Neurosonology: Transcranial Doppler

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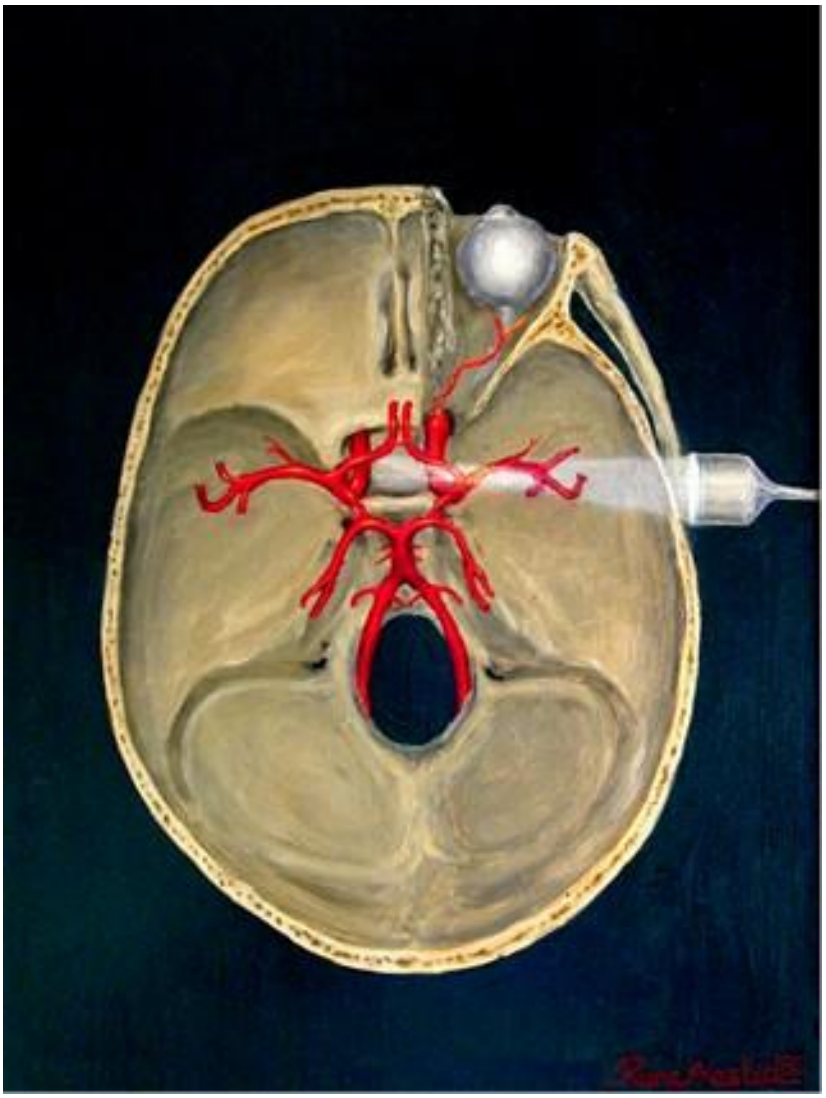


Contents

Transcranial Doppler (TCD) Services and Indications

What is TCD?

Transcranial Doppler, or TCD, is an ultrasound-based, safe, non-invasive means of dynamically surveying flow velocity and pathologic changes in the large arteries at the base of the brain. These include the middle cerebral arteries (MCAs), anterior cerebral arteries (ACAs), terminal internal carotid arteries (tICAs), posterior cerebral arteries (PCAs), ophthalmic arteries (OAs), intracranial vertebral arteries (VAs) and the basilar artery (BA).

What can be accomplished with TCD?

TCD provides information on flow velocity and direction of flow in a segment of the vessel investigated. The simplicity of the data acquired belies the many clinically useful findings that can be inferred from patterns of flow velocity and directional change. TCD is a useful tool for screening for major intracranial stenosis (> 50% luminal narrowing) and intracranial occlusions, validated against conventional and non-invasive angiography. TCD can also be affixed with a head frame and used as a monitoring tool to screen for right-to-left shunting of saline microbubble contrast, spontaneous asymptomatic microemboli, atypical reactions to a vasodilatory stimulus, and flow changes based on head and body movement.

When is TCD useful?

TCD has a number of inpatient and outpatient indications.

