Evaluation of a Novel Technique to Diagnose Carotid Artery Stenosis (CAS)

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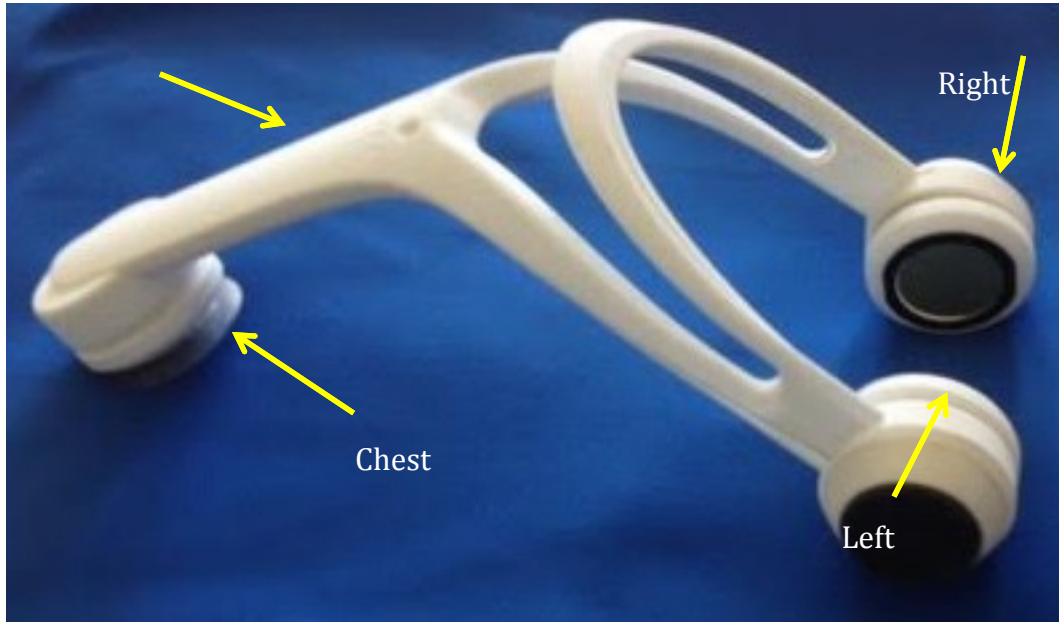Department of Cardiovascular Medicine
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Introduction:
Carotid atherosclerotic disease is associated with TIA, stroke and increased risk of major vascular events (1, 2). The prevalence of asymptomatic internal carotid artery (ICA) stenosis is low, but it increases with age (3). Other pathological disease states may involve the internal carotid arteries, such as fibromuscular dysplasia (FMD) and cervical artery dissection, and have distinguishing features on diagnostic imaging studies. The extracranial ICAs can be evaluated by different non-invasive modalities, namely carotid duplex ultrasound, MRA, and CTA. Each of these modalities has characteristic advantages and disadvantages, and each varies with regard to requirements for technology and trained technical and interpretive personnel. Catheter-based angiography is the gold standard for diagnosis and assessment of severity of ICA stenosis due to atherosclerotic disease or non-atherosclerotic pathologies, but is generally reserved for cases of uncertain or discrepant non-invasive testing or when intervention is indicated.

Screening for ICA stenosis could be used to identify patients at risk for cardiovascular events for whom cardiovascular risk reduction medical therapies may be considered, and to identify patients with significant ICA stenosis for whom additional imaging surveillance or revascularization (for severe ICA stenosis) may be indicated. Currently, carotid duplex ultrasound must be performed by a trained and certified vascular technologist using advanced duplex imaging equipment and with subsequent interpretation by a trained physician. It would be of value to develop an accurate, reliable, low cost, and easily accessible tool to screen for extra-cranial ICA disease in an office based setting. However, such a tool would require novel technology that allows for quick, accurate, reproducible, and safe evaluation.

This study will evaluate a new technology called the Carotid Stenotic Scan (CSS) developed by CVR Global, a medical device company. The CSS device uses principles of cardiovascular resonance to detect low frequency pressure fluctuations associated with

flow disturbances in areas of significant arterial narrowing. The CSS device consists of three non-emitting (passive) piezoelectric sensors contained in a cushioned gel pad, linked through a Y-shaped collar that positions one sensor over each carotid artery and one sensor on anterior central chest in the area of the heart (figure). These device pads lie on the skin surface and do not emit any energy into the body; they only gather data transmitted from within the body. The piezoelectric sensors in the device detect very low frequency pressure fluctuations generated by altered hemodynamics caused by narrowing

of the carotid artery. The CSS scan takes about 1-2 minutes to gather data for real-time analysis by the processor on the device cart.

