99% diameter reduction (category D), was found in 29% (41/142). Finally, 2% (3/142) of the patients were found to have a total occlusion of the internal carotid artery.

Asymtomatic Bruits

Figure 43.
Histogram demonstrating the Duplex category in the 142 carotid sides with a bruit.

The distribution of internal carotid artery disease in patients with bilateral bruits is shown in table XX. None of the patients with bilateral bruits were found to have normal internal carotid arteries. There were eleven patients with bilateral diameter reductions of 5-15% or less. A diameter reduction of less than 50% was found in 60% (28/47) of the patients with the remaining 40% (19/47) having a diameter reduction of more than 50%. Bilateral high grade lesions were found in 21% (10/47) of the patients. The asymptomatic occlusions were found with contralateral 50-99% diameter reduction in two and with a contralateral 5-15% diameter reduction in one patient. The incidence of high grade lesions (category D and E) were found in 32% (15/48) of the patients with unilateral and 21% (10/47) of the patients with bilateral bruits.

Table XX.
Duplex categories of the right and left internal carotid artery in patients with bilateral bruits. The right side is displayed on the horizontal and the left side on the vertical axis.

Bilateral Bruits						
Left Side	Right Side					
	0%	5-15%	16-49%	50-99%	100%	
0%						
5-15%	2	9	2	2		15
16-49%		2	13			15
50-99%		3	3	8	2	16
100%		1				1
	2	15	18	10	2	47

To evaluate the impact of the Duplex results on the managment of patients with asymptomatic bruits, the data of all new referrals were reviewed. Eighty-one of the 95 patients were new referrals, their data was used for further analysis. Of these 81 patients, 13 (16%) underwent contrast arteriography (see figure 44).

Asymptomatic Bruits

Figure 44.

Histogram demonstrating the Duplex category, the number of arteriograms and the number of operations in the 81 patients with asymptomatic bruits.

Eleven of these patients had high grade lesions with the remaining two having lesser degrees of involvement. Five patients underwent unilateral carotid endarterectomy, and in each case bilateral high grade stenoses were present.

6.3.3. Discussion.

The prevalence of high grade stenoses of the internal carotid artery in patients with asymptomatic bruits as documented with noninvasive tests varies from 21% to 37%^{60,96}. The prevalence of the high grade lesions (50-99% diameter reductions and total occlusions) in the present study was 31% (44/142), which is comparable with the other studies. Bilateral bruits were not associated with more arteriosclerotic disease than when bruits were found only on one side.

A major point of interest and controversy is the management of patients with asymptomatic bruits when arteriosclerotic disease is found. The policy of the referring physicians, sending their symptomatic patients to the vascular laboratory at the University of Washington has been discussed previously (6.2.3.). These physicians receive a report of the study findings expressed in diameter reduction of the internal carotid artery without any recommendations concerning either arteriography or operation. In the group of 81 new referrals with asymptomatic bruits 84% did not undergo further study. Of the 24 patients with high grade stenoses 46% (11/24) underwent arteriography. Of the five patients who underwent carotid endarterectomy, all had bilateral high grade stenoses. It appears that, rightly or wrongly, high grade stenoses were considered of clinical importance and in that respect influenced the subsequent workup and therapy of the patients. If physicians consider high grade lesions as the basis for further

treatment, there is an significant role for a test such as Duplex scanning. Of the 95 patients in the present study 29% were found to a 50-99% diameter reduction. If such a lesion is an indication for a more aggressive approach 71% of the patients would not be investigated further.

Unfortunately a review of the literature does not provide conclusive guidelines relative to this important clinical problem. However, it is becoming clear that the presence of a bruit in and of itself is of little help in predicting the site or extent of disease producing the finding. Ziegler¹⁸⁵ demonstrated with contrast arteriography that severe disease can be presented without bruits, David⁴⁹ and Riles¹⁴³ found an incidence of 47% and 61% respectively of high grade lesions in their arteriographic studies.

Given the obvious fallibility of the cervical bruit as an indicator of carotid disease, what is the subsequent course of patients followed without the benefit of accurate definition of disease at the carotid bifurcation? Heyman et al.⁸² reported a 5 to 7 year follow-up of 72 patients with asymptomatic cervical bruits in a rural southern community. They noted that the prevalence of bruits increased with age, was greater in females and in patients with hypertension. The striking finding was that the presence of a bruit was associated with a higher risk of stroke in males but not in females. Furthermore, the side of the bruit and the side of stroke were poorly correlated. In other words, male patients with asymptomatic bruits have a higher risk of stroke, but the side of the bruit does not predict the side of the stroke.

In the Framingham study Wolf et al.¹⁸² found asymptomatic bruits in 171 patients. In 8 years of follow-up these patients were found to be at higher risk for myocardial infarction and stroke. More often than not, cerebral infarction occurred in a vascular territory different from that of the carotid bruit. The authors concluded that a carotid bruit is clearly an indicator of increased stroke risk but also a sign of advanced general arteriosclerosis involving such major vascular beds as the coronary circulation.

Humphries, et al.⁸⁹ retrospectively analyzed 168 patients (182 arteries) with arteriographically confirmed stenoses of the internal carotid artery equal to or greater than 50% diameter reduction, who had no symptoms referable to that vessel. Of the 168 patients, 111 had undergone carotid endarterectomy on the opposite side. Of these patients followed an average of 32 months, 26 developed transient ischemic attacks, all of whom underwent successful endarterectomy. Three developed symptoms which were ignored and subsequently went on to a completed stroke. Only one patient sustained a stroke without warning symptoms. No information was provided on patients with lesser degrees of stenosis. The authors suggested that surgery was not required for the asymptomatic patient until transient ischemic attacks develop.

A contrasting view is that presented by Thompson's group^{167,170}, who advocate operating upon asymptomatic lesions which are "high grade" in nature. As stated by these authors, the major difficulty is related to identifying which patients should be investigated further with arteriography.

The approach at the University of Washington to the problem has been largely conservative both from the standpoint of arteriography and surgery. Even in patients who are candidates for major cardiovascular surgery, there is no firm

evidence that prophylactic carotid surgery is indicated^{14,33,36}. We are presently comfortable with the current approach to screen patients as described for the following reasons: (1) the accuracy of the test as compared with contrast arteriography is sufficiently good to identify the location and extent of the involvement; (2) once patients with disease are identified, it would appear prudent to follow them closely with repeat studies to document the natural history of the lesions; and (3) it is probably the only way prospective studies can be done which may answer many of the current questions.

Even given all uncertainties about the management of these patients, it is evident that the finding of a high grade lesion influenced the judgement of referring physicians. It appears that these patients for reasons yet unclear are considered to be more "stroke prone", although evidence for this view is not yet available. The question which needs to be answered is whether this is in fact the case.

To answer this question will require prospective studies to determine which lesions do in fact place the asymptomatic patient at risk. If emboli are the most important cause of stroke, then the degree of stenosis may bear no relevance to the clinical course of the patient. It is now clear that the necessary methods are currently available to carry out such a prospective study.

6.4. Carotid arterial disease in patients undergoing coronary bypass surgery.

6.4.1. Introduction.

The low incidence of transient and permanent complications following carotid thromboendarterectomy for symptomatic and asymptomatic carotid artery disease has led many authors to advocate this procedure as a measure to prevent stroke associated with coronary bypass surgery^{46,58,81}. The incidence of postoperative stroke following coronary bypass surgery, however, is relatively low^{2,141}. This suggests that patients with symptomatic ischemic coronary artery disease do not have a high incidence of significant carotid artery disease, or that in the group of patients undergoing coronary artery bypass surgery significant carotid arterial disease is not a major risk factor in the pathogenesis of postoperative stroke.

A prospective study with the ultrasonic Duplex scanner combined with spectral analysis as described in chapter 4 was undertaken to document the prevalence of extracranial carotid artery disease in patients undergoing coronary artery bypass surgery and to evaluate the practical use of this noninvasive method to screen patients preoperatively.

From January 1980 to July 1980, 102 patients who underwent coronary artery bypass surgery at the University Hospital, Seattle, were studied prior to operation. Of these patients, 23% (24/102) were referred for evaluation due to the presence of symptoms or signs related to carotid arterial disease (requested group); 77% (78/102) were evaluated as part of a study protocol (unrequested group) in which the result of the study was not reported to the patient's physician.

