NEUROSONOLOGY BASICS: TCD

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Neurosonology Basics: TCD

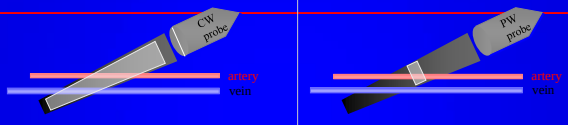
- Basics: Principles of TCD ultrasonography
- Clinical Applications:
  - TCD and extracranial disease
  - TCD and intracranial disease
  - TCD and acute stroke
  - TCD and Neuro-Critical Care
  - TCD Ans Intra-Operative Monitoring

BASICS

Principles of TCD Ultrasonography

- ***Pulse-echo principle***
- Sample Volume
- Spectral analysis
- Special problems (attenuation/aliasing)
- Safety consideration

‘CW’ - ‘PW’ Doppler Principle



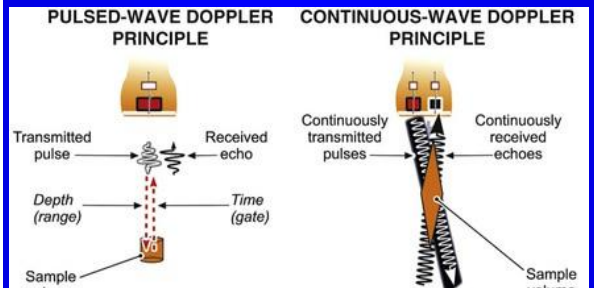
CW - Continious Wave

- Two crystals, one transmitter and one receiver
- Large Sample Volume
- Easy to pick up signals
- No depth information

PW - Pulsed Wave

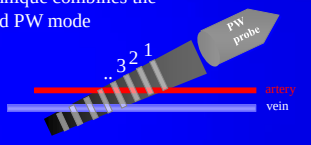
- One crystal is alternatively sending and receiving signals
- Adjustable Sample Volume
- Adjustable Depth
- Differentiation of vessels
- Necessary to do TCD

PW versus CW Doppler



‘Multi-Range’ Doppler

☞ The Multi-Range technique combines the advantages of CW and PW mode in one system!



Some Facts:

- Easy to pick up signals
- Large and adjustable Sample Volume
- Adjustable Depth
- Easy differentiation of vessels
- The new dimension gives easier orientation

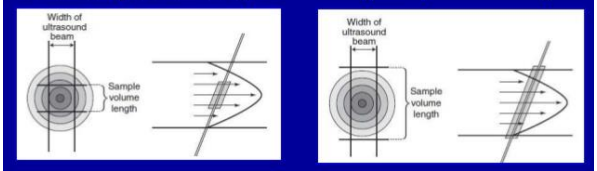
Principles of TCD ultrasonography

- Pulse-echo principle
- ***Sample Volume***
- Spectral analysis
- Special problems (attenuation/aliasing)
- Safety consideration

Sample volume length

Usually for TCD it ranges between 2 to 20 mm, usually we are working on 10-12 mm sample volume

Small sample volume length | **Large sample volume length**



Thrush A, Hartshorne T. Peripheral vascular ultrasound: How, why and when. Elsevier Churchill Livingstone, London, 2nd edition, 2005.

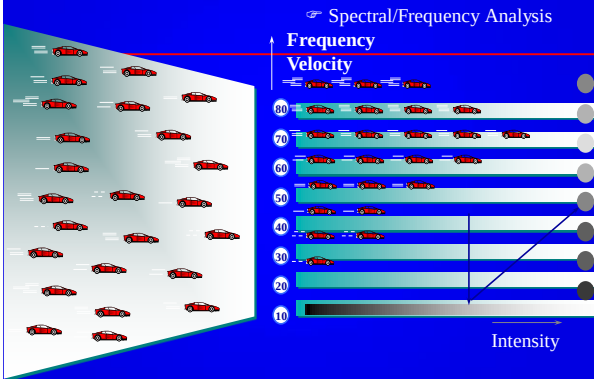
Principles of TCD ultrasonography

- Pulse-echo principle
- Sample Volume
- ***Spectral analysis***
- Special problems (attenuation/aliasing)
- Safety consideration

Spectral Analysis

- The ultrasound is reflected off the red blood cells and the energy of reflection is a function of the number of red blood cells flowing at a given velocity
- Since a spectrum of velocities can be found in the sample volume, a spectrum of colors will be seen on the screen

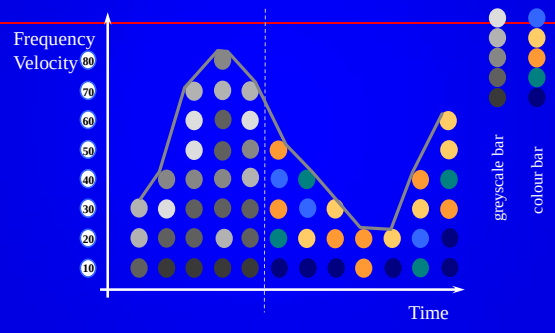
FFT - Fast Fourier Transformation



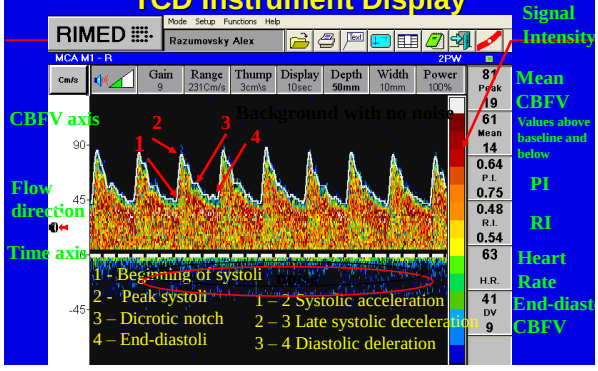
FFT - Fast Fourier Transform

- A spectrum analysis in the form of a mathematical transformation called Fast Fourier Transformation (FFT) is performed on the Doppler shift signal. The result is color coded blood flow spectrum display

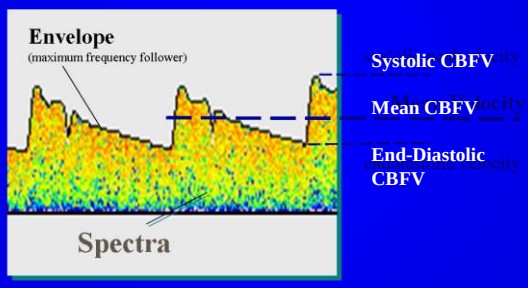
Spectral Display



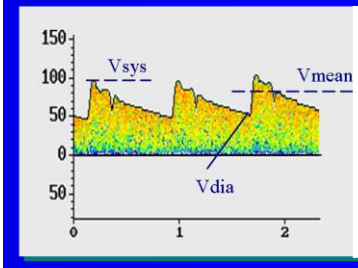
TCD Instrument Display



Spectral Display Indices



Pulsatility Indices



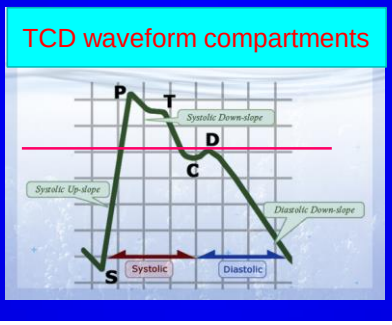
Gosling PI

PI =Vs – Vdias/V mean

Pourcelot Resistance Index

RI = Vs – Vdias/V dias

TCD Waveform



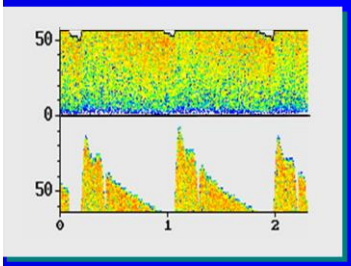
Principles of TCD ultrasonography

- Pulse-echo principle
- Sample Volume
- Spectral analysis
- **Special problems (attenuation/aliasing)**
- Safety consideration

Aliasing

- The PW Doppler device can evaluate a specific sample volume, but there must be adequate time between pulses for all signals to return from the defined depth
- *Aliasing* resembles an artifactual display of frequency shifts, resulting in false velocity readings

Aliasing Effect

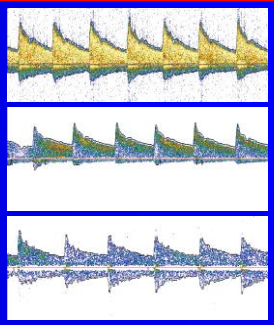


- Aliasing occurs when the flow velocities exceed the sampling frequency (half the PRF, Nyquist), the system does not sample fast enough
- The top of the spectra is cut and pasted to the bottom of the display
- In order to avoid Aliasing effects the Scale (PRF) setting can be increased or the Zero Line moved.

Attenuation

- Attenuation describes how the intensity of an ultrasonic beam predictably decreases in a homogeneous medium (brain) as the distance from the transducer increases
- Attenuation in soft tissue is directly related to the length of the sound pathway and the probe frequency

Attenuation

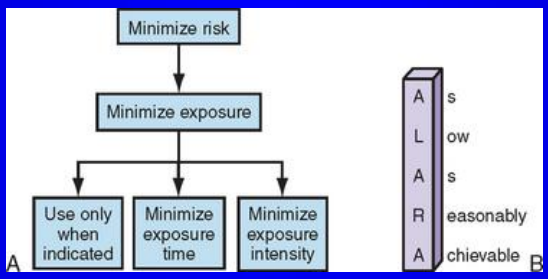


- Depth 85 mm
- Depth 98 mm
- Depth 112 mm

Principles of TCD Ultrasonography

- Pulse-echo principle
- Sample Volume
- Spectral analysis
- Special problems (attenuation/aliasing)
- ***Safety consideration***

Safety Considerations
ALARA Principle!!!