Description: Prospective study of evaluable patients presenting to the Cleveland Clinic Non-Invasive Laboratory for a clinically indicated complete carotid duplex ultrasound examination. We aim to enroll 300 subjects. We will enroll at least 100 patients who have moderate stenosis of one ICA based on prior ultrasound studies and up to 25 patients with known carotid FMD. Subjects who enroll in the study will undergo evaluation by both carotid duplex ultrasound and the CSS device. Carotid duplex studies will be read by a registered physician in vascular interpretation, blinded to the CSS device result, and degree of ICA stenosis will be determined according to velocity criteria adopted by Cleveland Clinic Non-Invasive Vascular lab. Findings from CSS device will be analyzed and degree of ICA stenosis will be categorized.

Objectives:
1. To determine agreement of degree of internal carotid artery narrowing as measured by the CSS device versus carotid duplex ultrasound.
2. To determine the reproducibility measures of carotid artery narrowing as measured by the CSS device.
3. To compare the degree of carotid artery narrowing as measured by the CSS device versus any other imaging modality used to evaluate the internal carotid artery (CTA, MRA or catheter based angiography) (pilot analysis)

4.   Exploratory data regarding CSS device output in the setting of carotid artery occlusions and fibromuscular dysplasia (FMD).

Study Subjects:
The study population will consistent of adult patients ($\geq$ 18 years) presenting to the Cleveland Clinic Non-Invasive Vascular Laboratory for a scheduled carotid duplex ultrasound to evaluate for carotid artery disease or in follow-up of known ICA stenosis. By design, we will enroll at least 100 patients who are known to have at least moderate stenosis of one ICA (i.e., PSV $\geq$ 125 cm/sec based upon the findings of prior imaging studies. In addition, a subset of up to 25 patients enrolled will include those with previously documented fibromuscular dysplasia of at least one ICA. Potentially eligible patients will be approached in the area where the ultrasound testing will be done by a qualified member of the study team prior to the ultrasound examination to explain the study and obtain appropriate informed consent.

Inclusion Criteria:
- Outpatients age $\geq$ 18 years sent to the vascular laboratory for carotid duplex examination for initial carotid ultrasound study or for follow-up of known carotid disease.
- Enrolled patients will include at least 100 subjects with at least moderate known stenosis (50-69% or greater, PSV $\geq$ 125 cm/sec) or occlusion of one or both ICAs
- Up to 25 patients with **known** fibromuscular dysplasia (FMD) of the internal carotid arteries.

Exclusion criteria:
- Age < 18 years.
- Hospitalized inpatients.
- Inability to provide informed consent.
- Prior history of carotid endarterectomy or carotid artery stent.
- Prior neck surgery
- Known prosthetic heart valve, known critical aortic stenosis, or study indication "preop" open heart or aortic surgery.

Study Visit Procedures: The research study will be conducted on the same day of the clinical carotid duplex study but may be performed prior to or after the scheduled carotid ultrasound (and any other vascular) examination(s), depending upon the patient schedule. After informed consent is obtained, limited medical history will be obtained, and self-reported height and weight will be recorded. The patient will undergo the standard of care carotid duplex examination and the CSS study procedure. Each subject will have a unique identifier number assigned that will be used on all ensuing study documents.

Medical History:

Data will be obtained by limited subject questionnaire and review of the electronic medical record, to include:

- Age on date of the study
- Sex
- Race, ethnicity
- Height and weight (self-reported)
- Study indication (first carotid duplex in lab, surveillance of known carotid artery stenosis, fibromuscular dysplasia, other)
- Treated medical conditions, including:
- Coronary artery disease (History of myocardial infarction, angina + abnormal stress test, or prior coronary artery bypass grafting or stenting/PCI)
- History of congestive heart failure
- Left ventricular ejection fraction (if known and date of echocardiogram within the past 1 year)
- Known peripheral artery disease (PAD)
- History of transient ischemic attack
- History of stroke
- Did patient have TIA, stroke or symptoms of retinal ischemia within 30 days of ultrasound study
- Hypertension requiring medication therapy
- Hyperlipidemia requiring medication therapy
- Diabetes requiring medication therapy or diet
- History of smoking cigarettes (> 100 in lifetime)
- Known diagnosis of fibromuscular dysplasia
- Known history of internal carotid artery dissection
- History of COPD
- Any correlative imaging studies (CTA, MRA, angiography) within 1 month prior to the day of the carotid duplex examination

Follow-up and Correlative Examinations:

Within 3 months (+/- 7 days) following the date of the study visit, the electronic medical record will be queried for any interval correlative imaging studies (CTA, MRA, or angiography) and reports performed up to 1 month prior and 3 months after the duplex examination date. Report of findings well be document (i.e., % ICA stenosis by CTA/MRA).

Study Procedures (Appendix B)

Standard Clinical Procedures:

The subject will undergo the clinically ordered clinical carotid duplex ultrasound as part of standard of care. Studies are performed using a standardized scanning protocol (Appendix C) by a Registered Vascular Technologist and interpreted by a Registered

Physician in Vascular Interpretation or otherwise qualified member of the medical staff. The vascular technologist and interpreting physician will be blinded to the output of the CSS study device.

