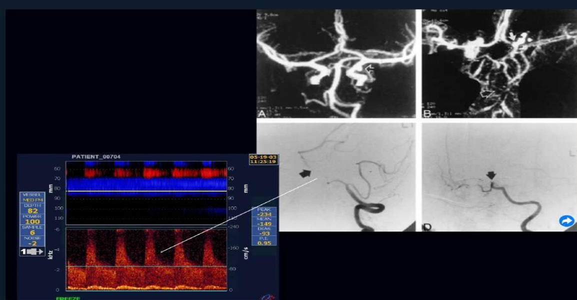
Transcranial Doppler (TCD): Practical Applications in Stroke



TCD In Stroke: A Review

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The Trillium Experience

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Disclosures

- No Honoraria for current presentation.
- Have Received Honoraria from Bristol-Myers Sqibb, Sanofi Aventi, Allergan and Boehringer Ingelheim.
- No other financial interests to disclose.

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Evaluation

For the **Provincial Stroke Rounds Planning Committee:**

- To plan future programs
- For quality assurance and improvement

- For **You**: Reflecting on what you've learned and how you plan to apply it can help you enact change as you return to your professional duties

- For **Speakers**: The responses help understand participant learning needs, teaching outcomes and opportunities for improvement.

[Transcranial Doppler (TCD): Practical Applications in Stroke]

Please take 2 minutes to fill the evaluation form out. Thank you!

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Objectives

•Explain the fundamental principles of Transcranial Doppler (TCD) and its clinical relevance in stroke assessment and what elements are outlined in the Canadian Stroke Best Practice Recommendations.

•Analyze case-based scenarios to illustrate the clinical application and interpretation of TCD findings in stroke management.

•Discuss practical considerations for implementing TCD in acute and ongoing stroke care.

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Part I: Technical Foundations

Principles, Technique & Waveform Recognition

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Principles, Technique & Waveform Recognition

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Introduction to Medical Ultrasound

🔊 Sound Wave Physics

Medical ultrasound uses high-frequency sound waves (1–20 MHz) transmitted into tissue. Echoes returning to the transducer are processed to create real-time anatomic images — no ionizing radiation.

🫀 Tissue Interaction

Different tissues reflect, scatter, or absorb sound differently. Bone reflects strongly (bright), fluid transmits freely (anechoic), and soft tissue spans a gradient — forming the basis of diagnostic contrast.

📡 The Doppler Effect

A frequency shift occurs when sound reflects off moving targets (e.g. red blood cells). This shift encodes velocity and direction of blood flow, enabling non-invasive hemodynamic assessment.

Clinical Modalities

- **B-Mode (2D Greyscale)**
  Structural imaging — vessels, parenchyma, cardiac chambers
- **Color Doppler**
  Flow mapping overlaid on B-mode; direction encoded red/blue
- **Spectral (Pulsed Wave)**
  Quantitative velocity waveforms at a single sample gate depth
- **Power Doppler**
  Highly sensitive low-velocity flow; direction-independent
- **Power M-Mode (PMD)**
  Multi-depth simultaneous spectral display — core of TCD emboli detection
- **Contrast-Enhanced US**
  Microbubble agents amplify signal; key for PFO/shunt studies

Kremkau FW. Diagnostic Ultrasound: Principles and Instruments, 8th ed. Saunders 2011 | Evans DH et al. Doppler Ultrasound, 2nd ed. Wiley 1999

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History of Transcranial Doppler

- **1982** — Aaslid et al. First TCD publication (Stroke 1982)
- **1990** — Emboli detection & HITS criteria established
- **1993** — TCD in sickle cell (Adams et al.) STOP trial
- **2001** — TIBI grading Demchuk et al. Stroke 2001
- **2002** — Power M-Mode (PMD) TCD Moehring & Spencer
- **2022** — BUBL study NovaGuide vs TTE ISC 2022

Key Contributions

• Rune Aaslid (Oslo, 1982): demonstrated transtemporal insonation of basal cerebral arteries through intact skull • STOP Trial (1998): TCD-guided transfusion reduced stroke risk in sickle cell disease by 92% — landmark prevention trial • Internation Consensus on MES: defined HITS criteria (>3dB, <300ms, unidirectional, random in cardiac cycle) • PMD (Moehring & Spencer, 2002): 33-gate power M-mode display enabling simultaneous multi-vessel insonation, simplified window finding, and enhanced emboli tracking — foundation of modern hands-free TCD

Aaslid R et al. Noninvasive transcranial Doppler ultrasound. J Neurosurg 1982 | Adams RJ et al. STOP Trial. NEJM 1998 | Markus HS et al. MES consensus. Stroke 1995 | Moehring MA & Spencer MP. Power M-mode Doppler. Ultrasound Med Biol 2002

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TCD in Stroke: Evidence-Based Recommendations from Major Guidelines

The following organisations have issued formal evidence-based recommendations supporting the use of TCD in specific stroke-related clinical settings:

CBPR — Canadian Best Practice 2023

- **PFO Detection — Cryptogenic Stroke**: TCD bubble study recommended as first-line R-to-L shunt screen in cryptogenic stroke/TIA. Superior sensitivity vs TTE; TEE remains anatomic gold standard for closure planning.
- **Emboli Monitoring (MES/HITS)**: TCD emboli surveillance post-CEA, during cardiac surgery, and in symptomatic carotid stenosis. Guides antiplatelet intensification; solid vs gaseous discrimination directs management.

AAN — American Academy Neurology Practice Advisory

- **Sickle Cell Disease — Stroke Prevention (Level A)**: Annual TCD screening in children 2–16 yrs. MCA/ACA TAMV ≥200 cm/s = high risk; initiate transfusion programme. STOP Trial (Adams 1998) — 92% stroke risk reduction.
- **Vasospasm in Subarachnoid Haemorrhage (Level B)**: Serial TCD recommended Days 3–14 post-aSAH. Lindegaard Ratio (MCA/ICA >3) distinguishes vasospasm from hyperaemia. MFV >200 cm/s = severe vasospasm requiring intervention.

ASNR — AJNR/ASNR Neurosonology Consensus

- **Intracranial Stenosis, Occlusion & Thrombolysis**: TCD criteria for MCA stenosis (MFV >80 cm/s) and occlusion validated vs MRA/DSA. TIBI grading endorsed for real-time recanalization monitoring during IV tPA.
- **Autoregulation & Cerebrovascular Reactivity**: TCD autoregulatory indices (Mx, PRx) endorsed for ICU monitoring in TBI and aSAH. Breath-holding index (BHI <0.69) identifies impaired vasomotor reserve predicting silent infarction risk.

ESO — European Stroke Organisation 2021

- **R→L Shunt Screening — ESUS & Young Stroke**: TCD bubble study recommended as initial screen in all cryptogenic stroke regardless of age. High-grade shunt (Spencer ≥3) + ASA = increased recurrence risk; refer for closure discussion.
- **Sonothrombolysis — Adjunct to IV tPA**: 2 MHz continuous insonation as adjunct to IV tPA (CLOTBUST trial). Trend to improved recanalization; recommended in trial settings pending definitive RCT evidence.

WFCCM — World Fed Critical Care Medicine Brain Death

- **Brain Death — Ancillary Confirmatory Study**: International consensus: bilateral absent diastolic flow, reverberant (to-and-fro) pattern, or systolic spikes only = cerebrovascular circulatory arrest. Accepted when clinical exam is confounded (Wijdicks 2010).
- **Raised ICP & Cerebral Perfusion Monitoring**: Pulsatility Index (PI >1.4 suggests ICP >22 mmHg) for non-invasive ICP estimation in TBI/hydrocephalus. Serial PI trending endorsed when invasive monitoring is unavailable.

CBPR 2023 | AAN Practice A... M 1998 | ASNR Neurosonology Consensus | ESO Guidelines 2021 | Wijdicks EFM et al. Neurology 2010 | Ducrocq X et al. WFCCM. J Neurol Sci 1998

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Perceived Limitations & How Advancing Innovations Have Addressed Them

⚠ Traditionally Perceived Pitfalls

Operator Dependency & Poor Reproducibility

TCD requires sustained manual probe positioning over a narrow acoustic window. Subtle angle changes alter velocity readings significantly, leading to wide inter-operator variability — a major adoption barrier.

Inadequate Temporal Window (~10–15% of Patients)

Dense temporal squamous bone — more common in elderly women and certain ethnicities — attenuates sound, making conventional B-mode and Doppler insonation impossible without signal.

Vessel Misidentification & Depth Errors

Without direct visualisation, the sonographer relies on depth, angle, and waveform morphology alone to identify which intracranial artery is being insonated — risking misattribution of MCA vs ACA vs ICA signals.

Single-Gate Emboli Detection: Low Sensitivity & False Positives

Classic single-depth pulsed-wave TCD monitors one sample volume. Artefacts (probe movement, patient speech) can mimic high-intensity transient signals (HITS), and real emboli at other depths are missed entirely.

✦ Advances That Overcome Them

Robotic Fixation Frames & Operator-Independent Systems

Hands-free headframe devices (NovaGuide, Digi-Lite) lock transducer angle with sub-millimetre precision, enabling prolonged automated monitoring and eliminating human positioning error. Validated in BUBL 2022 vs TTE.

Ultrasound Contrast Agents (Perflutren Microbubbles)

IV SonoVue / Definity dramatically amplify backscatter signal, restoring insonation in otherwise inadequate windows. Contrast TCD recovers signal in >80% of initially windowless patients (Stolz 2002, Seidel 2002).

Colour-Coded Duplex TCD (TCCD)

B-mode imaging plus colour Doppler overlays allow direct vessel visualisation through the temporal window, enabling anatomy-guided insonation with confirmed vessel identity — dramatically improving diagnostic accuracy (Alexandrov 2012).

Power M-Mode (PMD) Multi-Gate Simultaneous Display

PMD samples 8–33 simultaneous depth gates across the full MCA length in real time. True emboli appear as diagonal tracks spanning multiple gates; artefacts do not. Sensitivity and specificity for MES detection markedly superior to single-gate (Moehring 2002).

Alexandrov AV et al. J Neuroimaging 2012 | Stolz E et al. Contrast TCD. Stroke 2002 | Moehring MA et al. PMD-TCD emboli. Stroke 2002 | BUBL Study. ISC 2022

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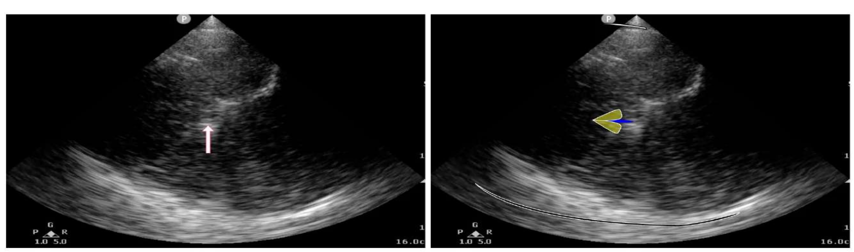
Doppler and Ultrasound Displays in Clinical Practice: Ultrasound "Modes": B-Mode Ultrasound

- **B-mode or 'brightness mode'**
- provides structural information utilizing different shades of gray (or different 'brightness') in a two-dimensional image (Figure 1)
- Brightness is determined by the amplitude of returning echoes

The following images have a side by side comparison of 2D ultrasound and anatomic landmarks that are necessary for TCD. The preset for these images is the cardiac preset (flipped images from a TCD preset). We first focus our attention to the middle of the field and look for 2 hypoechoic structures that look like a butterfly on its side (see image below). These structure represent either the thalami or the peduncles. The third ventricle lies anterior to the 'butterfly'. The third ventricle is an anechoic space with hyperechoic walls.



Probe position and 2D image for the trans-temporal window. Cardiac preset has been selected. The yellow structure represents the thalami or the peduncles. In white and in the near field the ipsilateral meninges. In the far field and in black, the contralateral temporal bone. The blue structure is the third ventricle and is an anechoic structure with hyperechoic walls. The white arrow points towards the far field border of the third ventricle.