- Routine study
    - can identify narrowing of any of major vessels at the base of the brain and requires no contrast injection.
    - can also identify aberrant direction of flow, which can be seen as a pathological response to major cerebrovascular disease.
- Monitoring study
    - validated approach to identifying any right-to-left shunting, including a patent foramen ovale (PFO).
    - can also identify microemboli associated with cardiac or vascular hardware, atrial fibrillation, and asymptomatic carotid artery disease that can inform management
    - screen for vertebrobasilar insufficiency
    - test for “downstream exhaustion” of cerebrovascular autoregulation
    - monitor response to tPA with acute stroke and inform prognosis
    - test for vasomotor instability in migraine and concussion patients
    - intraoperative monitoring of cardiac and endovascular procedures for cerebral risk from emboli

Overview of TCD Ultrasonography

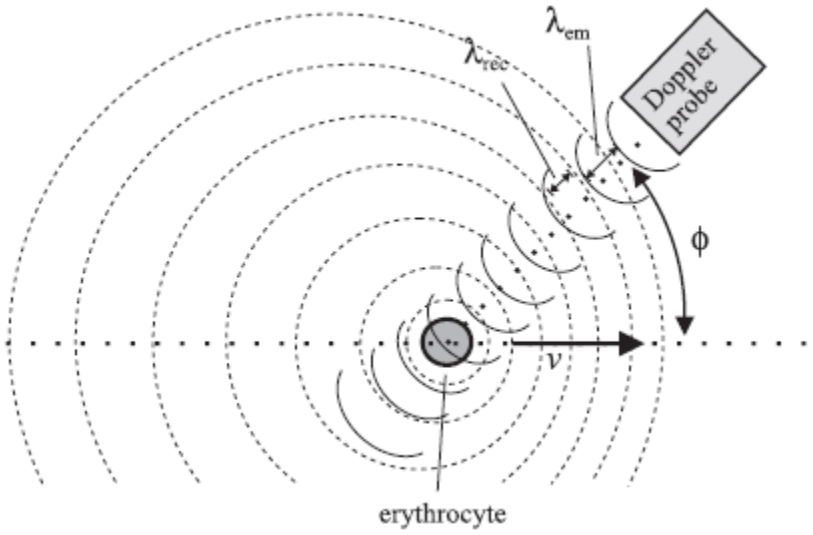
General Principles of TCD

TCD is a non-invasive means of measuring blood velocity and direction in large arteries of the brain

- Pros
  - Real-time
  - Continuous
  - Reproducible
  - Safe
  - No contrast (for most studies)
  - Relatively inexpensive
- Cons
  - Highly operator dependent
  - Absent/suboptimal windows for insonation in substantial minority of patients (~10%)

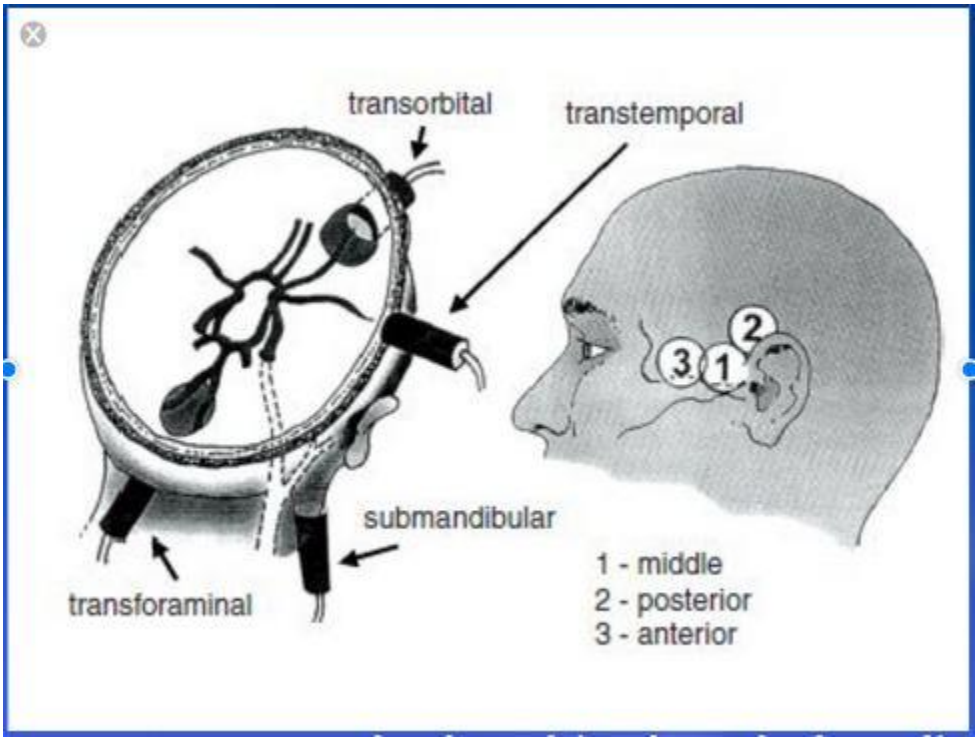
This procedure is predicated on a few simple premises, including the Doppler Effect, windows of insonation, expected cerebrovascular anatomy, cerebral hemodynamics, and the type of data TCD provides.