Safety Considerations

Nonthermal Effects

- *Stable cavitations* is the oscillation of the bubbles of fluid with the pressure variations induced by ultrasound
- *Transient cavitations* which occurs when the magnitude of bubble oscillations becomes so large that it causes sudden collapse of the bubbles, generating pressure discontinuities (so-called shock wave)

Safety Considerations

Nonthermal Effects

- A secondary complication of transient cavitations is the formation of free radicals and sonochemicals, which can cause further damage to the cell structure or even have a mutagenic effect.
- Till recently nobody demonstrated this effect *in vivo*

Safety Considerations

Thermal Effect

- Heating of the insonated brain resulting from the conversion of ultrasound energy is unavoidable
- Temperature elevation of 1^0C during an ultrasound study is usually considered to be inconsequential; however, scanning times should be considered carefully in patients with elevated body temperature
- Although not reported clinically, the theoretic risk of periosteal heating remains a concern

CLINICAL APPLICATIONS

Clinical Considerations

- Stroke, TIA and delayed consequences of cerebral ischemia remain common entities in ambulatory neurology practice
- Compelling indications for neurovascular testing include stroke, TIA, ocular ischemia. Tinnitus, dizziness/vertigo also represent complaints whereby TCD and CD may be indicated and justified
- The consequences of not performing such usual customary and reasonable medical maneuvers must be considered

Clinical Considerations (cont.)

- Different ICU:
  - NeuroCritical Care
    - SAH, TBI, Acute Stroke, Cryptogenic Stroke, Encephalopathy, Brain Death
  - Pediatric
  - Cardiac
  - Medical

Specific TCD Applications for Neurology

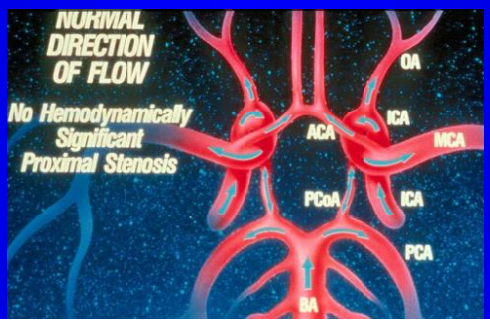
- Evaluation effect of extracranial lesion (carotid, vertebral, subclavian) on cerebral perfusion
- Evaluation of cerebrovascular reactivity
- Evaluation of intracranial arterial circulation (stenosis, Moya-Moya, cerebral arteritis)
- Evaluation of positional vertigo, syncope, dizziness, orthostatic hypotension
- Evaluation of Sickle Cell disease
- Acute/Subacute stroke/TIA
- Real-time monitoring of recanalization after t-PA and thromboectomy
- Monitoring of emboli
- Evaluation of PFO
- Dementia
- Meningitis, encephalitis, vasculitis
- Functional TCD

TCD AND EXTRACRANIAL CAROTID ARTERIES LESIONS

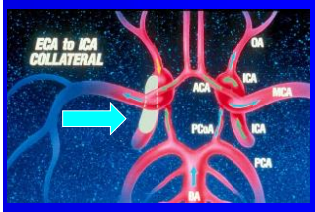
Carotid obstruction effect and TCD

- Mild to moderate stenosis < 75%: TCD is essentially normal
- Stenosis more than 75%: TCD wave form changes may include:
  - Decreased CBFV
  - Delayed systolic upstroke time
  - Decreased Pulsatility Index

Collateral Pathways

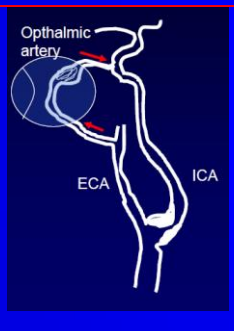


Collateral Pathways: OA

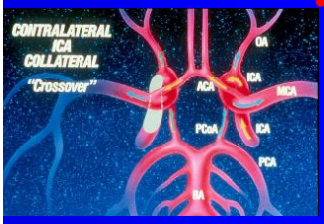


- **In the OA**
  - Retrograde OA flow direction when cross flow through the AComA is inadequate
  - The degree of collateralization through the OA ranging from flow confined to the cavernous portion, to flow extending to the distal MCA branches

Collaterals I - OA

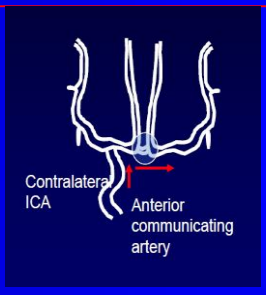


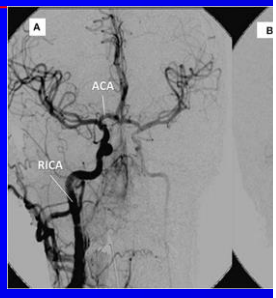
Collateral Pathways: ACA



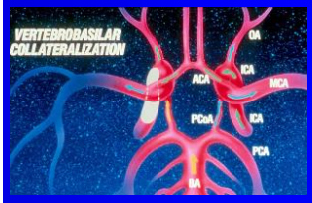
- **Patent ACommA:**
  - The contralateral ACA CBFV is approximately doubled
  - The ipsilateral ACA CBFV increase is approx. 50% with retrograde flow direction
  - A prompt MCA CBFV fall after compression of the non-occluded contralateral CCA

Collaterals III - ACommA



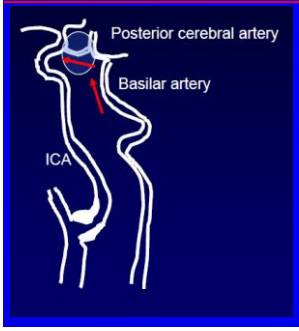


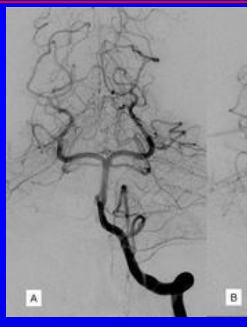
Collateral Pathways: BA



- **In the BA**
  - BA CBFV of more than 70 cm/s
  - A marked increase of BA CBFV after compression of the non-occluded CCA
  - An evident side-to-side asymmetry of the CBFV of the PCA's

Collaterals II - PCommA





Collateral Pathways

- Determination of altered collateral flow represent the most reliable indicator of CCA lesion by TCD

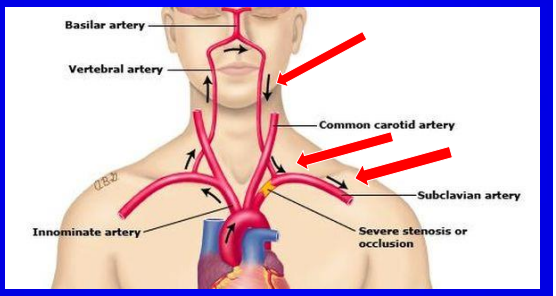
- Collateralization through the AComA (sensitivity – 93%, specificity – 100%)
- Collateralization through the PComA (sensitivity – 87%, specificity – 96%)
- Collateralization through the OA (sensitivity – 95%, specificity – 100%)

Cerebral Hemodynamics with Extracranial Arterial Disease

- In most cases the side-to-side difference in CBFV serves as the most sensitive and reliable quantitative criterion for the presence or absence of flow abnormalities

TCD AND SUBCLAVIAN STEAL

Subclavian Steal



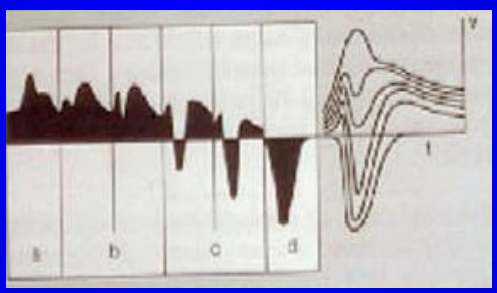
Subclavian Steal

- Atherosclerosis
- Traumatic
- Iatrogenic
- Dissecting aneurysm
- Congenital anomaly
- Necrotizing arteritis

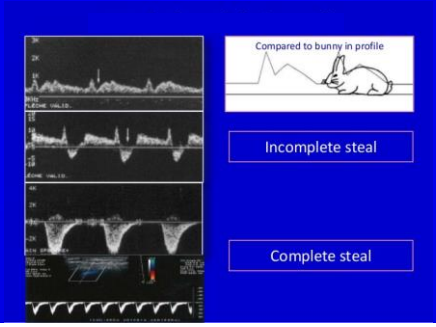
Subclavian Steal

- Systolic deceleration in the VA (moderate to severe stenosis of the subclavian artery)
- Alternating flow in the VA (incomplete steal)
- Retrograde flow in the VA (complete steal)

Transition of Waveform from Normal to Complete Steal Effect



Vertebral to Subclavian Crossflow



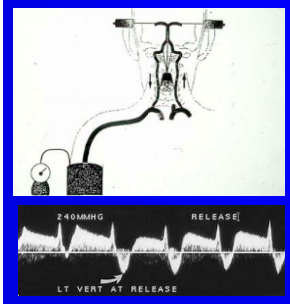
80-90% Stenosis of the Brachiocephalic Trunk

Right carotid siphon

Right MCA

Right VA

Subclavian Steal Protocol



- TCD study of the anterior and posterior circulation
- A brachial artery compression-decompression test
- At decompression there will be sudden increase in the steal in the VA/BA due to the reactive post-ischemic arm hyperemia

Role of TCD: Subclavian Steal

- Detects abnormal changes in Doppler spectrum waveform (systolic deceleration, alternating flow, retrograde flow) in the VA, and/or VA's, and/or BA
- Indicates low pressure in the BA
- Raises option of subclavian bypass surgery