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Doppler and Ultrasound Displays in Clinical Practice: Ultrasound "Modes": Doppler Modes

- **Doppler Modes: Based on Analysis of Moving Particles "Doppler Effect":**
- It is named after the physicist Christian Doppler, who described the phenomenon in 1842.
- "Über das farbige Licht der Doppelsterne und einiger anderer Gestirne des Himmels.." (On the coloured light of the binary stars and some other stars of the heavens)
- The hypothesis was tested for sound waves by Buys Ballot in 1845.] He confirmed that the sound's pitch was higher than the emitted frequency when the sound source approached him, and lower than the emitted frequency when the sound source receded from him.

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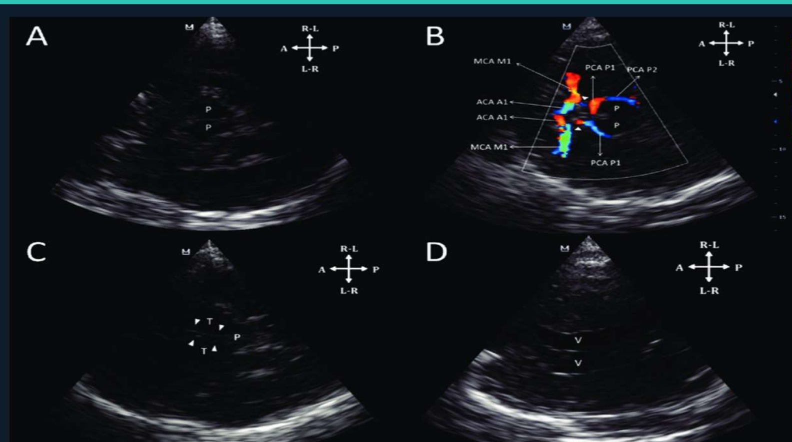
Color Doppler

- **Doppler Modes: Based on Analysis of Moving Particles "Doppler Effect":**
- Color Doppler ultrasound is also called Color-flow ultrasound.
- It is used to show blood flow or tissue motion in a selected two-dimensional area
- Direction and velocity of tissue motion and blood flow are Color coded and superimposed on the corresponding B-mode image (Figure A.)
- Red depicts movement towards the transducer, while blue depicts movement away from the transducer



from: Blanco,P, J Ultrasound Med 2016; 35:668–673

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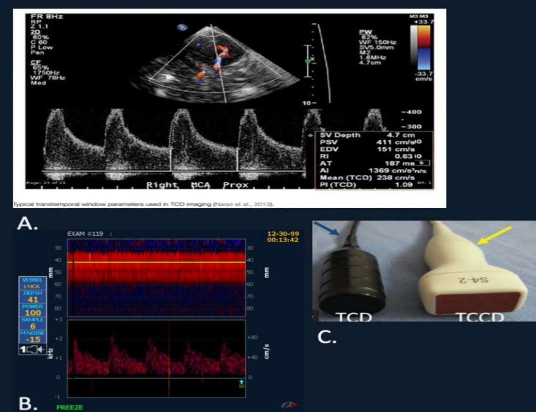
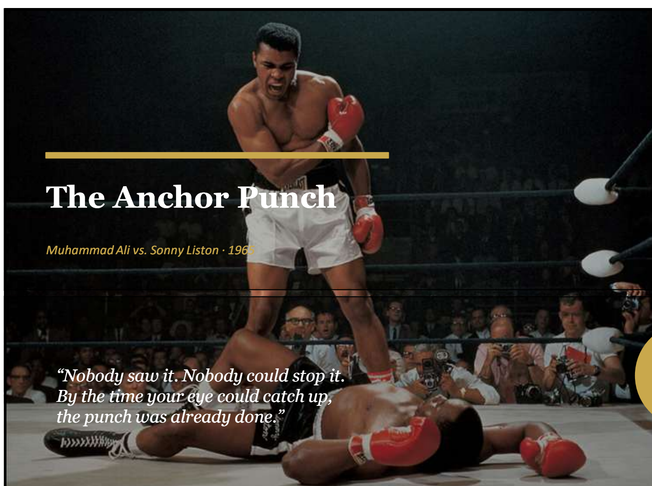
Spectral Doppler & Power M-Mode (PMD)

- **Doppler Modes: Based on Analysis of Moving Particles "Doppler Effect":**
- Spectral Doppler consists of a continuous and pulsed-wave form (Pulsed-wave spectral Doppler)
- Transducer sends pulses of ultrasounds to a predetermined depth
- Transducer then listens for returning echoes to determine flow velocities at that given location.
- Red blood cells move at a variety of speeds and directions
- Results in a spectrum of velocities within a given sample volume
- Hemodynamic changes also occur over time (with normal cardiac cycle)
- Result is spectrogram of the returned Doppler frequencies, plotted in a characteristic two-dimensional display (Figure A and B)
- PMD displays changes in signal Power from moving targets as change in color intensity; higher power is displayed as lighter color i.e., dark red for low power to pink for high power (Figure B.).
- Changes in velocity do not affect change in intensity of color of the PMD image.
- Dedicated TCD devices typically incorporate PMD, while multipurpose Vascular Ultrasound or POC Ultrasound devices will have Color, B-Mode and Spectral Analysis Displays. The probes for these varied devices are depicted in Fig. C





The Anchor Punch

Muhammad Ali vs. Sonny Liston · 1965

"Nobody saw it. Nobody could stop it. By the time your eye could catch up, the punch was already done."

Why nobody saw it:

- Too fast for the naked eye — gone before the frame refreshes
- Single vantage point missed the punch trajectory entirely

Power M-Mode TCD vs Color Doppler Ultrasound

Color Doppler ≈ Standard Camera

- Captures a narrow, 2D single-gate sample volume
- Misses emboli that travel outside the sample window
- Real-time emboli can 'pass unseen' between frames

VS

Power M-Mode ≈ High-Speed Multi-Angle Film

- Monitors 33 simultaneous sample gates across the vessel
- Catches every embolus regardless of where it travels
- Nothing passes unseen — superior sensitivity for emboli detection

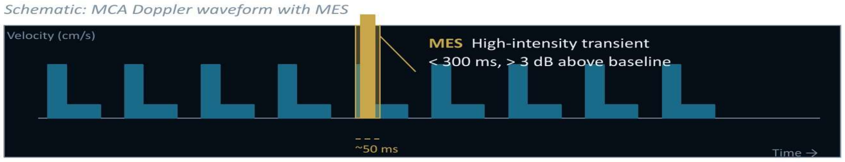
Ali's punch — like a microembolic signal — was always there. ***The right tool is what makes the invisible, visible.***

Microembolic Signals (MES) & HITS Criteria

⏱ Temporal Signature of a Microembolic Signal (MES)

Duration	Intensity	Direction
< 300 ms	**> 3 dB**	**Uni-dir.**
Typically 10–100 ms at peak intensity	Above background blood flow signal	Travels with flow — not bidirectional

Schematic: MCA Doppler waveform with MES



✗ Why Color Doppler Misses MES

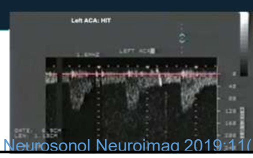
01 Frame Rate Too Slow Color Doppler frame rates are typically 10–30 fps. An embolic signal lasting < 100 ms occupies only 1–3 frames — easily aliased or averaged out.

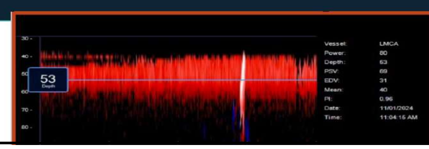
02 Single Fixed Gate Color Doppler samples one user-placed gate. If the embolus travels off-axis or through an unsampled depth, it is never interrogated.

03 Colour Averaging The colour map integrates velocity over time. A brief, bright MES is washed into the surrounding flow colour and its transient intensity spike is lost.

04 No Spectral Waveform MES diagnosis requires spectral Doppler with audio confirmation. Color mode provides no waveform, no dB readout, and no audio output.

HITS criteria (consensus): Duration < 300 ms · Intensity ≥ 3 dB above background · Unidirectional · Random in cardiac cycle · Characteristic audio (chirp/plop)





Kim j. J Neurosonol Neuroimag 2019;11(1):1-21

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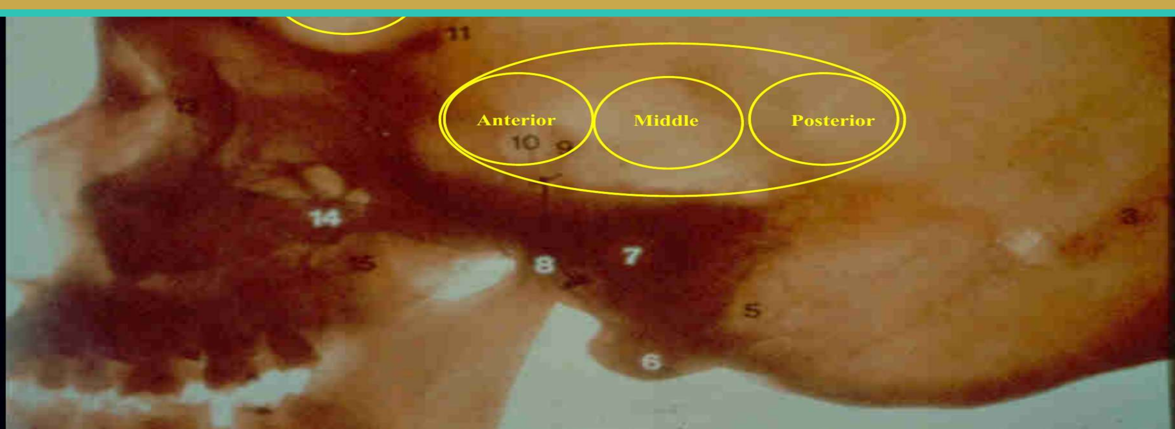
Transtemporal Insonation Windows



Transtemporal insonation windows

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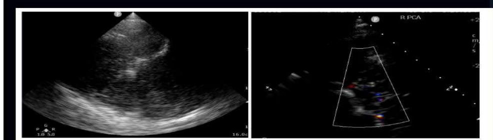
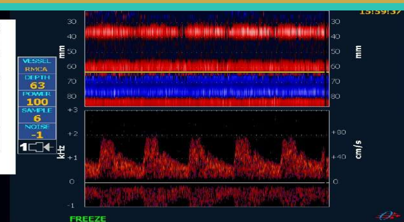
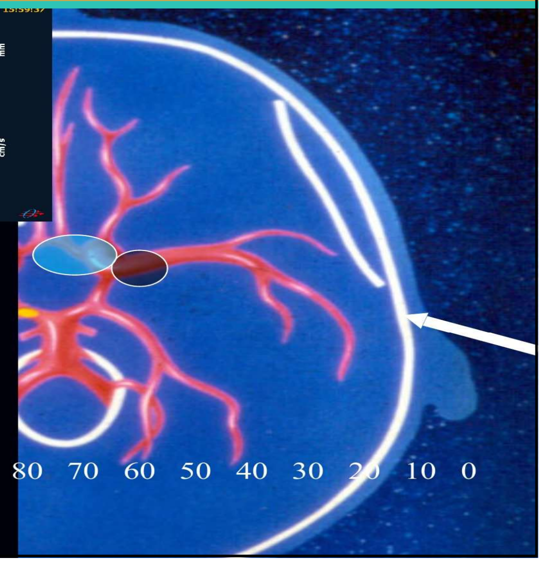
Temporal Window: Technique & Key Depths


CCDS of the trans-temporal window. On the left, the third ventricle is seen in 2D. On the right, we have lower the distance to be able to see the near field and turned on Color Flow Doppler. Making small movements of the hand to visualize the vessels that make up the circle of Willis.