The TCD instrument is able to measure flow direction via Doppler shifts. Velocity can also be calculated from these shifts with an assumed angle of insonance of 0° (e.g., parallel with flow).



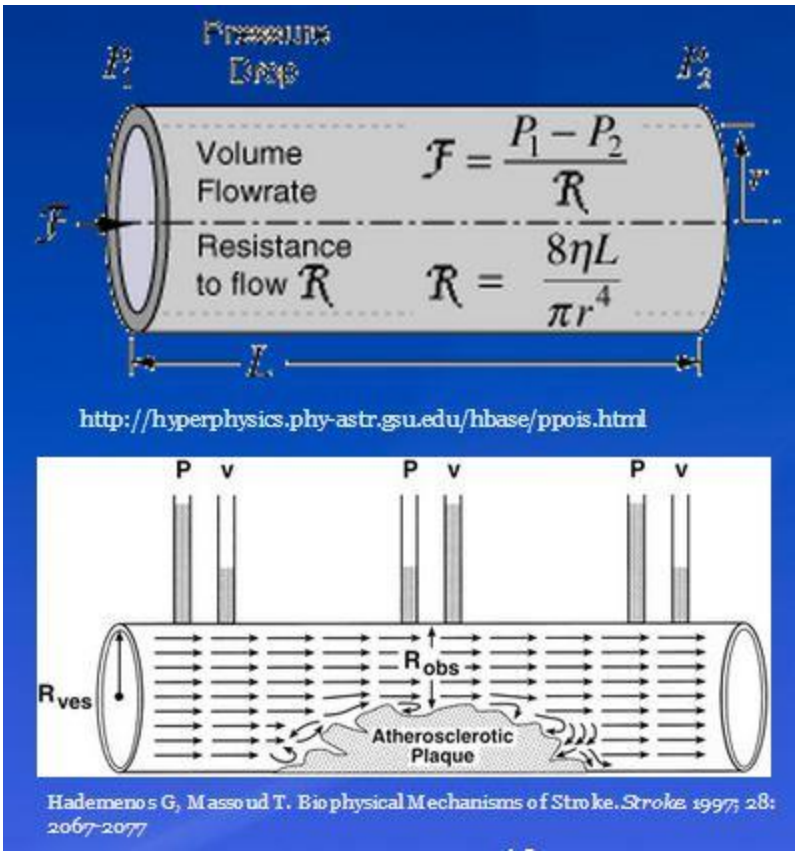
From: Deppe et al. NeuroImage 2004.

TCD has to be performed through certain “windows” because the skull attenuates the ultrasound. The transtemporal, transforaminal, submandibular and transorbital windows are shown below. Most of the arteries of the Circle of Willis are insonated via the transtemporal window, but the basilar and vertebral arteries are only accessible via the transforaminal window and the carotid siphon as well as the ophthalmic artery can only be insonated via the transorbital window.

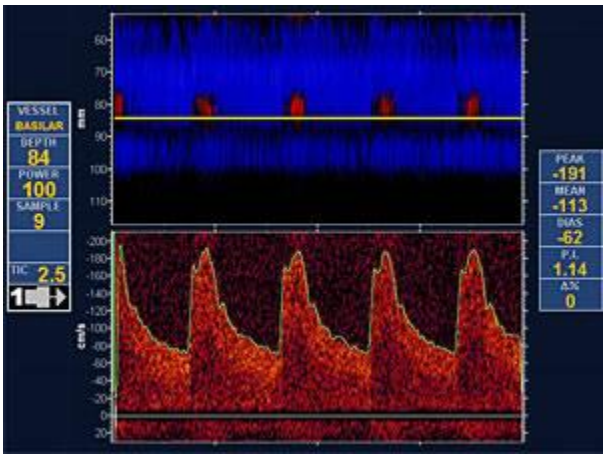


From: Alexandrov. Cerebrovascular Ultrasound in Stroke Prevention and Treatment. 2ed

Cerebral hemodynamics play a role in TCD performance and interpretation. Although the cerebral vasculature has complex mechanisms to ensure stable global cerebral blood flow, changes in cardiac output, blood viscosity, atherosclerotic plaque accumulation, vessel spasm, endothelial proliferation, and changes in partial pressure of arterial CO_2 can all precipitate potentially drastic focal changes in flow patterns.



TCD tells us the direction and velocity of flow. Within the segment of artery studied, TCD provides real-time, continuous, beat-to-beat information from peak systole through end diastole with many samplings in between. This allows for a mean velocity to be calculated and it is the mean velocity values we report and derive our inferences. The “peaks and valleys” in the figure below are a tracing of the beat-to-beat velocities as “heard” by the TCD device, referred to as the “spectral waveform.” Each major vessel has a characteristic appearance and sound.



