

Provincial Stroke Rounds

Wednesday October 1st, 2025



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.

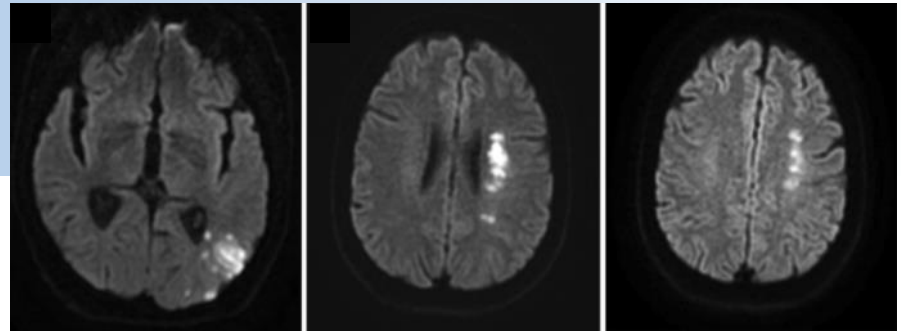
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Please take 2 minutes to fill the evaluation form out. Thank you!

Challenges in hemodynamic stroke: a multidisciplinary approach to chronic steno-occlusive disease

Joanna Schaafsma, MD PhD
Vascular Neurologist, Assoc. Prof.
University Health Network
University of Toronto



I have no relationships with for-profit or not-for-profit organizations for this program

1. Recognize the symptoms and signs of hemodynamic stroke
2. Understand existing imaging techniques for assessing chronic steno-occlusive arterial disease and cerebral hemodynamic status
3. Describe non-invasive strategies to prevent cerebral hypoperfusion

Outline



Clinical manifestations: how to recognize hemodynamic symptoms



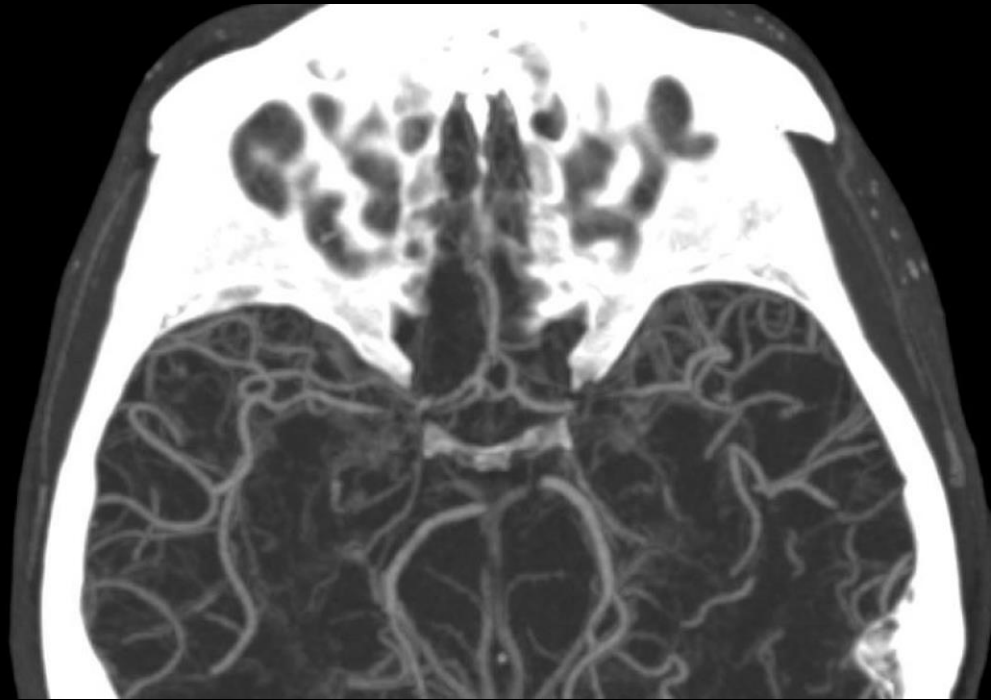
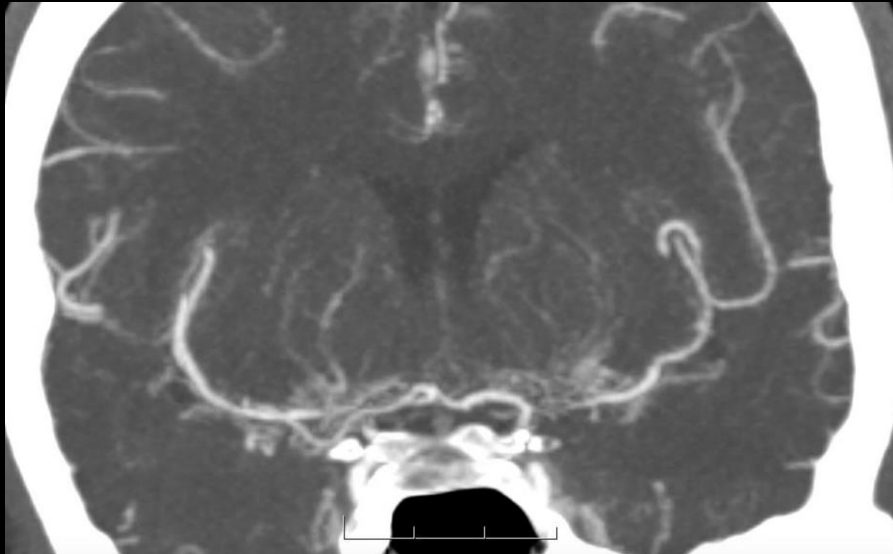
Diagnostic work up: how to confirm hemodynamic compromise



Treatment options & decision-making

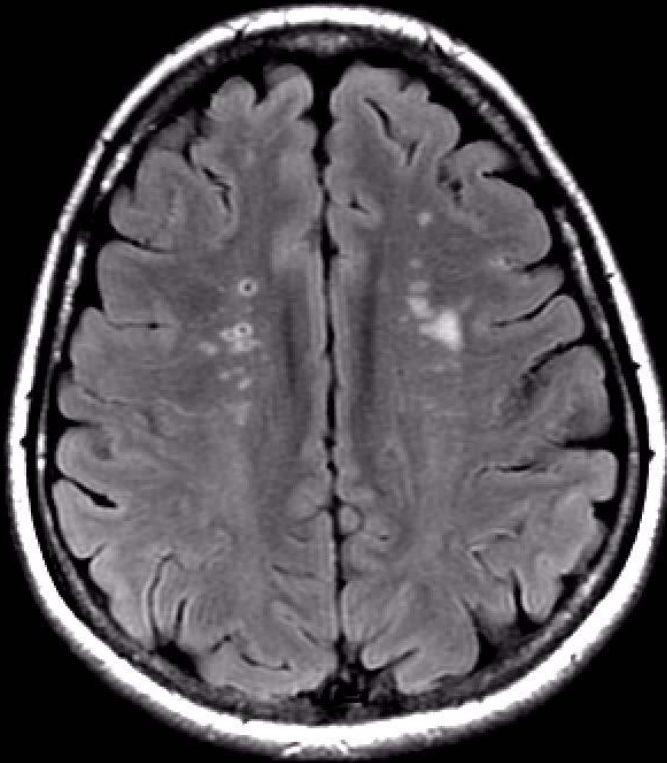
Thirty-three-year-old woman

- Episodic right arm weakness and shaking
- Trigger: feeding a child, heavy menses (endometriosis)
- Migraine-like L-sided headaches
- From the Philippines, twin sister with a history of ICH
- Baseline blood pressure 120/70 mm Hg
- EEG unremarkable



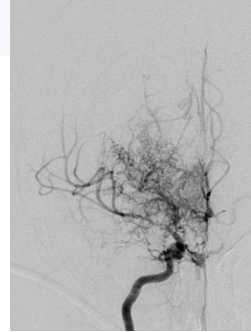
Distal ICA, M1, A1 stenosis with collateral network

MRI/MRA



- Bradyphrenia
- Language impairment

Diagnosis: Moyamoya disease



Moyamoya disease

- Rare: 0.005–0.009/10⁴ non-Asian, vs 0.9-2.3/10⁴ Asian
- Female predominant: 1.8:1
- Progressive distal ICA/M1/A1 (PCA) occlusion + frail collateral network
- Moyamoya disease vs syndrome
 - Down, Sickle Cell Disease, NF1, radiation-induced MMA
- Children: progressive cognitive impairment, ischemic events
- Adults: ischemic and hemorrhagic events

Chronic occlusive cerebrovascular disease

Other causes than Moyamoya arteriopathy

- **Atherosclerosis**
- Unhealed dissections
- Unhealed vasculitis
- Radiation-induced arteriopathy without MMA
- ...

Stroke burden: (recurrent) stroke risk

Moyamoya disease	Adults	~10% per year (reports up to 80% over 5 years) 40% post ICH
	Children	3-12% per year
ICA occlusion		14% in the first year
Vertebrobasilar steno-occlusive disease		12% in the first month 10-15% annually; 26% over 4 years

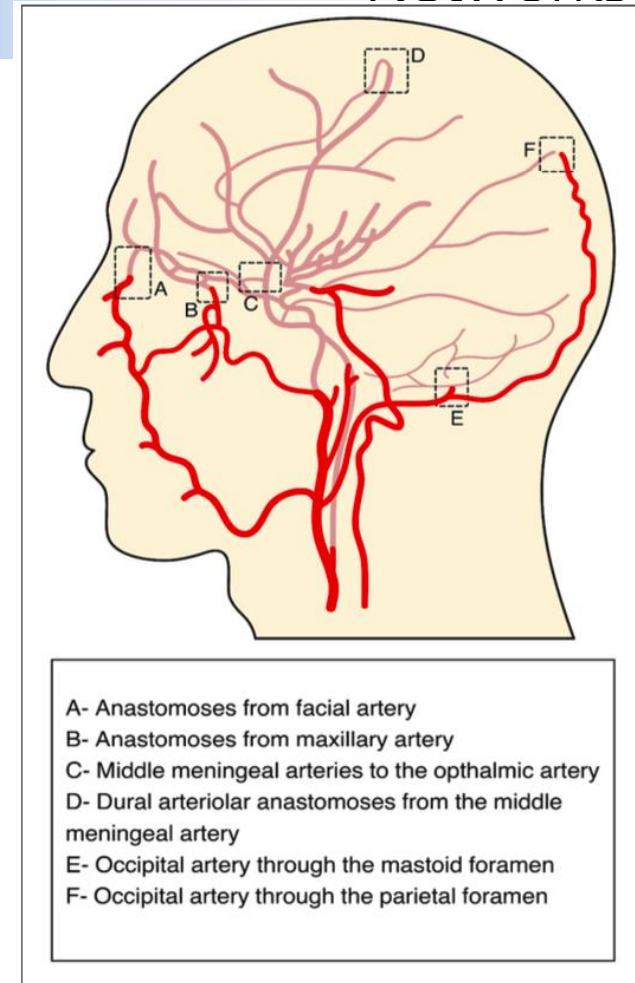
Gulli Stroke 2013; Li Lancet Neurol 2015; Tanaka J Stroke Cerebrovasc Dis 2022; Markus Stroke 2008; Kang Stroke 2019