- For purposes of this study, degree of ICA stenosis will be reported according to SRU consensus velocity criteria., Primary SRUCC parameter to determine % ICA stenosis will be peak systolic velocity, unless there is a clear indication for the use of a secondary parameter (ICA/CCA ratio, EDV), such as contralateral occlusion, tandem lesions, discrepancy between visual assessment of the plaque and PSV and others(4).

SRU Consensus Criteria (4)

	Primary Parameters		Secondary Parameters	
Degree of stenosis (%)	ICA PSV (cm/sec)	Plaque Estimate (%)*	ICA/CCA PSV Ratio	ICA EDV (cm/sec)
Normal	< 125	None	<2.0	<40
< 50	< 125	<50	<2.0	<40
50-69	125-230	≥50	2.0-4.0	40-100
≥ 70 but less than near occlusion	>230	≥50	>4.0	>100
Near occlusion	High, low, or undetectable	Visible	Variable	Variable
Total occlusion	Undetectable	Visible, no detectable lumen	Not applicable	Not applicable

*Plaque estimate (diameter reduction) with gray-scale and color Doppler US.

- Degree of stenosis per the Cleveland Clinic Non-invasive Vascular Laboratory will also be recorded (ECST based):
    - 0-19% stenosis PSV < 105 cm/sec no plaque
    - 20-39% stenosis PSV < 105 cm/sec plaque visualized
    - 40-59% stenosis PSV 105 – 150 cm/sec
    - 60-79% stenosis PSV > 150 cm/sec but EDV ≤ 135 cm/sec
    - 80-99% stenosis PSV > 240 cm/sec and EDV > 135 cm/sec
    - Occlusion – absent flown on extensive Doppler interrogation
    - Ultrasound features of carotid FMD (increased velocity and turbulent flow mid to distal ICA).

The following ultrasound parameters will be recorded for each side:
- Distal CCA peak systolic velocity
- Highest origin/proximal to mid ICA peak systolic velocity (PSV)
- Associated end diastolic velocity (EDV) for highest PSV
- ICA/CCA PSV Ratio
- Presence of plaque in the ICA (defined as wall thickness ≥ 1.5 mm)
- Presence of distal ICA waveform dampening (qualitative)

- Presence of post-stenotic spectral and/or color Doppler turbulence
- SRU Consensus Criteria % ICA Stenosis
- Cleveland Clinic Criteria % ICA Stenosis

For FMD subset: highest ICA mid/distal PSV and associated EDV

CSS Study Procedures:
Subjects will have a noninvasive CSS assessment as described below before or after the carotid duplex ultrasound. It is expected that the entire CSS evaluation will take approximately ten minutes. See Appendix A for the CSS Study Procedure.

Study Data Collection
Each subject will have a hard copy file with case report information and source documents, medical history questionnaire, CSS output, and the ultrasound reports. These individual files will be maintained with identifiers, including the signed consent form, and maintained in a locked filing cabinet accessible to the study coordinator and the authorized investigators. A Redcap database will be developed and maintained for clinical data entry and this will be housed on a password-protected network. All data that the sponsor receives will either be aggregate data or de-identified case report files. Deidentified ultrasound images and de-identified correlation study images and report may be requested by the sponsor for cases in which CSS results and duplex findings were discrepant.

Statistical Analysis Plan and Power Calculation: Primary analysis % agreement CSS and carotid duplex ultrasound (SRUCC interpretation) for ICA stenosis. Agreement will be assessed using the intraclass kappa coefficient (and corresponding 95% confidence intervals) for categorical data. Percent stenosis from both the CSS measurement and the duplex ultrasound will be categorized as follows:

Carotid Duplex by SRU Consensus	Simplified Duplex Category by SRU Consensus	CSS Device
Normal	<50%	<50%
<50%	<50%	<50%
50-69%	50-69%	50-69%
≥70%	≥70%	≥70%
Occlusion	Occlusion	Exploratory data
U/S Features of FMD	FMD	Exploratory data

It is anticipated that approximately 40% of total patients will have an ICA stenosis of 50% or greater. A sample of at least 300 patients (up to 500 carotid arteries) will have 90% power to detect an intraclass correlation coefficient of 0.80, assuming a null hypothesis of 0.65, with a 2-sided alpha of 0.05.

The secondary endpoint of reproducibility of the CSS measurement will be analyzed using the continuous stenosis measurement. Each CSS measurement will be repeated and the Intraclass Correlation Coefficient (ICC) will be calculated. The ICC in an index of the reliability of measurements from the same operator. Pearson and/or Spearman correlation coefficients and plots may also be produced.