From: www.thebarrow.org

- ## TCD Technique

Basic TCD technique involves the placement of a probe over a window of insonation and directing the probe such that it orients directly with the expected trajectory of an intracranial vessel. The intricacies of the technique come in the adjustments necessary to maximize signal (e.g., make the ultrasound beam as close to directly in line with flow as possible). This study requires the use of ultrasound gel, typical of other ultrasound studies. Monitoring studies require the use of a head-frame harness to hold probes in place, but the same principles of probe direction apply (see below).

- ## Patient Safety

TCD was first described in 1982 and, since then, no reported adverse events have been attributed to the use of even prolonged TCD monitoring (6+ hours continuously) with the FDA-approved frequency of 2 MHz. Most routine studies take < 30 minutes and monitoring studies take ~1 hour.

TCD is typically comfortable for the patient and well tolerated. The head frame for monitoring studies, while designed to be “snug,” can be adjusted for maximal patient comfort while still attaining a technically superb study.

Evidence Compendium by Indication

Cerebrovascular Disease

Intracranial artery stenosis/occlusion

	Sensitivity, %	Specificity, %	Reference standard
Intracranial steno-occlusive disease			Conventional angiography
Anterior circulation	70–90	90–95	
Posterior circulation	50–80	80–96	
Occlusion			
MCA	85–95	90–98	
ICA, VA, BA	55–81	96	
Extracranial ICA stenosis			Conventional angiography
Single TCD variable	3–78	60–100	
TCD battery	49–95	42–100	
TCD battery and carotid duplex	89	100	

- Routine study
- Any cause of stenosis
    - Most typically atherosclerosis
    - Sickle cell anemia
        - 92% relative risk reduction of first stroke in kids age 2-16
    - Can assess patency of stents
    - Can help differentiate “congenital atresia vs atherosclerotic narrowing”
- Alternative means of screening for intracranial atherosclerotic disease for patients who cannot tolerate MRI or CT
    - Claustrophobia
    - Poor renal function
        - Inability to safely receive contrast agents

- Demchuk AM, Christou I, Wein TH, et al. Accuracy and criteria for localizing arterial occlusion with transcranial Doppler. J Neuroimag 2000;10:1–12.
- Rorick MB, Nichols FT, Adams RJ. Transcranial Doppler correlation with angiography in detection of intracranial stenosis. Stroke 1994;25: 1931–1934.
- Ley–Pozo J, Ringelstein EB. Noninvasive detection of occlusive disease of the carotid siphon and middle cerebral artery. Ann Neurol 1990;28: 640–647.
- DeBray JM, Joseph PA, Jeanvoine H, et al. Transcranial Doppler evaluation of middle cerebral artery stenosis. J Ultrasound Med 1988; 7:611–616.
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- Mull M, Aulich A, Hennerici M. Transcranial Doppler ultrasonography versus arteriography for assessment of the vertebrobasilar circulation. J Clin Ultrasound 1990;18:539–549.

- Zanette EM, Fieschi C, Bozzao L, et al. Comparison of cerebral angiography and transcranial Doppler sonography in acute stroke. Stroke 1989;20:899–903.
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- Camerlingo M, Casto L, Censori B, et al. Prognostic use of ultrasonography in acute non-hemorrhagic carotid stroke. Ital J Neurol Sci 1996;17:215–218.
- Wong KS, Li H, Chan YL, et al. Use of transcranial Doppler ultrasound to predict outcome in patients with intracranial large-artery occlusive disease. Stroke 2000;31:2641–2647.
- Kushner MJ, Zanette EM, Bastianello S, et al. Transcranial Doppler in acute hemispheric brain infarction. Neurology 1991;41:109–113.
- Schwarze JJ, Babikian VL, DeWitt LD, et al. Longitudinal monitoring of intracranial arterial stenoses with transcranial Doppler ultrasonography. J Neuroimag 1994;4:182–187.
- Arenillas JF, Molina CA, Montaner J, et al. Progression and clinical recurrence of symptomatic middle cerebral artery stenosis: a long-term follow-up transcranial Doppler ultrasound study. Stroke 2001;32: 2898–2904.
- Wong KS, Li H, Lam WWM, Chan YL, Kay R. Progression of middle cerebral artery occlusive disease and its relationship with further vascular
- Adams RJ, McKie VC, Hsu L, et al. Prevention of a First Stroke by Transfusions in Children with Sickle Cell Anemia and Abnormal Results on Transcranial Doppler Ultrasonography. NEJM 1998;339:5-11.