Collaterome

Anatomical classification:

1. Collaterals between extracranial -
> intracranial arteries

Facial artery, IMA, ILT, MHT, MMA, occipital artery



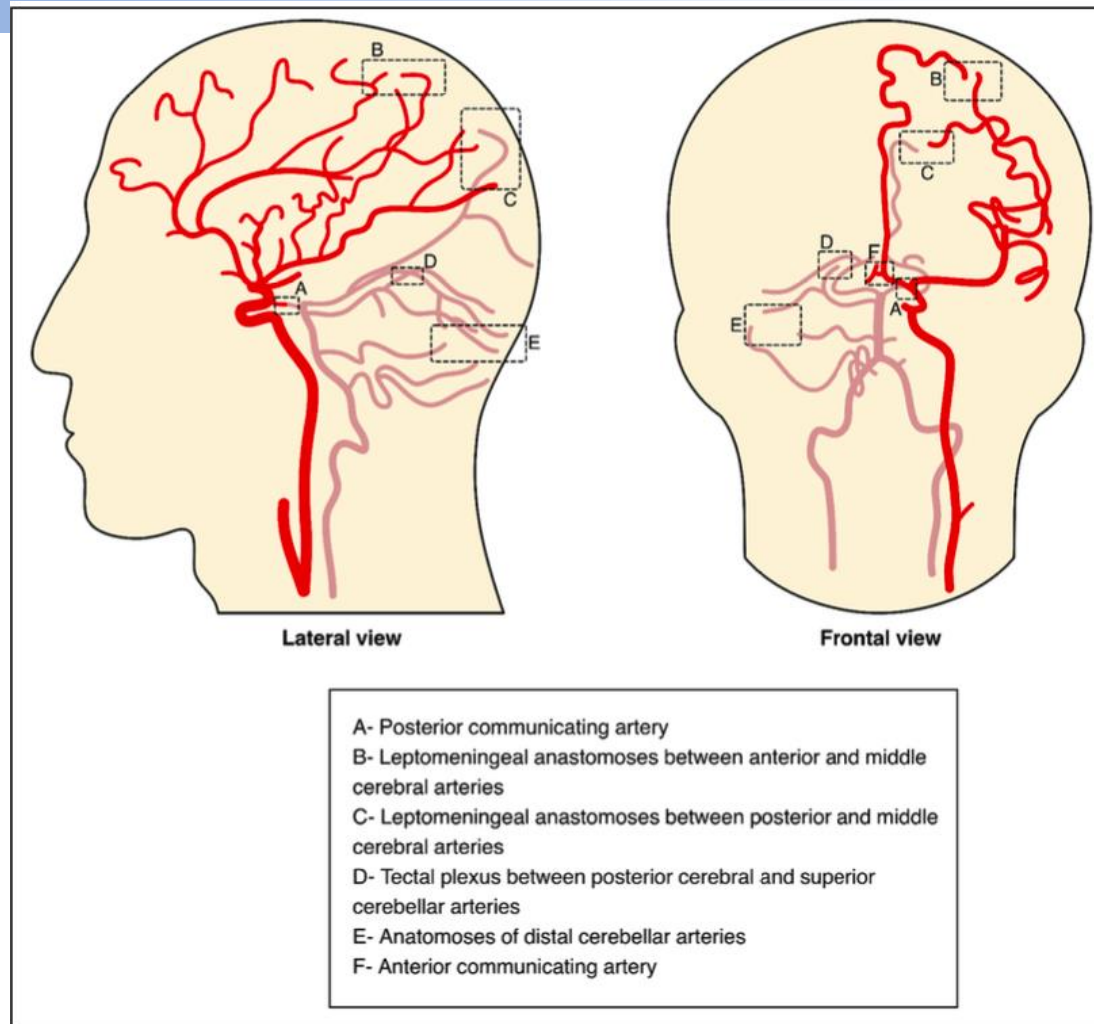
Patel, Liebeskind - Translational Stroke Research 2023

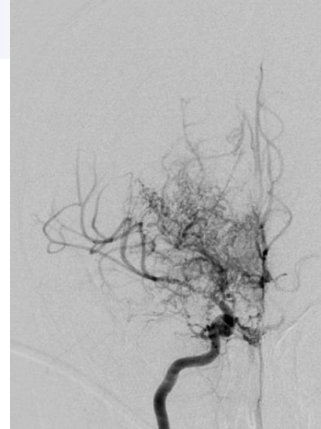
Fig. 1 Extracranial arterial collateral circulation

Collaterome

Anatomical classification:
2. Collaterals between
intracranial arteries:

- ACOM/PCOM
- Pial or leptomeningeal
collaterals (retrograde)
- End-to-end anastomoses of
distal cerebellar arteries

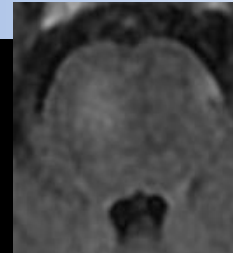




- The ability to recruit pre-existing collaterals is dependent on:
 - Anatomy
 - Timing:
 - Acute occlusions: instant recruitment of pre-existing collaterals
 - ‘Good quality’, non-tortuous
 - Chronic obstructive occlusions: gradual recruitment of pre-existing collaterals (days-weeks)
 - They become tortuous with remodelling of luminal diameter
 - Due to aging, vascular endothelial dysfunction, cerebrovascular risk factors: fewer and smaller collaterals
- Potential additional process:
 - Angiogenesis (Neovascularization): collateral network
 - Functional collaterals?
 - Frail

Importance of collaterals

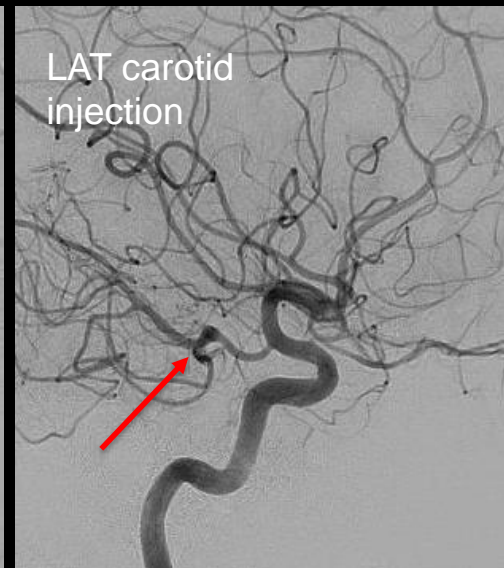
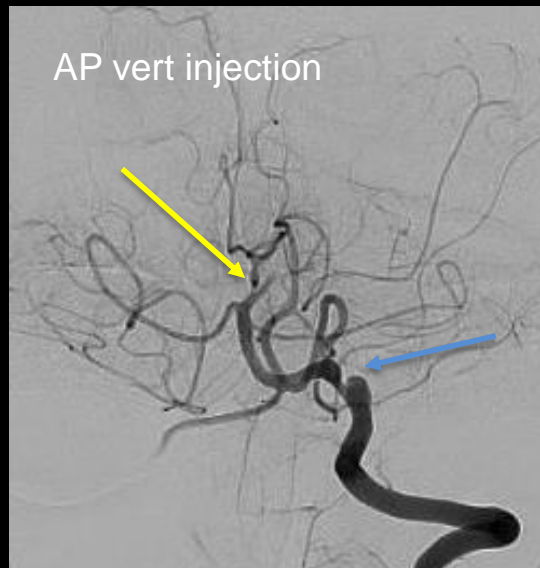
- 37F
- Severe head/neckpain while cycling
- Acute **transient** tetraplegia, GCS15



MR
FLAIR



MR DWI pons t=0



- Ischemic stroke caused by hypoperfusion: supply does not meet demand
 - Decreased supply:
 - Steno-occlusive disease
 - +/- hypotension, anemia
 - Increased demand:
 - Exercise
- Impaired washout of emboli

- **History**

- Fluctuating stereotyped symptoms
- Limb shaking
 - <5'
 - whole limb
 - paresis during/after (80%)
- Monocular symptoms triggered by bright light: retinal claudication
- Episodic non-focal symptoms (dizzy, unsteady, brainfog)
 - strongest predictor is focal + non focal symptoms
- Hemodynamic trigger to symptoms:
 - rising, exercise, new or ↑ antihypertensives, blood loss (menses)

- **History: Headache**

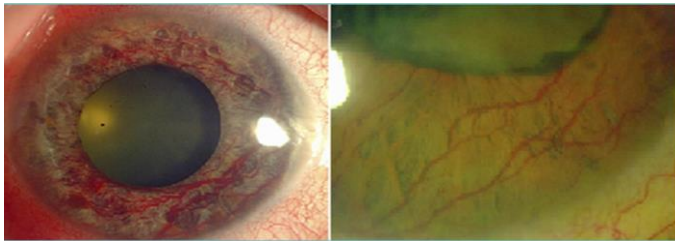
- Up to 72% in MMA^{1,2}
- Migraine mimic
- Children and adults
- Disabling: VAS 5, Sick leave: 60%
- Partially reversible after EC-IC bypass surgery:
 - Headache improvement in 68% of 59 patients
 - Related to hemodynamic status on BOLD CVR (OR 5.4; 95%CI: 1.2-23.5)
 - VAS: 5 -> 2.5 (*p* 0.002)
 - Analgesic use: 84% -> 40% (*p* 0.007)
 - Sick leave reduction: 60% -> 16% (OR 1.4; 95%CI: 1.6-121.4)

- **Cognitive changes**

- 50% of patients with symptomatic ICAO¹
- Improvement of cortical thinning after EC-IC bypass²
- RECON-trial:
 - Symptomatic ICAO + increased oxygen extraction fraction on PET
 - No cognitive change after EC-IC bypass surgery compared to MM³
 - Cognitive improvement related to hemodynamic state on PET
- *Awaiting CREST-H results (2027)⁴*
 - *Asymptomatic carotid stenosis and hemodynamic impairment on MR perfusion*
 - *Δ Cognition after medical management vs revascularization*

¹Bakker Stroke 2003; ²Fierstra Stroke 2011, ³RECON-trial, ⁴Marshall Int J Stroke 2018

- **Physical exam**
 - Hemodynamic challenge
 - Blood pressure: test for orthostatic hypotension
 - Rubeosis iridis:
 - iris neovascularization
 - Associated with ocular ischemic syndrome