TCD AND POSITIONAL VERTIGO, DIZZINESS, BOW HUNTER SYNDROME…

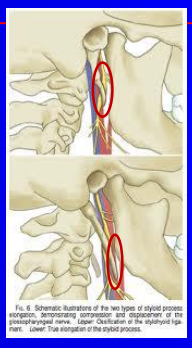
VB iIschemia and Head Turns

- Bow hunter's syndrome (BHS) is characterized by transient vertebrobasilar ischemia brought on by head turning, but reports in the literature are rare
- Identification of diminishing blood flow velocities by TCD can be performed accurately at the bedside, and such findings are associated with clinical symptoms

Eagle Syndrome

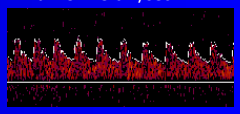
- Eagle syndrome is a rare condition where an elongated temporal styloid process (more than 30mm) is in conflict with the adjacent anatomical structures
- Two forms of eagle syndrome exists: The classic form and the vascular form

Eagle Syndrome

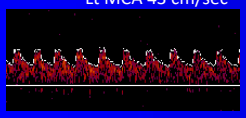


36 yo male with episodes of blurry visions and lightheadedness due to neck extensions when extending his neck while hunting and doing other activities associated with head movement, r/o vascular form of styloid process syndrome

Rt MCA 45 cm/sec

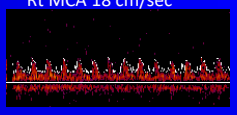


Lt MCA 43 cm/sec

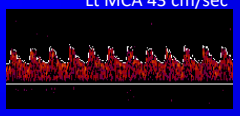


This study showed a hemodynamically significant abrupt CBFV decrease in the right MCA by 60% during head extension to the back with accompanying symptoms of dizziness and blurry vision. There was immediate disappearance of the symptoms with normal positioning of the head. This finding supports the presence of a right styloid process syndrome that involves mechanical irritation and compression of a vessel by an elongated styloid process

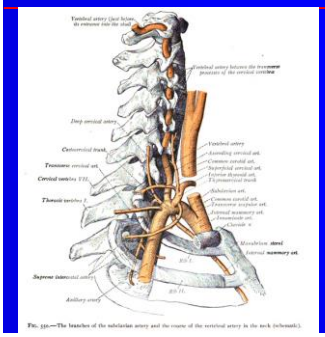
Rt MCA 18 cm/sec

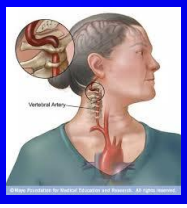


Lt MCA 43 cm/sec



VA

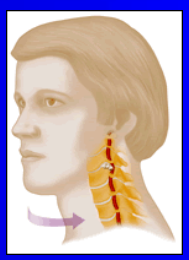




Owl and Head Rotation for 270º No Problem!

Bones in owls' necks have adaptations designed to facilitate extreme rotation. VA's feeding the birds' brains passes through holes in the vertebrae, called transverse foramine; these holes were 10 times larger in diameter than the artery. This extra space creates air pockets that allow the artery to move around when twisted; 12 of the vertebrae in the owls' necks had this adaptation

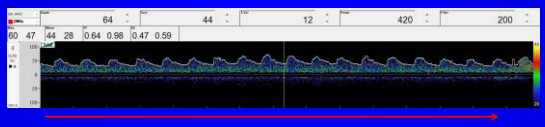
Head Turns



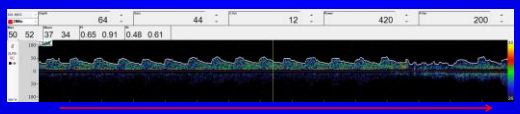
- Provocative maneuvers with head turns
- In normals BA CBFV decrease is no more than 20%

Rt VA

Neutral position, manually measured CBFV here was 52 cm/sec



Left turn, manually measured CBFV here was 36 cm/sec



Role of TCD: Head Turns

- TCD will be helpful to determine the cause of symptoms
- TCD will eliminate the vascular component if there will be no CBFV's changes observed during head turns
- TCD will confirm the vascular compromise if there will be abnormal CBFV changes in the proximal BA observed during head turns

TCD, EMBOLI AND EXTRACRANIAL CAROTID DISEIASE

Effects of Intensive Medical Therapy on Microemboli and Cardiovascular Risk in Asymptomatic Carotid Stenosis

Spence et al, 2009

- OBJECTIVE: To assess the effect of more intensive medical therapy on the rate of TCD MES and cardiovascular events in patients with asymptomatic carotid stenosis (ACS)
- DESIGN: A prospective study
- PATIENTS: 468 patients with ACS greater than 60% by Doppler peak velocity
- MAIN OUTCOME MEASURES: We compared (1) the proportion of ACS patients who had MES on TCD, (2) cardiovascular events, (3) rate of carotid plaque progression, and (4) baseline medical therapy, before and since 2003
- RESULTS: Cardiovascular events and MES on TCD have markedly declined with more intensive medical therapy. Less than 5% of patients with ACS now stand to benefit from revascularization; patients with ACS should receive intensive medical therapy and should only be considered for revascularization if they have MES on TCD

Asymptomatic embolisation for prediction of stroke in the Asymptomatic Carotid Emboli Study (ACES): a prospective observational study

Markus et al, Lancet Neurology, 2010

- The Asymptomatic Carotid Emboli Study (ACES) was a prospective observational study in patients with asymptomatic carotid stenosis of at least 70% from 26 centrs worldwide. To detect the presence of embolic signals, patients had two 1 h TCD recordings from the ipsilateral middle cerebral artery at baseline and one 1 h recording at 6, 12, and 18 months.
- Patients were followed up for 2 years. The primary endpoint was ipsilateral stroke and TIA. All recordings were analysed centrally by investigators masked to patient identity.

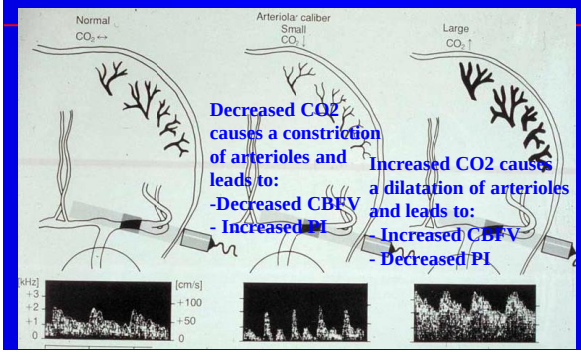
Asymptomatic embolisation for prediction of stroke in the Asymptomatic Carotid Emboli Study (ACES): a prospective observational study

Markus et al, Lancet Neurology, 2010

- **RESULTS**: 482 patients were recruited, of whom 467 had evaluable recordings. Embolic signals were present in 77 of 467 patients at baseline. The absolute annual risk of ipsilateral stroke or TIA between baseline and 2 years was 7.13% in patients with embolic signals and 3.04% in those without, and for ipsilateral stroke was 3.62% in patients with embolic signals and 0.70% in those without. Controlling for antiplatelet therapy, degree of stenosis, and other risk factors did not alter the results.
- **INTERPRETATION:** Detection of asymptomatic embolization on TCD can be used to identify patients with asymptomatic carotid stenosis who are at a higher risk of stroke and TIA, and also those with a low absolute stroke risk. Assessment of the presence of embolic signals on TCD might be useful in the selection of patients with asymptomatic carotid stenosis who are likely to benefit from CEA.

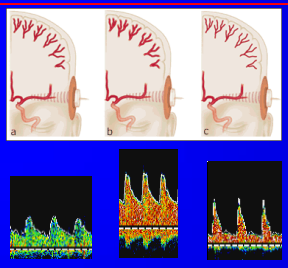
TCD AND CEREBRAOVASCULAR REACTIVITY

Cerebrovascular Reactivity



Physiologic Testing of CVR

- Increased CO2 causes a dilatation of the resistance vessels and results in:
  - Increased CBF/CBFV
  - Decreased Pulsatility Index
- Decreased CO2 causes a constriction of the resistance vessels and results in:
  - Decreased CBF/CBFV
  - Increased Pulsatility Index



Physiologic Testing of CVR: Assumptions

- The diameter of the basal cerebral vessels is not significantly altered by hypercapnia or hypocapnia
- Consequently the CBFV is directly proportional to the CBF
- The end-expiratory pCO2 is directly proportional to the arterial pCO2

Physiologic Testing of CVR

- During the ischemia, the compensatory mechanism of vessel dilatation (CVR or VMR) is nearly or already exhausted
- During maximal dilatation of the resistance vessels in order to counterbalance a critical drop of perfusion pressure, the cerebral arterioles are no longer able to react to CO2 stimuli
- Cerebral CO2 induced CVR can be used as an indicator of exhausted vasomotor reserve

Impaired CVR: Why it is important?