- **Right-to-left shunting (PFO, extracardiac)**

	Sensitivity, %	Specificity, %	Reference standard
Right-to-left cardiac shunts	70–100	>95	Transesophageal echocardiography

- Routine + Monitoring study with microbubble injection with/without Valsalva
- Can diagnose cardiac & extracardiac right-to-left shunts
  - PFO
  - Pulmonary AVM
  - Other
- Complementary and technically superior to echocardiography due to ability to diagnose extracardiac shunts and achieve better effort with Valsalva
- No sedation required
- Easier Valsalva for the patient without sedation

- Komar M, Olszowska M, Przewlocki T, et al. Transcranial Doppler ultrasonography should it be the first choice for persistent foramen ovale screening? Cardiovascular Ultrasound 2014, 12:16
- Tobe J, Bogiatzi C, Munoz C, et al. Transcranial Doppler is Complementary to Echocardiography for Detection and Risk Stratification of Patent Foramen Ovale. Canadian Journal of Cardiology. August 2016 Volume 32, Issue 8, Pages 986.e9–986.e16
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- Belvis R, Leta RG, Marti-Fabregas J, Cocho D, Carreras F, Pons-Llado G, Marti-Vilalta JL. Almost perfect concordance between simultaneous transcranial Doppler and transesophageal echocardiography in the quantification of right-to-left shunts.
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- Schwarze JJ, Sander D, Kukla C, et al. Methodological parameters influence the detection of right-to-left shunts by contrast transcranial Doppler ultrasonography. Stroke 1999;30:1234–1239.
- Droste DW, Lakemeier S, Wichter T, et al. Optimizing the technique of contrast transcranial Doppler ultrasound in the detection of right-to-left shunts. Stroke 2002;33:2211–2216.

• Vasospasm after subarachnoid hemorrhage

- Routine study
- Standard screening test in the setting of aneurysmal subarachnoid hemorrhage
  - Findings correlate well with angiographic spasm

- Lysakowski C, Walder B, Costanza MC, Tramer MR. Transcranial Doppler versus angiography in patients with vasospasm due to a ruptured cerebral aneurysm: a systematic review. Stroke 2001;32:2292–2298.
- Grosset DG, Straiton J, McDonald I, et al. Use of transcranial Doppler sonography to predict development of a delayed ischemic deficit after subarachnoid hemorrhage. J Neurosurg 1993;78:183–187.
- Kyoi K, Hashimoto H, Tokunaga H, et al. Time course of blood velocity changes and clinical symptoms related to cerebral vasospasm and prognosis after aneurysmal surgery. No Shinkei Geka 1989;17:21–30.
- Sloan MA, Burch CM, Wozniak MA, et al. Transcranial Doppler detection of vertebrobasilar vasospasm following subarachnoid hemorrhage. Stroke 1994;25:2187–2197.
- Burch CM, Wozniak MA, Sloan MA, et al. Detection of intracranial internal carotid artery and middle cerebral artery vasospasm following subarachnoid hemorrhage. J Neuroimag 1996;6:8–15.
- Vora YY, Suarez–Almazor M, Steinke DE, Martin ML, Findlay JM. Role of transcranial Doppler monitoring in the diagnosis of cerebral vasospasm after subarachnoid hemorrhage. Neurosurgery 1999;44: 1237–1248.
- Sloan MA, Haley EC, Kassell NF, et al. Sensitivity and specificity of transcranial Doppler ultrasonography in the diagnosis of vasospasm following subarachnoid hemorrhage. Neurology 1989;39:1514–1518.

- **Carotid artery disease**

- Routine and monitoring studies
- Significant carotid artery disease can make for a low-flow state to the brain
  - Screen for aberrant flow from other arteries to compensate
  - See if "reserve" is exhausted (vasomotor reactivity)
    - Predicts higher risk of stroke from asymptomatic carotid artery with 70% stenosis
    - Annual rate 4.1% normal reactivity, 13.9% abnormal reactivity
    - Severely exhausted reactivity independent predictor of stroke/TIA (OR 14.4)
    - Independent patient-data analysis of 754 patients in 9 studies
      - Impaired reactivity independently associated with risk of stroke (HR 3.69; CI 2.01-6.77) and the risk was similar between recently symptomatic and asymptomatic patients
  - Screen for asymptomatic microemboli
    - Emboli from asymptomatic carotid artery of at least 70% stenosis confer higher stroke risk
      - Stroke or TIA HR 2.54 over 2 years, stroke alone HR 5.57; absolute risk 3.62% in patients without emboli, 7.13% in patients with emboli