Oller et al JVascSurg 2012

Ocular Ischemic Syndrome

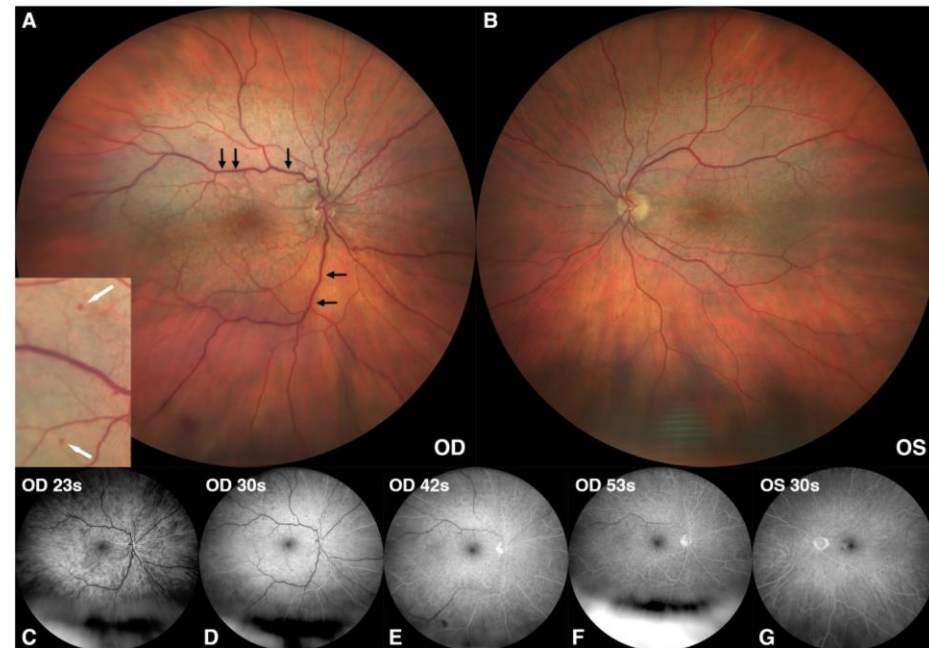
30% of ICAO

Usually gradual vision loss over weeks

75F monocular vision loss + dull pain OD:

- Dilated inner retinal vasculature (A:black ↓)
- Peripheral dot-blot hemorrhages (white ↓)
- Delayed filling retinal arteries & veins (C-F)
- Normal transit in OS (G)

-> CTA: >90% stenosis ipsilateral ICA



Courtesy: Dr. Ballios, retinal specialist,
UHN

Hypoperfusion symptoms & Stroke risk

- Hypoperfusion symptoms alone are not strongly correlated with recurrent stroke risk
- Patients need imaging to assess their hemodynamic status

Amin-Hanjani, VERITAS study group 2020; Lutsep, SAMMPRIS study group 2015; Mazighi Neurology 2006



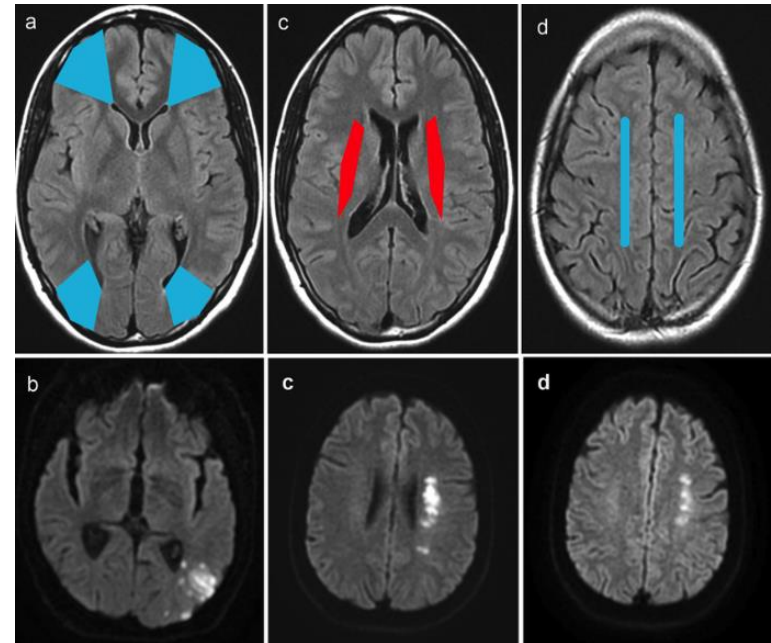
Structural imaging: MRI

Indirect signs of hemodynamic compromise:

- Infarcts in the watershed territories

Note:

- *infarct patterns do not always explain the stroke mechanism*
- \triangle *territories in MMA*



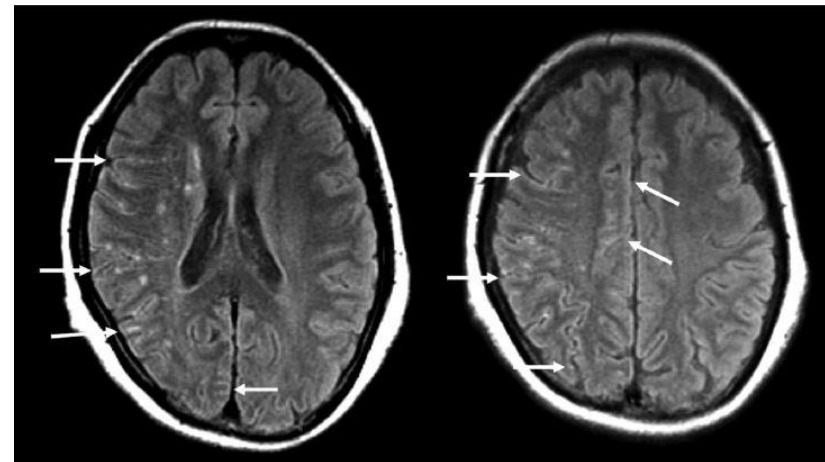
Case courtesy of Frank Gaillard, Mori AJNR 2009

Structural imaging: MRI

Indirect signs of hemodynamic compromise:

- Infarcts in the watershed territories
- Cortical thinning
- Ivy sign (slow flow in leptomeningeal collaterals)

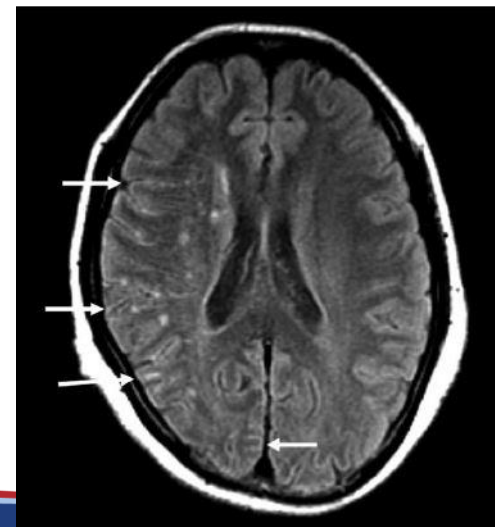
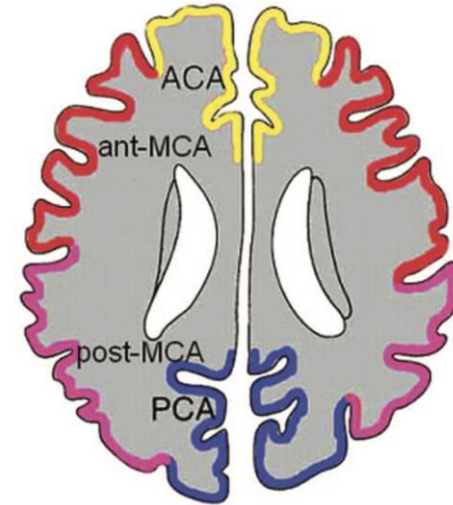
Case courtesy of Frank Gaillard, Mori AJNR 2009



Diagnostic value of ivy sign

- n=73 patients, 584 cortical regions
- *Index: Ivy sign on FLAIR*
- *Reference: BOLD cerebrovascular reactivity*

- Positive predictive value for impaired CVR: 79% (95%CI: 69-87)
- Negative predictive value for impaired CVR: 77% (95%CI: 74-79)
- Sensitivity to detect impaired CVR: 44% (95%CI: 35-54)
- Specificity to detect impaired CVR: 94% (95%CI: 90-97%)



O'Cearbhaill et al. ISC 2024

Imaging hemodynamics: angiography

Multiphase CTA

- Imaging the presence of collaterals, their caliber, and impression of filling time

DSA

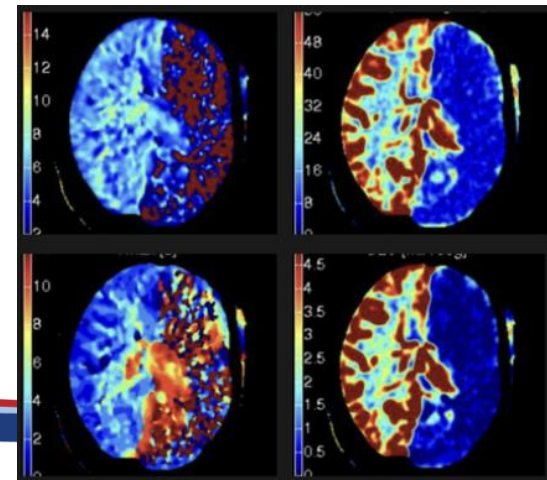
- Time-resolved imaging of collaterals
 - *Note: Poor inter and intra observer agreement of collateral grading**
- Neovascularization

*Ben Hassen JNIS 2019

Imaging hemodynamics: perfusion

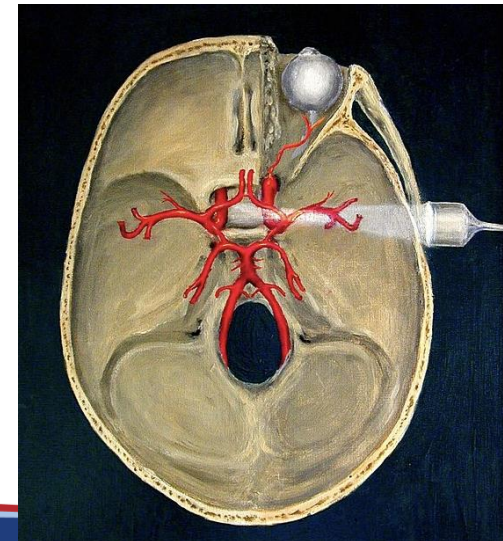
CTP/MRP:

- Maps of CBF, CBV, MTT, time to maximal contrast concentration
- Limited value to assess hemodynamic impairment:
 - Resting perfusion measures
 - No assessment of the quality of the collateral circulation
 - Limited spatial resolution and skull base artifact for posterior circulation
- Less reliable with increasing severity of disease: no functional information