- Defining a high-risk patient with asymptomatic carotid stenosis remains difficult. To date there is no evidence of any factor that may influence the prognosis of patients with asymptomatic carotid stenosis
- Evaluation of CVR will help physicians to predict cerebrovascular events in patients with asymptomatic carotid artery stenosis

Physiologic Testing of CVR

- **Carbon Dioxide**
  - Ability to test the reactivity of cerebral vessels; vasodilatation under hypercapnia and vasoconstriction under hypocapnia
- **Acetazolamide**
  - Ability to test the reactivity of cerebral vessels only with vasodilatation under hypercapnia
  - Less influenced by the patient's cooperation

Physiologic Testing of CVR with CO2. Protocol

- A mask placed on the subject's face, while breathing room air and relaxing to allow acclimation to the test situation
- Bilateral MCA monitoring
- The end-tidal CO2, BP, HR, ECG monitored non-invasively
- Air with CO2 concentration of 2%, 4%, 5% and 6% given for 2 to 3 minutes until steady states of MCA CBFV reached

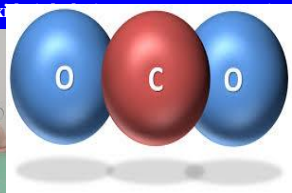
Physiologic Testing of CVR with CO2

Physiologic Testing of VMR with CO2. Protocol

- The mean MCA CBFV increase of 40% and more is being indicative of normal cerebral VMR

How CVR could be tested

Carbon dioxi… …hox injection



BREATH HOLDING INDEX (BHI)

The diagnostic and prognostic value of breath-holding

McMechan FH, Cal State J Med. 1922

- The breath-holding test in connection with the patient's response to other tests, when indicated, may be of diagnostic and prognostic significance, and may not only indicate therapeutic measures, but may also serve as a guiding sign to their effectiveness
- Used routinely at the bedside, in the office, and in the hospital, it can be made one of the most valuable assets of daily practice

Physiologic Testing of CVR with BHI. Protocol

- 2 MHz TCD probes bilaterally with helmet with any contemporary TCD machine
- Before the BHI test, the procedure must be explained to the patient in detail: "Please, breath normally, then take a normal breath and hold for 30 seconds, until I say okay, thereafter you are allowed to breath again normally"
- Careful instruction provided to patient to avoid or minimize a Valsalva maneuver during the breath-holding
- In cases where breathing was started earlier than 30 sec, we need to repeat the test and reported loudly the time each 5 seconds that elapsed from the beginning. It will facilitate the cooperation during the procedure

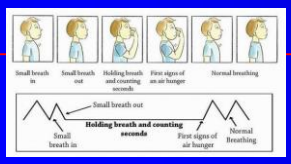
Physiologic Testing of CVR with BHI. Protocol

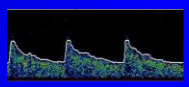
- Subject first breathed room air until a steady CBFV bilaterally recorded/ steady expiratory end-tidal CO2 level obtained
- *Patients must be instructed* ***to hold their breath after a normal inspiratory breath to avoid Valsalva maneuver***
- Three sequential breath-holding periods of 30 seconds duration performed with the subject lying supine. Between each breath-hold test, two minutes rest
- TCD continuous recording must start from the beginning of the breath-holding until additional 20 seconds after finishing breath-holding

Physiologic Testing of CVR with BHI. Protocol

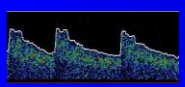
- The highest mean CBFV at the end of 30 seconds or after the end of breath-holding during next 20 seconds must be taken as V2
- Qualitative TCD wave form images documented
- Between each bBH test, two minutes rest
- All measurements and recording were repeated three times
- Changes from the baseline in the quantitative and qualitative recordings must be evaluated after the test
- For each MCA, the percent change in CBFV calculated for each three BH obtained. This is determined by formula (V2 – V1/V1) x 100%, where V1 is the baseline CBFV and V2 is the mean CBFV at the end of 30-40 sec or whatever breath holding was lasting. Therefore we are determining percentage of mean CBFV change for each of three BHs

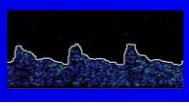
TCD and CVR



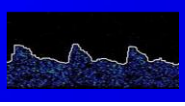


Normal



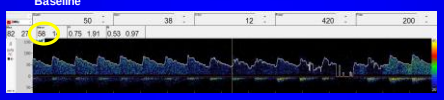


Abnormal

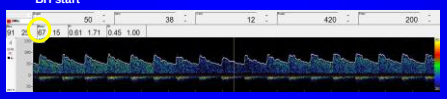


CVR test with Breath-Holding

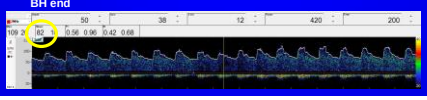
Baseline



BH start



BH end



BHI Normal Values

- The mean MCA BHI value was 1.48 %/s (Silvestrini et al, Journal of Cerebral Blood Flow & Metabolism, 1996)
- The mean MCA BHI were 1.59± 0.3 in women and in young (1.34±0.5) and old men (1.20± 0.4) (normal population) *(Matteis et al, Stroke, 1998)*
- The mean MCA BHI was 1.03-1.65 %/s (Zavoreo et al. Acta Clinica Groatica, 2004)
- The mean MCA BHI value was 1.45 +/- 0.50 %/s (Jiménez-Caballero et al. Rev Neurol. 2006)
- The mean MCA BHI value was 1.28 +/- 0.71 %/s (Molinari et al, J Neuroeng Rehabil. 2006)

Role of TCD: Cerebrovascular Reactivity

- CVR evaluation of asymptomatic or symptomatic patients with less than 70% of stenosis could provide valuable information to help make decision about preventive CEA
- CVR may have certain role in evaluation of patients concussion, dementia, prediction of outcome in critical care patients

Role of TCD: Extracranial Carotid or VB disease

- Detects impaired cerebral perfusion, emboli, presence or absence of altered collateral circulation
- CVR evaluation of asymptomatic or symptomatic patients with less than 70% of stenosis could provide valuable information to help make decision about preventive CEA
  - CVR may have certain role in evaluation of patients concussion, dementia, prediction of outcome in critical care patients
- High accuracy to detect effects of subclavian steal, Bow Hunter or Eagle syndromes
- Provides follow-up after medical, surgical, and endovascular treatment

TCD AND INTRACRANIAL ARTERIAL STENOSIS

IAS or Intracranial Arterial Stenosis (IAS)

- Secondary to:
  - Atherosclerosis
  - Vasculitis
  - Moya-Moya disease
  - Sickle Cell Disease

Criteria for Abnormal TCD Diagnosis of IAS

- An MCA, ICA and ACA stenosis were considered if CBFV > 80 cm/s
- ICA siphon stenosis if CBFV > 65 cm/s
- BA and VA stenosis if CBFV > 60 cm/s

Additional Criteria for Abnormal TCD Diagnosis of IAS

- Criteria for M1, A1, C1

CBFV (cms/sec)	STENOSIS
80-99	Mild
100-139	Moderate
> 140	Severe

- Criteria for VB system

CBFV (cms/sec)	STENOSIS
60-80	Mild
81-100	Moderate
> 100	Severe

Additional Criteria for Abnormal TCD Diagnosis of IAS

- Significant stenosis will be associated with delayed systolic upstroke distal to the lesion
- At the site of stenosis CBFV will be elevated Distal to the stenosis it will be reduced
- Proximal to stenosis, PI will often be elevated (>1). Distal to stenosis PI will be reduced

Role of TCD: Intracranial stenosis

- Detects stenosis of intracranial vessels
- Provides longitudinal follow up and monitor effects of treatment (medical, endovascular)
- Diagnosis of intracranial stenosis could be performed inexpensively and easily
- TCD accurately and noninvasively evaluate intracranial circulation without adverse side effects or discomfort
- Patients with Sickle Cell Disease must be monitored routinely with TCD: Practice Standard

CEREBRAL ISCHEMIA

AHA, Statistical Update

- **2000-2007:** On average, every 45 sec, someone in the United States has a stroke
- Each year, about 700,000 people experience a new or recurrent stroke. About 500,000 of these are first attacks and 200,000 are recurrent attacks

- **2008-2020:** On average, every 40 sec, someone in the United States has a stroke
- Each year, about 795,000 people experience a new or recurrent stroke. About 610,000 of these are first attacks and 185,000 are recurrent attacks

87% of Stroke are Ischemic

Stroke Diagnosis
Clinical and Neuroimaging

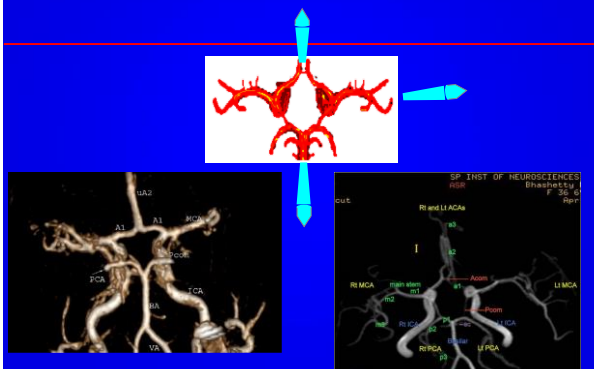
- CT
- CTA
- MRI (DWI and PWI)
- MRA
- CT-Xe^{133}
- Xe-^{133}
- SPECT
- PET

- However all these methods are not universally available
- MRI/MRA has certain contraindications
- Other methods using radioactive materials
- **TIME!** Even in sites equipped with them, the technique may not be immediately accessible
- **COST!!!** Neuroimaging technology is tremendously expensive, hard for smaller hospitals to afford

Acute Ischemic Stroke and Neuroimaging

- Stroke pattern imaging (CT/CTA & MRI/MRA) alone cannot identify stroke mechanism/s
- The lack of correlation between initial clinical presentation and imaging findings further justifies obtaining appropriate studies to define information about cerebrovascular hemodynamic
- Detailed and complete (carotid and TCD ultrasound) analysis of vascular condition is mandatory

Circle of Willis: CTA, MRA & TCD



TCD AND ACUTE STROKE DIAGNOSIS

TCD and Cerebral Ischemia

- Diagnosis for Acute Stroke
- Monitoring for Acute Stroke Treatment
- Emboli Monitoring
- PFO
- Sickle Cell Disease
- Thrombolysis
- *TCD in Neuro-ICU*