6.4.2. Results.

In the requested group, 14 patients (58%) were sent to the laboratory because of an asymptomatic bruit in the region of the carotid arteries. Ten patients (42%) were sent to the laboratory because the history revealed symptoms possibly related to extracranial carotid artery disease. The mean age of the patients, the male-female ratio, the incidence of a positive history for hypertension, diabetes mellitus and the use of cigarettes are shown in table XXI.

Table XXI.
Risk factors for extracranial carotid artery disease in the requested and unrequested group.

	Requested (n=24)	Unrequested (n=78)
Mean age	61.0	57.7
Male-female ratio	4:1	9:1
Hypertension	38%	44%
Diabetes Mellitus	12.5%	10%
Smoking history	97.5%	70%

The incidence of unstable angina, a cardiac risk factor for peri- operative cardiac complications for the requested and unrequested group is shown in table XXII. A neck bruit was present in 21 patient in the requested group, in eight of these bilateral bruits were noted. In the unrequested group four patients were found to have a cervical bruit when examined in the vascular laboratory.

Table XXII.
Prevalence of cardiac risk factors in the requested and unrequested group.

	Requested (n=24)	Unrequested (n=78)
Chronic angina	15	38
Angina at rest	7	25
Unstabel angina	2	16

A history of a recent focal transient ischemic attack was noted in three patients in the requested group. One patient in the unrequested group had experienced a transient ischemic attack approximately 10 years prior to the study with another sustaining a hemispheric stroke more than 10 years prior to study with complete neurological recovery. In the requested group five carotid endarterectomies were performed; two synchronously and three prior to the coronary bypass procedure. The prevalence and extent of carotid artery disease as estimated by the Duplex scanner combined with spectral analysis in the unrequested group is shown in

table XXIII. In this group five patients had unilateral or bilateral stenoses of more than 50% diameter reduction (category D) in the internal carotid artery, and 50 patients (64%) had no or minimal disease (category A or B).

Table XXIII.

Duplex categories of the right and left internal carotid artery in the unrequested group. The right side is displayed on the vertical and the left side on the horizontal axis.

Right Internal Artery	Unrequested Left Internal Carotid Artery				
	A	B	C	D	Total
A	2	8			10
B	3	37	12	1	53
C	1	5	5	2	13
D				2	2
Total	6	50	17	5	78

The prevalence and extent of carotid disease as estimated by the Duplex scanner combined with spectral analysis in the requested is shown in table XXIV. In this

Table XXIV.

Duplex categories of the right and left internal carotid artery in the requested group. The right side is displayed on the vertical and the left side on the horizontal axis.

Requested						
Right Internal Carotid Artery	Left Internal Carotid Artery					
	A	B	C	D	E	Total
A		1				1
B		2				2
C		1	7	4	1	13
D			3	4	1	8
E						0
Total	0	4	10	8	2	24

group, thirteen patients had at least one stenosis of more than 50% diameter reduction (category D and E) and three patients (13%) had no or minimal disease (category A or B).

One postoperative stroke occurred in a 49 years old male with a 16-49% diameter reduction (category C) of the appropriate internal carotid artery. One postoperative transient ischemic attack occurred in a 50 years old male with a 16-49% diameter reduction (category C) of the related internal carotid artery. Both of these were in patients in the unrequested group.

6.4.3. Discussion.

The incidence of postoperative stroke after myocardial revascularization procedures was 2% in the 1,287 patients reported by Reul, et al. ¹⁴¹ and Ashor et al. ² also reported a 2% stroke rate in 100 patients aged 65 years of more. Although the postoperative stroke rate is relatively low, the preoperative detection of carotid arterial disease both by invasive and noninvasive methods is advocated by many authors. It is less clear as to what the subsequent management of the patient should be, when concomitant carotid arterial disease is found in patients awaiting coronary artery bypass grafts for angina pectoris.

Carotid endarterectomy either prior to or combined with coronary bypass procedures have been advocated by many authors ^{46,58,81} both for symptomatic and asymptomatic patients. However, for the asymptomatic patient it is usually not stated how extensive the carotid disease needs to be before endarterectomy is undertaken. Others have remained skeptical of the relationship between asymptomatic carotid occlusive disease and the incidence of perioperative stroke. Barnes, et al. ¹⁴ found an incidence of 16% of severe carotid disease (50% or greater diameter reduction) in 102 patients who were candidates for major cardiovascular surgery. However, there were no perioperative strokes or transient ischemic attacks in this group of patients. In a follow-up study of these patients ¹⁶ Barnes noted that with severe carotid disease diagnosed by the noninvasive test patients had a greater chance of developing a myocardial infarction. In 330 patients screened by Doppler imaging and spectral analysis prior to cardiovascular surgery, Turnipseed, et al. ¹⁷⁴ noted no relation between the severity of carotid artery disease and the incidence of perioperative stroke.

In the present study the risk factors for neurological complications in the two group were comparable. In the unrequested group the cardiac risk factor (unstable angina) was found more frequently (16/78) than in the requested group (2/24). In the unrequested group, only 6% (5/78) had a stenosis of 50% diameter reduction or more of the internal carotid artery. In contrast, 54% (13/24) of the requested group had stenosis of 50% diameter reduction or more.

Of these thirteen patients with high grade lesions, five underwent carotid endarterectomy without focal neurological perioperative complications. The remaining eight patients with stenosis of 50% diameter reduction or more were patients with asymptomatic bruits, and were not considered candidates for carotid surgery by their physician. None of these eight patients had perioperative focal neurological complications.

The 49 year old male, who sustained a stroke related to the right cerebral hemisphere following coronary bypass surgery, had a 16-49% diameter reduction of the right and a 5-15% diameter reduction of the left internal carotid artery. The postoperative transient ischemic attack, related to the right hemisphere occurred in a 50 year old male with 16-49% diameter reduction noted bilaterally in the internal carotid arteries. In both patients who sustained perioperative focal neurological complications, the extent and severity of their carotid disease was established with the noninvasive test. However, in neither case was the degree of stenosis noted by Duplex scanning severe enough to suggest that these two patients were seriously at risk for stroke. One of the explanations could be that most perioperative neurological complications are caused by embolic events, coming from ulcerative plaques. Both arteriography and noninvasive test are not capable of identifying ulcerative plaques accurately.

The results reported in this study suggest that patients with symptoms or signs are more likely to have severe carotid disease as compared to asymptomatic patients awaiting coronary bypass surgery. However, like Barnes ^{14,16} and Turnipseed ¹⁷⁴, we found that preoperative noninvasive studies fail to predict which patients among those asymptomatic for carotid disease are at high risk for focal neurological perioperative complications. Adding the three studies together in a population of over 500 patients the incidence of perioperative strokes could not be related to the presence of high grade stenosis as detected by noninvasive tests.

Based upon our study and others, we no longer advocate arteriography prior to coronary bypass surgery even if high grade stenoses are found in patients who do not have a history of focal neurological symptoms. This does not mean, of course, that the patients with suspected carotid disease should not be screened. While the natural history of asymptomatic high grade lesions is as yet unknown it would appear wise to at least counsel both the patient and referring physician that disease is present and continued regular follow-up is to be carried out.

6.5. Velocity pattern changes following carotid endarterectomy.

6.5.1. Introduction.

The evolution of the role of surgery in the management of cerebrovascular insufficiency spans a short period of 25 years. Although the indications for prophylactic carotid surgery are still controversial (see 6.2.3 and 6.3.3), surgery has become one of the accepted forms of treatment for patients with focal symptoms secondary to extracranial carotid artery disease ^{29,62,169}. The American experience suggests that the complication rate of carotid endarterectomy ranges from less than 1% among experienced, skilled surgeons to as high as 15% when performed by the occasional vascular surgeon ¹⁷¹. Given these reports it is essential that each surgeon assess his or her own results when considering the place of carotid surgery.

Although the clinical results of carotid surgery are reasonably well documented, little is known about the hemodynamic changes that follow the surgical procedure. While the incidence of recurrent symptoms appears to be low in most reported

series, the actual rate of restenosis is unknown since arteriography is only performed when the patient develops recurrent symptoms.

The development of noninvasive methods have made it possible to evaluate the carotid bifurcation after operation. Turnipseed et al. ¹⁷³, using ultrasonic arteriography combined with spectral analysis, found restenoses of the proximal internal carotid artery in 9% of patients in a 3 year follow-up study. The authors concluded that asymptomatic postoperative internal carotid restenosis is more prevalent than generally reported. Kremen et al. ¹⁰⁶, using pressure oculoplethysmography (see 2.2.2.), found a recurrent rate of postoperative stenoses of 9%. Bodily et al. ³⁰, using Duplex scanning combined with spectral analysis, found flow abnormalities in 49% of the arteries after carotid surgery.