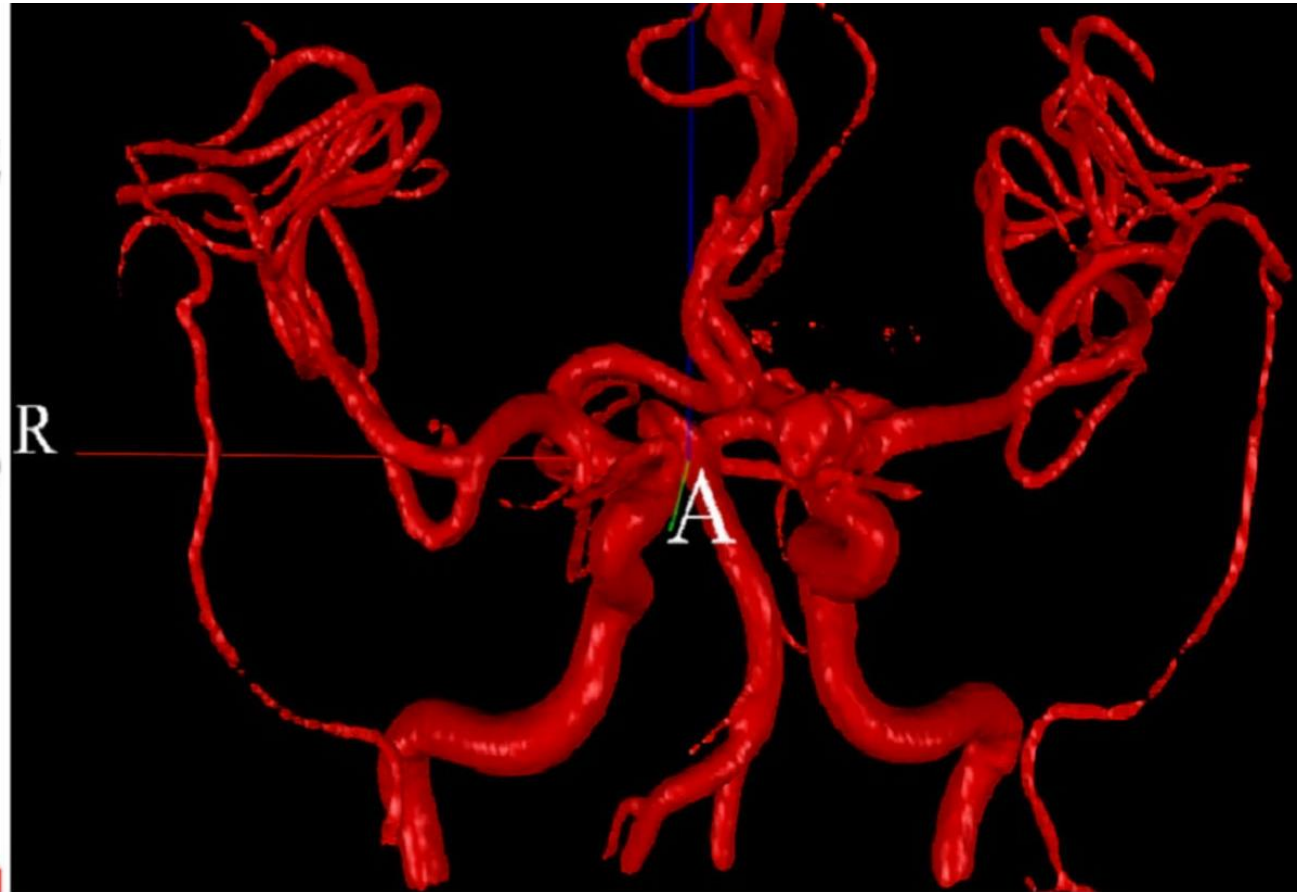
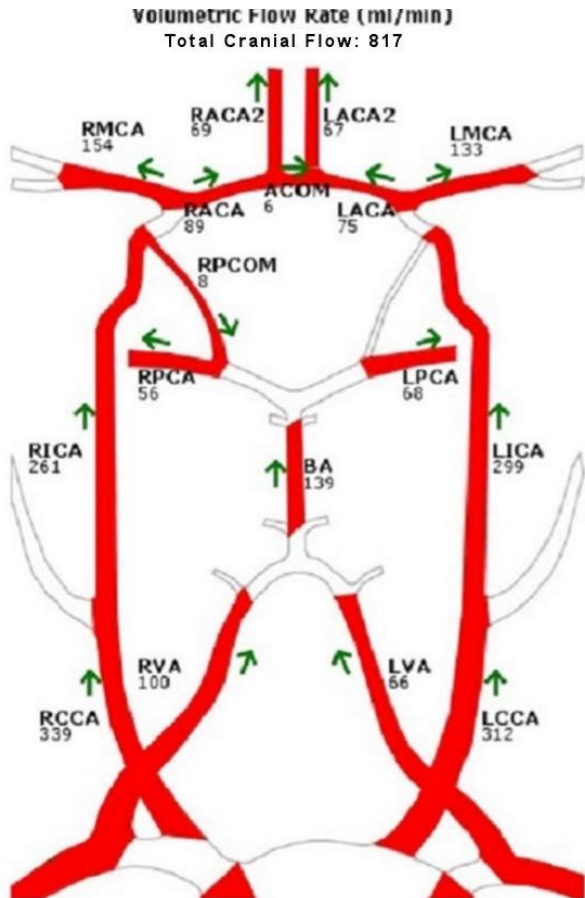
Transcranial Duplex Sonography

- Flow velocity
- Recruitment collaterals
 - Direct: ACOM/PCOM
 - Indirect: flow direction ophthalmic artery, leptomeningeal arteries
 - Increased flow in P2 ipsilateral to ICAO is related to hemodynamic impairment and stroke risk¹
- Hemodynamic impairment
 - Response to vasodilator (e.g. Diamox)
- Pros: accessibility (bedside)



Quantitative MRA (e.g. 'NOVA'):

- 2D Phase contrast MRA: direct volumetric flow measurements
- 3D TOF-MRA for anatomical correlation – selection of orthogonal plane of interest
- Clinical utility for posterior circulation assessed in the VERITAS study:
 - Flow measurements distal to symptomatic vertebrobasilar stenosis
 - Low distal flow: 28% recurrent stroke vs 9% in normal distal flow (HR 12; 95%CI: 2-71)



Li, Charbel, et al. J Neurol Res 2021

Imaging hemodynamics: vascular reserve

¹⁵O-water PET

- First imaging technique to assess brain perfusion (1980's)
- ICAO patients with ongoing TIAs:
 - Misery perfusion: ↓ CBF, ↑ CBV, ↑ oxygen extraction, normal O₂ consumption
- Hemodynamic reserve (vasodilatory capacity) assessed with acetazolamide

Alternative: MRI BOLD with cerebrovascular reactivity (CVR)

- “Brain stress test”
- Vasodilatory stimulus: CO₂
- Indirect measure for Δ CBF:
 - Δ deoxyHb \rightarrow Δ BOLD signal \rightarrow mapped per mmHg CO₂ change
- Assesses efficacy of collaterals: cerebrovascular reserve capacity

Cerebrovascular reactivity MRI: emerging technique



Dr. D.J. Mikulis
Neuroradiologist

Dr. J Fisher
Anesthesiologist



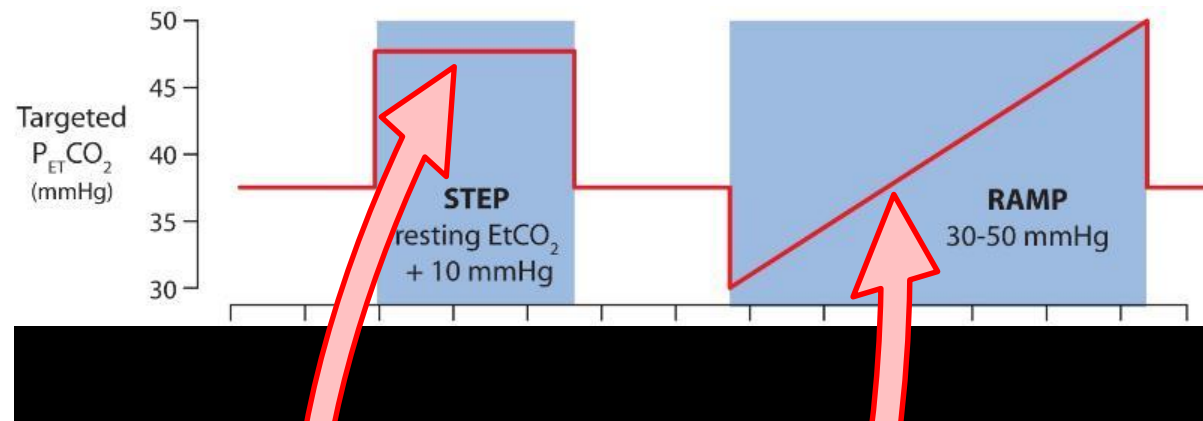
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Bhogal
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Duffin
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Forte
Klostranec
Kuo
Levine
Lim
Mandell
Mikulis
Niftrik
Poublanc
Sayin
Shafi
Skanda
Sobczyk
Schulman
Uludag
Venkatraghavan
Vibhute
Wasserman
Wood
Wu



- Vaso active stimulus (CO₂) using Respiract
- Full brain mapping of cerebrovascular responses to precise session-to-session vasoactive stimuli during MRI
- End-tidal CO₂ = arterial CO₂