Separate exploratory analyses will address the following:

1) Correlation of CSS results to duplex ultrasound results in those with ICA by duplex occlusion
2) Correlation of severity of stenosis from CTA, MRA, or catheter based angiography (when available) to CSS results.
3) Correlation of CSS stenosis results to duplex ultrasound results in those with known ICA FMD (approximately 25 patients)

Data and Safety Monitoring
This protocol poses no physical risk and the need for a formal Data Safety and Monitoring Board (DSMB) is not anticipated. However, reporting of any adverse events will follow the standard procedures of Cleveland Clinic. The only risk to the subject is loss of confidentiality and this will be protected to the best of the sponsor's ability.

Potential Risks: This is a low risk protocol. The CSS devise is non-invasive and passive and does not cause any discomfort. The only risks relate to confidentiality and the study team will minimize these risks as discussed above. In the unlikely event of a study-related adverse event, the Principal Investigator, IRB and CVR Global will be notified.

Potential Benefits
There will be no direct benefit to the subject for participation, though study participants will receive a parking pass. There may be benefit to society as a whole when the accuracy and efficacy of the device as a rapid, noninvasive means to diagnose carotid artery disease has been shown.
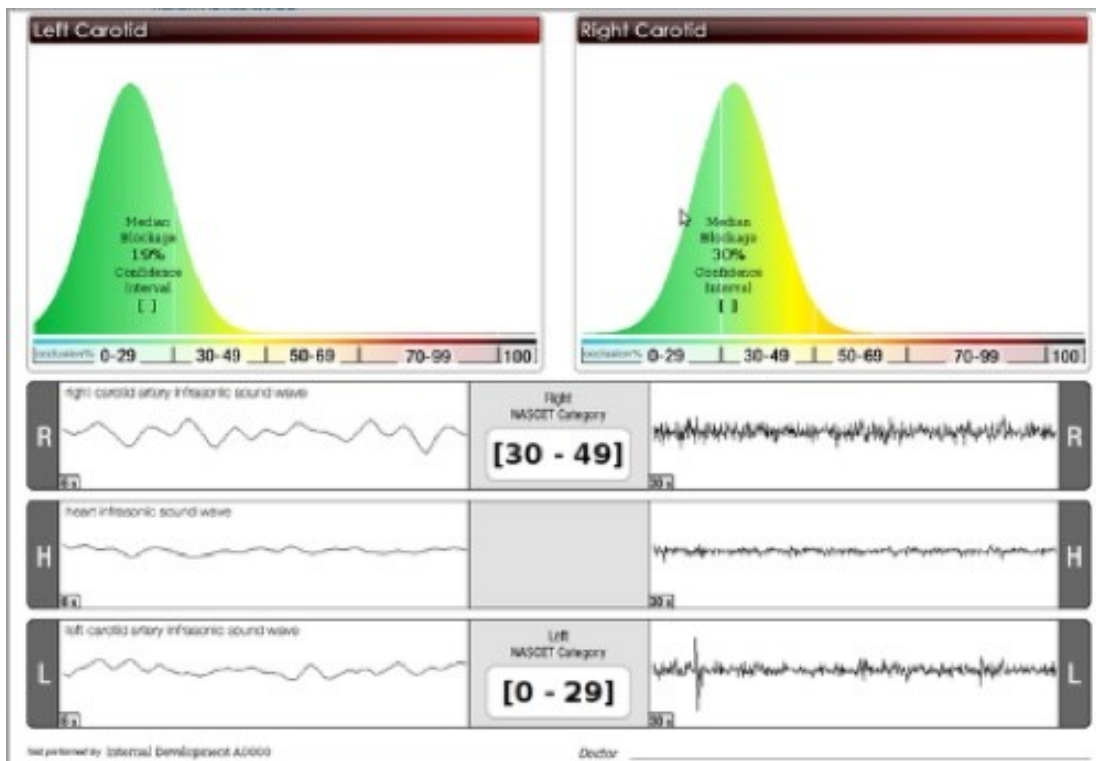
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APPENDIX A
CSS STUDY PROCEDURE
Study is performed with patient in a seated position (chair)

1. Prior to placement on the subject's neck, wipe the device clean and place clean unused gel packs over the piezoelectric sensors. Have the subject sit upright and straight in a comfortable chair.

2. Open a new subject file in the CSS device program and enter the assigned subject number.

3. Place the device on the subject assuring good contact over each carotid artery (just at or above the bifurcation) and the anterior chest wall.

4. Verify on the display that the device is sensing the signals.

5. Instruct the subject to sit very still and breathe quietly while holding the collar component of the device.

6. Select the "Start" button on the display touch screen for signal verification to begin; once the device notes signal verification select the "Start" button again.