100 % Power

Transducer : between the ear and frontal process of zygomatic bone

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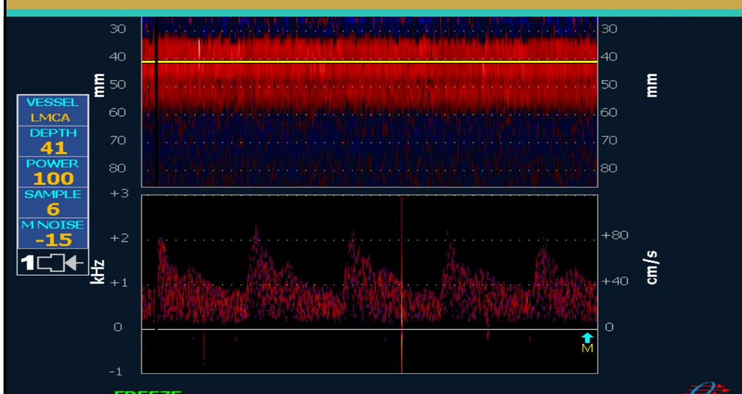
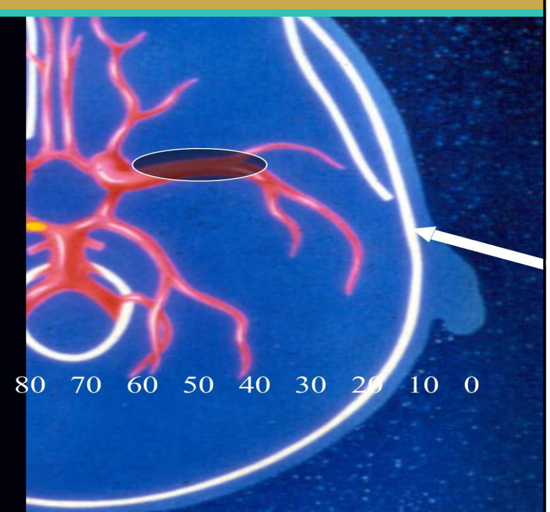
MCA Signature: Power M-Mode Display





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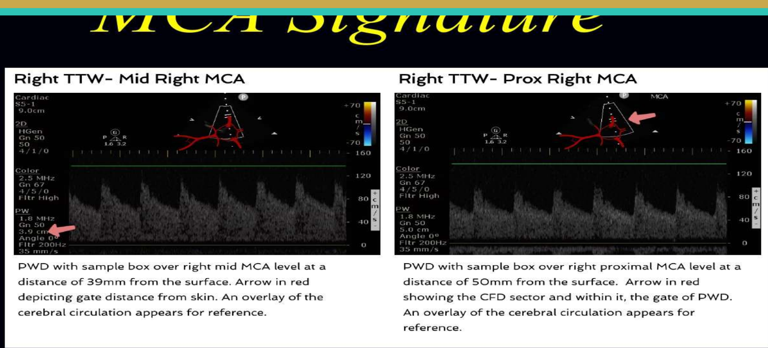
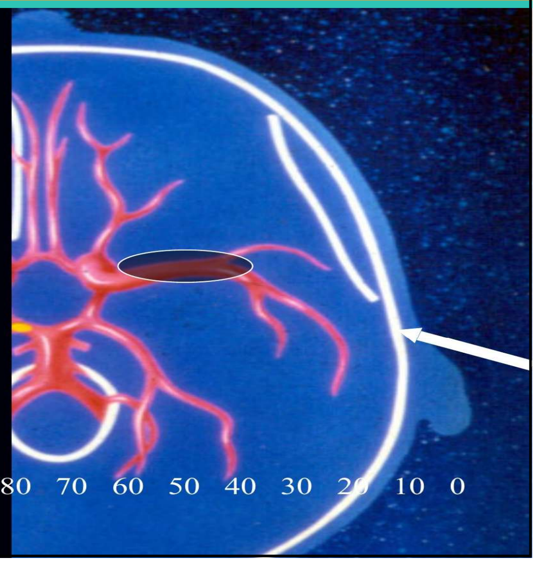
MCA Signature: Proximal vs. Mid Segment





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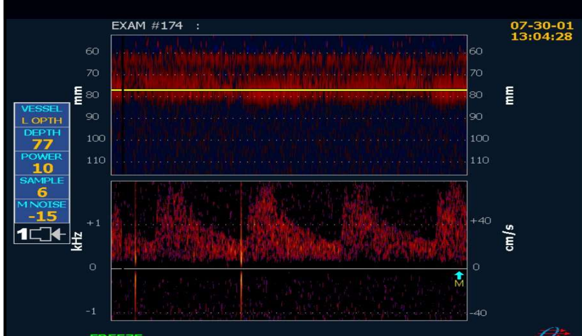
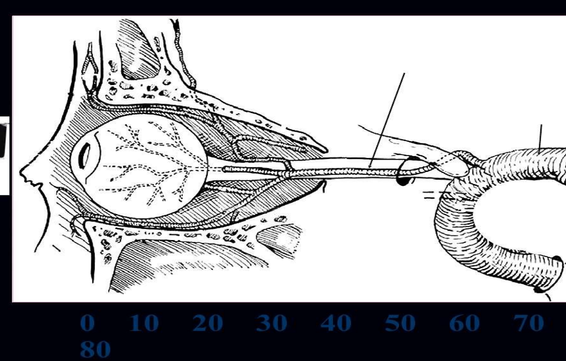
Orbital Window: ICA Siphon Signature





ICA siphon signature at 60 to 80 mm depth, Decreased Power 10%

⚠ Safety: Use 10% power only for orbital window

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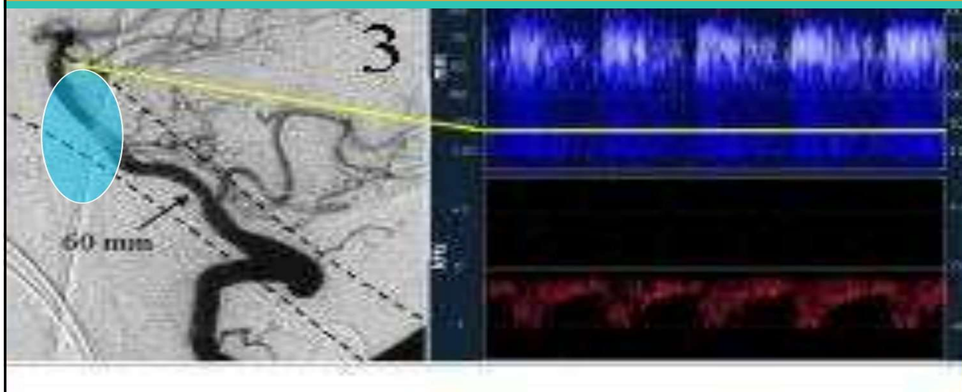
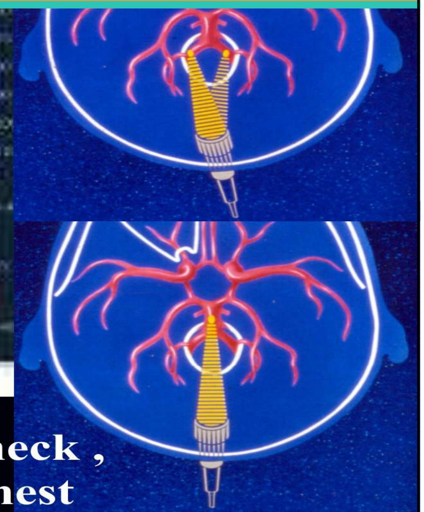
Transforaminal Window: Posterior Circulation (M-Mode TCD)





Space between Atlas and skull base: Bend neck , lateral decubitus position and head tilt to chest

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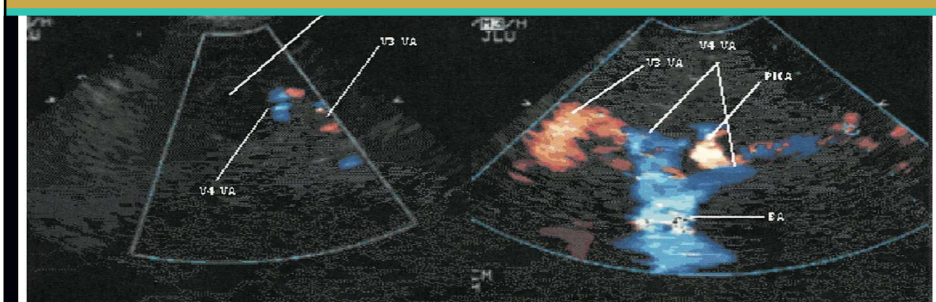
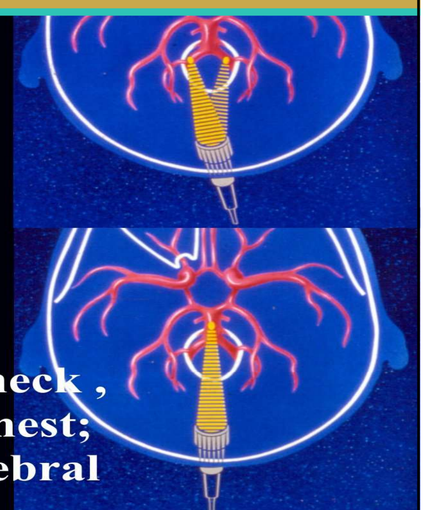
B-Mode TCD / Color Doppler: Posterior Circulation





Space between Atlas and skull base: Bend neck , lateral decubitus position and head tilt to chest; Depth of ROI demonstrative of V3,V4 vertebral artery

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Part II: Case Reviews

Clinical Applications of TCD in Stroke

Part II: Case Reviews

Clinical Applications of TCD in Stroke

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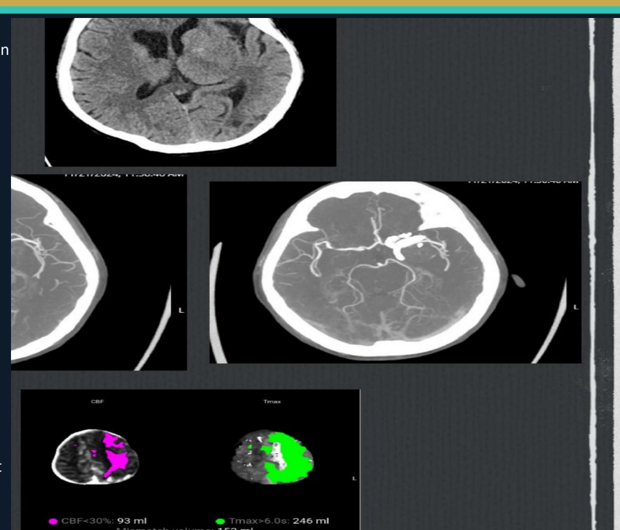
Case 1: Acute Stroke

- 71 y.o. male presenting with weakness with right sided predominance and speech arrest.
- and recent history of arterial embolic stroke on DAPT.Status post insertion of flow diverting stent in his carotid siphon with coiling of aneurysm, a year ago.
- Three weeks prior to current presentation was admitted to hospital for embolic stroke from his stent and his DAPT was advanced to ASA and Ticagrelor.
- Presently, the patient was NPO for a colonoscopy and thus had his Ticagrelor held. His ASA was retained given his indwelling stent.
- He was last seen normal at 10:30 last night. He awoke to an apparent weakness necessitating his wife helping him to bed from the bathroom. She noted he was unable to communicate. He was transported via the acute stroke pathway bypassing his home hospital BCH.

• Past Medical History
Aneurysm, Angina pectoris, Arthritis, Chronic kidney disease, Coronary artery disease, Diverticular disease, GERD, Gout, Hearing deficit, Heart valve disease, Hypercholesterolemia, Hypertension, Shortness of breath.

• Vitals & Exam
BP 108/68, pulse 74, temperature 36.4°C, resp rate 16, SpO2 100%. Mixed aphasia with some appropriate verbal responses; drowsy but rousable. Right arm in flexed with tremulousness. Left leg flaccid. NIHSS: 13.