TCD and Acute Stroke

- Different stroke therapies may offer a benefit for one mechanism but not for other others
- If the mechanism can be determined in the first few hours after stroke, then patients with different stroke subtypes could be selected for specific therapies in clinical practice

TCD and Acute Stroke

- ***TCD, MRA and MRI in acute cerebral ischemia. Razumovsky et al, Acta Neurol Scan, 1999***

TCD showed a sensitivity of 96% and specificity of 33% for recognizing abnormal CBFV (anterior and posterior circulation vessels were evaluated together). For MCA lesions only (n=17) a specificity was 100% and a sensitivity was 93%

- ***Yield of TCD in acute cerebral ischemia. Alexandrov et al, Stroke, 1999***

TCD had 88% accuracy for abnormal (occlusion and stenosis) vs. normal vessels: sensitivity 87.5%, specificity 88.6%, PP 87.5% and NP 88.6%

- ***Diagnostic impact of early TCD on TOAST classification subtype in acute cerebral ischemia. Wijman et al, Cerebrovas Dis, 2001***

Initial TOAST classified correctly in 46% cases. After TCD (modified TOAST), 60% of patients were classified correctly, for an absolute benefit of 14% and a relative benefit of 30%

- ***Accuracy of TCD Compared With CTA in Diagnosing Arterial Obstructions in Acute Ischemic Strokes. Brunser et al, Stroke 2009.*** TCD demonstrated 34 intracranial occlusions and CTA 33. TCD sensitivity of 81.8%, and specificity of 94% for detecting an arterial occlusion in any specific artery. TCD is valid compared with CTA for the diagnosis of arterial occlusions in patients with acute ischemic stroke, especially in MCA obstructions.
- … and many more

Neurosonology in ER

Portable TCD and duplex

Fast track protocol

Use full power

Occlusion(s) location

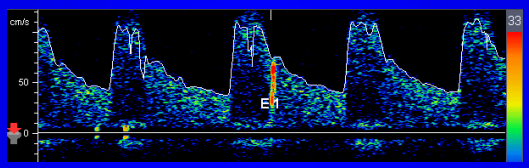
Monitoring set

Patient with Acute Cerebral Ischemia

67-yo AA female, acute onset of the left side hemiplegia
Late for i/v tPA but eligible for intra-arterial t-PA protocol

ARTERY	Normal CBFV cm/sec	Emboli	Right CBFV Mean	Right PI	Right Depth	Emboli	Left CBFV Mean	Left PI	Left Depth
A M1	41+-7	18	41	1.0	50		42	0.9	50
A M2		23	35	0.9	43		37	1.1	42
CV									
A AL	39+-9	12	33	1.0	68		36	1.0	72
C1	43+-12	31	39	0.8	64		40	1.1	64
A P1	36+-8		37	0.8	66				
A P2	36+-8								
		17	28	1.0	50		26	1.0	50
C2	41+-12								
C4		16	37	0.8	68		40	0.9	68
external									
	35+-7		33	0.6	64		39	0.7	64
proximal	35+-7		41	1.1	84				
mid									
distal									

TCD “signature” of emboli



Patient with Acute Cerebral Ischemia

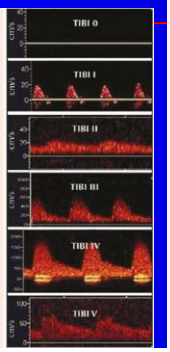
67-yo AA female, acute onset of the left side hemiplegia
Late for i/v tPA but eligible for intra-arterial t-PA protocol

- TCD exam in ER showed constant stream of emboli through the right anterioir circulation vessels
- PMH: two days ago stenting of the right extracranial ICA
- Decision: no intra-arterial t-PA, transfer to regular floor and i/v heparin
- Two days later: no emboli, no symptoms

TCD CRITERIA FOR ACUTE CEREBRAL ISCHEMIA

TIBI (Thrombolysis in Brain Ischemia) Grading

TIBI 0: Absent	No flow signals or lack of regular pulsatile flow signals despite varying degrees of background noise
TIBI I: Minimal	Systolic spikes of variable velocity and duration Absent diastolic flow during all cardiac cycles; reverberating flow is a type of minimal flow
TIBI II: Blunted	Flattened or delayed systolic flow acceleration compared with control side Positive end-diastolic velocity Pulsatility index < 1.2
TIBI III: Dampened	Normal systolic flow acceleration Positive end-diastolic velocity ≥ 30% decrease in mean flow velocity compared with control side
TIBI IV: Stenotic	Mean flow velocity ≥ 80 cm/s and velocity difference > 30% compared with controlside; if velocity difference is < 30%, look for additional signs of stenosis (ie, turbulence, spectral narrowing) Affected and comparison sides have mean flow velocities < 80 cm/s due to low end-diastolic velocities; mean flow velocity > 30% compared with control side; signs of turbulence
TIBI V: Normal	< 30% mean flow velocity difference compared with control side



Criteria for CBFV Asymmetry

- A side-to-side difference greater than 30% considered abnormal
- Moderate CBFV decrease with CBFV asymmetry more than 21%
- Major CBFV decrease with a significantly reduced CBFV lower than 30 cm/s (for anterior circulation vessels)

Role of TCD: Acute Stroke

- TCD can identify hemodynamically significant abnormalities and lesions of the brain vasculature
- TCD within 24 hours of symptoms onset improves the early accuracy of stroke subtype diagnosis, especially in patients with large artery atherosclerosis
- Early detection affects therapeutic strategies in patients with acute/subacute cerebral ischemia
- TCD is an accurate indicator of blood flow status and may be as reliable as angiography and correlated well with MRI, MRA, DSA, and CTA at a **fraction of the cost and no risk** for patients
- TCD could identify the active source of embolism in a very cost-effective manner
- TCD can be performed rapidly and effectively in acute setting (ER, OR, ICU) or done longitudinally to evaluate progression and/or regression of disease

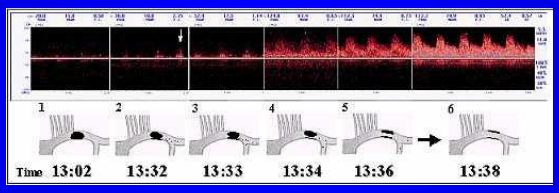
TCD MONITORING OF ACUTE STROKE TREATMENT

Reperfusion Effect after t-PA or Thromboectomy

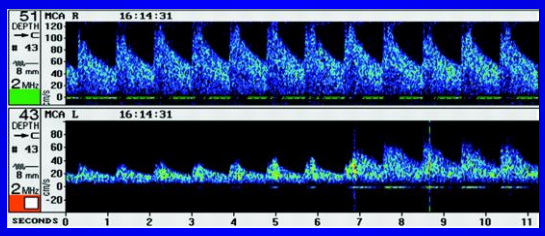
- Cerebral hemodynamic evaluation after recanalization therapy, can help identify patients with high risks of reperfusion-associated complications
- Post-stroke hypoperfusion is associated with infarct expansion, while hyperperfusion, which once was considered the hallmark of successful recanalization, is associated with hemorrhagic transformation
- Either the hypo- or the hyperperfusion may result in poor clinical outcomes. Individual BP target based on cerebral hemodynamic evaluation was crucial to improve the prognosis

MCA Reperfusion with i/v t-PA

Alexandrov et al, 2004



Left MCA Reperfusion



TCD Monitoring

- The beginning, speed timing, amount of recanalization represent important parameters of reperfusion therapy for stroke and are measured by following parameters:

1. Waveform change by >1 TIBI scale
2. Appearance of embolic signal
3. CBFV improvement by >30% at constant angle of insonation
4. Appearance of flow signals with variable Pulsatility Indices and amplitude of systolic peaks

Role of TCD: Monitoring of acute stroke treatment

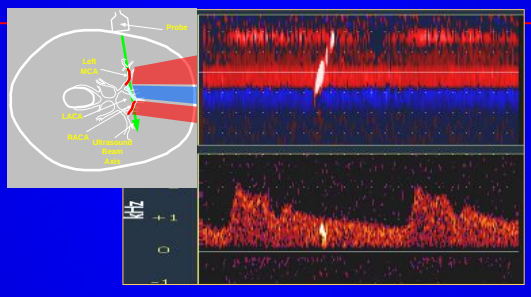
- TCD could be ideal to guide aggressive treatment
- *TCD can help in the primary and repetitive diagnosis of the vessel occlusion by indicating whether the lesion is present at all, still present or already re-canalized*
- TCD can be done repetitively and close to the anticipated time of fibrinolysis
- Asymmetrical CBFV observed by TCD is a sign that can suggests a thromboembolic lesion in the acute phase of ischemic stroke, therefore, the examination could provide a basis for early reperfusion therapy, which has been shown to significantly improve outcome after stroke

Role of TCD: Monitoring of acute stroke treatment

- TCD ultrasound can provide real-time monitoring of thrombolysis or thromboectomy
- TCD provides useful information to understand the pathophysiological changes after restoration of cerebral blood flow in patients with large vessel occlusion that undergo reperfusion therapy
- Outcome prediction/prognosis
- Treatment monitoring
- Treatment effect evaluation

TCD, EMBOLI AND ACUTE STROKE

TCD and Emboli



TCD and Emboli

- Etiology of stroke is embolic in 32%
- TCD technique is the “gold” standard to detect emboli in real-time while emboli going through the cerebral circulation
- TCD emboli monitoring could be useful for patients with acute stroke, TIA, potential cardiac sources of emboli, etc.
- Emboli monitoring: surrogate marker for plaque activity and risk of macroembolism

Role of TCD: Emboli Monitoring

1. Quantitative count of emboli
2. Localization of the embolic source responsible of stroke
3. Identification of high-risk patients for stroke recurrence
4. Monitoring of the therapy effectiveness
5. Monitoring of cardiovascular surgery
6. Monitoring different type of invasive procedures

TCD AND PFO

PFO Screening and Diagnosis: Contrast-TCD vs. c-TTE or c-TEE?