“Step” and “Ramp” standard CO₂ Stimulus

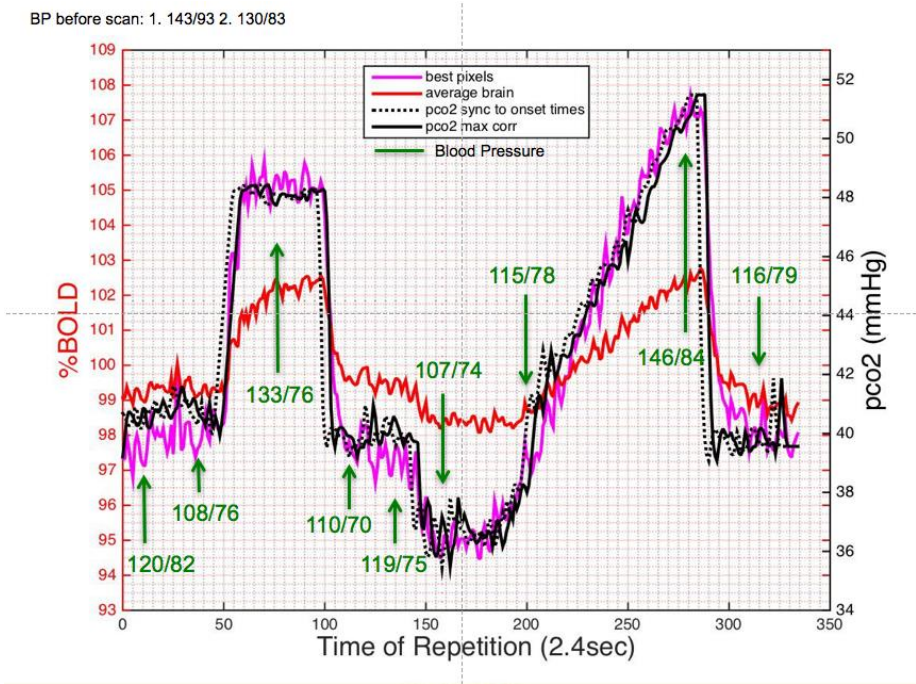


Step stimulus : CVR Speed of response response

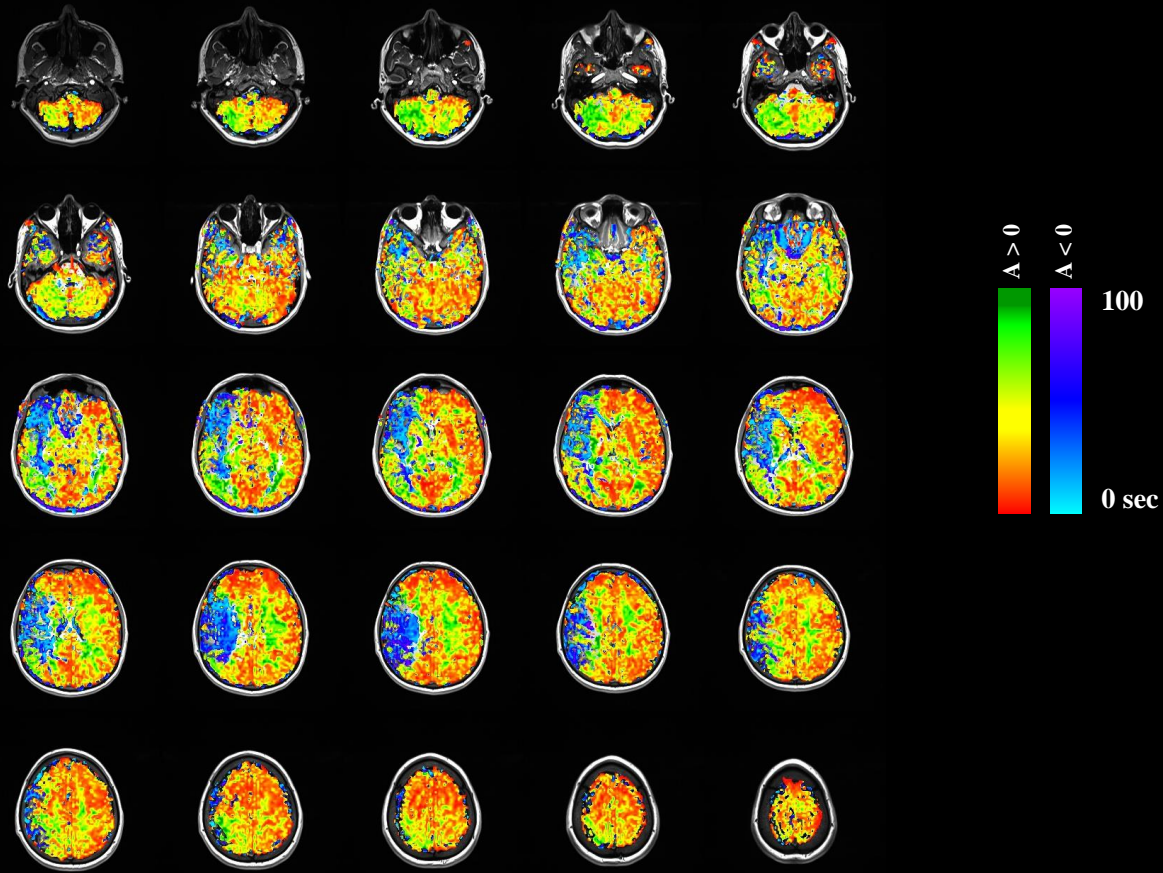
Ramp stimulus: CVR Magnitude of

CVR response

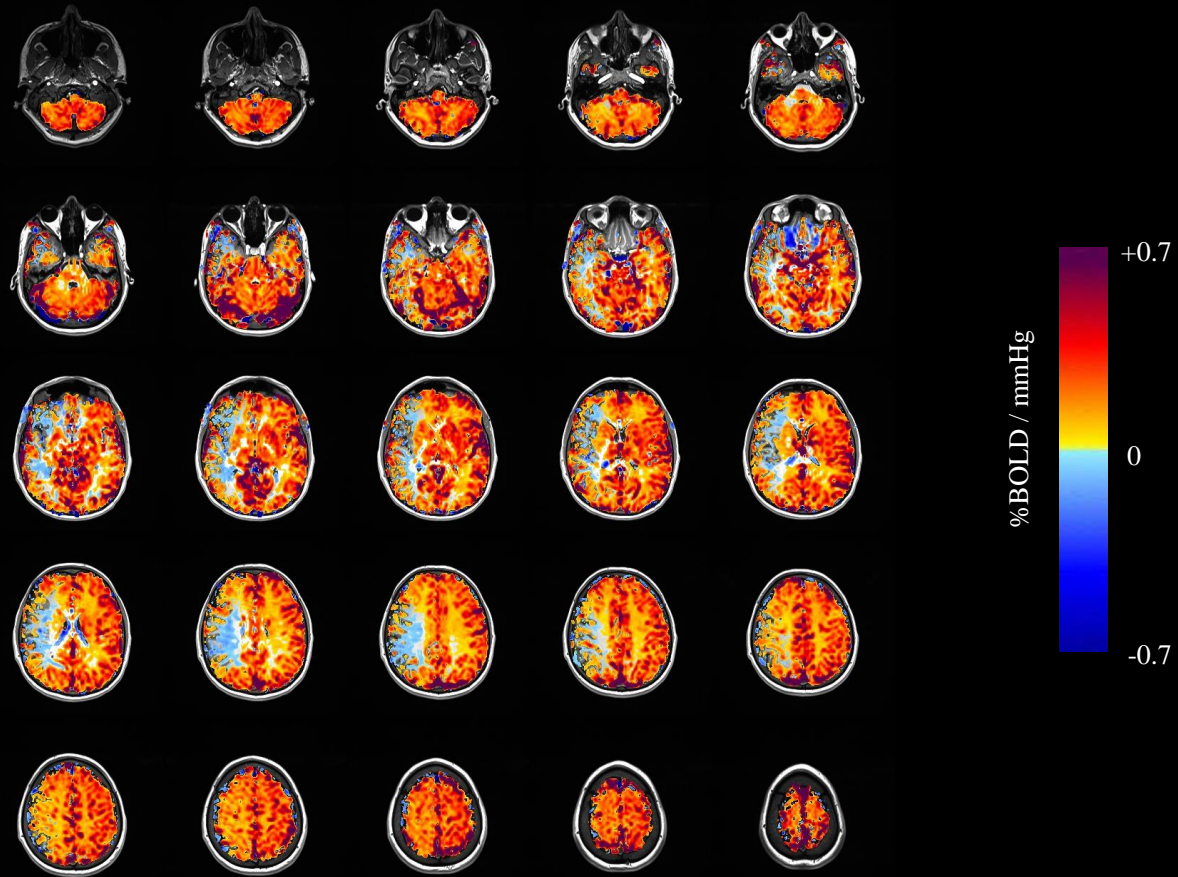
Linear correlation between:
 the % change in the BOLD signal
 per mmHg change in CO₂
 for each voxel in the brain
 for every BOLD image



CVR Speed - step



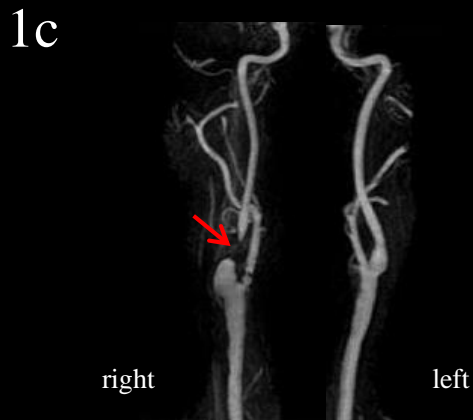
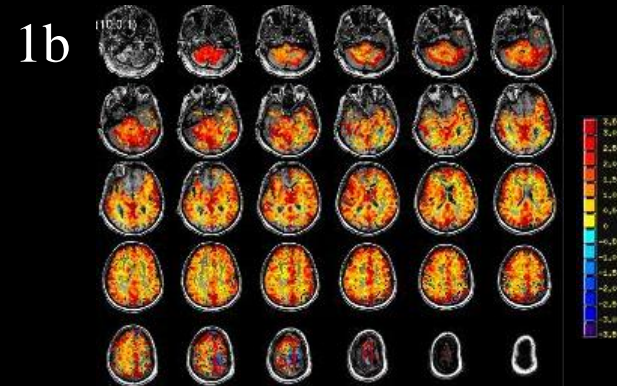
CVR Magnitude - Ramp



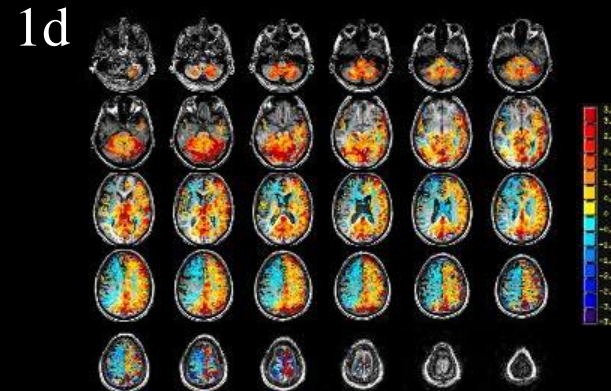
CVR patterns: 2 patients with TIAs



Effective collaterals



Ineffective collaterals

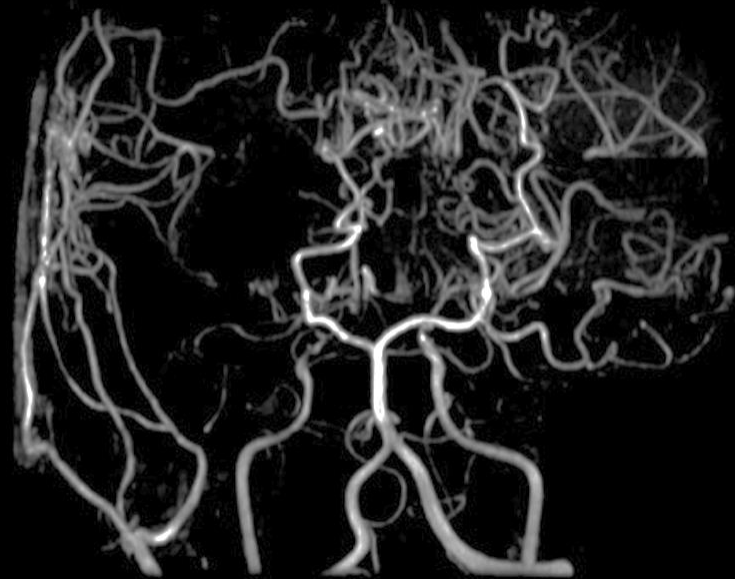
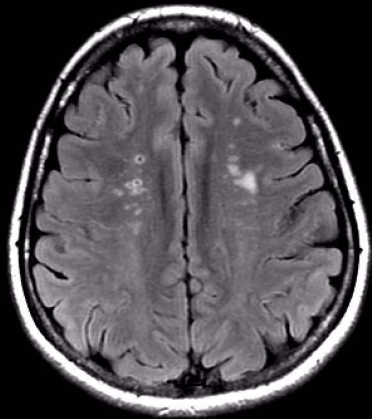