At the University of Washington patients undergoing carotid surgery are routinely studied pre and postoperatively following a strict study protocol. The purpose of the present study was to evaluate the sequential changes that occurred in the velocity patterns of 88 patients who had undergone carotid surgery.

All patients of the study were studied with the Duplex scanner prior to carotid surgery. After carotid surgery the patients were studied at three, six, twelve and twenty-four months postoperatively. Although not all patients were seen at three months follow-up, all 88 patients were seen at least once within six months. Sixty-four patients (69 sides) were studied at three months, 56 patients (60 sides) at six months, 54 patients (58 sides) at 12 months, and 27 patients (29 sides) at twenty-four months after operation.

6.5.2. Results.

The distribution of internal carotid artery disease as classified by the velocity patterns and confirmed by contrast arteriography prior to surgery is shown in table XXV. Four percent (3/69) were found to have a 5-15% diameter reduction

Table XXV.
Duplex categories preoperative and three months postoperative of 69 internal carotid arteries.

Duplex Category Preoperative		Duplex Category 3 Months Postoperative				
Number of Operated Sides		A	B	C	D	E
A						
B	3	2		1		
C	8	5		3		
D	58	20		32	6	
E						

(category B), 12% (8/69) were found to have a 16-49% diameter reduction (category C). A 50-99% diameter reduction was found in 84% (58/69). For obvious reasons there were no normals or total occlusions in the group of patients who were candidates for carotid endarterectomy.

Of those sides with a B lesion prior to surgery, two sides were found to have spectral broadening in the deceleration phase of systole (B category) 3 months after surgery, one side showed spectral broadening throughout systole (category C). Of the sides classified as C prior to surgery, five sides were found to have spectral broadening in the deceleration phase of systole (category B), three sides were found to have spectral broadening throughout systole (category C). Of the 58 preoperative D lesions, 20 sides had spectral broadening in the deceleration phase of systole (category B), 32 sides had spectral broadening throughout systole (category C), and six sides had systolic peak frequencies above 4 KHz with spectral broadening throughout systole (category D).

The results of the 6 months follow-up studies are shown in table XXVI. Of those two classified as B prior to surgery, both were found to have spectral broadening in the deceleration phase of systole. Of the three preoperative internal carotid

Table XXVI.
Duplex categories preoperative and six months postoperative of 60 internal carotid arteries.

Duplex Category Preoperative	Duplex Category 6 Months postoperative				
Number of Operated Sides	A	B	C	D	E
A					
B 2	2				
C 3	1 2				
D 55	10 34 11				
E					

arteries classified as C, one was found to have spectral broadening in the deceleration phase of systole (category B) and two were found to have spectral broadening throughout systole (category C). Of the patients with B or C lesions prior to surgery, none was found with a D velocity pattern after 6 months. Of the 55 sides with a D classification prior to surgery, ten sides had spectral broadening in the deceleration phase of systole (category B) after surgery, 34 sides had spectral broadening throughout systole (category C), and eleven sides had systolic peak frequencies well above 4 KHz with spectral broadening throughout systole.

The results of the 12 months follow-up study are shown in table XXVII. Of the two internal carotid arteries classified as B prior to surgery, both were found to

Table XXVII.
Duplex categories preoperative and twelve months postoperative of 58 internal carotid arteries.

Duplex Category Preoperative		Duplex Category 12 Months Postoperative				
Number of Operated Sides		A	B	C	D	E
A						
B	2		2			
C	5		2	3		
D	51		17	23	11	
E						

have spectral broadening in the deceleration phase of systole (category B). Of the five patients having a C classification of the internal carotid artery prior to operation, two were found to have spectral broadening in the deceleration phase of systole (category B) and three were found to have spectral broadening throughout systole (category C) in the 12 months follow-up study. None of the patients with a B or C category of the internal carotid artery developed a velocity pattern with systole peak frequencies above 4 KHz and spectral broadening (category D).

Of the 51 sides which were classified as D lesions preoperatively, 17 sides had spectral broadening in the deceleration phase of systole, 23 sides had spectral broadening throughout systole, and eleven sides had systolic peak frequencies well above 4 KHz with spectral broadening after 12 months follow-up (table XVII).

After 24 months follow-up 29 sides were studied (table XVIII). One B categorized internal carotid artery prior to surgery was found to have spectral broadening in the deceleration phase of systole after 24 months follow-up. Of the four sides categorized as C prior to surgery, one was found to have spectral broadening in the deceleration phase of systole (category B) and three were found to have spectral broadening throughout systole (category C). Of the 24 sides with a D categorized internal carotid artery prior to surgery, four sides had spectral broadening in the deceleration phase of systole (category B), 15 sides had spectral broadening throughout systole (category C), four sides had systolic peak frequencies well above 4 KHz with spectral broadening (category D), and one side was occluded (category E). Again of the sides with a B or C lesion prior to surgery, none developed high systolic peak frequencies in combination with spectral broadening.

Table XXVIII.

Duplex categories preoperative and 24 months postoperative of 29 internal carotid arteries.

Duplex Category Preoperative	Duplex Category 24 Months Postoperative				
Number of Operated Sides	A	B	C	D	E
A					
B 1		1			
C 4		1	3		
D 24		4	15	4	1
E					

In the last three years seven patients have undergone contrast arteriography after carotid endarterectomy. Four of these patients are in the present follow-up protocol, with the three remaining not studied preoperatively by the Duplex scanner and therefore not in the present follow-up protocol. The diameter reduction as estimated by Duplex scanning and contrast arteriography are shown in table XXIX.

Table XXIX.

Diameter reduction estimated by contrast arteriography and Duplex scanning in patients after surgery.

Number of Patients	Arteriographic Diameter Reduction	Duplex Scanning Diameter Reduction
1	20%	5-15%
2	60%	50-99%
3 *	30%	16-49%
4 *	45%	50-99%
5 *	10%	5-15%
6	90%	50-99%
7 *	20%	16-49%

* Patients in present follow-up study.

Five patients demonstrated recurrent symptoms related to the operated sides, two patients developed symptoms related to the contralateral side. Amaurosis fugax related to the operated side was found in one patient with a B velocity pattern and

in one patient with a C velocity pattern. Motor weakness related to the operated side was found in two patients both with a C velocity pattern. One frank stroke related to the operated side occurred in a patient with a B velocity pattern. Of the two patients with symptoms not related to the operated side one patient with a C lesion on that side sustained a frank stroke, the other developed amaurosis fugax with a D velocity pattern on that side.

6.5.3. Discussion.

In order to interpret the velocity patterns from the carotid bifurcation after operation, it is important to review the changes in the arterial segment that are known to occur. The endarterectomized area in time will be covered by proliferation of myointimal cells⁶⁷. Early postoperative arteriograms often show wall irregularities as well as some dilatation of the carotid bulb^{50,150}. Schutz et al.¹⁵⁰ in a series of 50 arteriograms reported wall irregularities in 12 and local dilatation of the bulb in 6 instances. The wall irregularities appeared to decrease with time, while the dilatation persisted. Diaz et al.⁵⁰ found local dilatation and circumferential defects in the majority of 50 early postoperative arteriograms. The circumferential defects disappeared in subsequent arteriograms. In the present series of 88 patients four underwent arteriography after operation, in two cases dilatation of the bulb was found, and in all four wall irregularities were present.

The fact that a normal velocity pattern is not commonly found in our follow-up studies is not surprising since flow disturbances can occur with minimal changes in the intimal surface. In all follow-up studies spectral broadening throughout systole (category C) was found most frequently followed by spectral broadening in the deceleration phase of systole (category B). Both the B and C category can be considered as postoperative findings not related to a recurrent high grade stenosis.

Whenever systolic peak frequencies were noted above 4 KHz with spectral broadening throughout systole (category D), the velocity pattern was classified as consistent with a high grade stenosis (50-99% diameter reduction). This was found in 9% after 3 months, 18% after 6 months, 19% after 12 months, and 17% after 24 months follow-up.

Of interest is the fact that of the 6 sides where a D velocity pattern was noted after three months, in four sides the classification changed to a C velocity pattern after 12 months. Of the eleven sides where a D velocity pattern was found after 6 months, in five instances a C velocity pattern was noted after 24 months. These findings suggest that there are changes in the carotid bulb in these patients, similar to those described by Schutz¹⁵⁰ and Diaz⁵⁰ in their arteriographic studies. Our findings are consistent with the thesis that myointimal proliferation can occur early after operation but in some patients may regress with time.