• Acute Stroke Imaging Summary
Left MCA fills from left A1 and circle-of-Willis. Stable encephalomalacia related to left frontal and left occipital parietal infarct.
No definite CT evident acute intracranial infarct. NEW left internal carotid artery non-opacification/occlusion compared to prior angiogram — large thrombosed left ICA aneurysm; please consider NIR opinion.



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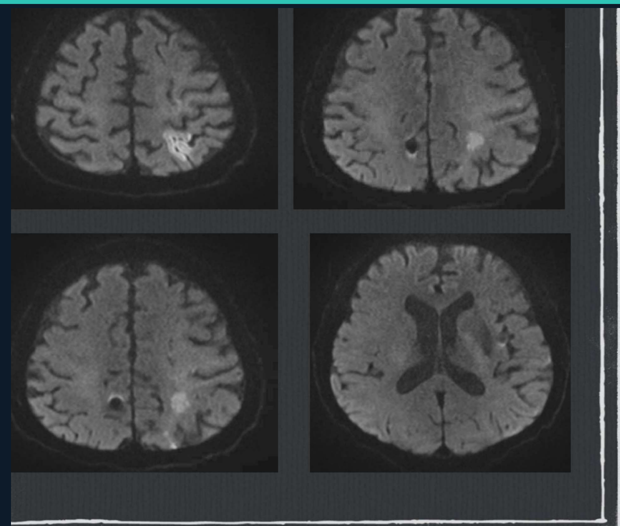
Case 1: Acute Stroke

MR HEAD STROKE UNENHANCED 3D — FINDINGS

Peripheral gyriform diffusion restriction in left posterior parietal lobe near vertex, extending to periventricular left parietal white matter. Scattered foci in posterior left frontal lobe within cortex near vertex. Compatible with evolving focal acute/subacute infarcts.
Encephalomalacia/gliosis within left frontal region near vertex — related to remote infarct. Additional old focal cortex and centrum semiovale white matter infarcts. Chronic infarcts within left lateral occipital and medial left occipital lobe.
Expected evolution of previously seen right globus pallidus/anterior limb internal capsule infarct — now chronic with focal encephalomalacia.
Giant left ICA aneurysm redemonstrated with susceptibility artifact. Aneurysm sac 4.8 × 3.2 × 4.0 cm — grossly unchanged vs prior MRI from August. Protrusion of medial aspect into sphenoid sinus similar to prior.
Scattered nonspecific foci of susceptibility artifact bilaterally — combination of remote chronic microhemorrhage and hemosiderin deposition on left side.
Ventricular system unchanged. No midline shift. No herniation.

SUMMARY

Multifocal areas of diffusion restriction near vertex involving left parietal lobe and posterior frontal lobe — evolving acute/early subacute infarcts



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Case 1: Acute Stroke

EXAM: CV US TRANSCRANIAL DOPPLER

Clinical Indication

Acute carotid siphon stent occlusion check for distal emboli and retained perfusion in left MCA.

Visibility

Bilateral MCA and ACA territories insonated with good spectrographs and M-Mode Dopplers visualized.

Findings

Clear asymmetry left to right. Right MCA: mfv 58 cm/s, pfv 102 cm/s, pfv delta 34 cm/s. Left MCA: mean flow velocity 27 cm/s with blunted parvus et tardus morphology.
Attempts to demonstrate compensatory hyperperfusion through anterior communicating artery unsuccessful — suggesting partial obstruction of the anterior communicating artery.

Summary

Examination suggests extension of occlusion in the carotid stent into the A1 region of the Anterior Cerebral artery. May suggest possibility of thrombus propagation and impending collateral failure. Results discussed with neuro-interventionalist on call

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Case 1: “Last-Stop…Terminal ICA Occlusions”

Preop: Left ICA Occlusion | Procedure: Endovascular Thrombectomy + Intracranial Stent for Aneurysm Embolization

Clinical Summary

71 y.o. male with large left ICA aneurysm treated with flow diverter stenting July 2024. Presented with aphasia and hemiplegia — found to have thrombosed left ICA stent. Good intracranial collateral circulation. Offered endovascular thrombectomy after failing conservative measures.

Operative Summary

8-French flowgate balloon catheter navigated over H1 slip catheter and Terumo glide wire into left ICA. AP lateral runs demonstrated full stent occlusion. Phenom 21 microcatheter navigated via Sofia 6F aspiration catheter. Multiple passes with aspiration; focal stenosis near distal stent required 6F Sofia — eventually passed. RED 62 aspiration catheter placed over Phenom 21 past distal stent; TICI 3 achieved.

Severely stenosed area in mid-portion of stent treated with SL-10 navigated inside Sofia 6F; deployed 4.5 mm × 21 mm Atlas stent across stenosis. Final run showed vessel open with good perfusion into MCA.

Summary: Successful revascularization of ICA occlusion related to flow diverting stent. Placement of intracranial stent for aneurysm. Procedure done after 5pm on urgent basis. Patient started on integrelin infusion.

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TIBI (Thrombolysis in Brain Ischemia) vs. mTICI (Modified Thrombolysis in Cerebral Infarction) — TCD & Angiographic Grading Correlation

TIBI (TCD-based)			mTICI (Angiographic)			Clinical Correlation
TIBI	TIBI Name	TCD Waveform Description	mTICI	mTICI Name	Angiographic Description	Clinical Correlation
0	Absent	No flow signal. Flat line. No systolic or diastolic component detected.	0	No Perfusion	No antegrade flow beyond the point of occlusion. Complete vascular obstruction.	Complete occlusion. No recanalization. High risk of infarct progression.
1	Minimal	Minimal systolic signal only. No diastolic flow. Reverberant/bidirectional blips.	0b	Trickle / Backfill	Faint anterograde flow or retrograde filling only. Distal territory not opacified.	Functionally absent perfusion. Equivalent to failed reperfusion. Poor prognosis.
2	Blunted	Low pulsatile flow, reduced velocity, prolonged systolic accel. (parvus et tardus).	1	Partial Occlusion	Contrast beyond obstruction but fails to opacify >50% of distal territory.	Severely impaired perfusion. Parvus-tardus on TCD = proximal residual stenosis.
3	Dampened	Abnormally low velocities, flat systolic peak. Reduced PI. Flow present but attenuated.	2a	Partial (<50%)	Partial but incomplete reperfusion; <50% of distal target territory opacified.	Incomplete reperfusion. TCD dampening may indicate high-resistance distal bed.
4	Stenotic	High-velocity turbulent signal ≥80 cm/s MFV or >30% asymmetry. Aliasing on M-Mode.	2b	Partial (≥50%)	Substantial reperfusion; ≥50% but incomplete distal territory opacified.	Substantial reperfusion with residual stenosis. Elevated TCD velocities post-EVT.
5	Normal	Normal waveform. MFV within normal range. Normal PI. Sharp systolic upstroke.	3	Complete Reperfusion	Complete antegrade flow with full opacification incl. cortical branches.	Complete recanalization. Optimal EVT target. TCD normalisation → good mRS.

References:

TIBI: Demchuk AM, Burgin WS, Christou I, et al. Thrombolysis in brain ischemia (TIBI) transcranial Doppler flow grades predict clinical severity, early improvement, and outcome in patients with intracranial carotid occlusions. Stroke. 2001;32(1):89–93.

mTICI: Zaidat OO, Yoo AJ, Khatri P, et al. Recommendations on angiographic revascularization grading standards for acute ischemic stroke. Stroke. 2013;44(9):2650–2663. [Original TICI: Higashida RT et al. Stroke. 2003;34(8):e109–e137.]

Correlation: Burgin WS, Malkoff M, Felberg RA, Demchuk AM, Christou I, Grotta JC, Alexandrov AV. TCD ultrasound criteria for recanalization after thrombolysis for MCA stroke. Stroke. 2000;31(5):1128–1132. | Felberg RA et al. Usefulness of triphasic Doppler ultrasonography of the MCA for evaluating recanalization and thrombolysis monitoring. J Neuroimaging. 2002;12(2):145–151. | Alexandrov AV et al. Speed of intracranial clot lysis with IV tPA: sonographic classification and short-term improvement. Circulation. 2001;103(24):2897–2902. | Molina CA et al. Improving predictive accuracy of recanalization on stroke outcome in patients treated with tPA. Stroke. 2004;35(1):151–156.

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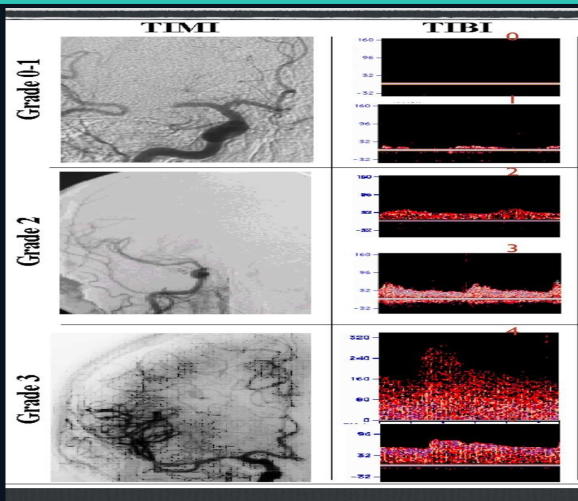
TIMI vs. TIBI — Angiographic & TCD Correlation | Burgin et al., Stroke 2000;31:1128



Persisting Occlusion (TIMI 0–1 ↔ TIBI 0–1 or 2–3)

- TIMI Grade 0–1 angiographically = no or minimal distal flow
  - Correlates with TIBI 0 (Absent) or TIBI 1 (Minimal) on TCD
  - TIBI 2–3 (Blunted/Dampened) may also reflect persistent proximal occlusion
- No detectable Doppler shift distal to occlusion site (TIBI 0)
  - Absent end-diastolic flow with a short systolic spike (TIBI 1)

Complete Recanalization (TIMI 3 ↔ TIBI 4–5)

- TIBI 4–5 vs. TIMI 3 angiographic recanalization:
  - **Sensitivity 91% for MCA recanalization**
  - **Specificity 93% for MCA recanalization**
- TIBI 4 (Stenotic): low-resistance flow with focal velocity increase ≥80 cm/s
  - May be associated with hyperemia post-recanalization
- TIBI 5 (Normal): no significant velocity asymmetry vs. contralateral side

Key Validation Points

- Complete MCA recanalization on TCD accurately predicts angiographic findings
  - Normal TCD signal → complete angiographic resumption of flow
  - Partial TCD improvement (TIBI 2–3) may correspond with persistent occlusion on

Reference: Burgin WS. Malkoff M. Felberg RA. Demchuk AM. Christou I. Grotta JC. Alexandrov AV. Transcranial Doppler ultrasound criteria for recanalization after thrombolysis for middle cerebral artery stroke. Stroke. 2000;31(5):1128–1132.

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Case 2

- 52 year old woman, independent CEO, presented to the Mackenzie Health Region as Code Stroke.
- No history of uncontrolled hypertension, regimented exercise routine and dietary control.
- Hyperacute assessment and Imaging indicated BG ICH.
- Transferred to regional ICU for BP management.
- Collaboration with UHN to acquire DSA over course of hospitalization given age — Negative for AVM.
- MR Imaging acquired acutely and on follow up.
- Initial Blood Pressures only modestly elevated 140s.
- ICU stay associated with therapeutic titration of BP; nursing records suggest pressures varying between the 110 and 140 range over the first week.