7. After 30 seconds of uninterrupted recording, stop the scan and have the subject release the collar device.

8. To test for reproducibility, repeat steps (1) through (7) one more time.

Typical output display at end of CSS test (subject to change as software is developed)

APPENDIX B:
CSS STUDY VISIT CHECKLIST

Inclusion (all must be answered "YES"/checked off):
□ Patient at least 18 years old
□ Seen as an outpatient
□ Scheduled for a carotid duplex ultrasound examination for initial or follow-up evaluation of known carotid disease
□ Able to give informed consent in English

Patient known to qualify for subgroup?:
□ At least moderate stenosis (PSV > 125 cm/sec) or occlusion of one or both ICAs on a prior CCF duplex study
□ Known fibromuscular dysplasia of one or both ICAs

□**Exclusion criteria checked (confirm none of the following are true):**
•   Prior history of carotid endarterectomy or carotid artery stent
•   Prior history of prosthetic heart valve
•   Known critical severe aortic stenosis (AVA < 1 cm/sec)
•   Indication for carotid duplex ultrasound is "pre-op" for open heart surgery or aortic surgery
•   Prior neck surgery

Study Procedures:
□ Informed consent complete and copy given to patient
□ Generate subject ID number
□ Medical history form, height and weight
□ Carotid duplex ultrasound study completed (can be done before or after consent or CSS exam)
□ 5 minute rest period
□ 1st CSS measurement
□ 2nd CSS measurement
□ Validate parking
□ Code database form

_____   _____
Research Coordinator/ Investigator Signature   **Date**

APPENDIX C: Cleveland Clinic Non-Invasive Laboratory Carotid Duplex Examination Protocol (Native Carotid Arteries)

EXTRACRANIAL CAROTID DUPLEX ULTRASOUND

I. PURPOSE
Duplex scanning permits accurate localization of disease in the extracranial carotid and vertebral arteries. Spectral analysis of velocity waveform permits accurate classification of disease in the internal carotid artery into categories based on the extent of diameter reduction.

II. INDICATIONS
    A. Transient ischemic attack (TIA)
    B. Asymptomatic cervical bruit
    C. Stroke/cerebrovascular accident (CVA)
    D. Suspected subclavian steal
    E. Screening of patients prior to cardiac or vascular surgery with asymptomatic bruit or high risk for carotid artery stenosis
    F. Post carotid intervention patients (endarterectomy, stent, etc.)
    G. Pulsatile mass in either the carotid or subclavian region
    H. Follow up studies on patients with known carotid disease
    I. Suspected carotid artery dissection

III. LIMITATIONS
    A. Recent neck surgery (i.e., endarterectomy)
    B. Patients who are unable to lie flat or still may prove difficult to scan
    C. Patients with very thick, muscular necks are a challenge. Note: Asking the patient to reach for his/her hips may help to bring the shoulders down and out of the way
    D. Patients with mental status issues unable to cooperate with the Examination
    E. Bedside exams which may limit access to the patient or his/her anatomy

IV. PATIENT PREPARATION
    A. Review report and/or images of any prior examinations in the vascular lab.
    B. Explain the examination to the patient and why it is being performed.
    C. Patient history is obtained for relevant vascular information (e.g., prior endarterectomy or stenting).
    D. Answer any questions or concerns the patient may have before proceeding.
    E. Patient should be positioned in a manner that allows for maximum access to the vessels being examined.

V. PROCEDURE: GENERAL CONSIDERATIONS
    A. *Technique*: Reproducible and constant velocity measurements require that the data be obtained in the same manner at each site and time. Since the criteria for the disease states are based on spectral velocity waveforms, it is of the utmost

importance that the protocol be adhered to as closely as possible. Bilateral studies are critical for a complete exam. A limited study should be performed only in very special circumstances (e.g., intra-operative carotid examination).

B. *Angle*: A constant angle measurement should be maintained between the ultrasound beam and the axis of the vessel and/or direction of flow. The axis of the vessel is defined as an imaginary line drawn parallel to the vessel wall. The angle cursor should be placed in this position before recording a spectral waveform. The classifications for disease used in this protocol were validated using a constant angle of 60 degrees. In tortuous vessels where obtaining a 60 degree angle may be difficult, take the most favorable angle close to 60 degrees and always document it for future studies. Never take spectral waveforms at angles above 60 degrees, as the cosine value changes rapidly, and small errors in angle measurements cause large errors in the peak velocity calculations.

C. *Sample volume size*: Keep the sample volume as small as possible to obtain the most discrete spectral information. In the case of an occlusion or a very tight lesion, the sample volume may be increased to help locate the flow channel.

D. *Sample volume placement*: Place the sample volume in the center of the vessel or the flow channel.

E. *Scan planes*: The examination should include multiple views (anterior, lateral, postero-lateral) of the vessels in both the longitudinal and transverse planes. Doppler velocity waveforms should be generated from the longitudinal plane, which provides the most favorable angles between the Doppler ultrasound beam and the axis of the vessels.