An important question is whether the changes found by Duplex scanning combined with spectral analysis are in fact real or due to errors in our study technique. The latter is very unlikely, based upon our current experience with the Duplex scanner. Another important question relates to the accuracy of the velocity patterns seen after operation in predicting the degree of involvement. As noted in table XXIX, the results in the seven patients who underwent repeated arteriography agreed quite well. Thus, this method of study is not only suitable for

screening patients with suspected extracranial carotid artery disease but is also useful in predicting the state of the carotid bulb in patients after carotid endarterectomy.

Symptomatic recurrent stenosis after carotid endarterectomy is reported to occur in 1-4 percent of patients ^{45,67,155}. Asymptomatic recurrent stenosis, as detected by noninvasive tests, are reported in approximately 10% ^{106,173}. Reasons for restenoses, except for technical errors, are mainly caused by myointimal hyperplasia or recurrent arteriosclerosis ^{45,67}. Myointimal hyperplasia is expected within the first 24 months after surgery, whereas arteriosclerotic changes as cause for recurrent stenosis is expected after a longer postoperative period. In the present study, approximately 20% of the patients developed velocity patterns consistent with a high grade stenosis. However, the development of such flow patterns was not associated with recurrent of symptoms in the majority of these patients. This is not surprising since most of the early lesions which develop are smooth and do not ulcerate and do not become potential sites for embolization. Also, as indicated above, there is evidence that with time, these velocity patterns will change in some patients towards a more normal range.

The present study has demonstrated that the Duplex scanner combined with spectral analysis is a reliable method to follow patients after carotid endarterectomy. The study shows that approximately 20% of the operated sides develop a velocity pattern consistent with a 50-99% diameter reduction. The number of patients and follow-up time in this study is not large or long enough to draw definitive conclusions. It is clear however, that a noninvasive test such as used will in years to come provide more valuable information about symptomatic and asymptomatic recurrent stenosis after carotid endarterectomy.

Chapter 7

General Discussion.

Stroke ranks as the second most common cause of death due to vascular disease in the United States ¹⁰⁸. In addition, it is also the cause of disability for an estimated one million Americans. Episodes of transient ischemic attacks are recognized as precursors of stroke since approximately 40% of affected patients are likely to have a cerebral infarction within the first five years after the initial event ¹⁷². Furthermore, at least 75% of patients with completed strokes will give a history of previous transient ischemic attacks.

The relationship between extracranial carotid artery disease and stroke became fully realized with the development of cerebral arteriography. Arteriographic studies indicated that 74% of patients with ischemic stroke syndromes had at least one significant lesion in the extracranial vasculature ⁷⁵. In most patients with transient ischemic attacks, arteriography will demonstrate that the common site of narrowing is at the origin of the internal carotid artery. For many years, only high grade stenoses or occlusions were considered important in the pathogenesis of transient ischemic attacks (hemodynamic theory). At present, emboli from ulcerated plaques are considered to be the most common cause of transient cerebral ischemia (embolic theory) ¹⁶⁶. It is now accepted that the release of trombi into the bloodstream from an ulcerated area within a plaque can lead to both transient and permanent neurological changes. While embolization is often difficult to prove, the best evidence for such occurrences is found in patients with transient monocular blindness where emboli may be seen in the retinal arteries ¹²⁶.

The finding that the lesion responsible for emboli is generally localized at an accessible side, i.e. the carotid bulb, made surgical treatment possible. Good long term results after carotid surgery made carotid endarterectomy one of the accepted forms of treatment for patients with transient ischemic attacks ¹⁶⁹.

Contrast arteriography remains the ultimate diagnostic procedure for patients, who are candidates for carotid surgery. Since contrast arteriography has a small but real risk of serious complications ¹⁶⁴, ideally only those patients considered candidates for carotid surgery should undergo this invasive procedure. This creates a need for accurate noninvasive tests which could be used to screen patients with suspected extracranial arterial disease.

Noninvasive methods are readily separated in indirect and direct tests. Indirect tests such as supraorbital Doppler or oculoplethysmography are the most common noninvasive tests employed today for the detection of extracranial carotid artery disease. The reason for this is to be found in the simplicity and low cost of these tests. Supraorbital Doppler studies alone are unsuitable as diagnostic test for

patients with suspected extracranial carotid artery disease¹⁵. Pressure oculoplethysmography seems to be accurate for high grade stenoses. Eikelboom⁵⁶ described the results, using this device, in 309 patients where the extent of carotid disease was documented by contrast arteriography. For stenoses of 65% or more, the sensitivity and specificity were 87% and 84% respectively.

There are two major disadvantages with all indirect tests: (1) minimal disease (non flow-pressure reducing lesions) cannot be detected. This is important when it is realized that 50% of the patients in Thiele's study¹⁶⁶ with TIA's did not have stenoses of sufficient magnitude to reduce pressure or flow; and (2) it is not possible to differentiate between total occlusions and high grade stenoses. This distinction is an important one from a diagnostic standpoint.

Direct noninvasive tests operate without or with imaging systems. Those operating without an imaging system are in general based upon the evaluation of velocity changes using continuous wave Doppler devices^{2, 134, 148}. Direct noninvasive tests that employ imaging systems can be divided in those that provide a flow map and those which provide a B-mode image.

The continuous wave ultrasonic arteriograph, as described by Spencer et al.¹⁵³ provides a flow imaging system, which is accurate in predicting high grade stenoses of the carotid system. However, Weaver et al.¹⁷⁷ found that lesions in the 0-50% diameter reduction range were not readily detected using this device. This is not surprising, since differentiation between the presence or absence of spectral broadening, as a reflection of flow disturbance produced by minimal lesions, is on theoretical grounds impossible using a continuous wave device.

With the development of pulsed Doppler ultrasound it became possible to detect blood flow at discrete points across the arterial lumen⁷, and assess the velocity patterns proximal to, in and distal to sites of stenoses. To increase the clinical utility of the pulsed Doppler, it is necessary to combine it with a method of acoustical imaging. There are a variety of approaches to this problem. Hokanson et al.⁸⁷ were the first to develop an ultrasonic arteriograph, which provides anatomical information by generating a flow map that can be used as a guide for precise placement of the pulsed Doppler sample volume.

Clinical results from the University of Washington, using Hokanson's ultrasonic arteriograph, were reported by Blackshear et al.²⁴. The agreement between this ultrasonic device and contrast arteriography was 91% (20/22) for 50-99% diameter reductions, and 59% (13/22) for 10-49% diameter reductions. There was one false negative in the 8 normal vessels included in the study. A larger series, using Hokanson's arteriograph, was reported by Sumner et al.¹⁶³. Using a diameter reduction greater than 20% as criterion for a positive test, the sensitivity of the method was 81% and the specificity 88% in 209 carotid bifurcations. These results demonstrate that ultrasonic pulsed Doppler imaging systems can be used to detect extracranial carotid artery disease encompassing the spectrum of involvement from normal to total occlusion. The system is relatively inexpensive and when combined with spectral analysis is suitable for both clinical and research orientated studies.

The initial attempts to evaluate carotid disease with a B-mode system alone quickly demonstrated its deficiencies. The first patient studied with this device at the University of Washington appeared to have a patent internal artery on the B-mode image, but was found to have a total occlusion by contrast arteriography. Subsequent studies showed that both thrombus and non-calcified plaques may have the same acoustic properties as flowing blood⁷⁶. This finding prompted the development of a device which combined the B-mode image system with a pulsed Doppler device. The B-mode image permitted identification of the walls of the artery, visualization of calcified plaques, and served as a guide for the accurate placement of the sample volume of the pulsed Doppler at any desired point within the vessel. This concept of combining the two systems into the Duplex scanner was first described by Barber et al.¹¹. Since its initial development the system has undergone continuous modification to make it usable in clinical practice. This sequence and its results were described by Phillips et al.¹³³.

For all of the validation studies, contrast arteriography has been used for comparison, since it is considered to be the standard for quantifying the location and degree of narrowing of the extracranial carotid arteries. Although considered the gold standard, it became apparent, that there was considerable variability in reporting the results of carotid arteriograms related to both the intra- and interobserver variability. Chikos et al.⁴¹ highlighted this problem in a carefully designed study of 128 multiplanar selective arteriograms of the carotid arteries. The intraobserver agreement for a "normal" internal carotid artery was 75% with an interobserver agreement of 57%. This variability is one of the reasons that total agreement between arteriography and any noninvasive test, especially for evaluating normal and minimally diseased vessels, will probably never be possible.