Initial CT Head: "Code Stroke"

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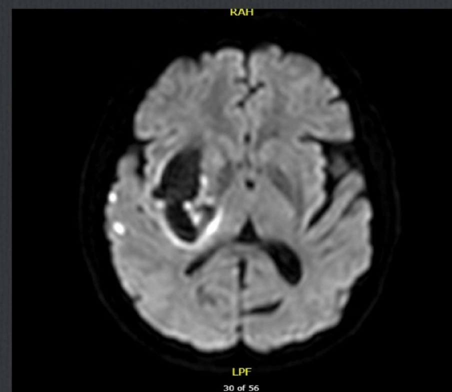

Initial MRI Head: DWI

Initial MRI Head: DWI

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Case 2

Initial CT Head: "Code Stroke"

Initial MRI Head: DWI

Left: Initial CT Head "Code Stroke" | Right: Initial MRI Head DWI

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Case 2

- Primary ICH can be difficult to distinguish from Hemorrhagic Transformation of Infarction in the setting of reperfusion injury.
- Conversely, Remote Diffusion-Weighted Imaging Lesions and Intracerebral Hemorrhage (RDWILS, DWIL, NIL etc.) are described in setting of ICH, 2–>7 days onset.
- While associated with increased risk of poor outcomes as well as prospective risk of ischemic events, radiographic associations include cerebral micro bleeds and leukoariosis, as well as a subcortical distribution of ischemic lesions. Clinical associations include high SBP on admission.

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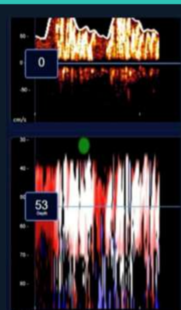
Case 2: PFO and Stroke: “Red Herring or Red Handed”



Alternative mechanism of cardio-embolism was considered. The patient had undergone TTE during her initial hospital stay as part of stratification of Vascular Risk.

TTE Findings

IAS: Interatrial septum is poorly visualized. Right Atrium: normal size. Mitral Valve: Minimally thickened leaflets. Trace mitral regurgitation. Aortic Valve: cusps not visualized due to suboptimal images. No aortic valve regurgitation. AV Vmax: 1.32 m/s.
Thus TCD based PFO study was considered.

TCD Bubble Study

Bilateral MCA and ACA territories insonated with good spectrographs and M-Mode Dopplers visualized.
Upon initial injection at rest: grade 3 degree of spontaneous shunting demonstrated by high intensity transients (HITS).
Upon First Valsalva: clear bilateral embolic signal of grade 4 degree.
Upon Second Valsalva: deferred due to clear positivity demonstrated on previous trials.

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Case 2: … "Closure"

The patient was heparinized and an InQwire wire was used to cross the PFO
with a JR4 diagnostic catheter. The LA pressure was 16/12 (11). An LA angiogram was performed to delineate the left atrial size and the left atrial size and location of the interatrial septal crossing point. A #25 Talisman device was prepared in usual fashion. An 8-French Talisman delivery catheter was advanced into the left upper pulmonary vein over an Amplatz extra stiff wire. The ECT was confirmed to be greater than 300. #25 Talisman device was prepared in the usual fashion and deployed under
fluoroscopic guidance in a satisfactory position. No complications occurred.

A 6-French Angio-Seal device was used to seal the LFA puncture site and the Talisman delivery catheter was replaced with a 8-French short sheath, which will be pulled in the cardiac catheterization recovery area. The patient was loaded with aspirin and Plavix and will be discharged on DAPT
for 3 months. Protamine was administered. She will be discharged home this evening.

Referral to Interventional Cardiology — "En route" Follow Up TEE

TEE Impressions:
LAA: no LA or LAA thrombus visualized. RA + VC: very small left to right tunnel PFO. Positive saline bubble study with some early bubbles crossing R to L. MV Morphology and Function: Minimally thickened mitral valve leaflets. Trace mitral regurgitation.

Notwithstanding discrepancy between TCD and TEE, Patient underwent Catheterization with "ICE" which verified high grade tunnel/PFO

The patient successfully underwent closure of the PFO after consultation and discussion with Cardiology Staff. And remains clinically stable.

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PFO & Cryptogenic Stroke — That was Then…

Epidemiology & PICSS Study

- Present in 30% of general population
- In cryptogenic stroke <55 years: 6× increased prevalence vs general population
- Potential treatments: ASA/Plavix, Coumadin, Endovascular or Surgical closure
- PICSS Study recruited from WARSS — ~630 patients randomised ASA vs. Warfarin
  - No significant difference in recurrent stroke rate with vs without PFO
  - No difference by PFO size (small / medium / large)
  - No difference between Aspirin and Warfarin groups
- PICSS: level 1 evidence for natural history, level 2 for treatment (limited power)
  - Mean INR in WARSS 2.1; median INR in PICSS 1.8 | Mean age 59 ± 12 y

Suggested Management Principles

- Treatment must be individualised; antiplatelet favoured as first line
- High Risk PFO considered for endovascular/surgical closure

Table 4. Factors Suggesting a Need for Closure of a Patent Foramen Ovale (PFO)

Younger patient (age <50 y)
No other cause of stroke identified
Large PFO
Coexisting atrial septal aneurysm
Recurrent neurologic events
Valsalva maneuver associated with previous events
Failure of anticoagulation therapy to prevent events
Intolerance of anticoagulation
High risk of recurrent deep venous thrombosis or pulmonary embolus

Wu LA et al. Arch Intern Med. 2004;164(9):950–6 | Homma S et al. (PICSS) Circulation 2002;105:2625–31

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…"This is Now": PFO & Cryptogenic Stroke - RoPE Score & Attributable Risk

$$\text{PFO Attributable Fraction} = 1 - \left(\frac{\text{Prevalence of PFO in controls} \times [1 - \text{Prevalence of PFO in CS cases}]}{\text{Prevalence of PFO in CS cases} \times [1 - \text{Prevalence of PFO in controls}]}\right)$$

RoPE Score (Kent et al. Neurology 2013;81:619–625)

- Development of scale to predict attributable risk of PFO-related stroke in cryptogenic stroke population
- Scale predicts likelihood of causal association
  - Risk of stroke is higher in 'cryptogenic' population with alternate vascular risk factors — recurrence rate is lowest in this strata
- Higher RoPE score = younger, healthier patient = PFO more likely to be causative
  - Score 0–3: ~10% PFO-attributable fraction | Score 9–10: ~88% attributable fraction

Predictors of Non-PFO Cause (OR table, right)

- Older age, diabetes, hypertension, current smoking, prior stroke/TIA, and deep (vs cortical) infarct all predict lower likelihood of PFO causality (all P < 0.001)

Term in model*	OR (95% CI)	p Value
Age, per 10-y increase	0.72 (0.67–0.77)	<0.0001
Diabetes	0.65 (0.51–0.83)	0.0006
Hypertension	0.68 (0.57–0.81)	<0.0001
Current smoker	0.60 (0.50–0.71)	<0.0001

Abbreviations: CI = confidence interval; OR = odds ratio; PFO = patent foramen ovale.
* Adjusted for sex and index stroke vs TIA.

Table 4 RoPE score calculator

Characteristic	Points	RoPE score
No history of hypertension	1	
No history of diabetes	1	
No history of stroke or TIA	1	
Nonsmoker	1	
Cortical infarct on imaging	1	
Age, y		
18–29	5	
30–39	4	
40–49	3	
50–59	2	
60–69	1	
≥70	0	
Total score (sum of individual points)		
Maximum score (a patient <30 y with no hypertension, no diabetes, no history of stroke or TIA, nonsmoker, and cortical infarct)		10
Minimum score (a patient ≥70 y with hypertension, diabetes, prior stroke, current		0

Kent DM et al. (RoPE Score) Neurology 2013;81:619–625

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PFO in Cryptogenic Stroke: Young Patients & Benefit of Closure

~25% of general population have a PFO

~40–50% of cryptogenic stroke patients have PFO

6× increased PFO prevalence in CS patients <55 yrs

NNT 20 strokes prevented per 20 closures (CLOSE trial)

RoPE Score — Who Benefits Most?

7–10	**High attributable risk**	Strong benefit from closure; recurrence driven by PFO
0–3	**Low attributable risk**	PFO likely incidental; address competing vascular risks
4–6	**Intermediate**	Individualise — anatomy (ASA, large shunt) guides decision

Kent DM et al. Neurology 2013;81:619–625

Landmark RCTs: Closure vs Medical Therapy

RESPECT	RRR 62%	NNT 45	Long-term extended follow-up favours closure; AF ↑ periprocedurally
REDUCE	RRR 77%	NNT 28	HR 0.23 at 2 yrs; Helex/Cardioform device; AF signal persists
CLOSE	RRR 97%	NNT 20	0 recurrent strokes in closure arm at 5 yrs; ASA comparator

Mas JL CLOSE NEJM 2017 | Sondergaard L REDUCE NEJM 2017 | Carroll J RESPECT NEJM 2013/2017

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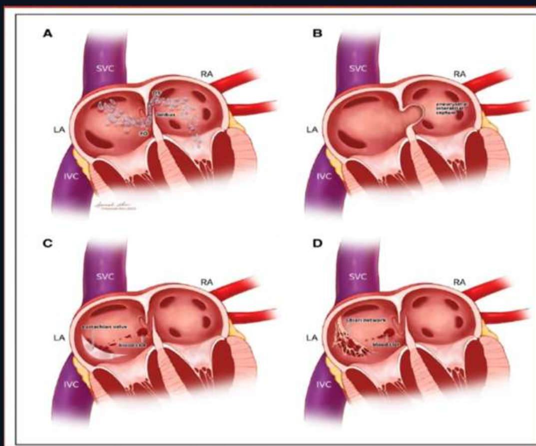
Patent Foramen Ovale — Diagnosis & High Risk Features



Diagnostic Modalities

- Diagnostic techniques include TTE, TEE and TCD
- TEE/TCD > TTE for sensitivity
  - Spencer et al: TCD — 98% sensitivity, 94% accuracy detecting PFO
  - TEE — 91% sensitivity, 99% accuracy (J Neuroimaging 2004;14:342–9)

Clinical Evidence

- Mojadidi et al: overall sensitivity 97%, specificity 93% for detection of RLS with c-TCD vs c-TEE
  - JACC Cardiovasc Imaging. 2014 Mar; 7(3):236–50
- TCD may have an important role in assisting diagnosis of PFO

High Risk Structural Components

- PFO Size >25–30 microbubbles passing in 3–5 cardiac cycles (TCD SLS 3–5)
- Atrial Septal Aneurysm (>10 mm)
- Persisting Eustachian tube and Chiari Network — felt to impede PFO Closure

High Risk PFO Features: L. Sposato et al. Stroke Jan 2024

Spencer MP et al. J Neuroimaging 2004;14:342–9 | Mojadidi MK et al. JACC Cardiovasc Imaging 2014;7(3):236–50 | Sposato LA et al. Stroke 2024 Jan

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BUBL Study — Robot-Assisted TCD vs. TTE for Right-to-Left Shunt Detection

Rubin MN et al. Stroke 2023;54:2846–2850 | NCT04604015 | 6-site prospective single-arm trial, n=129 evaluable

Study Design

- Prospective, multicenter, single-arm device trial
  - 6 clinical sites across the USA
- 154 enrolled — 129 evaluable (intent to scan), 121 per protocol
  - Population: adults with ischaemic stroke or TIA (embolic etiology on differential)
  - Enrolled Oct 2020 – Oct 2021
- Robot-assisted TCD (raTCD): NeuraSignal NovaGuide™ system
  - Bilateral automated probe placement — no TCD training required
- Compared to standard-of-care TTE with agitated saline

Why TTE Fails

- TTE sensitivity for RLS: only ~45% vs TEE
  - Chest wall and rib obscure atrial images
  - Sedation limits Valsalva in TEE; TTE Valsalva hard to confirm
  - Valsalva confirmed on raTCD by ≥25% drop in MCA velocity

Primary Outcome — Any RLS Detection

64% raTCD detected RLS — 83/129 patients

20% TTE detected RLS — 26/129 patients

3× more RLS detected by raTCD vs. TTE (absolute difference 44%, P < 0.001)

Secondary — Large RLS Detection

27% raTCD large RLS — 35/129 patients

10% TTE large RLS — 13/129 patients

TTE completely missed 18/35 large intervenable shunts (P < 0.001)