- Reinhard M, Schwarzer G, Briel M. Cerebrovascular reactivity predicts stroke in high-grade carotid artery disease. Neurology 2014;83:1–8
- Markus HS, King A, Shipley M, Topakian R, Cullinane M, Reihill S, Bornstein NM, Schaafsma A. Asymptomatic embolization for prediction of stroke in the Asymptomatic Carotid Emboli Study (ACES): a prospective observational study. Lancet Neurol. Jul 2010; 9(7): 663-671
- Markus H, Cullinane M. Severely impaired cerebrovascular reactivity predicts stroke and TIA risk in patients with carotid artery stenosis and occlusion. Brain 2001;124:457–467.
- Silvestrini M, Vernieri F, Pasqualetti P, et al. Impaired cerebral vasoreactivity and risk of stroke in patients with asymptomatic carotid artery stenosis. JAMA 2000;283:2122–2127.

- **Acute Stroke/tPA monitoring/sonothrombolysis**

- Routine + monitoring study
- TCD can be used to monitor recanalization "progress" after tPA is given for stroke
  - Early recanalization (and lack thereof) informs prognosis

- Physical properties of ultrasound may assist in thrombolysis process ("sonothrombolysis")

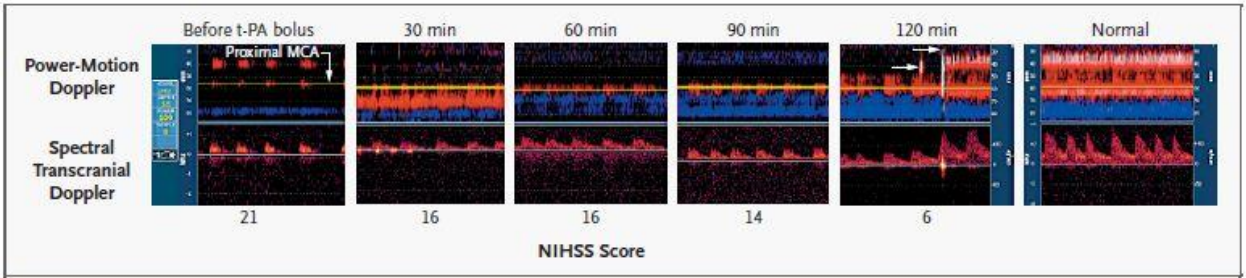

Figure 1. Complete Recanalization with the Use of Power-Motion Transcranial Doppler Ultrasonography.

Spectral wave forms from the proximal middle cerebral artery (MCA) were obtained at a depth of 58 to 60 mm (left-hand image, arrow) from the left transtemporal window. A minimal, grade 1, signal as measured on the TIBI scale, with absent diastolic flow is seen on power-motion Doppler images (top) and spectral-transcranial Doppler images (bottom) obtained before the administration of a t-PA bolus. Thirty minutes after the t-PA was given, TIBI grade 3 dampened signals (i.e., cycles with positive end-diastolic flow) indicate the beginning of the recanalization of the proximal middle cerebral artery. TIBI grade 3 signals remain at 60 and 90 minutes. At 120 minutes, embolic tracks are shown by power-motion Doppler display (top, arrows), followed by restoration of low-resistance normal flow in both proximal and distal parts of the middle cerebral artery. Normal flow through the unaffected middle cerebral artery is shown in the far right-hand image for comparison. Corresponding National Institutes of Health Stroke Scale (NIHSS) scores are provided below each frame. (In the general population with stroke, scores range from 0 to 34, with higher scores indicating greater neurologic deficits.) At 24 hours, this patient had an NIHSS score of 4. At three months, he had no residual neurologic deficits, and his modified Rankin score was 0.

- Alexandrov AV, Molina CA, Grotta JC, Garami Z, Ford SR, Alvarez-Sabin J, Saqqur M, Demchuk AM, Moye LA, Hill MD, Wojner AW. Ultrasound-enhanced systemic thrombolysis for acute ischemic Stroke. N Engl J Med. 2004 Nov 18;351(21):2170-8

• Vertebrobasilar insufficiency

- Routine study + monitoring study
- Patients with positional and/or neck-rotational symptoms of lightheadedness, vision changes, weakness and/or numbness or frank clinical stroke may have vertebrobasilar insufficiency
- TCD of the vertebral arteries and/or PCAs during head rotation and/or extension can be performed to screen for positional hemodynamic changes in the setting of symptom production.