A great deal of effort has been expended in attempting to assess the amount of diameter reduction of the internal carotid artery using spectral patterns obtained with the pulsed Doppler. Giddens et al.⁷¹ demonstrated, using hot film anemometry in an animal model, that flow disturbances can be detected immediately downstream of stenoses which do not reduce pressure or flow. Thiele et al.¹⁶⁵ were able to verify this in a similar animal model using a high frequency pulsed Doppler velocimeter. These authors demonstrated that the pulsed Doppler could be used to assess the velocity disturbances that occur with varying degrees of stenoses. The most useful parameter to detect these flow disturbances was the estimation of spectral width. Hutchinson et al.⁹⁰ noted that broadening of the spectrum with non-pressure reducing stenoses occurred first during the deceleration phase of systole. As the stenoses became more severe (16-49%), broadening was noted throughout the entire pulse cycle. In clinical studies of the carotid bifurcation, it is possible by combining the onset of spectral broadening with the peak systolic frequencies to estimate the degree of narrowing for discrete categories ranging from normal to total occlusion. Fell et al.⁵⁹ have shown that using this approach it is possible to estimate the diameter reduction of the internal carotid artery with reasonable accuracy.

In January, 1980, the prototype PV III Duplex scanner was replaced by a commercially available unit. The improvements made were results of the previous

experience obtained with the earlier systems. The agreement between arteriography and ultrasonic Duplex scanning using the short focus scanhead for normal carotid arteries was 50%, for the 5-15% diameter reduction category the agreement was 69% and for the 16-49% diameter reduction category 70%. Using the medium focus scanhead agreement between arteriography and Duplex scanning was 94% for the 50-99% diameter reduction category and 93% for total occlusions.

The accuracy in differentiating between high grade stenoses and total occlusions improved as compared with previous results of the PV III Duplex scanner⁵⁹. This was a result of the appreciation of the changes in the velocity patterns of the common carotid artery (see 5.2.). The capability to differentiate accurately between high grade stenoses and total occlusions makes the Duplex method superior to all indirect noninvasive tests.

The introduction of an algorithm to estimate the degree of involvement in patients with stenoses in the 50-99% diameter reduction category is promising and will likely play a role in documenting progression of disease for lesions in this category¹⁰⁵.

Analyzing the results of the Duplex Scanner combined with spectral analysis and comparing them with other noninvasive methods, we are confident that this system provides an accurate screening method for patients with suspected extracranial carotid disease³⁷. The method is suitable for screening patients who are considered possible candidates for contrast arteriography. Furthermore, since the method has the potential to detect disease varying from minimal lesions to total occlusions, the method may be suitable for studies designed to document the progression of disease.

Given the accuracy of Duplex scanning, will it replace contrast arteriography? At present the answer must be no, but it will clearly modify the indications for the invasive study. Since the technique is relatively new, each laboratory which employs the method will have to be confident of their results before basing clinical decisions on the findings of the Duplex study. In our laboratory, the accuracy of the method for the detection of high grade lesions and total occlusions approaches 94%. Thus, in certain patients, it is entirely reasonable to base a decision to proceed with arteriography on the results of a Duplex scan.

Another question frequently asked is the role of scanning in patients with a clinical presentation that would normally demand arteriography. Should these patients be subjected to Duplex scanning or is it superfluous? Our feeling is that they should be studied for the following reasons: (1) there are situations in which the Duplex studies may be instrumental in the diagnostic approach that is followed. For example, the finding of a totally occluded internal carotid artery may remove the need for arteriography; (2) the noninvasive studies will provide a baseline examination that will be useful for follow-up; and (3) prospective studies of patients with extracranial arterial disease will require repetitive follow-up of such patients.

Of the patients referred for study, about one-third have focal TIA's as the basis for the referral (see 6.2.). Short of those found to have a total occlusion, there is

general agreement that arteriography should be done to determine the basis for the problem. However, the decisions with the remaining two-third of patients who do not have focal TIA's, the problem is more complex. For example, the group of patients with nonfocal symptoms present difficult problems, especially when the clinical picture is vague which is often the case. We are more willing to perform arteriography in this group of patients when bilateral disease is found by the Duplex study, especially when a total occlusion is found in one internal carotid artery with a high grade stenosis on the other side. The literature for this group of patients is rather confusing, although most authors consider bilateral high grade stenoses (diameter reduction of more than 50%) a cause for the nonfocal symptoms^{62, 65, 119}.

Our own approach to patients with asymptomatic bruits has been largely conservative both from the standpoint of arteriography and surgery. One of the reasons for this attitude is that it is still not clear that carotid endarterectomy will protect these patients for stroke. Recent publications^{82, 181, 182} have demonstrated that, although the overall risk for stroke is increased in this group of patients, the strokes that do occur may not be related to the side of the bruit. Thus, an asymptomatic bruit appears to be a good predictor of subsequent cardiovascular events, i.e. myocardial infarction and stroke. Since there is a need for prospective studies to obtain information about the natural history of this group of patients, we have embarked upon such a study. It will require another five years before the results of this study will provide meaningful data.

Given our own policy, it was of interest to see what referring physicians did with the information provided to them from our laboratory (see 6.2.). A surprising finding was that even though patients were classified as having focal symptoms lasting less than 24 hours by the referring physicians, there remained a considerable number who did not have arteriography. Only 22% in the 5-15% diameter reduction group and 27% in the 16-49% diameter reduction group underwent contrast arteriography. Whether this approach is a correct one can only be answered by follow-up studies. It is our plan to follow the patients who did not undergo arteriography because it is only by this approach that we can find the answer to this question. It also became apparent that the referring physicians considered the finding of a high grade stenoses of greater clinical importance in both the nonfocal and asymptomatic bruit group (see 6.2. and 6.3.). The number of patients with a 50-99% diameter reduction who underwent arteriography in these two groups was significantly higher than those with lesser degrees of involvement.

Whether or not prophylactic carotid surgery should be performed in patients who are candidates for coronary bypass surgery is still controversial. As a result of our study on 102 patients (see 6.4.) and Barnes studies^{14, 16}, we no longer advocate arteriography prior to coronary bypass surgery even if high grade stenoses are found in patients without a history of focal neurological symptoms. This does not mean that the patients with suspected carotid disease should not be screened. It would appear reasonable to counsel the patient and referring physician that disease is present and continued regular follow-up is to be carried out until the natural history of asymptomatic high grade lesions is known.

Although the indications for carotid surgery are not well established to everyone's satisfaction, carotid endarterectomy is the most commonly performed vascular procedure in the United States of America. In good centers, the procedure can be performed safely with a low complication rate. This fact does not appear to be widely accepted by some neurologists as evidenced by the differing views concerning the role of endarterectomy. There is no doubt that the results do vary from region to region and reflect the skill and experience of the surgeon. Whenever carotid endarterectomy is indicated, it should only be done by surgeons whose complication rate is less than 2%¹⁷¹.

Although carotid endarterectomy appears to be a durable procedure with good results, little is known about the hemodynamic changes that follow the operation. Our results from 88 patients with a follow-up of two years demonstrate that recurrent asymptomatic restenoses is found in 9% after three months, 18% after six months, 19% after twelve months, and 17% after twenty four months follow-up. Longer follow-up studies will be required to assess the importance of restenosis with respect to the development of recurrent symptoms. It is our impression that the Duplex scanner is an ideal means of following patients postoperatively. The method provides hemodynamic data on the flow patterns across the operated segment. The finding of flow disturbances is extremely common even when high grade stenoses are not found. If these flow disturbances are a factor in the cause of myointimal hyperplasia or secondary to such a change remains to be determined.

There have been reports in the literature describing the use of objective velocity waveform parameters for the detection and classification of disease of the carotid arteries. Blackshear et al.²⁷ and Knox et al.¹⁰⁵ introduced simple parameters to quantitate the degree of stenosis of the internal carotid artery. Rutherford et al.¹⁴⁸ used discriminant analysis of selected waveform parameters to identify normal and diseased internal carotid arteries. Greene et al.⁷³ at the University of Washington developed a similar technique using computer selected waveform parameters employing a stepwise discriminant analysis to classify disease into four categories. Data from the Duplex scanner with ECG data are recorded on audiotape for further analysis. The Doppler information of 20 suitable heart beats are chosen by the computer and subjected to the fast Fourier spectrum analysis from which an ensemble averaged spectrum is produced. The averaged spectrum is then analysed by a software package developed to perform pattern recognition⁷³. A stepwise algorithm is used to go through the following decisions: (1) normal or diseased; (2) if diseased, greater or less than 50% diameter reduction; and (3) if less than 50%, greater or less than 20% diameter reduction.