- Reproducible
- RespirAct Health Canada approval (Aug 2022)
- Gradual integration into clinical practice

Diagnostic yield:

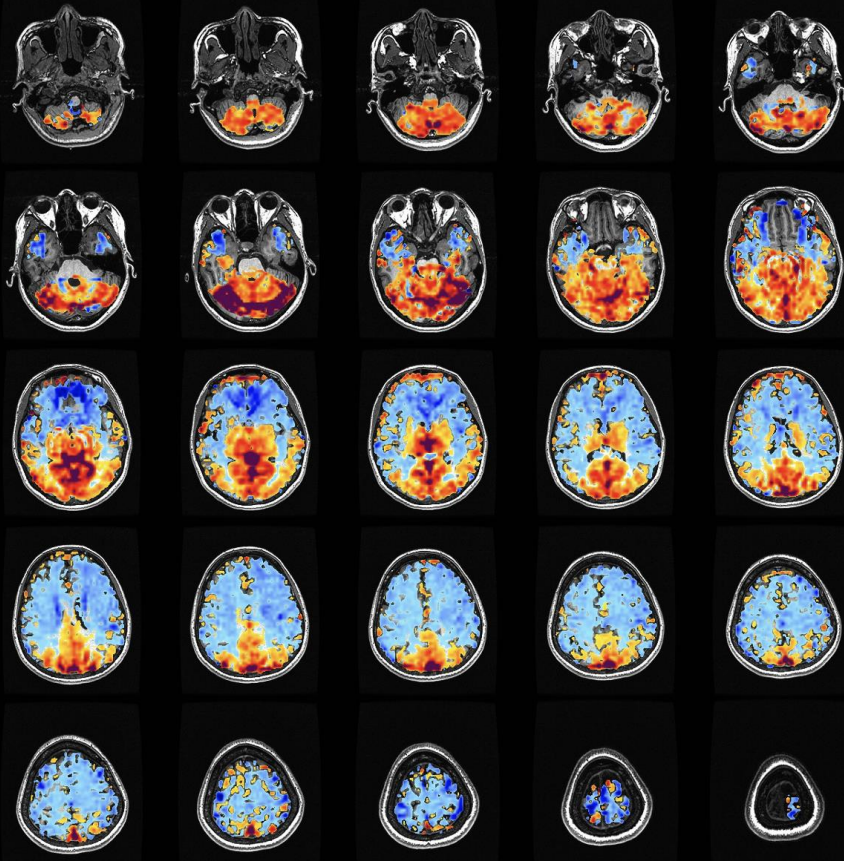
- BOLD-CVR vs [^{15}O]H₂O-PET (gold standard): Good agreement
- BOLD-CVR impairment is associated with recurrent ischemic stroke
- *?Future: acute stroke – failed EVT*

Back to our patient: 34F L MCA symptoms & limbshaking

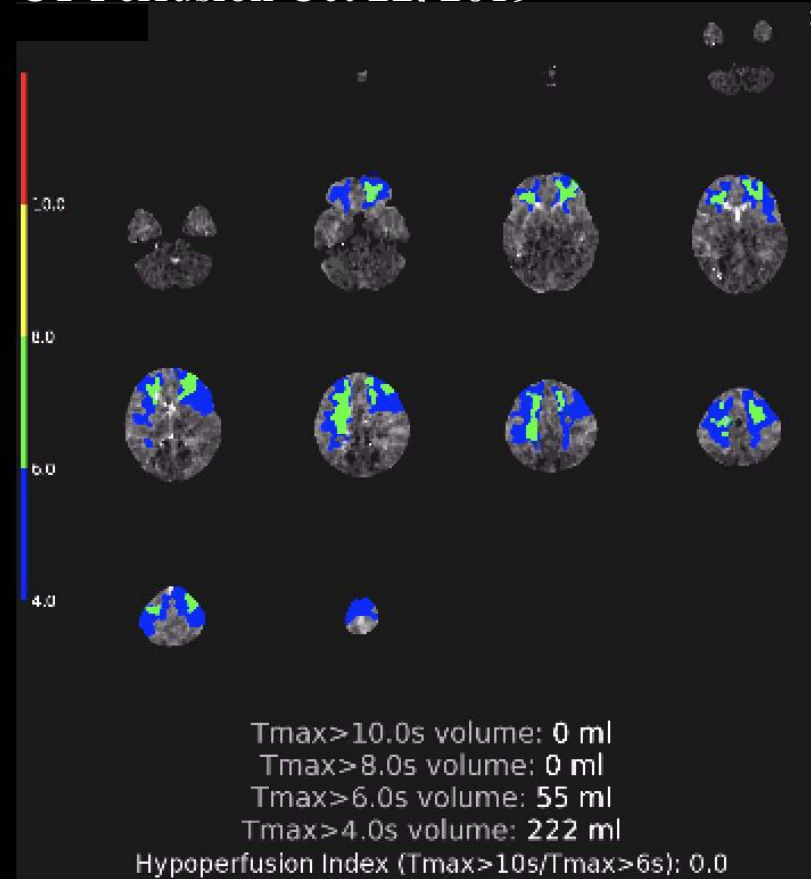


MRI with Cerebrovascular Reactivity

CVR Aug 12, 2019



CT Perfusion Oct 22, 2019



Recommendations for Imaging Work-up MMA

Moyamoya arteriopathy ESO Expert consensus (absence of evidence):

- Hemodynamic assessment is recommended to support decision-making:
 - In both asymptomatic and symptomatic MMA patients, to identify the territories at risk for stroke
- Use the imaging modality that the individual institution has the most experience with
- Include PCA/posterior circulation assessment in all (especially pediatric) MMA patients

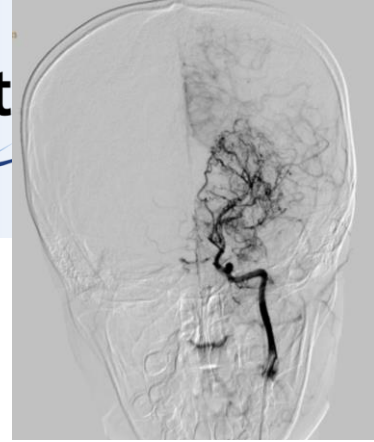
Management options **Moyamoya arteriopathy**

- **Medical management: all patients**
 - Optimizing perfusion
- **Surgical revascularization: selected patients**
 - Flow augmentation (Indirect or direct methods)
- **No endovascular treatment** with stent or angioplasty (unless ruptured moyamoya aneurysms)

Japanese guidelines for the Management of Moyamoya disease. 2021
Miyamoto S. Japan Adult Moyamoya trial. Stroke. 2014
Esposito G. Cerebral Bypass surgery level of evidence. 2018

Medical management Moyamoya angiopathy

- Ischemic stroke prevention:
 - Optimize hemodynamics, avoiding triggers: dehydration, hyperventilation, fever, hypotension, regular sleep
 - Treat anemia
 - Hydroxyurea in sickle cell disease patients
 - Headache treatment:
 - Hydration, sleep
 - Avoid vasoactive agents (beta-blockers, calcium channel blockers, triptans)
 - Fludrocortisone? Midodrine?
 - Antiplatelet therapy?
 - Secondary prevention: Low-dose aspirin or clopidogrel (decreased embolic washout)
- Secondary hemorrhagic stroke prevention:
 - Avoid hypertension + hypotension
 - No aspirin if no ischemic event



- **Hemorrhagic Moyamoya disease**
 - 1 RCT (JAM trial): STA-MCA bypass
 - Decreased risk of events: 34->14% over 4 yrs (Level of evidence IB)
- **Ischemic Moyamoya disease**
 - No randomized data
 - Trend event ↓: RR 0.54 (95%CI:0.28-1.01)
 - Natural course: 10-80% recurrent stroke over 5 years.
 - Selected patients with hemodynamic impairment (BOLD CVR; PET; CBF-SPECT)

Japanese guidelines for the Management of Moyamoya disease.
2021

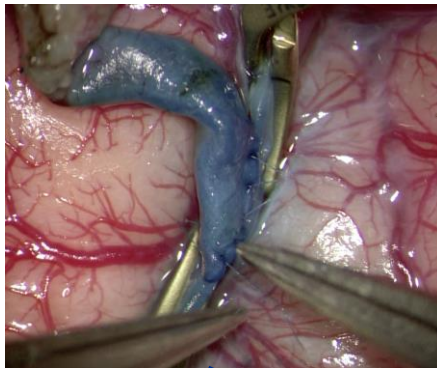
Miyamoto S. Japan Adult Moyamoya trial. Stroke. 2014
ESOC guidelines 2023

Surgery in Moyamoya: ESO Guidelines - AHA/ASA Statement

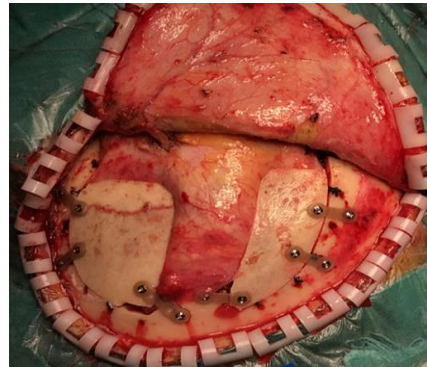
- Adults with hemorrhagic presentation: direct STA-MCA bypass. *Quality evidence: low*
- Expert opinion: Consider surgery in case of:
 - Clinical ischemic presentation and imaging markers of hemodynamic impairment
 - Silent infarcts and hemodynamic impairment in the same region
 - 6-12 weeks post-event