- Sturzenegger M, et al. Dynamic Transcranial Doppler Assessment of Positional Vertebrobasilar Ischemia. Stroke. 1994;25:1776-1783
- Vilela MD, et al. Rotational vertebrobasilar ischemia: hemodynamic assessment and surgical treatment. Neurosurgery 2005. 56(1):36-45.
- Schneider PA, et al. Noninvasive evaluation of vertebrobasilar insufficiency. Journal of Ultrasound Medicine, 1991. 10(7):373-379

• Cerebral circulatory arrest (brain death ancillary test)

- TCD is a validated ancillary test in the setting of suspected brain death

- As cerebral edema and intracranial pressure increase, the heart is unable to pump blood to the brain

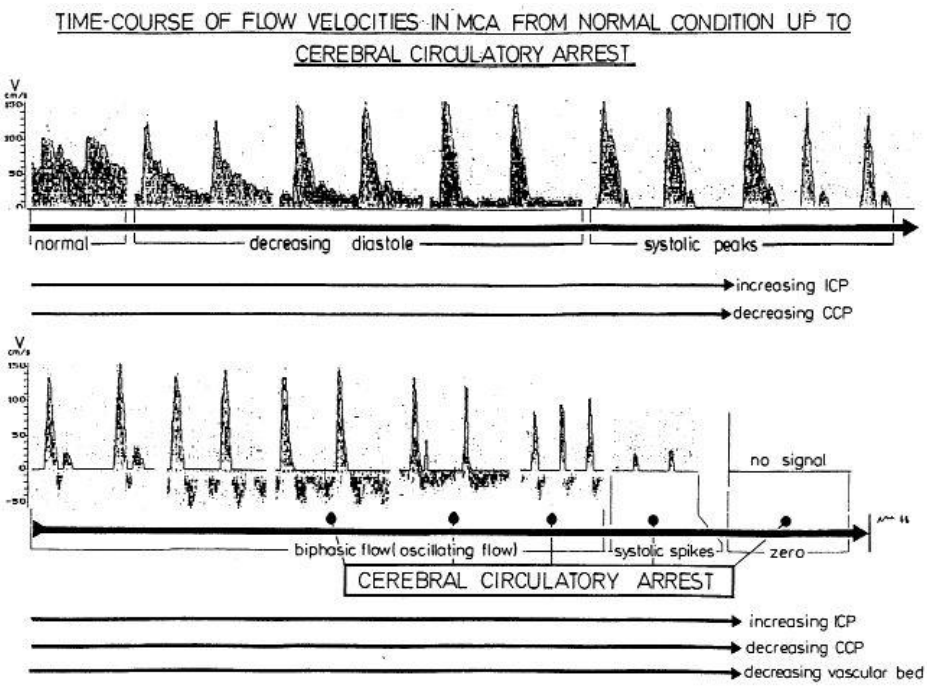

Fig. 1. Doppler spectral wave forms of the MCA monitoring the development from a normal recording to the complete extinction of flow signals due to increasing intracranial pressure. In the upper row signals can be seen which are characterized by increasing pulsatility. But there is no reverse flow phase. In the lower row reverse flow is shown, however, the first two curves show an asymmetric distribution with a preponderance of forward flow. This does not correspond to a complete cerebral circulatory arrest. This is only confirmed if the forward and reverse flow components are equal. (Reprinted from [10].)

- Ducrocq X, et al. Consensus opinion on diagnosis of cerebral circulatory arrest using Doppler-sonography. Task Force Group on cerebral death of the Neurosonology Research Group of the World Federation of Neurology. Journal of the Neurological Sciences. 1998;15:145-150

- **Intra/peri-operative monitoring (carotid endarterectomy [CEA] or stenting [CAS])**

- Routine study + monitoring study
- An approach to monitoring for peri/post-operative cerebrovascular complications of carotid artery surgery (CEA or CAS)
    - Emboli detected during dissection and wound closure, >90% decrease in ipsilateral MCA velocity at cross clamping, >100% increase in pulsatility index in MCA at clamp release are associated with operative stroke in CEA
        - Can inform surgical technique during dissection/closure, raise awareness for post-operative complications
    - Patients with frequent emboli in the first hour after carotid endarterectomy have a 15-fold increased risk of ipsilateral stroke/TIA
    - Serial monitoring of MCA velocities after CEA and CAS can predict risk of carotid hyperperfusion syndrome

- The European Society for Vascular Surgery identifies intraoperative TCD as one measure "which virtually abolished intra-operative stroke"

- Ackerstaff RGA, et al. Association of intraoperative transcranial Doppler monitoring variables with stroke from carotid endarterectomy. Stroke. 2000;31:1817-1823
- Naylor AR, et al. Closing the loop: a 21-year audit of strategies for preventing stroke and death following carotid endarterectomy. Eur J Vasc Endovasc Surg. 2013 Aug;46(2):161-70
- Abbott AL, et al. Timing of clinically significant microembolism after carotid endarterectomy. Cerebrovasc Dis 2007;23:362-367
- Pennekamp CW, et al. Prediction of cerebral hyperperfusion after carotid endarterectomy with transcranial Doppler. Eur J Vasc Endovasc Surg. 2012 Apr;43(4):371-376