At present, 24 normal internal carotid arteries and 81 diseased internal carotid arteries with arteriographic confirmation have been analysed. Of the 24 normal internal carotid arteries 18 were so classified by the computer. Of the 10 internal carotid arteries with 5-15% diameter reduction, 7 were classified correctly by the computer. Of the 39 with a 16-49% diameter reduction, 19 were classified correctly, and of the 32 with 50-99% diameter reduction, 22 were correctly identified by the computer. These results are promising, although more work has

to be done before a microprocessor can be developed which can be used on-line to make these decision steps.

What are the research goals for the future? Basically these can be divided into two categories: (1) signal processing and (2) long-term clinical studies.

Signal processing will follow two directions. The computer recognition programs will have to be refined further with the goal of developing a microprocessor which can be used on-line to analyze the Doppler spectrum at the time the patient is being studied. In addition, work is ongoing to evaluate the feasibility of analyzing averaged data which varies from 1-20 heart cycles. Dr. D.J. Phillips has started on this latter program at the University of Washington using data from the Duplex scanner. This work is a logical, intermediate step between the current approach described in chapter five of this thesis and the more complex work, being done by F.M. Greene with the computer pattern recognition program⁷³. One of the questions which needs to be answered is the number of cycles one should average to obtain a velocity waveform that is adequate for further analysis. Selecting too many cycles could result in the loss of non-periodic information through averaging that could be useful. Averaging too few can result in the analysis of non-meaningful beat to beat variations. Having the option to change the number of heart cycles to be averaged, creates a new dimension for the analysis of spectral data. It is possible that some important parameters will be best depicted in an averaged velocity waveform where others may be observed only in a non-averaged waveform.

Documenting progression of disease will be the other main goal for future work. As has been stated previously, the Duplex concept is suitable for this sort of study because the method can be used repetitively to provide accurate reproducible hemodynamic information concerning the carotid bifurcation. Based upon our experience, we are confident that this important issue can best be addressed by obtaining repetitive velocity data from the same anatomic sites.

However, which patient groups should be followed and which parameters should be chosen? The first part of this question is not difficult to answer. Basically, those patients should be followed in which progression of disease is of clinical importance. It is clear that there is a need for information about the natural history of patients with asymptomatic bruits. The next group of patients are those who have undergone carotid surgery. Does restenosis play a role in the development of recurrent symptoms? Another group of patients, where the long-term follow-up is important are those patients with TIA's not treated surgically. Perhaps, it will be possible to answer the question concerning the role of antiplatelet agents in preventing disease progression.

At present it is not possible to decide which parameters should be chosen to document progression of disease. The computer pattern recognition program as it stands today does not seem to be sufficient, since diameter reduction changes within the 50-99% category cannot be documented. This will require the addition of new algorithms such as described by Knox et al.¹⁰⁵ to cover the entire spectrum of disease. Although many problems remain to be solved, it seems clear that using the averaged velocity waveforms from the common and internal carotid artery

with the help of computer controlled stepwise discriminant analysis will be sufficient to answer these questions.

In conclusion, the results of the studies presented in this thesis have answered only a few of the questions concerning the diagnosis and treatment of extracranial carotid artery disease. With such a method available to document the extent of disease, the ultimate question comes to mind: Is it possible to predict clinical outcome on the basis of the degree of diameter reduction of the internal carotid artery? This question has not yet been answered and it will take probably another ten years before the answer is found. However, it can be expected that noninvasive tests such as described will be useful in approaching this problem objectively. A great deal of knowledge about this difficult issue is being slowly accumulated by people working in the field of ultrasound. As long as the noninvasive studies are used to carry out long-term studies, progress with regard to the natural history of carotid atherosclerosis will be made.

Summary

The studies in this thesis evaluate the practical value of ultrasonic Duplex scanning combined with spectral analysis in the detection of extracranial carotid artery disease. The method is based on the combination of real-time B-mode imaging and a 5 MHz pulsed Doppler device. The B-mode images are used as a guide for placement of the sample volume of the pulsed Doppler in the centerstream of the vessel of interest. The basic principle of the method is the estimation of diameter reductions of the internal carotid artery with velocity waveform parameters obtained from the pulsed Doppler device, subjected to Fast Fourier Transform spectral analysis.

In four studies the issue of the accuracy of the ultrasonic method, as compared to multiplanar contrast arteriography, were presented. The first study evaluated the value of velocity waveform information of the common carotid artery in predicting disease in the internal carotid artery. In the second study the accuracy of Duplex scanning was evaluated in 246 carotid bifurcations. The third study concerned the evaluation of velocity waveform changes due to an increase of total blood flow in normal subjects as a means to unmask lesser degrees of stenoses. The fourth study concerned the evaluation of a parameter for accurate detection of severe carotid artery disease.

Given a certain accuracy the ultrasonic device was used in four clinical orientated studies. The first two studies concerned the influence of Duplex scanning on the management of referring physicians in patients with symptomatic and asymptomatic extracranial carotid artery disease. The third study evaluated the incidence of carotid artery disease in patients who were candidates for coronary bypass surgery, the fourth study concerned the issue of recurrent stenoses after carotid surgery.

Chapter 1. This chapter provides the reader with a short review of the anatomy and pathology of the extracranial carotid artery systems. Clinical considerations of carotid artery disease are discussed.

Chapter 2. Contrast arteriography is traditionally considered the screenings method of carotid artery disease. The use of this invasive procedure both as screenings device and gold standard for noninvasive methods is described. The variability in reading arteriograms, especially with no or minimal disease present, and the consequences of this variability for noninvasive methods are mentioned.

The second part of this chapter is a review of the noninvasive screenings techniques available for detecting extracranial carotid artery disease. Basically they can be divided in indirect and direct noninvasive tests. The method used in this thesis is a direct ultrasonic test, obtaining information from the carotid bifurcation.

Chapter 3. In this chapter some basic principles of fluid dynamics are introduced. Changes in the velocity profiles of the carotid system obtained by the Doppler technique will be more meaningful with the knowledge of these basic principles.

Chapter 4. This chapter describes the current status of ultrasonic techniques. The fundamental differences between continuous wave and pulsed Doppler are described. Detecting velocity information from discrete points in the vessel of interest, as provided by a pulsed Doppler system, justifies the use of a parameter like spectral broadening. This parameter allows the detection of arteriographic lesions which are non pressure or flow reducing. The additional anatomical information, required to obtain relevant pulsed Doppler information, is with Duplex scanning provided by B-mode images.

Using five categories, the pulsed Doppler information combined with spectral analysis can be classified as followed:

(A) normal, 0% diameter reduction; (B) 5-15% diameter reduction; (C) 16-49% diameter reduction; (D) 50-99% diameter reduction; and (E) total occlusion, 100% diameter reduction. The parameters used for this classification are: (1) spectral width during systole; (2) systolic peak frequency; and (3) diastolic frequencies.

Chapter 5. The basis for this chapter are four studies performed with both data from the prototype PV III Duplex scanner and the commercially available Mark V Duplex scanner. The first study was performed to assess in an objective fashion the frequency of flow to zero during late systole or diastole in the velocity waveform of the common carotid artery as related to disease in the proximal internal carotid artery. Of 156 patients, who underwent multiplanar contrast arteriography, the velocity patterns of the common carotid artery were reviewed. Flow to zero during diastole in the common carotid artery was found in three groups of patients: (1) patients with flow to zero in both common carotid arteries not related to disease in the proximal internal carotid artery; (2) patients with a tight stenosis (90-99% diameter reduction) in the internal carotid artery; and (3) patients with a total occlusion of the internal carotid artery. Although flow to zero during diastole in the common carotid artery is very commonly observed with a total occlusion of the internal carotid artery, it may also be seen with a high grade stenosis. Thus when found, it is essential to ascertain if flow is, indeed, present in the internal carotid artery. The appreciation of the characteristics of the velocity pattern of the common carotid artery improved the overall accuracy in detecting extracranial carotid artery disease.