Surgical Revascularization

Direct bypass



Indirect methods



STA-MCA
OA-MCA
OA-PCA
STA-ACA-
MCA

Combination

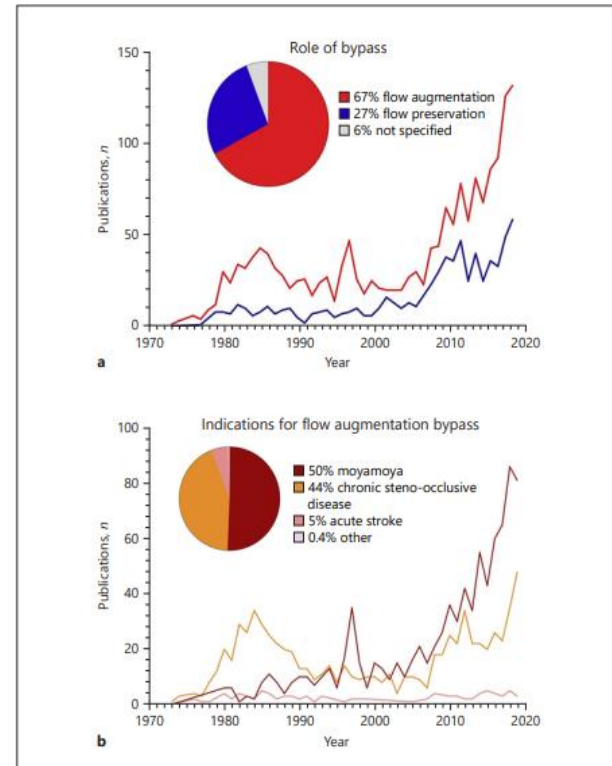
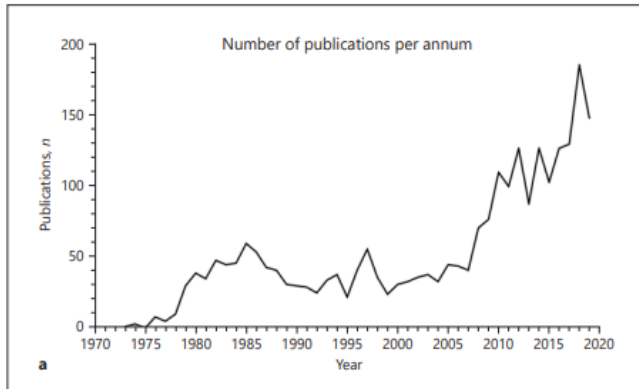
- Encephalo-myo-synangiosis (EMS)
- Encephalo-duro-arterio-synangiosis (EDAS)
- Encephalo-duro-arterio-myo-synangiosis (EDAMS)
 - Omental-cerebral transposition
 - Burr holes

- Ensure per operative normotension, normocapnia, normovolemia
- Risk of postoperative stroke (surgical site)
 - Adults (7%)
 - Pediatric (2%)
- Hyperperfusion syndrome (3-5%)
- Wound healing problems (Depends on surgical strategy)
 - 1.7 – 5.1% Direct bypass
 - 4.4 - 14% Combined treatment

Trends in Literature on Cerebral Bypass Surgery: A Systematic Review

Basil E. Grüter^{a,b} Lazar Tomic^{a,b} Stefanos Voglis^{a,b} Flavio Vasella^{a,b}
Valentino Mutschler^b Oliver Bichsel^{a,b} Natalie Scherrer^{b,c} Luca Regli^{a,b}
Giuseppe Esposito^{a,b}

^aDepartment of Neurosurgery, University Hospital Zurich, Zurich, Switzerland; ^bClinical Neuroscience Center, University Hospital Zurich, Zurich, Switzerland; ^cNeurointensive Care Unit, University Hospital Zurich, Zurich, Switzerland

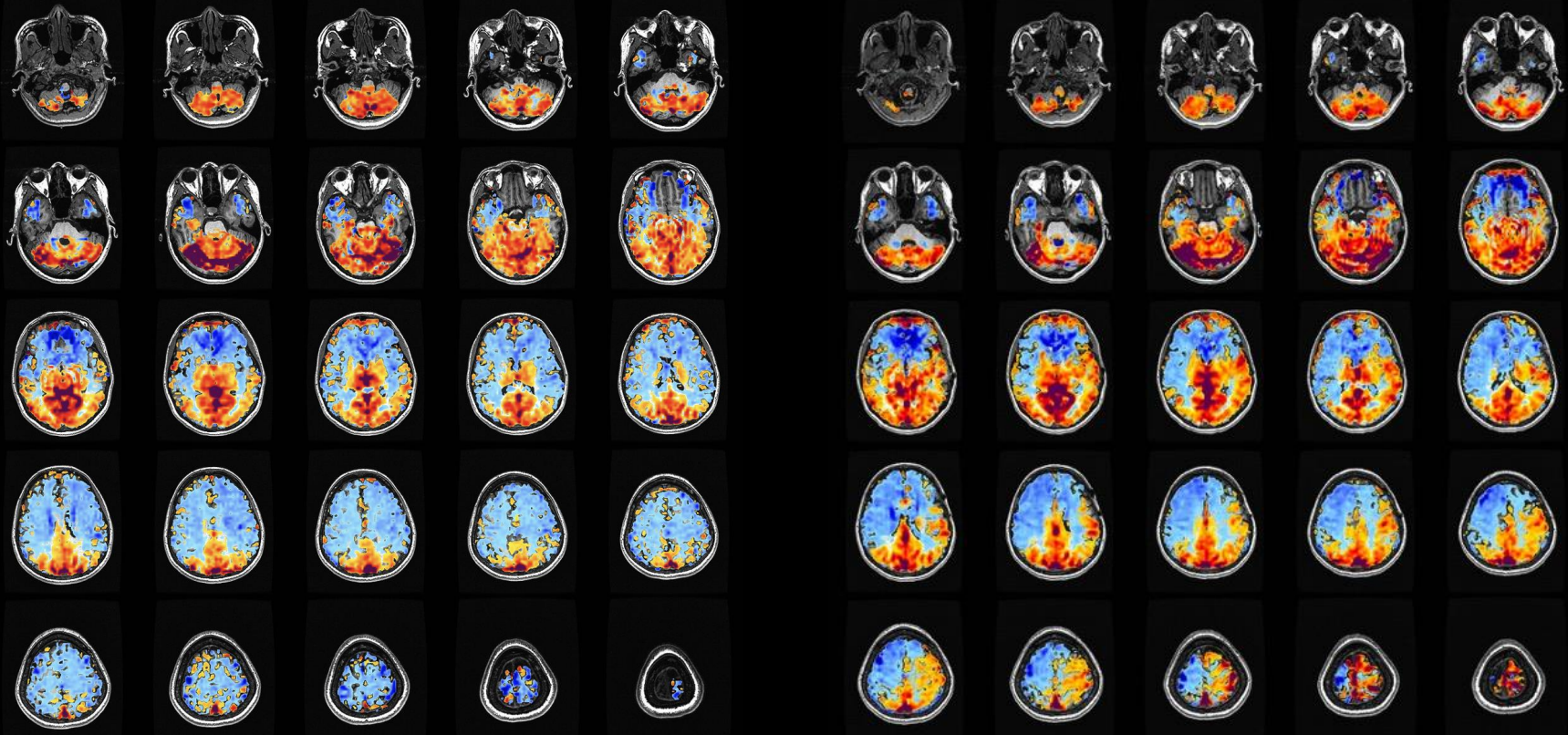


Back to our patient

- Underwent left-sided EC-IC bypass surgery in 2020
- Uncomplicated course
- Significant improvement in her headaches
- No episodes of left MCA symptoms anymore
- Left-sided CVR improvement post-bypass:

CVR pre left ECIC by-pass
Aug 12, 2019

CVR post left ECIC By-pass
Jan 2020

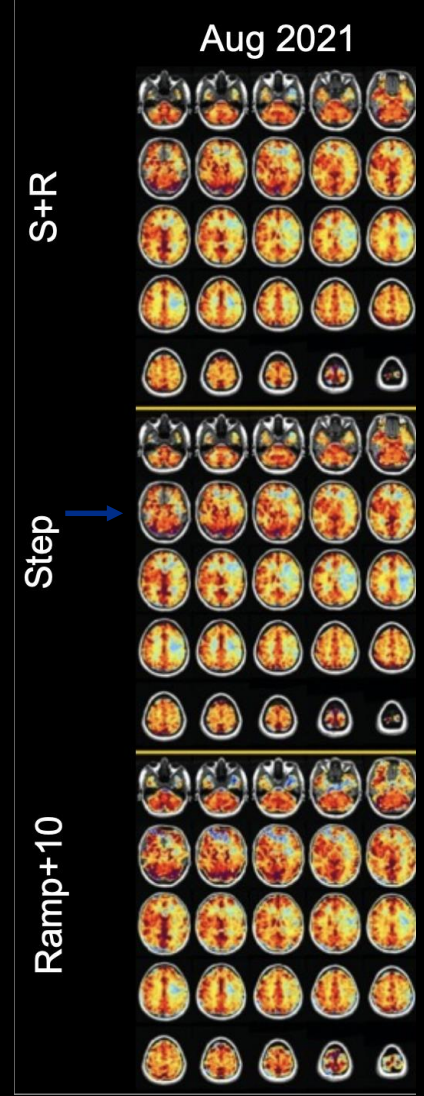
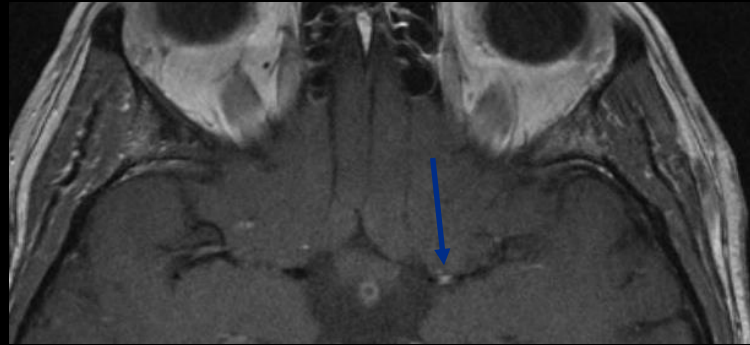
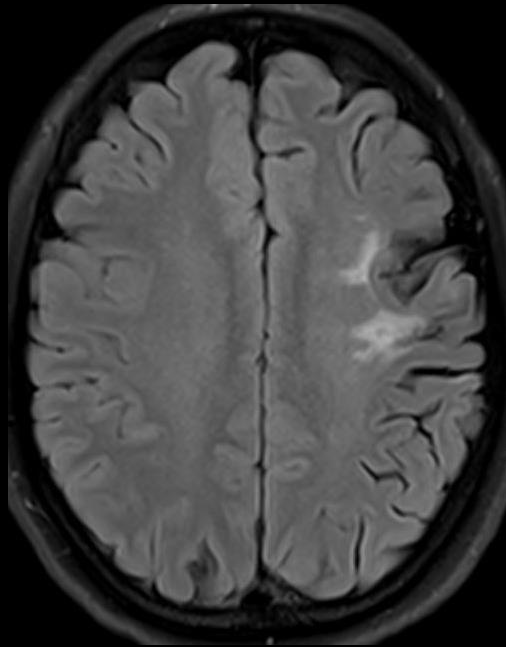