Key Metrics vs. TEE (gold standard)

Metric	raTCD	TTE
Sensitivity	96%*	45%
Specificity	92%*	99%
Any RLS (BUBL)	64%	20%
Large RLS (BUBL)	27%	10%
No raTCD false-neg vs TEE	0	—

** Prior TCD meta-analyses vs TEE reference (Katsanos et al. Ann Neurol 2016)*

Clinical Significance

- Reliance on TTE alone = underdiagnosed RLS, missed PFO closure candidates
  - ~5% of all ischaemic strokes attributable to RLS — 10% in young/middle-aged
- raTCD operated by non-TCD-trained staff with equivalent accuracy

Reference: Rubin MN, Shah R, Devlin T et al. Robot-Assisted Transcranial Doppler Versus Transthoracic Echocardiography for Right to Left Shunt Detection. Stroke 2023;54(11):2846–2850. | Also: Katsanos AH et al. Ann Neurol 2016;79:625–35

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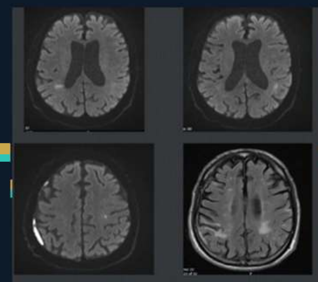
Case 3: "ESUS AIN'T AGEIST"



- Patient is a 70 y M independent to IADLs on initial presentation. Presented with Subacute speech arrest-impaired fluency.
- Imaging showed multifocal left Perisylvian/frontal lesions.
- Patient history of biprosthetic valve replacement, endocarditis work up negative. TTE negative for valvular disease and Right to left shunt.
- Holter and prolonged Holter negative.
- Recurrent presentation for at home hospital "confusional episodes" ×2 over the ensuing year. Each occasion associated with recurring ischemic, bihemispheric lesions.
- Followed up in SPC, and started on empiric DOAC, presumed PAF
- Despite empiric anticoagulation. Recurrent "Confusional Event" Re-Admitted to Home Hospital
- Functional decline, multi-infarct dementia. Discharging Physician Called to arrange SPC follow up;
- Patient transferred to THP-M Site as Complex Non-acute Stroke Patient for in-hospital reassessment.
- On latest presentation, LP and repeat cardiac work up TEE— negative.
- Embolic? Vasculopathy?
- Platelets noted persistently elevated for first time.
- Discussion with Neurosurgery for Brain/Meningeal Biopsy.
- TCD Considered as Non-invasive Preliminary Test for Emboli Monitoring and PFO study

- TCD positive for High Grade Right to left shunting, and on emboli monitoring spontaneous emboli.
- JAK mutation positive. Diagnosis: Essential thrombocytosis, started c Hydroxyura by Hematology with anticipated
- Patient unable to return home, discharged to Nursing Home Dementia unit.

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PFO in ESUS: The Elderly, Malignancy & Secondary Causes

ESUS (Embolic Stroke of Undetermined Source): non-lacunar infarct with no AF, <50% stenosis, no cardiac thrombus, and no other determined cause — Hart RG et al. Lancet Neurol 2014

PFO in Elderly ESUS — What the Data Show

- PFO prevalence in ESUS remains ~25% even in patients >60 yrs
- RoPE score lower in elderly → attributable fraction is lower, not zero
- NAVIGATE & RESPECT ESUS: no benefit of anticoagulation over antiplatelet in unselected ESUS
- Post-hoc: PFO + ASA may still benefit from closure regardless of age
- AHA/ASA 2021 Class IIa: consider closure if high-risk PFO features even age 60–65

Malignancy, Hypercoagulability & ESUS

- Active malignancy: 10–15% of ESUS — lung, pancreas, GI adenocarcinomas predominate (Schwarzbach 2012)
- NBTE and LICA are key mechanisms — often coexist
- Cardinal clues: D-dimer ↑, multi-territorial DWI infarcts (Nam HS et al. Ann Neurol 2017)
- Trousseau syndrome: migratory thrombophlebitis + emboli via mucin/TF hypercoagulability
- Workup: CT CAP, tumour markers, PET-CT; anticoagulation preferred over antiplatelet

Other Secondary Causes of ESUS to Systematically Exclude

Cardiac:	Paroxysmal AF (prolonged monitoring), LAA dysfunction, valvular disease, intracardiac thrombus	**Vascular:**	Aortic arch atheroma ≥4mm, cervicocranial arteriopathy, vasculitis, FMD
Haematologic:	APS, thrombocytosis, hyperviscosity, JAK2 mutation, PNH, occult coagulopathy	**Paradoxical:**	PFO + DVT/PE, pulmonary AVM (HHT), pulmonary hypertension — TCD bubble study crucial

Hart RG et al. ESUS. Lancet Neurol 2014 | Schwarzbach CJ et al. Cancer & Stroke. Stroke 2012 | Nam HS et al. DWI patterns in cancer stroke. Ann Neurol 2017 | Powers WJ et al. AHA/ASA Guidelines 2021

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TCD Bubble Study: Protocol for PFO / R→L Shunt Detection

Indication: Cryptogenic stroke / TIA, ESUS, pre-closure workup, PFO surveillance. Principle: IV agitated saline microbubbles (>10 μm) cannot cross pulmonary capillaries — MCA detection implies cardiac or pulmonary R→L shunt.

Step-by-Step Protocol

1. **Patient Positioning & Probe Setup**
   Supine. Bilateral temporal windows; depth 50–55 mm. Optimise MCA signal (TIBI ≥3). PMD multi-gate preferred for simultaneous bilateral display.
2. **Contrast Preparation**
   9 mL saline + 1 mL blood + 0.5 mL air via 3-way stopcock. Agitate 10× until opaque. Inject within 30 s via antecubital IV (18–20G).
3. **Baseline Injection (Rest)**
   Rapid IV bolus over 3–5 s. Monitor MCA bilaterally for 40 s post-injection. Document any MES. Record Spencer Grade at rest.
4. **Provocation: Valsalva Manoeuvre**
   Repeat injection. At 5 s post-injection: sustained Valsalva strain (>40 mmHg) for 5–10 s, then release. Reverses inter-atrial gradient — unmasks latent PFO. Confirm adequacy by
5. **Grading & Reporting (Spencer Scale)**
   Grade 0: none • 1–2: 1–10 MES • 3–4: 11–25 MES • 5: curtain. Timing: <8 cardiac cycles = cardiac shunt; late (>8 cycles) = pulmonary AVM. Document rest and provocation grades separately.

Quality Indicators & Common Pitfalls

✓ Adequate Valsalva
Patient strains audibly against closed glottis for 5–10 s, beginning 5 s after injection. Confirm by visible MCA velocity dip ≥25% on Doppler trace before release. Inadequate Valsalva is the most common cause of false-negative results.

✓ Bubble Quality & IV Access
9 mL saline + 1 mL blood + 0.5 mL air agitated 10× until uniformly opaque. Inject within 30 s — bubbles dissolve rapidly. Antecubital or medial cubital vein preferred; hand or wrist IV increases bubble dissolution before reaching right heart.

⚠ False Positive — Pulmonary AVM
Right-to-left shunting via pulmonary arteriovenous malformation (e.g. HHT) produces MCA signals LATE — typically >8 cardiac cycles after injection. Cardiac PFO shunting appears EARLY (<5 cycles). Timing of first MES relative to injection is therefore critical to document.

⚠ False Negative — Common Causes
Inadequate Valsalva (most common) • Distal or small-bore IV site • Over-diluted or poorly agitated contrast • Inadequate temporal window (use contrast agent) • Patient positioning — avoid semi-recumbent if possible during injection phase.

Reporting Standard: State — (1) laterality of insonation, (2) Valsalva adequacy, (3) Spencer Grade at rest and with Valsalva, (4) timing of first MES relative to injection (early <8 cycles = cardiac; late = pulmonary)

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Right-to-Left Shunt Grading — Spencer Logarithmic Scale (TCD) vs. TEE

TCD: HITS counted in bilateral MCA for 40 s after agitated saline injection ± Valsalva | TEE: microbubbles in LA within 3 cardiac cycles after right atrial opacification

Grade	TCD — HITS (MCA, 40 s)	TCD Description	Shunt Severity	TEE — Bubbles in LA (3 cycles)	Clinical Implication
0	No HITS	No signal detected in MCA — complete absence of microbubbles	None	0 bubbles	No RLS — PFO absent or closed
I	1–10 HITS	Individual, countable microbubbles — small embolic shower	Trivial / Small	1–9 bubbles (Small)	Minimal clinical risk; may not warrant closure alone
II	11–30 HITS	Multiple discrete bubbles — moderate embolic show	Small–	10–20 bubbles ...rate)	Consider further risk stratification with RoPE score
▲ LARGE RLS THRESHOLD — SLS Grade III+ = intervenable shunt ▲					
III	31–100 HITS	Dense shower — bubbles begin to coalesce; difficult to count individually	Moderate–Large	21–30 bubbles (Large)	SLS ≥ III threshold for large RLS in BUBL/closure trials; consider TEE + closure discussion
IV	101–300 HITS	Continuous embolic shower — partially dense; multiple overlapping signals	Large	>30 bubbles (Large/Very large)	High-risk PFO; strong indication for closure in cryptogenic stroke <60 y
V	>300 HITS ("Curtain")	Curtain pattern — MCA signal completely obliterated by dense embolic shower	Massive	LA fully opacified	Very high-risk; complete opacification equivalent; strong closure indication

Notes: TCD (SLS) grading uses bilateral MCA Power M-mode; HITS counted within 40 s of injection ± Valsalva. Adequate Valsalva confirmed by ≥25% drop in MCA velocity. TEE grades based on bubble count in LA within 3 cardiac cycles of RA opacification; >3 cycles suggests PAVM (extracardiac). **SLS Grade ≥ III (>30 HITS) correlates with TEE large shunt (>20–30 bubbles in LA) and is the threshold used in BUBL trial & closure RCTs.**

References

1. Spencer MP, Moehring MA, Jesurum J, et al. Power M-mode transcranial Doppler for diagnosis of patent foramen ovale and assessing transcatheter closure. J Neuroimaging. 2004;14(4):342–349.
2. Zanferrari C, Buffon D, Cattelan AM, et al. Detection of right-to-left shunts: comparison between the International Consensus and Spencer Logarithmic Scale criteria. Neurol Sci. 2008;29(1):9–14.
3. Katsanos AH, Psaltopoulou T, Sergentanis TN, et al. Transcranial Doppler versus transthoracic echocardiography for detection of patent foramen ovale in cryptogenic cerebral ischemia: systematic review and meta-analysis. Ann Neurol. 2016;79(4):625–635.
4. Rubin MN, Shah R, Devlin T, et al. Robot-Assisted Transcranial Doppler Versus Transthoracic Echocardiography for Right to Left Shunt Detection (BUBL Study). Stroke. 2023;54(11):2846–2850.
5. Palazzo P, Ingrand P, Agius P, et al. Transcranial Doppler to detect right-to-left shunt in cryptogenic acute ischemic stroke. Brain Behav. 2019;9(2):e01091.
6. Homma S, Sacco RL. Patent foramen ovale and stroke. Circulation. 2005;112(7):1063–1072.