The second study presented the results concerning the accuracy of the Mark V Duplex scanner combined with spectral analysis. For comparison between multiplanar contrast arteriography and the ultrasonic device were available 246 carotid sides, 169 sides were studied with the medium and 77 sides with the short focus scanhead. The agreement between arteriography and ultrasonic Duplex Scanning using the short focus scanhead for normal carotid arteries was 50%, for the 5-15% diameter reduction category 69%, and for the 16-49% diameter reduction category 70%. These results were clearly better than the results obtained with the medium focus scanhead in the same three categories.

The agreement between arteriography and ultrasonic Duplex scanning in high grade stenoses (50-99% diameter reduction) was 94%, using the medium focus scanhead and 89% using the short focus scanhead. The agreement for total

occlusions was 93% for the medium focus scanhead and 100% for the short focus scanhead. In high grade lesions and total occlusions there was no marked difference between the two scanhead.

The third study was designed as pilot study in order to find a means of unmask lesser degrees of stenoses and separate them from normal carotid arteries. Five normal subjects increased the total blood flow to their brains by breathing 6.8% carbon dioxide. Changes in flow were quantified by features derived from the velocity waveforms of the common, internal, and external carotid artery. An increase in velocities during diastole correlated well with the expected increase in total blood flow induced by breathing 6.8% carbon dioxide. Increases in spectral width reflected the development of flow disturbances not apparent under basal conditions. The study suggests that marked increase in flow produced by intracranial vasodilatation can dramatically alter the velocity patterns normally observed.

The fourth study concerned the evaluation of an algorithm for accurate detection of severe carotid artery disease. The study was performed in order to estimate the degree of involvement in the 50-99% diameter reduction category. The algorithm used is the ratio of peak systolic velocity in the internal carotid artery to the end diastolic velocity in the common carotid artery. The ratio was evaluated in 68 diseased and 30 normal carotid arteries. The algorithm permitted gradation of disease into 60% diameter reduction and more with 95% accuracy, 65% diameter reduction and more with 97% accuracy, and 90% diameter reduction and more with 100% accuracy. The values of the 30 normal sides studied, fell below those of the 60% diameter reduction group. The algorithm seems to be useful in further gradation of stenoses in the 50-99% diameter reduction range.

The four studies of this chapter demonstrated that the accuracy of ultrasonic Duplex scanning combined with spectral analysis justifies the use of the method as a screenings device for patients with extracranial carotid artery disease. Furthermore, the method has the potential to document progression of disease. Critical, however, is the knowledge of the limitations of the method, as has been shown by the use of the medium focus scanhead in patients with minimal disease.

Chapter 6. This chapter is based on four clinical studies performed with the Mark V Duplex scanner combined with spectral analysis. The first study was performed to assess the influence of the Duplex studies on the management of patients with suspected symptomatic extracranial carotid artery disease. Data on all new referrals (n=410) during one year were reviewed. The patients were grouped according to their reason of referral: (1) patients with focal neurological symptoms lasting less than 24 hours (n=156); (2) patients with focal symptoms lasting longer than 24 hours (n=107); and (3) patients with nonfocal neurological symptoms (n=147). For all groups there was a statistically significant relationship between the reporting of the presence of a high grade stenosis (50-99% diameter reduction) and the likelihood that the patient would undergo contrast arteriography. The finding of a high grade stenosis on the arteriograms resulted in a greater number of patients undergoing carotid surgery. The results of this study indicate that the report of the noninvasive test influenced the decision making process in the

management of patients with suspected carotid artery disease. For patients with focal neurological symptoms lasting less than 24 hours this was a surprising finding, since it is our own policy that these patients will undergo contrast arteriography regardless the percentage of stenosis.

In the second study 95 patients referred to the vascular laboratory because of an asymptomatic bruit were evaluated with the Mark V Duplex scanner. Unilateral bruits were found in 48 patients and bilateral bruits in 47 patients. Out of the 142 carotid sides with a bruit 2% (3/142) were found to be normal, 30% (42/142) were found to have a 5-15% diameter reduction, 37% (53/142) were found to have a 16-49% diameter reduction, 29% (42/142) had a 50-99% diameter reduction, and 2% (3/142) of the patients were found to have a total occlusion of the internal carotid artery. When a high grade stenosis (50-99% diameter reduction) is considered to be an

indication for contrast arteriography then this invasive procedure could be avoided in 71% of the cases. Our own approach of this problem is largely conservative both from the standpoint of arteriography and surgery. Even in patients who are candidates for coronary bypass surgery there is evidence that prophylactic carotid surgery is not indicated for patients without neurological symptoms. We perform Duplex studies in patients with asymptomatic bruits as a part of a follow-up study in order to address the issue of documenting progression of disease. Only such studies will give the answer whether or not prophylactic surgery should be performed in patients with asymptomatic carotid disease such as asymptomatic bruits.

The third study was performed to obtain a better understanding of the incidence of carotid occlusive disease in candidates for coronary bypass surgery and evaluate the practical use of a noninvasive method to screen patients preoperatively.

Hunderd and two patients were evaluated preoperatively with the Mark V Duplex scanner, 24 studies were requested on the basis of either previous neurological problems or the presence of a bruit and 78 studies were performed as part of the study protocol. In the unrequested group 6% (5/78) of the patients had a stenosis of 50% diameter reduction or more. In the requested group 54% (13/54) had a stenosis of 50% diameter reduction or more. In the postoperative phase one stroke and one transient ischemic attack were noted among the unrequested group and none in those suspected of having carotid disease on clinical grounds. Neither patient had a high grade stenosis. Based on this study and others there is little evidence to support the contention that noninvasive screening of patients free of symptoms or signs of carotid disease prior to coronary artery bypass surgery is a valuable method of screening patients who will sustain a focal neurological event.

In the fourth study sequential changes in the velocity patterns after carotid endarterectomy were evaluated, 88 patients were studied prior to and following carotid surgery with the ultrasonic Duplex device. Patients were studied at three, six, twelve and twenty-four months after surgery. The velocity patterns of all patients demonstrated flow disturbances following carotid endarterectomy. Velocity patterns consistent with recurrent high grade stenoses (more than 50% diameter reduction) were found in 9% at three months, 18% at six months, 19% at twelve months, and 17% at twenty-four months follow-up. Most restenoses are

considered to be caused by myointimal hyperplasia, which could be the result of the documented flow disturbances. The results of this study demonstrated that: (1) flow disturbances occur after carotid endarterectomy even without recurrent stenoses; and (2) the development of early restenoses is higher than the incidence of recurrent symptoms.

Chapter 7. In the general discussion the most prominent findings of chapter 5 and 6 are reviewed. These findings demonstrate that Duplex scanning combined with spectral analysis is an accurate method to detect extracranial carotid artery disease. The method has proven to be suitable for clinical and research orientated study protocols.

Further goals for the research orientated studies will be: (1) to improve signal processing, and (2) to find algorithms to document progression of extracranial carotid artery disease. These algorithms will probably be found with the development of a variable averaging spectrum velocity pattern program combined with a computer controlled stepwise discriminant analysis program.

Samenvatting

Gedurende de laatste jaren heeft het "niet-invasieve" onderzoek van de extracraniële cerebrale circulatie een stormachtige ontwikkeling doorgemaakt. Deze ontwikkeling is toe te schrijven aan een toenemende behoefte op gefundeerde gronden patiënten te kunnen selecteren voor contrast-arteriografie. Dit proefschrift beschrijft een niet-invasieve methode met als doelstelling de klinische betekenis ervan te evalueren. De gebruikte methode is gebaseerd op het "Duplex" principe, een combinatie van echografie en een pulsed-Doppler systeem. De met echografie verkregen anatomische informatie stelt het pulsed-Doppler systeem in staat een representatief snelheidsprofiel van de extracraniële vaten te verkrijgen. Spectraal-analyse van het snelheidsprofiel maakt het vervolgens mogelijk, aan de hand van hemodynamische parameters, de diameterreductie van een arterie te bepalen.

Traditioneel wordt de nauwkeurigheid van niet-invasief onderzoek bepaald door vergelijking met contrast-arteriografie, waarbij de arteriografie als "gouden standaard" wordt gebruikt. In dit proefschrift wordt de nauwkeurigheid van het Duplex principe in combinatie met spectraal-analyse aan de hand van de resultaten van vier studies besproken.

Naast de functie om patiënten te kunnen selecteren voor arteriografie kunnen met een nauwkeurig niet-invasief onderzoek carotis afwijkingen in bepaalde patiënten populaties worden geïdentificeerd en eventueel vervolgd. Het doel van deze studies, waarvan er vier in dit proefschrift zijn opgenomen, is het verkrijgen van meer inzicht in de betekenis van de aanwezigheid van arteriosclerotische carotis afwijkingen en het optreden van eventuele progressie.