PFO Screening Accuracy

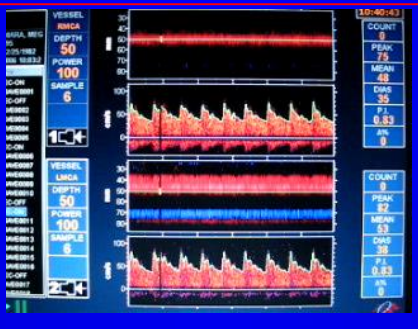
- **TTE (63% accuracy)**
  - 30% false negative
  - Poor sensitivity
- **TEE (88% accuracy)**
  - Invasive
  - 15-20% false neg.
  - Inability to perform calibrated Valsalva
  - Patient sedated
- **TCD (94% accuracy)**
  - Minimally invasive
  - Highly sensitive
  - Calibrated Valsalva to standardize strain
- ***Demonstrates passage of bubbles through the cerebral circulation***

Contrast-TCD for the Right-to-Left Shunt Testing

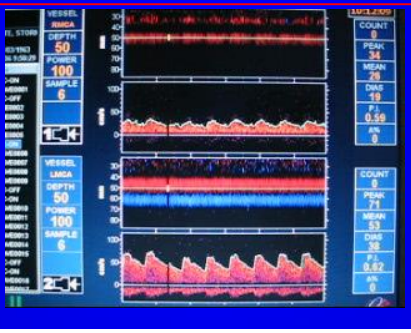
- *TCD, unlike TTE/TEE, is quantitative*
- TCD "bubble-test" is a new, simple, accurate, reliable, cost effective, and safe method for testing for Right-to-Left shunt/PFO
  - excellent non-invasive test
  - excellent sensitivity (especially with Valsalva)
  - excellent specificity
  - can be done in neurologists' office

Contrast-TCD

Positive Bubble-TCD with Valsalva



Positive Valsalva (shower)



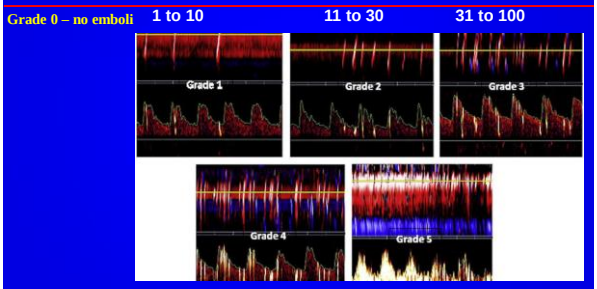
Consensus Statement
Cerebrovasc Dis, 2000

A 4-level categorization was accepted according microemboli appearance using unilateral MCA monitoring:

1. No occurrence of microemboli
2. 1-10 microemboli
3. >10 microemboli but no curtain
4. curtain or shower where a single microemboli cannot be discriminated within the TCD spectrum

Dr. M. Spencer 6-level Logarithmic Scale

Spencer MP et al, J Neuroimaging, 2004



Role of TCD: Stroke & R-to-L shunt

- The efficient use of c-TCD among patients with acute ischemic stroke will decrease the number of cases labeled as cryptogenic and will lead to more informed choices among current long-term therapeutic options or endovascular interventions

TCD AND SICKLE-CELL ANEMIA

Sickle cell disease

- Sickle cell is in many nationalities:
  - African Americans,
  - Africans,
  - Arabs,
  - Greeks,
  - Italians,
  - Latin Americans, and those from India

STOP Trial

- Children with SCD who had been found to be at high risk for stroke on the basis of elevated CBFV greater or equal 200 cm/sec
- Two abnormal comparable TCD's are needed to identify patients at higher risk of stroke (CBFV greater than 200 cm/sec on two separate occasions
- If CBFV is equal or greater than 170 cm/sec – conditional
- TCD screening recommended and standard of care

TCD ENHANCED THROMBOLYSIS

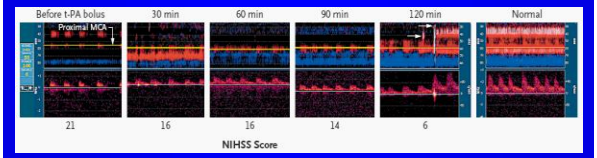
Possible favorable effect of ultrasound on recanalization after acute onset of ischemia

- The potential therapeutic use of external high-intensity focused US was explored by Lynn et al. (J Gen Physiology, 1942)
- Lynn et al. postulated that external HIFU can induce localized tissue damage at a focal point within the body with no effect on the surface or on the overlying or surrounding tissue

Current approach

- In vivo arterial clot dissolution can be achieved:
  - With i/v microbubbles and transcutaneous US
  - With i/v thrombolysis facilitated by transcutaneous US
  - By transcutaneous therapeutic US
  - Catheter based therapeutic US

CLOTBUST Primary End-points: Complete MCA Recanalization and Dramatic Clinical Recovery within 2 hrs after t-PA bolus



Alexandrov et al, New Engl J Med 2004;351:2170-2178.

Role of TCD: Thrombolysis

- TCD can augment residual flow and speed up thrombolysis, allowing patients to recover from stroke more rapidly
- TCD has the potential as an adjunct to improve thrombolytic therapy
- Administration of Micro Bubbles induces further acceleration of US-enhanced thrombolysis in acute stroke, leading to a more complete recanalization and to a trend toward better short- and long-term outcome

What TCD service Could Achieve for Patients with Acute Cerebral Ischemia

- Immediate bed-side results in ER, OR, Recovery Room, ICU or hospital ward
- Provides accurate CBFV information for determination of disease severity
- Detects even minimal cerebral hemodynamic changes
- Detects emboli
- TCD allows **rapid, non-invasive and cost-effective** evaluation of the blood flow status in basal cerebral arteries
- TCD has an established clinical value in the diagnostic workup of stroke patients and is an essential component of a comprehensive stroke center
- Ideal tool for following disease progression, therapeutic, radiological, surgical or endovascular revascularization, stages of recovery and long-term therapeutic effects

TODAY IN USA …

Memphis, TN
Mobile Stroke Unit

Acuson P300
Duplex scanner

Siemens Somatom Scope CT

TCD ST3 Spencer's

TCD AND NEURO-CRITICAL CARE

Specific TCD Applications for Neuro-Critical Care/Neurosurgery

- Vasospasm diagnosis, monitoring and treatment effect evaluation after TBI, SAH, intracranial hemorrhage, tumor resection, etc.
- Acute stroke diagnosis, monitoring and treatment effect evaluation
- PFO screening for cryptogenic stroke and risk assessment
- Emboli and Fat emboli monitoring
- Thromboectomy effect monitoring
- CEA/CAS effect evaluation
- Neuroradiology stenting (pre, during and post)
- Pre- and post-treatment AVM evaluation
- Septic patients evaluation
- Diagnosis and monitoring of intracranial hypertension
- Total cerebral circulation cessation/brain death clinical diagnosis confirmation

TCD AND VASOSPASM DIAGNOSIS

Physiologic Variables affecting TCD

- Age
- Hematocrit
- Vessel Diameter
- Gender
- Fever
- Metabolic Factors
- Cardiac Output
- Heart Rate
- Brain Activity

Intensive Care TCD Protocol must include:

HR: MAP: PaCO2: Hct: ICP: Temp:

SAH and TBI

- Up to 70% of SAH patients develop angiographic vasoconstriction
- Only 20–30 % develop DCI
- Up to 60% of TBI patients will have post-traumatic SAH

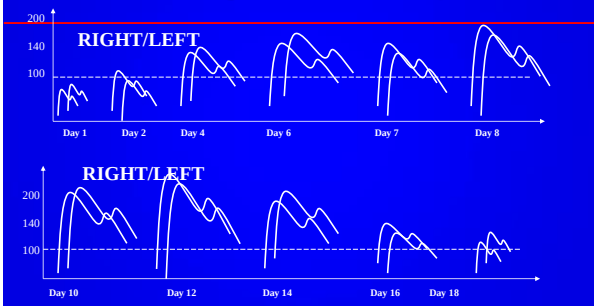
TCD Criteria for Diagnosis of MCA vasospasm

Mean CBFV (cm/s)	MCA/ICA ratio (Lindegaard Ratio)	Interpretation
<100	< 3	Nonspecific
100-139	3-6	Mild
140-199	3-6	Moderate
>200	>6	Severe

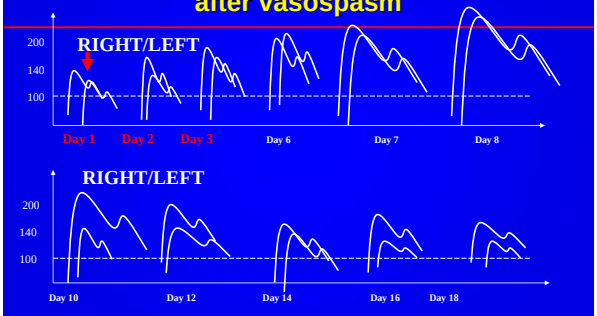
TCD criteria for vasospasm (mean CBFV)

• Newell D et al, 1990	**120 cm/sec = significant VSP on DSA**
• Mascia L et al, 2003	TCD, threshold value of 100 cm/s for DSA VSP and 160 cm/s for clinical VSP detection
• Krejza J et al, 2005	94 cm/sec with TCCS and DSA
• Razumovsky A et al, 1991- 2016	100 cm/sec with TCD

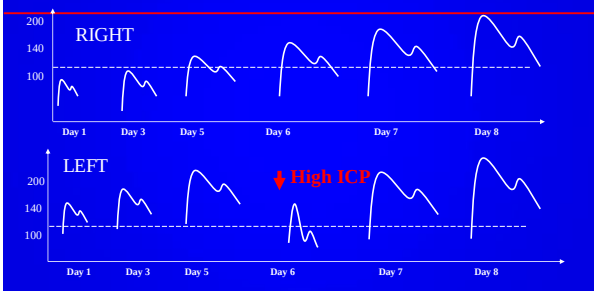
TCD changes after vasospasm



Early onset abnormal TCD changes after vasospasm



Unilateral TCD changes after vasospasm



TRAUMATIC BRAIN INJURY

TBI

Civilian

- Every 21 seconds, one person in the US sustains TBI

Battlefield

- *Okie, NEJM, 2005:* Among surviving soldiers wounded in combat in Iraq and Afghanistan, TBI appears to account for a larger proportion of casualties than it has in other recent U.S. wars. According to the Joint Theater Trauma Registry, 22% had injuries to the head, face, or neck.