F. *Documenting stenosis*: The classifications of disease are based on locating the highest peak systolic and end-diastolic velocities. It is essential that the sample volume be moved throughout the area of stenosis. **Stenotic segments** should be **documented with spectral waveforms for three locations**.
   1. **Pre-stenotic waveform** (it may be a dampened signal)
   2. **Stenotic waveform** (taken at the point of maximum velocity)
   3. A **post stenotic waveform** (demonstrates post stenotic turbulence) This waveform should be identified with every high-grade stenosis to verify a true velocity increase attributable to a stenosis.

VI.   PROCEDURE: TEST PROTOCOL
   A. *Patient setup*: The test is performed with the patient supine with a small towel placed under the neck for support. The technologist is seated at the head of the bed. The patient's head is slightly hyperextended and turned toward the contralateral side. The head position can be changed to optimize visualization of the vessel.
   B. *Scan technique*: A study of the carotid system should be evaluated with grayscale and color and spectral Doppler analysis. In grayscale, plaque should be described by echo characteristics (e.g., homogeneous, heterogeneous) as well as by surface characteristics (e.g., smooth, irregular). With color Doppler waveform and spectral analysis, areas of narrowing within the lumen, color disturbances or absence of color flow should be noted. The sample volume of the Doppler should be moved continuously throughout the length of the vessel searching for regions of

increased velocity or flow disturbance. It is important to note that a stenosis may be very focal and the flow distal to it may normalize over a short distance. The sample volume must not be skipped around but rather moved methodically through the vessel. Spot recordings of velocity waveforms may overlook a significant lesion. Color flow imaging facilitates the identification of anatomy, areas of interest, and the area of greatest stenosis.

C. *Transducers*: Selected based on vessel depth while allowing for the best display of both grayscale and color and spectral Doppler imaging.

D. *Common carotid artery*: The artery is evaluated throughout its length for the presence of visible plaque, tortuosity, and changes in the velocity. A spectral waveform should be taken from the most proximal segment of the vessel, mid, and distal segments. The characteristic of the waveform is that of a low-resistance vessel. The end-diastolic velocity should be above the baseline. In the proximal common carotid artery waveform, a higher resistive or hybrid type signal may be seen, but the distal common carotid artery waveform should have a low-resistance pattern. Important hemodynamic information from the common carotid artery may indicate proximal or distal disease. If there is a high-grade stenosis of the internal carotid artery or a total occlusion, the blood will be shunted through the external carotid artery. The common carotid will take on the characteristics of the external carotid artery with flow of zero or very close to zero in end-diastole. In the presence of a significant stenosis at the origin of the common carotid artery, the ipsilateral common carotid artery may be dampened with low velocity and a slower slope to peak systole compared with the contralateral common carotid waveform. The ipsilateral common carotid waveform may also appear post-stenotic in character.

E. *External carotid artery*: The external carotid supplies the structure of the face, neck, and scalp. The waveform has a sharp upstroke to systole, followed by a prominent dicrotic wave, which may reverse at end-systole/early diastole, and velocities reaching zero in end-diastole (waveforms rest on the baseline). The peak systolic velocity of the external carotid is normally higher than that of the internal carotid artery. Branches may be visualized near the origin, which may help distinguish the external carotid from the internal carotid, which has no branches in the neck. The use of superficial temporal oscillation ("temporal tap" maneuver) can help distinguish the external carotid artery from the internal carotid artery by causing a disturbance in the spectral Doppler waveform. The external carotid artery normally will lie in an anterior medial plane.

F. *Carotid bulb*: The bulb is usually located in the proximal portion of the internal carotid artery; however, the location is variable. The normal flow patterns become complicated as the blood moves through the dilation and the angled branches of the bifurcation. These normal anatomic features cause a flow separation and reversal of flow at the outer walls. The profile of waveforms taken across the bulb usually demonstrates unidirectional flow along the divider of the bifurcation, and a transient reversal of flow at

peak systole near center stream, and at the outer wall opposite the flow divider.

G. ***Proximal to mid internal carotid artery***: The characteristic Doppler waveform is that of a low-resistance vessel. The normal flow disturbances of the carotid bulb may extend into the mid segment and be reflected in the waveform. The mid internal carotid artery waveform is generally taken distal to the normally placed bulb in an area where the vessel is no longer dilated. The carotid artery normally will lie in a posterior/lateral plane.

H. ***Distal internal carotid artery***: The distal internal carotid artery is that segment of the vessel beginning at least three (3) cm above the bifurcation. Atherosclerosis will usually develop in the first two (2) cm of the internal carotid artery and rarely will be seen in the distal internal carotid artery. The distal internal carotid artery typically will dive away from the transducer or will be tortuous and difficult to visualize. Caution should be used in this area because of inaccurate angle measurements, which may lead to overestimation of velocity increases and hence misdiagnosis of stenosis. There are cases where true increases in velocity are detected in the distal internal carotid artery. Fibromuscular dysplasia, (which causes the typical string of beads appearance of the vessel) develops in this region. To fully evaluate for fibromuscular dysplasia, a lower-frequency curved array transducer should be used to scan high in the neck.