In hoofdstuk 1 wordt een overzicht gegeven van de anatomie en pathologie van de extracraniële cerebrale circulatie. De klinische betekenis en eventuele behandeling van arteriosclerotische afwijkingen ter hoogte van de carotis-bifurcatie worden besproken.

Hoofdstuk 2. Diagnostisch onderzoek van de carotis-bifurcatie bestaat uit invasief en niet-invasief onderzoek. Contrast-arteriografie wordt traditioneel beschouwd als het definitieve onderzoek om carotis-bifurcatie afwijkingen te diagnostiseren. De betrouwbaarheid en risico's van dit invasieve onderzoek worden besproken.

Niet-invasief onderzoek kan worden ingedeeld in "indirecte" en "directe" methoden. Indirecte methoden registreren veranderingen in het collaterale systeem ten gevolge van carotis-bifurcatie afwijkingen, directe methoden registreren ter plaatse van de bifurcatie. Het Duplex concept is gebaseerd op registraties ter hoogte van de carotis-bifurcatie en is daardoor een directe methode.

Hoofdstuk 3. Met behulp van hemodynamische parameters wordt het geanalyseerde snelheidsprofiel geclassificeerd; de parameters zijn spectrale verbreding, maximale systolische en diastolische frequenties. Met bekendheid van enkele hemodynamische basisprincipes krijgt het gebruik van de gekozen parameters meer betekenis. Relevante principes worden in het kort beschreven.

In hoofdstuk 4 worden de kenmerken en verschillen van continuous wave en pulsed-Doppler technieken beschreven. Een pulsed-Doppler systeem stelt de gebruiker in staat hemodynamische informatie vanuit het midden van een arterie te verkrijgen. Hierdoor is het mogelijk veranderingen in de spectrale verbreding van het snelheidsprofiel, als gevolg van minimale arteriosclerotische vaatwandafwijkingen, te registreren. In het Duplex concept wordt de anatomische informatie, nodig ten einde de localisatie van het pulsed-Doppler systeem te bepalen, verkregen door echografie.

Gebruik makend van eerder genoemde parameters kan het snelheidsprofiel van de arteria carotis interna in één van de volgende vijf categoriën worden ingedeeld: (A) normaal, 0% diameterreductie; (B) 5-15% diameterreductie; (C) 16-49% diameterreductie; (D) 50-99% diameterreductie; en (E) totale occlusie, 100% diameterreductie.

In hoofdstuk 5 wordt aan de hand van de resultaten van vier studies de nauwkeurigheid van het Duplex concept in combinatie met spectraal-analyse besproken. In de eerste studie wordt het snelheidsprofiel van de arteria carotis communis gebruikt om de nauwkeurigheid van het registreren van arteria interna afwijkingen te verhogen. Het normale arteria carotis communis profiel vertoont een continue voorwaartse stroomrichting gedurende de diastole fase. Deze continue voorwaartse stroomrichting blijkt in drie situaties niet aanwezig te zijn: (1) bij patiënten met een totale occlusie van de arteria carotis interna; (2) bij patiënten met een 90-99% diameterreductie van de arteria carotis interna; en (3) bij patiënten met centrale pathologie, niet gerelateerd aan arteria carotis interna afwijkingen. In deze laatste categorie is de voorwaartse stroomrichting beiderzijds niet aanwezig. Met de waardering van de veranderingen in het snelheidsprofiel van de arteria carotis communis, is de nauwkeurigheid van het diagnostiseren van totale occlusies toegenomen.

De tweede studie geeft aan de hand van een vergelijkende studie de nauwkeurigheid van het Duplex concept in combinatie met spectraal-analyse. Gebruik makend van een "short focus" transducer is de overeenstemming tussen Duplex en arteriografie 50% voor categorie A (0% diameter-reductie), 69% voor categorie B (5-15% diameterreductie), en 70% voor categorie C (16-49% diameterreductie). Gebruik makend van een "medium focus" transducer is de overeenstemming tussen Duplex en arteriografie, 94% voor categorie D (50-99% diameterreductie) en 93% voor categorie E (totale occlusie).

De resultaten van dit vergelijkende onderzoek tonen aan dat het niet-invasieve onderzoek 50-99% diameterreducties en totale occlusies met een hoge nauwkeurigheid registreert. Het scheidend vermogen tussen een normale arteria carotis interna en een 5-15% diameterreductie zou theoretisch kunnen worden vergroot door de totale hoeveelheid bloed per tijdseenheid dramatisch te verhogen. Teneinde het snelheidsprofiel van een normaal carotis systeem te kunnen beoordelen bij een toename van de totale bloedstroom werd in de derde studie bij vijf gezonde proefpersonen voor en tijdens CO₂-inhalatie een Duplex studie verricht. Ten gevolge van de CO₂-inhalatie trad bij alle proefpersonen, als uiting van een vermindering van de stabiliteit van de bloedstroom, een verbreding van het spectrum in het snelheidsprofiel op. Alvorens de waarde van dit fenomeen

te kunnen beoordelen, zal de studie eveneens verricht moeten worden met patiënten bekend met een 5-15% diameterreductie van de arteria carotis interna.

In de vierde studie wordt een nieuwe parameter geïntroduceerd, met behulp waarvan afwijkingen in de 50-99% diameterreductie categorie kunnen worden herverdeeld. Met deze parameter blijkt het mogelijk een 90-99% diameterreductie categorie te creëren, waardoor toename van arteriosclerotische afwijkingen in follow-up studies voor de 50-99% diameterreductie categorie kunnen worden gedocumenteerd.

Hoofdstuk 6 bestaat uit vier klinische studies die de invloed en betekenis van het gebruik van het Duplex principe in patiënten populaties evalueren.

In de eerste studie wordt de invloed van het niet-invasieve onderzoek op de verdere behandeling van patiënten met neurologische symptomen besproken. Het vermelden van een 50-99% diameterreductie van de arteria carotis interna blijkt, onafhankelijk van het klachtenpatroon, de kans op arteriografisch onderzoek significant te verhogen.

De tweede studie registreert het voorkomen van afwijkingen in de arteria carotis interna bij patiënten met een asymptomatische soufflé in de hals. Van de 142 carotis-bifurcaties met een soufflé in de hals wordt de arteria carotis interna in 2% geclassificeerd als normaal, in 30% met een 5-15% diameterreductie, in 37% met een 16-49% diameterreductie, in 29% met een 50-99% diameterreductie en in 2% met een totale occlusie. Als een hemodynamisch significante stenose een indicatie is voor contrast-arteriografie in patiënten met een asymptomatische soufflé, kan het niet-invasieve onderzoek dit invasieve onderzoek 71% van de patiënten besparen.

In de derde studie wordt het voorkomen van carotis afwijkingen, in patiënten die coronair chirurgie ondergaan, gedocumenteerd. In 6% van de patiënten zonder neurologische symptomen werd een 50-99% diameterreductie van de arteria carotis interna geregistreerd. De optredende peri-operatieve neurologische complicaties waren niet gerelateerd aan het voorkomen van hemodynamisch significante stenosen.

In de vierde studie worden hemodynamische veranderingen geregistreerd in patiënten die carotis chirurgie hebben ondergaan. De resultaten van deze studie tonen aan dat een postoperatieve restenosering over het algemeen asymptomatisch verloopt en relatief frequent optreedt.

Hoofdstuk 7. In de algemene discussie worden de belangrijkste bevindingen van hoofdstuk 4 en 5 nader besproken. De resultaten van de eerste vier studies tonen aan, dat het niet-invasieve Duplex onderzoek in combinatie met spectraal-analyse nauwkeurig arteria carotis interna afwijkingen registreert. De methode is principieel superieur aan elke indirecte methode door de nauwkeurigheid waarmee een hemodynamische significante stenose kan worden onderscheiden van een totale occlusie. De vier studies van hoofdstuk 6 demonstreren de klinische waarde van een nauwkeurig niet-invasief onderzoek voor de carotis-bifurcatie afwijkingen.

Toekomstig werk met de Duplex scanner dient te zijn gericht op het verbeteren

van het scheidend vermogen tussen een normale arteria carotis interna en een arteria met minimale artériosclerotische afwijkingen. Verder zullen een aantal follow-up studies worden verricht ten einde een beter inzicht te krijgen op het natuurlijke verloop van arteriosclerotische carotis-bifurcatieafwijkingen.

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Curriculum Vitae

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