Clinical Significance: Vasospasm after TBI represent Important Source of Morbidity and Mortality

MacPherson et al., 1973

- 41% of patients who died from TBI had PTV 24% with massive tSAH developed ischemic symptoms in contrast to 3% of patients with mild tSAH

Taneda et al, 1996

- Ischemic symptoms accompanying arterial VSP following tSAH are comparable to those found following aneurysmal SAH
- Some reports of cases of patients with mTBI w/o initial tSAH who develop PTV published

Servadei F et al, Neurosurgery, 2002

- European Brain Injury Consortium, data were prospectively collected for 1005 patients with moderate or severe TBI who were admitted to one of the 67 European neurosurgical units during a 3-month period in 1995
- Complete data on early clinical features, CT findings, and outcomes at 6 months were available for 750 patients, of whom 41% exhibited evidence of tSAH on admission CT scans

There is a strong, highly statistically significant association between the presence of tSAH and poor outcomes

Children and TBI

O'Brien N et al, Crit Care Med, 2015

- Vasospasm occurs in a sizeable number of children with moderate and severe traumatic brain injury

La Rovere KL et al, J Neurotrauma 2016

- 16 articles from January 2005 to July 2015 that met inclusion and exclusion criteria. TCD parameters were used to assess autoregulation, intracranial pressure, and vasospasm, and to predict neurological outcome. Altered TCD CBFVs and PIs can demonstrates vasospasm and intracranial hypertension across studies, respectively. Outcomes seem to be related to altered TCD-derived CBFVs while in the ICU

All current literature recommends aggressive screening for posttraumatic vasospasm in pediatric TBI patients. TCD may impact day-to-day management in the Pediatric ICU, and potentially improve outcomes in children with TBI

TBI: Pathophysiology

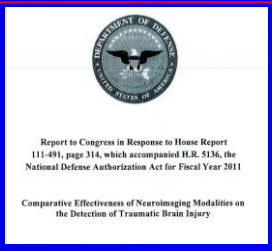
Primary Injury:
- Contusions/Hemorrhages
- Diffuse Axonal Injury (DAI)

Secondary Injury (Intracranial) occurs hours to weeks/years after injury:
- Blood Flow and Metabolic Changes
- **Cerebral Ischemia**
- Traumatic Hematomas
- Hydrocephalus
- **Cerebral Edema/Increased Intracranial Pressure/Herniation**
- PTSD

Clinical Significance

- The reported incidence of traumatic vasospasm ranges from 19%-68%, the true incidence remains unknown due to variability in protocols for its detection *(Kramer et al, 2013)*
- Extrapolation of current data suggests that as many as 279,000 to 1.2 million patients a year may suffer from post-TBI vasospasm in the USA and 10,800 to 40,000 might experience a resultant clinical decline *(W. Rutland-Brown et al, 2006)*
- Ischemic symptoms accompanying arterial vasospasm following tSAH are comparable to those found following aneurysmal SAH

Neuroimaging Effectiveness


Report to Congress in Response to House Report 111-491, page 314, which accompanied H.R. 5136, the National Defense Authorization Act for Fiscal Year 2011

Comparative Effectiveness of Neuroimaging Modalities on the Detection of Traumatic Brain Injury

- In 2012 DoD prepared a report to Congress where based on experts evaluation only CT and TCD have high clinical applicability for moderate and severe TBI *(Note: today there is data showing TCD utilization for concussion /mild TBI)*

Transcranial Doppler to Predict Neurologic Outcome after Mild to Moderate TBI

Bouzatt et al, 2016

- A prospective observational study across 17 sites
- TCD was performed upon admission in 356 patients with GCS from 9 to 15 with mild lesions on CT
- Normal TCD was defined as a PI of less than 1.25 and diastolic CBFV higher than 25 cm/s in the two MCAs
- The primary endpoint was secondary neurologic deterioration on day 7
- **Results:** TCD thresholds had 80% sensitivity and 79% specificity to predict neurologic worsening. Patients with abnormal TCD on admission (24%, 86 patients) showed a more altered score for the disability rating scale on day 28 compared to those with normal TCD (257 patients)

- **Conclusions:** TCD measurements upon admission may provide additional information about neurologic outcome after mild to moderate traumatic brain injury. *This technique could be useful for in-hospital triage in this context*

Role of TCD: Post SAH/TBI vasospasm

- It is useful to perform TCD test on admission (or ASAP after surgery) and perform daily TCD studies when patient is in the ICU
- The frequency with which TCD should be performed may be guided by patient clinical presentation, knowledge of risk factors for vasospasm, early clinical course
- TCD studies should be performed after endovascular treatment to identify patients with recurrent vasospasm

Role of TCD: Post SAH/TBI vasospasm

- Elevated CBFV's in asymptomatic patients warrant meticulous observation in some closely supervised setting until CBFV's begin trend downward
- Elevated CBFV's in a particular vascular territory can focus subsequent neurologic examinations to detect subtle changes earlier in their clinical course

Role of TCD: Post SAH/TBI vasospasm

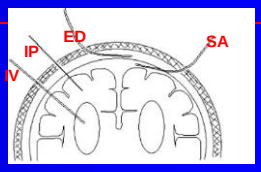
- In symptomatic patients, elevated CBFV's most likely represent significant vessel narrowing and may obviate the need for cerebral angiography. At this point, aggressive medical therapy can be initiated or advanced
- Asymptomatic patients w/o elevated CBFV's probably can avoid additional angiography. However, we need to consider patient's age because elderly patient's could develop vasospasm in normal or slightly abnormal CBFV's range

Role of TCD: Post SAH/TBI vasospasm

- The presence and temporal profile of CBFV's in all available vessels must be detected and serially monitored
- The pattern of CBFV's elevation may indicate the need to follow patient carefully for evidence of deficits related to specific vascular territory
- Waveform appearance either regionally, or globally may be clinically significant

TCD AND INTRACRANIAL HYPERTENSION

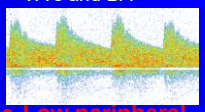
ICP Monitoring Methods



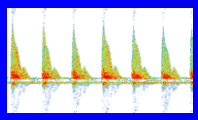
- **ED Probe**
  - Limited accuracy
  - Relatively delicate
- **SD Probe**
  - Limited accuracy
  - High failure rate
  - Periodic flushing necessary
- **IV catheter "Gold Standard"**
  - Most invasive method
  - High infection rate
  - May be difficult to insert
  - Simultaneous CSF drainage and ICP monitoring not possible
- **I/P Probe**
  - Measures local pressure
  - Drift of zero over time

Representative Morphology of TCD Wave-Form

- MCA (M1 and M2 segm)
- ICA (C1, C3 and C4 segm)
- ACA (A1 segm)
- PCA (P1, P2 segm)
- VA's and BA

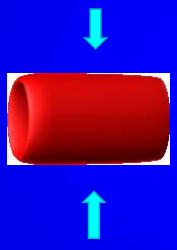


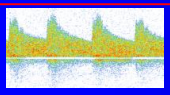
- **Low peripheral resistance and PI less than 1**
- OA



- **High peripheral resistance and PI more than 1**

TCD for non-invasive ICP evaluation

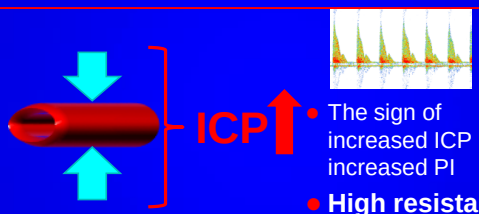




Normal ICP

- **Low resistance**
- **PI less than 1**

TCD for non-invasive ICP evaluation



- The sign of increased ICP is increased PI
- **High resistance**
- **PI more than 1**

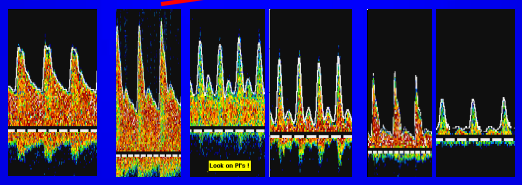
TCD wave-form changes with development of intracranial hypertension

Moreno et al, 2000; Belner et al, 2004; et al, 2005; Splavski et al, 2007; Melo et al, 2011; de Riva et al, 2012 and many, many others

PI ≥ 1.25 (Bouzat et al, 2011)
PI ≥ 1.26 could reliably predict CSF-P ≥ 20 cm H_2O or 14.7 mmHg (Wakerley et el, 2015)

Normal ICP

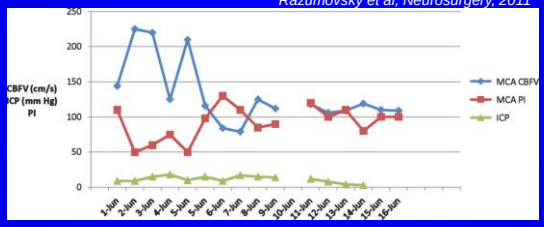
ICP 20 mm Hg and higher



Patient with GSW

Trend shows almost direct inverse relationship between CBFV and PI but epidural ICP values normal

Razumovsky et al, Neurosurgery, 2011



How to Interpret PI changes?