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Case 4: Recurring Arterial Events

- A 79 year old right hand dominant male presented with acute onset of expressive aphasia and right hemi-body weakness preceded by an episode of left amaurosis fugax.
- Past history of hypertension, hyperlipidemia, rheumatoid arthritis, smoking and metastatic SCC of the scalp treated with resection and radiation.
- Initial NIHSS was 17 which improved to 3 shortly after administration of tPA. CTA head and neck revealed a distal left M2 occlusion as well as a short segment left ICA stenosis in the region of an elongated styloid process on the left. Elongated styloid processes seen bilaterally; left and right styloid process was 5 cm and 3.8 cm long respectively.
- While on aspirin, he experienced recurring episodes of left eye amaurosis fugax. Bedside TCD revealed asymmetric embolic signal occurring exclusively on the left. Started on IV heparin but continued to experience transient left eye vision loss. MRI brain revealed scattered diffusion restriction in the left hemisphere.
- Follow up CTA showed new left carotid intraluminal thrombus extending into carotid siphon of the left ICA. Resolution of micro-embolic signal on TCD and of recurring symptoms was associated with titration of i.v. Heparin dosing.
- Despite ongoing clinical stability, vessel progressed to complete occlusion. PET scan revealed no malignancy while hypercoagulable work-up was positive for antiphospholipid antibodies. Eventually bridged to warfarin;

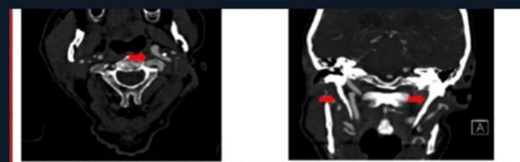

Figure 1: CTA head and neck. Axial view (A) showing left carotid artery stenosis. Coronal view (B) showing elongated styloid process bilaterally. Left and right styloid process was 5 cm and 3.8 cm long respectively.

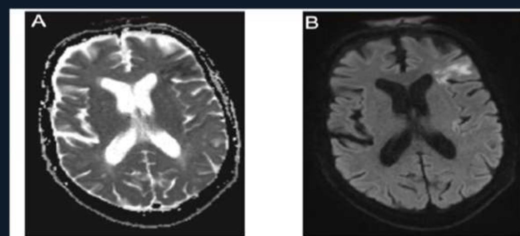

Figure 2: MRI brain. Axial ADC (A) and DWI (B) sequences show diffusion restriction in the left inferior frontal gyrus, pars opercularis.

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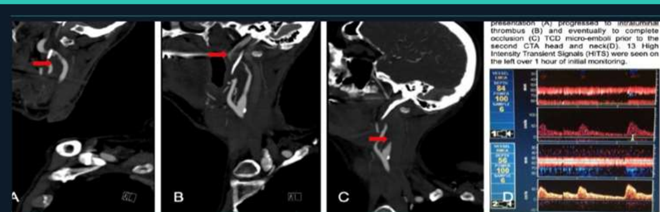
Case 4: Vascular Eagle's Syndrome "A Rare Bird"

- Eagle's Syndrome is generally rare. Prevalence of abnormally long (>2.5 cm) styloid process is 4 to 7.3%; only 4 to 10% will be symptomatic. This case demonstrates the importance of recognizing elongated styloid process or calcified stylohyoid ligament as a potential cause of stroke and TIA. Typical mechanism is non-traumatic carotid artery dissection, dissecting aneurysm, or carotid artery stenosis/compression.
- There are no guidelines when it comes to treating Vascular Eagle's syndrome. TCD can be used to identify a symptomatic ICA when there is suspicion of vascular Eagle's Syndrome — a viable complementary bedside modality. Sonographic evidence of micro-emboli may also necessitate more aggressive treatment, especially in the context of a hypercoagulable state. Moreover, TCD can monitor a carotid artery dissection during a styloid process resection.
- This Case is also representative of the application of TCD in the setting of Emboli monitoring for both diagnostic of symptomatic extra- and intracranial lesions, and allowing for the assessment of efficacy of medical antithrombotic strategies (e.g. Intra-luminal Carotid Thrombus, Symptomatic Intracranial Atherosclerosis).



Treating Subclinical Emboli "Blocking the Jabs, and Preventing the Knock Out Punch"

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Case 5

- 84 y.o. male presenting with recurrent left sided weakness correlating with punctate ischemic lesions on MRI. Appropriately on serial trials of DAPT post extracranial carotid stenting. CTA Showed Intracranial Right MCA occlusion vs. Critical Stenosis. Suspected Atherosclerotic Moya Moya Syndrome.
- PMH: BPH, CAD, Carotid artery stenosis, Diabetes mellitus type 2, Dyslipidemia, H/O coronary angiogram (13/07/2024), Hypertension, Iron deficiency anemia, NSTEMI (13/07/2024), Sleep apnea, Stroke, and TIA.
- PSH: Trigger finger release; Cardiac catheterization; Coronary angioplasty.
- Etiology?: Distal Emboli? Hypoperfusion?

TCD Study

Bilateral MCA and ACA territories insonated; good spectrographs and M-Mode Dopplers visualized. ~1 hour of monitoring with no microembolic signal.

Patient showed signs of prestenotic jet with markedly increased velocities in distal ICA and MCA — showing "trickle flow" through proximal and mid MCA. Resultant turbulence stimulated emboli filters, but did not correlate to true appearances of high intensity transients.

Contralaterally, distal ICA and MCA showed compensatory hyperperfusion without blunting seen in ACA on the right. No hyperperfusion in PCA.

This is a negative study for evidence of microembolic signal in the distribution of his vascular lesion or in an alternative distribution; however stagnant flow predisposing to distal embolization is supported by the ultrasound. This provides a rheologic basis for introduction of combination DOAC and ASA in the setting of recurring events given the cited challenges in the viability of intracranial stenting. Findings discussed with stroke team and consensus about treatment on discharge was attained and discussed with family.

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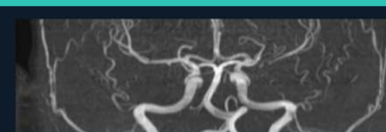
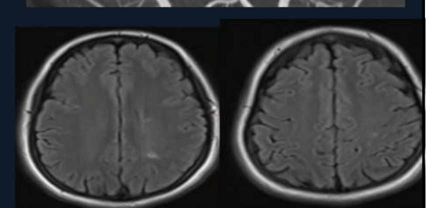
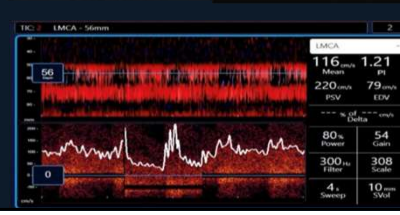
Case 6







Recurrent ongoing stereotyped right-sided numbness possibly weakness with dysarthria on 1 occasion. MR signal changes only in the left hemisphere.

Follow Up MR and CTA suggested Moya Moya Pattern. However Given Age, Demographic and Lesions on MRI.

Patient presents to West GTA Stroke Prevention Clinic for a TCD based Emboli monitoring study, as well as a complete TCD study including Cerebral Vasoreactivity/BHI.

Bilateral MCA and ACA territories insonated with good spectrographs and M-Mode Dopplers; approximately 1 hour of monitoring with no microembolic signal.

Left MCA showed evidence of a post stenotic jet manifesting as aliasing and mfV >100 cm/s, beyond this region the mid M1 MCA region velocities (mfV) were in the normal range 49–52 cm/s with lowering of velocities in the most distal M1/M2 junction with velocities in the 39 cm/s (compared to 67 cm/s contralaterally).

Testing for cerebrovascular reactivity showed breath holding index on symptomatic side (left hemisphere) of 0.192. Right side: 0.537. Substantially below normal, more likely reflection of the observed poor compliance with reliable breath holding.

This is a negative study for evidence of microembolic signal. Suggests efficacy of current antithrombotic regime. In terms of mfV, shows "High-High" or "High-Normal" gradient across the MCA territory. Patient only begins to show lower velocities in the distal M1/M2 junctions with apparent asymmetry relative to the contralateral side — suggesting indeed Moya-Moya Disease vs. That of Moya-Moya Syndrome. VMR reactivity not reliable; unfortunately no access to performance of L-arginine or Acetazolamide of Hypercapnia tests in the Stroke Prevention Clinic.

Foreseeable first step is to reassess her post vessel wall imaging. She remains asymptomatic at this time, and expressed a refusal for lumbar puncture however is amenable to reconsidering post investigation.

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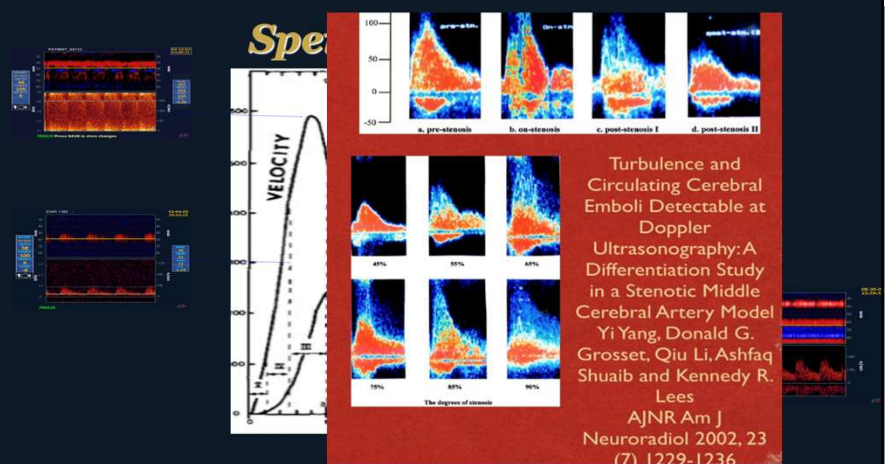
Cases 5,6-Steno-Occlusive Disease: "Not all about the Watershed"

- Decrease in Turbulent Flow results in alterations which correlate to degrees of stenosis and location along stenotic segment.
- This Rheologic Change may be seen in diverse disease states including steno-occlusive disease such as Moya-Moya, Sickle Cell Disease, or Cerebral Vasospasm.
- Segmental Nature of Pathology can make accurate isolation challenging. Remaining Alert to Background evidence of Aliasing associated with high velocities and traversing length of vessel using M-Mode Depth references important to isolate evidence of vasculopathy.
- Complimentary tests depending on clinical context can include: emboli monitoring, tests for Vaso-motor reactivity, or colour Doppler Contrast.
- Multiple Modalities e.g. CTA enhance both clinical suspicion and guide technique.



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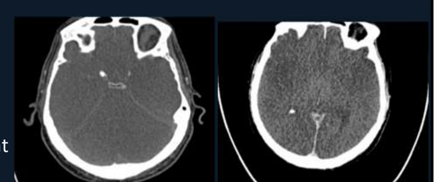
Case 7

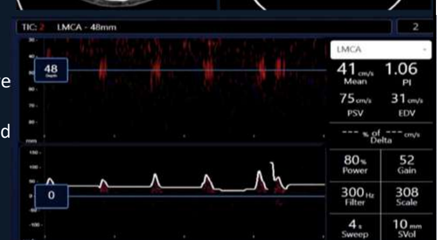
PMH
Coronary artery disease, Diabetes mellitus, Ischemic cardiomyopathy, Non-insulin dependent diabetes mellitus, Peripheral vascular disease, Smoker.

CT HEAD — Brain Parenchyma
Diffuse loss of gray-white matter differentiation, marked supratentorial and infratentorial edema with complete effacement of the sulci. Persistent mass effect on the ventricular system, with persistent effacement of the 3rd ventricle and 4th ventricle. Relative hyperdensity of the basal cisterns and some subarachnoid spaces — pseudo SAH. Persistent tonsillar herniation and effacement of the prepontine cistern.

CTA COW
Contrast opacification to distal petrous ICAs in anterior circulation. In posterior circulation, contrast to the leve of extradural vertebral arteries but no contrast opacification intracranially in the posterior circulation.
DELAYED: Contrast opacification in bilateral MCAs to distal M3 segments, bilateral distal A2 ACA segments and bilateral P2 PCA segments posteriorly. Questionable faint contrast in transverse, straight and transverse sinuses.

CV US TRANSCRANIAL DOPPLER — Brain Death Exam
Bilateral MCA territories insonated at a depth of 48–49 mm consistent with Mid M1 regions bilaterally.
Findings: Patient showed high resistance spikes with absent diastolic flow.
Summary: Study compatible with the evolving changes post brain death; warrants further supportive investigations including CTA, nuclear medicine perfusion scanning, and if warranted follow up TCD.