Headache

Migraine with and without aura

- Routine + monitoring studies
- Migraine with & without aura: cerebrovascular reactivity is abnormally low during attacks
- Migraine with aura: cerebrovascular reactivity is abnormally elevated between as compared to controls and migraine without aura. Functional reactivity to visual stimulus is also greater in migraine with aura
    - Can help solidify diagnosis, especially if confounders
    - May be a trackable biomarker for response to medications
    - Interesting biomarker for research protocols
- Right-to-left shunting studies for exertional headache
    - Presence of right to left shunt thought to contribute to headache, prompts antiplatelet therapy

- Fiermonte G, et al. Cerebrovascular CO_2 reactivity in migraine with aura and without aura. A transcranial Doppler study. Acta neurologica Scandinavica. 1995;92(2):166-169.
- Silvestrini M, et al. Estimation of cerebrovascular reactivity in migraine without aura. Stroke. 1995;26:81-83.
- Harer C, et al. Cerebrovascular CO_2 reactivity in migraine: assessment by transcranial Doppler ultrasound. J Neurol. 1991 Feb;238(1):23-6

Concussion

- Routine + monitoring study
- Vascular reactivity after sport-related mTBI is abnormal shortly after injury

- Serial studies may be an objective biomarker of recovery
  - Inform return to play
- Interesting biomarker for future research

- Len TK, et al. Cerebrovascular Reactivity Impairment after Sport-Induced Concussion. Medicine & Science in Sports & Exercise. 2011; 2241-2248
- Len TK, et al. Serial monitoring of CO_2 reactivity following sport concussion using hypocapnea and hypercapnea. Brain injury, March 2013;27(3):346-353

Dementia

- Routine + monitoring studies
- Intracranial stenosis can inform vascular contribution to cognitive impairment
- Impaired vasomotor reactivity downstream from a significantly narrowed carotid artery is associated with cognitive impairment
  - Risk of decreasing Mini Mental Status Examination score increases progressively in patients with bilaterally normal to unilaterally abnormal to bilaterally abnormal carotid arteries
    - 3-year MMSE: 27→26 in bilaterally normal carotid arteries, 26.5→25 in unilaterally abnormal carotid arteries, 27→24 in bilaterally abnormal carotid arteries
  - Left carotid artery stenosis and impaired vasomotor reactivity are associated with poor performance on Verbal Fluency testing compared to controls
  - Right carotid artery stenosis and impaired vasomotor reactivity are associated with poor performance on Colored Progressive Matrices and Complex Figure Copy Test
- Asymptomatic microemboli in the setting of Alzheimer- or vascular-type dementia predict a poor cognitive trajectory
  - 2-year deterioration in ADAS-Cog of 15.4 in patients with emboli vs 6.0 in those without emboli

- Buratti L, et al. Cognitive Deterioration in Bilateral Asymptomatic Severe Carotid Stenosis. Stroke. 2014;45 ePub ahead of print June 5, 2014
- Balucani C, et al. Cerebral hemodynamics and cognitive performance in bilateral asymptomatic carotid stenosis. Neurology 2012;79;1788-1795
- Purandare N, et al. Association of Cerebral Emboli with Accelerated Cognitive Deterioration in Alzheimer's Disease and Vascular Dementia. Am J Psychiatry 2012;169:300-308

Dysautonomia

- Routine study + monitoring studies
- TCD during tilt table testing can inform mechanism of (pre)syncope
  - Vasovagal: significant drop in diastolic flow velocity but preserved systolic velocity

    - Postural Orthostatic Tachycardia Syndrome (POTS): significant drop in both systolic and diastolic flow velocity
        - Can assist in diagnosis if vital sign changes are equivocal
        - May allow for stopping a tilt study prior to syncope, which is uncomfortable and stressful
- Measurable disturbances in physiologic rhythmicity of cerebral blood flow and impaired vasomotor reactivity can inform patterns of dysautonomia
    - Ancillary support of a diagnosis of generalized dysautonomia
    - Easily acquired, non-invasive objective biomarker of dysautonomia that can be tracked for treatment response
    - Interesting research biomarker

- Diehl R, et al. Spontaneous blood pressure oscillations and cerebral autoregulation. Clinical Autonomic Research 1998;8(1) 7-12
- Zunker P, et al. Detection of central and peripheral B-waves with transcranial and laser Doppler sonography. Cerebrovasc Dis 1996;6(3):6-7
- Hermosillo AG, et al. Cerebrovascular blood flow during the near sync opal phase of head-up tilt test: a comparative study in different types of neutrally mediated syncope. Europace 2006;8:199-203