Increased PI

- Increased ICP
- Encephalopathy
- Hydrocephalus
- Fulminant hepatic failure
- Bacterial meningitis
- Focal distal stenosis
- Brain death

Decreased PI

- Vasospasm
- Hyperemia
- AV malformation

TCD PI in the management of intracranial hypertension

- PI measurements permit the early identification of patients with low CPP/high ICP and great risk of cerebral ischemia
- *In emergency situations it can be used alone when ICP monitoring is contraindicated or not readily available*

Role of TCD: Intracranial hypertension evaluation

- TCD wave-form changes indicates abnormally high ICP, especially after 20 mm Hg
- TCD changes may alarm Neuro-ICU personnel and may indicate malfunctioning of ICP probe
- Abnormally globally decreased pattern of the CBFV's in parallel with increased PI's indicate onset of diffuse intracranial hypertension
- Sudden onset of asymmetrical CBFV's and PI's changes may indicate potential mid-line shift
- *TCD quantitative and qualitative analysis must be taken into account for evaluation of intracranial hypertension; however, MAP, PaCO2 and cardiac output must be within the normal limits*

Non-Invasive ICP monitoring would enable

- Triage at the point of contact
  Battlefield, football field, ambulance, ER…
- In-time and evidence-based application of therapy
  Titrate therapy to ICP targets
- Long-term monitoring
  Without the risk of infection or damage to vital brain structures
- Expansion of patient pool for which monitoring might be beneficial
  Mild and moderate TBI, migraines, pediatric patients,…

TCD AND BRAIN DEATH/TOTAL CEREBRAL CIRCULATORY ARREST

Andreas Vesalius (1514-1564)

- Madrid
- Anatomist
- At autopsy: thorax opened → heart beating!
- Forced to leave Spain

This event and others need for formal pronouncement of death

Reasons for Interest Shift to Brain Death Determination

- The mechanical ventilator (Bjorn Ibsen: mid-20th Century), especially combination of mechanical ventilator and new cardiac stimulation measures
- The creation of intensive care units (ICUs), neuro-intensive care units (NICUs) and cardiac ICUs
- The issue of organ procurement for transplantation purposes
  - ***Existence of certain cultural and religious barriers that are often limits procedures for organ donation***

Standards for Determining Brain Death

- 1968 Harvard Criteria
- 1981 Uniform Declaration of Death Act
- 1995 American Academy of Neurology

American Academy of Neurology Guidelines (1995)

- Demonstration of coma
- Evidence for the cause of coma
- Absence of confounding factors, including hypothermia, drugs, electrolyte, and endocrine disturbances
- Absent brainstem reflexes
- Absent motor responses
- Apnea
- A repeat evaluation in 6 hrs is advised, but the time period is considered arbitrary
- Confirmatory laboratory tests are only required when specific components of the clinical testing cannot reliably be evaluated

Brain Death Concept

- Brain death is legally equivalent to death of the individual
- Transplantation of organs is allowed after neurological death determination, provided consent is obtained
- In the USA by law require two physicians to declare brain death

HOWEVER…

2009 CONTROVERSIES IN THE DETERMINATION OF DEATH

THE PRESIDENT'S COUNCIL ON BIOETHICS

Controversies in the Determination of Death

- The irreversible loss of brain-dependent functions occurs while the body, with technological assistance, continues to circulate blood and to show other signs of life. In such cases, there is controversy and confusion about whether death has actually occurred
- There is controversy as well about the use of the traditional cardiopulmonary standard in the organ procurement practice known as "controlled donation after cardiac death" (controlled DCD)
- There is debate about whether, at the time that organs are taken, the donor is truly dead. But, with controlled DCD, there is also a more acute danger that the quality of end-of-life care for the patient-donor will be compromised

The Washington Post December 23, 2015

"terminal wean" at Tomball Regional Medical Center (Tomball, TX)

Alabama 'miracle' boy wakes before doctors pull plug

BBC News, 2018

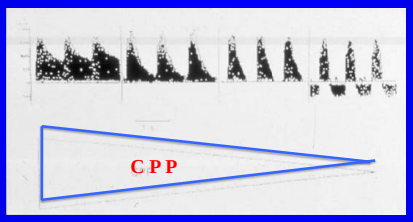
- A 13-year-old boy in the US state of Alabama regained consciousness just after his parents signed the paperwork to donate his organs

QUESTION IS: HOW CAN WE AVOID THE INACCURATE DIAGNOSIS OF BRAIN DEATH WITH MAXIMUM CERTAINTY?

CONFIRMATORY TESTS OF BRAIN DEATH IN ADULTS

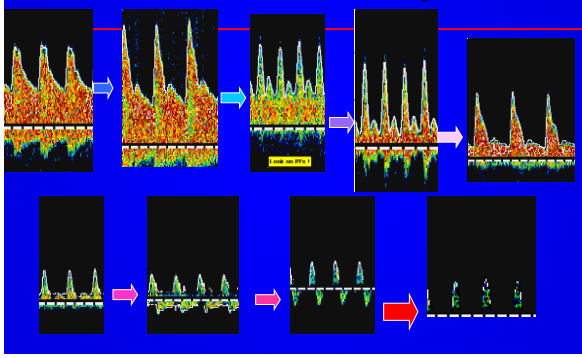
- Electroencephalography (EEG)
- Cerebral Angiogram
- **Transcranial Doppler Sonography (TCD)**
- Magnetic Resonance Imaging (MRI)
- Single Photon Emission Computed Tomography (SPECT)
- Evoked Potentials
  - Brainstem Auditory Evoked Potentials (BAEP)
  - Somatosensory Evoked Potentials (SSEP)
- Spiral Computed Tomography Scan (Spiral CT Scan)

TCD Waveform Progression from Intact CBFV to Circulatory Arrest

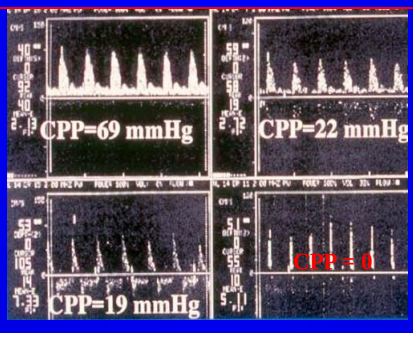


Hassler et al., 1988

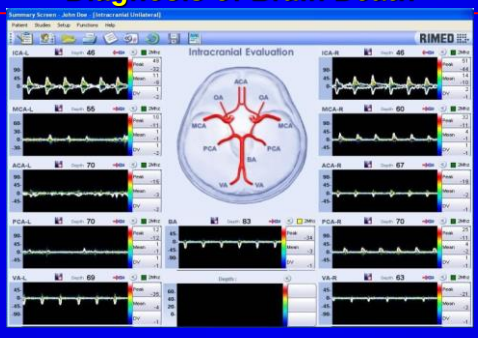
TCD Waveform Progression from Intact CBFV to Circulatory Arrest



TCD Waveform Progression



TCD Report in Patient with Clinical Diagnosis of Brain Death



Guidelines for the Use of TCD as Confirmatory Test of Brain Death

- The cause of coma has been established
- Intoxication, hypothermia, severe arterial hypotension, metabolic disorders and others have been excluded
- Clinical evaluation by experienced examiners shows no evidence of cerebral and brainstem function

Brain Death: Complete TCD Test

- **Examination of anterior circulation: extracranial ICA, MCA, ACA bilaterally, and posterior circulation: VA bilaterally and BA is strongly recommended**
- **Optional examination of the PCA and OA bilaterally**

Clinical Value of TCD for Critical Care

- ***Detect a Change from Baseline/Normal Values Early in the Course of Illness and Before Irreversible Damage Occurs***
- Contributes to the pharmacological management, further diagnostic testing and/or interventional treatment

TCD is a Critical Tool *(Quantitative Biomarker)* in Critical Care

- The use of TCD at hospital admission allows identification of patients with brain hypoperfusion due to the stroke, vasospasm after SAH/TBI and/or intracranial hypertension
- In such high-risk patients, early TCD goal-directed therapy can restore normal cerebral perfusion and might then potentially help in reducing the extent of secondary brain injury
- TCD represent effective tool to monitor effects of treatment and interventions

TCD is a Critical Tool in Critical Care

- The value of TCD in clinical practice is well established, especially to measure and grade vasospasm following SAH and TBI
- Based on AHA, AAN, NCS Guidelines and many years of clinical practice TCD is a tool employed by the Neurosurgeon, Neurointensivist and Neurologist in the management of vasospasm, acute/subacute stroke and/or hypoperfusion or hyperperfusion of CBF

MULTIPLE PERSPECTIVES

TCD Advantages

- Rapid assessment of cerebral vasculature, provides physiological and hemodynamics data
- Quantitative
- Repeatable
- Changes often precede clinical symptoms
- Changes precede angiographic narrowing

TCD Advantages

- No contraindications
- Portable
- Non-invasive
- Safe and not painful
- Cost-effective alternative to neuroimaging choices

T…s"

- Operator…
- N. Ameri…ging very broadly v…retation: True
- Neuroima…and overutiliz…
- Absence…e
- From 201…e doing only TCD and…credentials called NVS (Neurovascular Specialist) introduced by ASN

Questions?

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