   A high resistance waveform suggests a change in resistance of the distal vascular bed. It may suggest the presence of a significant siphon lesion, intracranial stenosis, or distal carotid dissection.

   The internal carotid waveform may also be found to have markedly elevated end-diastolic velocities in comparison with the contralateral internal carotid artery. The elevation in overall flow rate will be noted throughout the common carotid as well. This pattern of flow may indirectly suggest a decrease in the resistance of the distal vascular bed as in the presence of a distal arteriovenous malformation.

I. ***Vertebral artery***: The origin of these vessels from the subclavian artery lie deep under the clavicle and are difficult to scan. The vertebrals can be small, tortuous, and asymmetric in size.

   The scanhead is initially placed low in the neck, and the common carotid artery is identified as a landmark. The scanhead is then moved out laterally and tipped inferiorly. The vertebral artery may then be seen lying deep to the common carotid. Color Doppler helps to readily locate the vertebral arteries, followed by a confirmation with the spectral waveform. The typical spectral waveform from a vertebral artery is that of a low-resistance vessel similar to the internal carotid artery. The vertebral artery is assessed for its flow direction (antegrade or retrograde). Subclavian stenosis or occlusion at its origin may cause the vertebral artery flow to reverse direction to supply the arm (subclavian steal). Proper identification of the direction of flow is important. A blunted, post-stenotic waveform in the vertebral artery should prompt investigation for more proximal stenosis.

J. *Subclavian artery*: The subclavian artery is located under the clavicle and is difficult to access with some transducers. The flow velocity in the subclavian artery is classically peripheral in its character. It should have the typical triphasic character, a forward systolic component, a reversal component in late systole/early diastole, and a second forward component in late diastole.

K. *Innominate artery*: The innominate artery is the first branch that arises from the aortic arch. The distal portion of the artery can be accessed from above the clavicle. The proximal and mid portions of the vessel cannot typically be visualized due to bony structures. The transducer can be angled transversely down into the sternoclavicular notch giving sight to the distal portion of the vessel.   The Doppler spectral appearance is triphasic in character.

VII: PLAQUE CHARACTERISTICS

Sonographic images of atheromatous carotid plaques should be carefully evaluated to determine plaque extent and location, severity, surface contour, and texture. Most importantly, the plaque texture should be classified as appearing either homogeneous or heterogeneous. A diagnosis of ulcerative plaque cannot be made accurately by merely identifying that the plaque surface is irregular.

Homogeneous plaque usually has a smooth surface, and its uniform acoustic texture corresponds pathologically to dense fibrous connective tissue. Heterogenous plaque may have either a smooth or irregular surface and its complex acoustic appearance can be associated pathologically with the presence of intraplaque hemorrhage.

Surface characteristics

Smooth: Intimal surface appearance is continuous and shows no irregularities

Irregular: Intimal surface is discontinuous and is not completely smooth

Ulcerated: Ulcer cavity with blood flow within a plaque seen on multiple planes of view

Plaque textures

Homogeneous: Homogeneous plaques usually produce a uniform echo pattern. The surface of homogeneous plaques is usually smooth.

Heterogeneous: Heterogeneous plaque has a complex echo pattern that contains at least one focal sonolucent area. The intimal surface may be either smooth or irregular. Acute hemorrhage can, at times, be identified by a pattern of plaque containing a large sonolucent area. A false diagnosis of intraplaque hemorrhage may occasionally be made if there are large deposits of lipids within the plaque.

Calcified: Heterogeneous (dense) plaque with very bright and highly reflective echoes. This plaque contains areas of calcium that produces acoustic shadowing.

This shadowing causes an interruption in the color and spectral Doppler waveform signal which may result in an erroneous calculation in the percentage of stenosis.

VIII: VERTEBRAL ARTERIES

The characteristics of the Doppler spectrum obtained from the vertebral artery are those of a scaled-down internal carotid artery (see pp. 3-4 for examples). The intracranial circulation is a low-resistance flow bed: consequently, the flow waveform has a sharp well-defined systolic peak followed by a gradual fall off in flow velocity through diastole. In normal circumstances, antegrade flow is maintained throughout the cardiac cycle.

1. If no flow is detected when the Doppler sample volume is placed in the mid point of the artery, this is diagnostic for vertebral artery occlusion.
2. If retrograde flow is present, this is diagnostic of subclavian steal.
3. Bi-directional flow can be indicative of a stenosis in the proximal subclavian artery. This is consistent with an incomplete subclavian steal.
4. In the setting of a more proximal subclavian or vertebral artery stenosis, there can be a blunted vertebral artery waveform (parvus-et-tardus) or a "bunny rabbit" pre-steal waveform which can be seen prior to bi-directional flow.
5. High velocities can occur when the vertebral artery is providing compensatory flow for an occlusive lesion elsewhere in the cerebral vascular system.
6. Loss of diastolic flow in a vertebral artery ("high resistive" waveform) may indicate distal vertebral artery or basilar artery (if bilateral) stenosis or occlusion.