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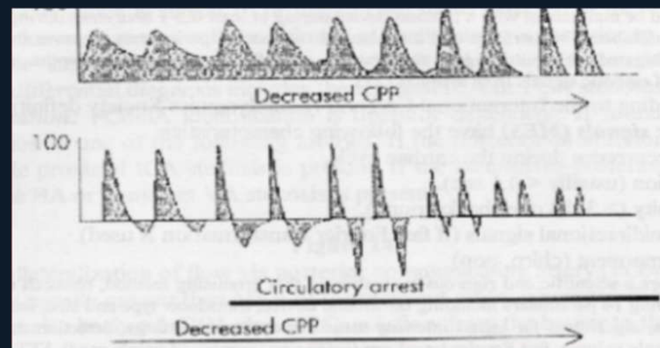
Case 7

- Considerations of possible Brain Death will occur in the setting of catastrophic insult, and persistent coma.
- Establishment of Brain Death is a tragic though important clinical milestone to assist families in decision making pertaining to goals of care.
- International Guidelines have recently been revised to include TCD as a supportive ancillary investigation, in conjunction with CTA, and Radionuclide Perfusion Scans.
- Emerging Scales (7 point scale, 4 point scale) for use with CTA which quantify degree of circulatory failure by evaluating cortical veins bilaterally along with GCV and Arterial Perfusion in the CoW have shown good correlation (sensitivity and specificity) when compared to DSA. Thus when used in conjunction with TCD, particularly with serial TCD, and evolving correlative changes allows for highly sensitive, highly specific multimodality assessment of this tragic clinical setting.



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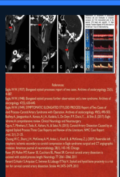
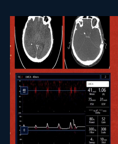
TCD in Stroke: Diverse Roles Across the Care Continuum



Case 4 — Eagle's Syndrome

Demonstrating Efficacy of Anti-Thrombotic Rx

- Guides antiplatelet/anticoagulant intensification
- Eagle's Syndrome / Dissection
- Thrombocytosis
- Moya-Moya high-gradient detection
- ICAD (Intracranial Atherosclerotic Disease)



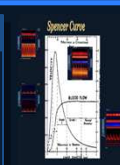
Case 7— Brain Death

Brain Death Assessment

- Cerebrovascular circulatory arrest pattern
- Reverberant / to-and-fro systolic spikes
- Absent diastolic flow → net zero cerebral perfusion
- Accepted ancillary test per international guidelines

Diagnosis & Vessel Assessment

- Occlusion localisation (MCA, ICA, BA)
- Stenosis grading — Spencer Curve velocity model
- Parvus-tardus pattern: proximal occlusion
- Collateral flow assessment (AComA, PComA)
- Vasospasm
- Steno-occlusive disease / Moya-Moya / ICAD



Spencer Curve (Cases 5,6)

Cerebrovascular Reactivity (CVR)

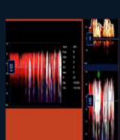
- Breath-holding index (BHI): vasodilatory reserve
- Impaired CVR predicts silent infarction risk
- Guides EVT candidacy in steno-occlusive disease

Emboli Monitoring (MES/HITS)

- Detects circulating microemboli in real time
- Guides antiplatelet/anticoagulant intensification
- **Solid and Gaseous Emboli**

Real-Time Cerebral Blood Flow Assessment

- Detection of blood flow velocities allow for graphing a "Spectrum" across Cardiac Cycle
- Color Doppler and PMD allow for precise anatomic localization of desired vessel



Case 2— PFO Closure

PFO / R→L Shunt Detection

- Agitated saline bubble study via temporal window
- 3× superior sensitivity vs TTE (BUBL 2022)
- Detects pulmonary AVM shunts not seen on TEE

Thrombolysis Monitoring (TIBI)

- Real-time recanalization tracking during IV tPA
- TIBI Grade 0–5: absent → normal flow
- Early recanalization predicts functional outcome
- Sonothrombolysis: ultrasound-augmented lysis (?)

Case 1 — EVT

Alexandrov AV et al. Consensus on TCD. J Neuroimaging 2012 | Demchuk AM et al. TIBI. Stroke 2001 | Ringelstein EB et al. Brain death TCD. ASNC 2006 | BUBL Study ISC 2022

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Organizing a TCD Service

- Identify Existing Resources:
- TCD dedicated device?
- Multipurpose TCD? Stroke Clinic for Carotids? Cardio-diagnostics? ICU, POCUS I'm ER?, Vascular Surgery? Radiology?
- Define Needs, and Viable Targets:
- TCD to supplement Carotids? Postural Studies? Opthalmic Artery in setting of Carotid occlusion? Steno-occlusive disease? Dedicated TCD with Power M-Mode?-PFO/RLS-Cryptogenic Stroke/ESUS Protocol, In-patient vs outpatient
- Potential Benefits? Resource utilization, the combination of TTE and TCD will often preclude need for TEE, when negative. In inpatient setting, an accessible bedside exam can decrease LOS.
- Identify Multidisciplinary Partners in Care for Follow-up Care; eg, Streamlines pathways for referral to Interventional Cardiology, Hematology, Rheumatology, Neurointerventional Radiology and Med-Oncology all part of the important "hand-over" after identifying relevant etiological factors in our patients.
- Thus organizing a TCD service allows for an impetus to enhancing stroke care across multiple aetiologies, and phases of disease

"Team TCD "

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Organizing a TCD Service (Continued)

- After acquiring access to TCD; who will support investigations and how?
- Brain-stroming solutions.
- THP-SPC: Stroke in Young/ESUS Clinic Protocol with TCD: Dedicated Days for TCD Clinic, with dedicated nurse for on-site iv access, and U/S Tech, and Stroke neurologist. Arrangement with Lab services allow for immediate post testing for thrombophilia work up to be drawn in clinic, prior to patient departure.. And relevant "builds" into the EMR allow for streamlined pathways of referral to Cardiology; Rheumatology; Vascular Surgery, NIR.
- In patient studies may be performed in clinic or at the beside and on non designated days to facilitate test acquisition and decrease LOS.
- Next Steps? Dedicated In patient and Acute Stroke Service, with greater logistic flexibility and capacity.

"Team TCD "

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In Conclusion: "Me, We"

- TCD is a modality that is non-invasive and portable and if available has valuable applications in both acute and elective settings of stroke care.
- Bedside accessibility allows for application in a diversity of settings of diagnostic uncertainty in both acute inpatient and secondary preventive outpatient settings.
- Innovations of Technology have reduced limitations associated with User Dependence
- Further Collaboration is required towards developing regional TCD programs that consider local logistics, resources and practice patterns.

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Thank You

Muzaffar Siddiqui MD FRCPC | Division of Neurology | Trillium Health Partners

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Evaluation

For the **Provincial Stroke Rounds Planning Committee:**
- To plan future programs
- For quality assurance and improvement

- For **You**: Reflecting on what you've learned and how you plan to apply it can help you enact change as you return to your professional duties

- For **Speakers**: The responses help understand participant learning needs, teaching outcomes and opportunities for improvement.

Transcranial Doppler (TCD): Practical Applications in Stroke

Please take 2 minutes to fill the evaluation form out. Thank you!

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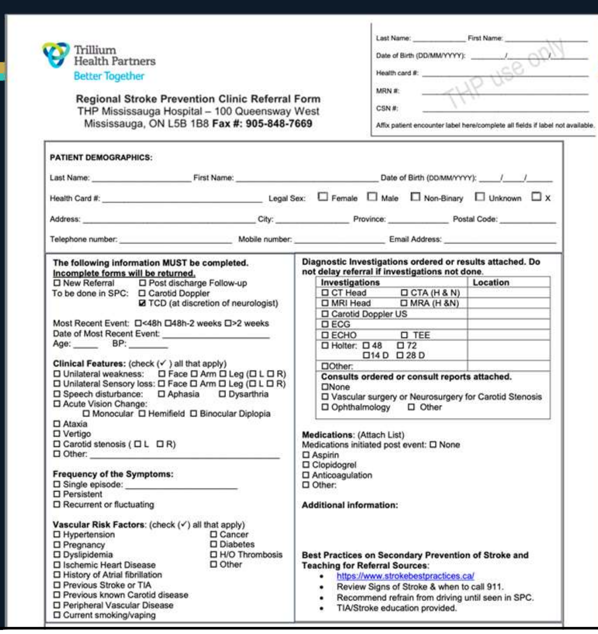
Resources:



Trillium Health Partners
Better Together

Regional Stroke Prevention Clinic Referral Form
THP Mississauga Hospital – 100 Queensway West
Mississauga, ON L5B 1B8 **Fax #: 905-848-7669**

Last Name: ____ First Name: ____
Date of Birth (DD/MM/YYYY): ___/___/___
Health card #: ____
MRN #: ____
CSN #: ____
Affix patient encounter label here/complete all fields if label not available.
THP use only

PATIENT DEMOGRAPHICS:
Last Name: ____ First Name: ____ Date of Birth (DD/MM/YYYY): ___/___/___
Health Card #: ____ Legal Sex: ☐ Female ☐ Male ☐ Non-Binary ☐ Unknown ☐ X
Address: ____ City: ____ Province: ____ Postal Code: ____
Telephone number: ____ Mobile number: ____ Email Address: ____

The following information MUST be completed.
Incomplete forms will be returned.
☐ New Referral ☐ Post discharge Follow-up
To be done in SPC: ☐ Carotid Doppler
☑ TCD (at discretion of neurologist)

Most Recent Event: ☐<48h ☐48h-2 weeks ☐>2 weeks
Date of Most Recent Event: ____
Age: ____ BP: ____

Clinical Features: (check (✓) all that apply)
☐ Unilateral weakness: ☐ Face ☐ Arm ☐ Leg (☐ L ☐ R)
☐ Unilateral Sensory loss: ☐ Face ☐ Arm ☐ Leg (☐ L ☐ R)
☐ Speech disturbance: ☐ Aphasia ☐ Dysarthria
☐ Acute Vision Change:
☐ Monocular ☐ Hemifield ☐ Binocular Diplopia
☐ Ataxia
☐ Vertigo
☐ Carotid stenosis (☐ L ☐ R)
☐ Other: ____

Frequency of the Symptoms:
☐ Single episode: ____
☐ Persistent
☐ Recurrent or fluctuating

Vascular Risk Factors: (check (✓) all that apply)
☐ Hypertension ☐ Cancer
☐ Pregnancy ☐ Diabetes
☐ Dyslipidemia ☐ H/O Thrombosis
☐ Ischemic Heart Disease ☐ Other
☐ History of Atrial fibrillation
☐ Previous Stroke or TIA
☐ Previous known Carotid disease
☐ Peripheral Vascular Disease
☐ Current smoking/vaping

Diagnostic Investigations ordered or results attached. Do not delay referral if investigations not done.

Investigations	Location
☐ CT Head ☐ CTA (H & N)	
☐ MRI Head ☐ MRA (H &N)	
☐ Carotid Doppler US	
☐ ECG	
☐ ECHO ☐ TEE	
☐ Holter: ☐ 48 ☐ 72 ☐ 14 D ☐ 28 D	
☐Other:	

Consults ordered or consult reports attached.
☐None
☐ Vascular surgery or Neurosurgery for Carotid Stenosis
☐ Ophthalmology ☐ Other

Medications: (Attach List)
Medications initiated post event: ☐ None
☐ Aspirin
☐ Clopidogrel
☐ Anticoagulation
☐ Other:

Additional information:

Best Practices on Secondary Prevention of Stroke and Teaching for Referral Sources:
- https://www.strokebestpractices.ca/
- Review Signs of Stroke & when to call 911.
- Recommend refrain from driving until seen in SPC.
- TIA/Stroke education provided.

Kim j, Pictorial Essay: Transcranial Doppler Findings of the Intracranial and Extracranial Diseases
.J Neurosonol Neuroimag 2019;11(1):1-21

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