DIAGNOSTIC CRITERIA
I. Internal Carotid Artery (ICA) Interpretation:

Classifications of Internal Carotid Artery Stenosis

Diameter Reduction	Peak Systole	End Diastole	Flow Character and Grayscale
0 – 19%	<105 cm/sec	*	Mild spectral broadening during the deceleration phase of systole
20 – 39%	<105 cm/sec	*	Plaque present Spectral broadening present
40 – 59%	105-150 cm/sec	*	Plaque present Increased spectral broadening
60 – 79%	>150 cm/sec	*	Plaque present Marked spectral broadening present
80 – 99%	>240 cm/sec	and >135 cm/sec	Plaque present Marked spectral broadening present
Occluded	N/A	N/A	No flow signal. A characteristic "thump" may be noted at the stump or origin of the occlusion. Common carotid artery diastolic component low or reversed flow

*End-diastolic velocity values are only used as stenosis classification for 80-99% diameter reduction lesions. *A lesion associated with PSV > 240 cm/sec but EDV < 135 cm/sec is generally a 60-79% stenosis.*

Note: This classification is only accurate for predicting the amount of diameter reduction in the **first 3 cm of the internal carotid artery**. It is not reliable for accurately predicting disease in the external carotid artery or in the setting of fibromuscular dysplasia. The statement **"ultrasound features consistent with fibromuscular**

dysplasia" will be used when **turbulent flow and a velocity shift** are noted in **mid or distal ICA and/or beading** is present.

Note: When a patient does **not have plaque present**, but has **elevated velocities** throughout the ICA and the CCA (i.e., normal ICA/CCA ratio <2) the statement **"elevated velocities, no plaque seen. Likely normal study"** will be used in place of calling a category of stenosis.

*Note***:** Although our criteria are based upon PSV and EDV, ICA/CCA ratios are included on our reports. These **criteria are added** for use in interpretation of cases in which **PSV may not accurately reflect the degree of stenosis** (e.g., tandem lesions in innominate or CCA, contralateral occlusion, and elevated velocities in all vessels due to underlying cardiac disorder). In general, an ICA/CCA ratio of > 4 is suggestive of a > 70% stenosis (NASCET criteria).

Note: In the setting of a contralateral ICA occlusion, there is potential for overestimation of stenosis due to compensatory flow. This should be noted in the interpretive report when appropriate (e.g., velocities in 80-99% category contralateral to occlusion).

II. Common carotid artery interpretation:
50-99% stenosis   Velocity shift with doubling of PSV across an area of plaque

III. External carotid artery interpretation:
Elevated velocities, plaque noted   PSV > 200 cm/sec with significant plaque
                                             visualized

IV. Subclavian artery interpretation:
50-99% stenosis   Velocity shift with doubling of PSV across an area of plaque
                     or PSV > 275 cm/sec in proximal subclavian artery with turbulent
                     flow and plaque noted
If turbulent flow is present but no plaque is visualized, findings may suggest more proximal subclavian artery stenosis

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DOCUMENTATION

DOPPLER:

Common:	Right origin, proximal, mid, and distal vessel
	Left proximal, mid, and distal (origin if possible) vessel
Internal:	Origin, proximal, mid, and distal (as far distal as possible) vessel
External:	Origin
Vertebral:	Mid vessel
Subclavian:	Right origin, left proximal
Innominate:	Distal (if possible)

Grafts: Proximal, mid, distal and anastomotic sites

GRAYSCALE:
- Common
- External
- Internal
- Grafts: anastomosis sites and body

COLOR POWER ANGIOGRAPHY (CPA):
- Suspected occlusion

ADDITIONAL NOTES
ANY TIME A **VELOCITY SHIFT IS IDENTIFIED IN **ANY** VESSEL, THE AREAS PROXIMAL TO THE SHIFT, AT THE SHIFT, AND DISTAL TO THE SHIFT SHOULD BE DOCUMENTED

***For incidental finding of thyroid nodule: report maximal diameter of nodule and use standard reporting language to suggest dedicated thyroid ultrasound.

URGENT VALUE NOTIFICATION
The following urgent values require **direct verbal communication** with the ordering provider or service:
1. 80 – 99% ICA stenosis
2. 60 – 79% ICA stenosis with PSV >300 cm/sec or ICA/CCA ratio >4.0
3. 100% ICA occlusion not previously documented at the Cleveland Clinic
4. Carotid artery dissection not previously documented at the Cleveland Clinic

*Notification: The name and pager number of the person who was notified must be documented on the report along with the date and time of notification.