- Developed ischemic events from **right** hemisphere
- Worsening of occlusive disease and CVR on the right
- She was offered a second EC-IC bypass, now on the right in 2021 (1 year later)
- No complications
- No recurrent ischemic events. Headaches continued to improve

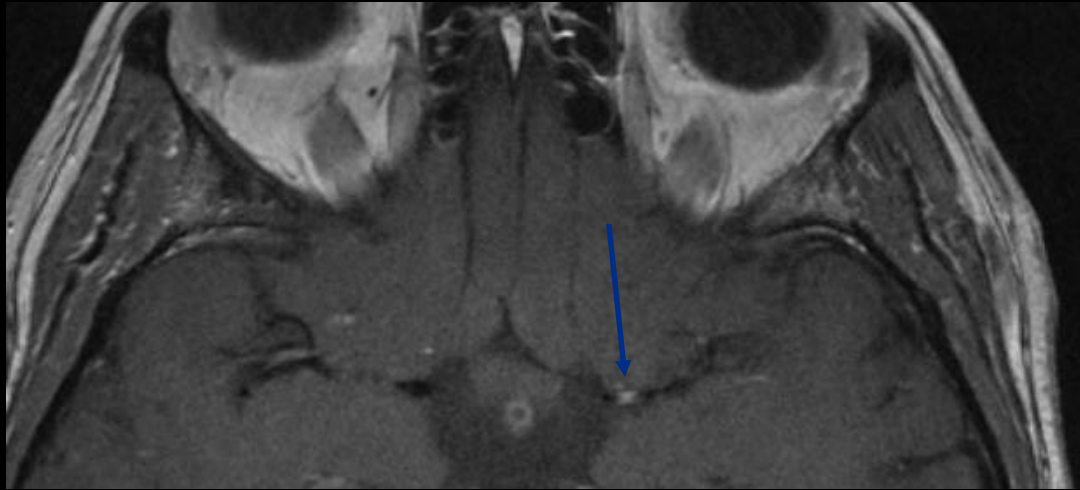
Workup & treatment of **MMA** occlusive disease

35-year-old woman

- 2021: Recurrent symptomatic left MCA stenosis: embolic stroke and TIAs
- No hemodynamic trigger
- Left-sided headache, 'brain fog'
- The nature of the stenosis is not well understood
 - Vasculitis work-up was negative (including LP)
 - New diagnosis of DM2, DLD, HTN.
 - Working diagnosis: ICAD



MRI Vessel wall imaging



- Circumferential eccentric enhancement -> ICAD



SAGITTAL



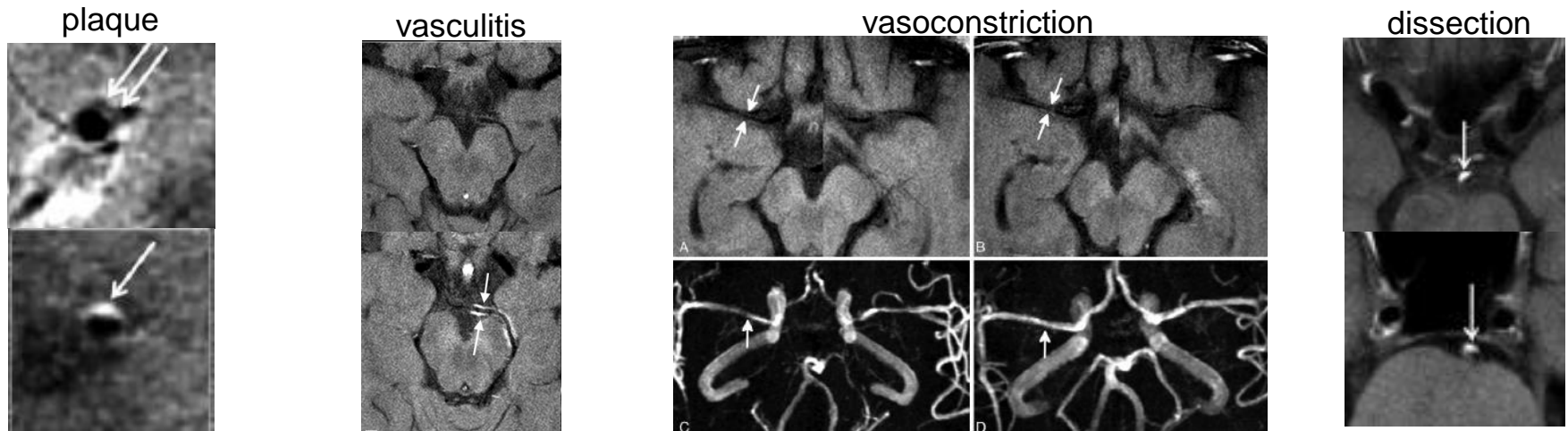
AXIAL



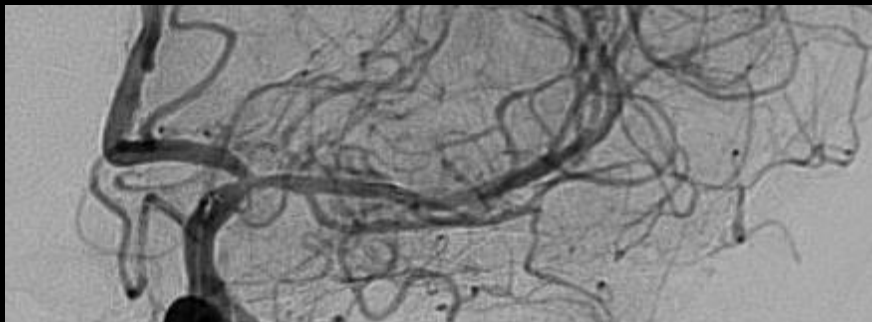
CORONAL

Yield of Vessel Wall Imaging in Stroke

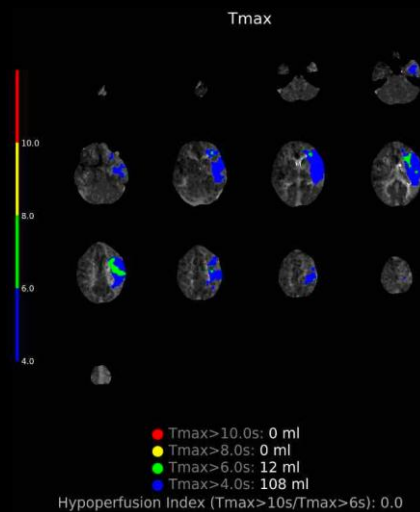
- Framework VWI interpretation
 - Atherosclerosis: eccentric thickening +/- eccentric enhancement
 - Vasculitis: circumferential concentric thickening +/- enhancement
 - Vasoconstriction: concentric thickening +/- mild enhancement
 - Dissection: eccentric thickening with homogenous eccentric enhancement



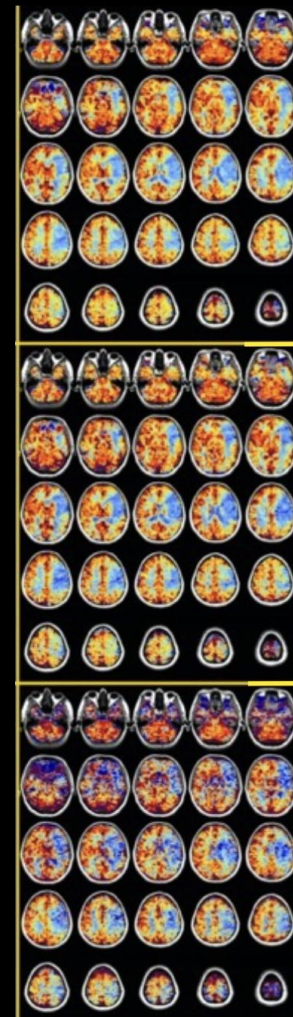
L MCA stent



1 year post L MCA stent



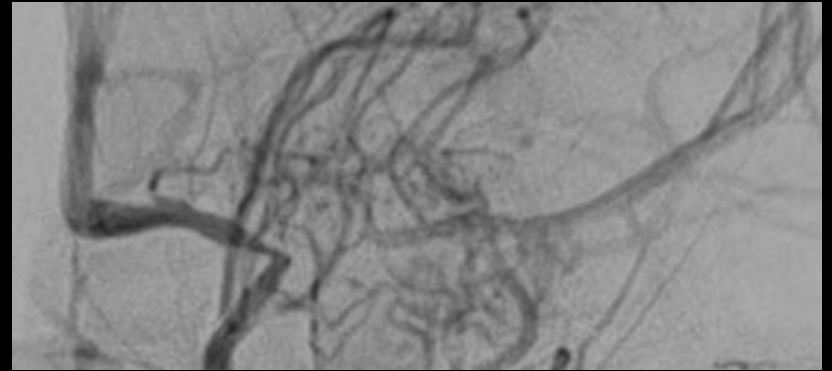
Oct 2022



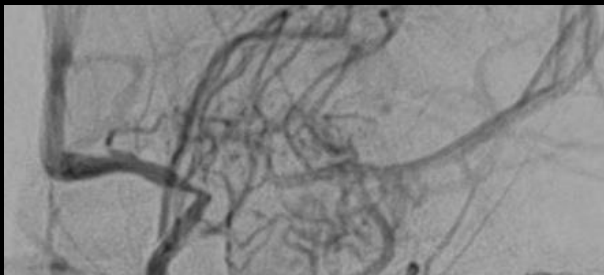
A1 patent



1 year later:
Stent occluded
New L A1 stenosis



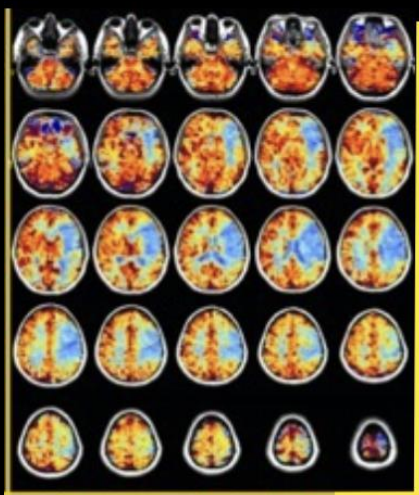
Pre angioplasty L A1



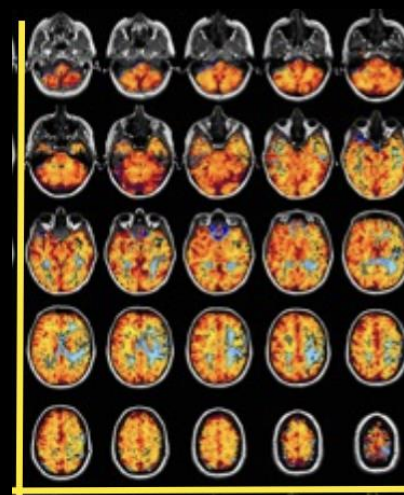
Post angioplasty L A1

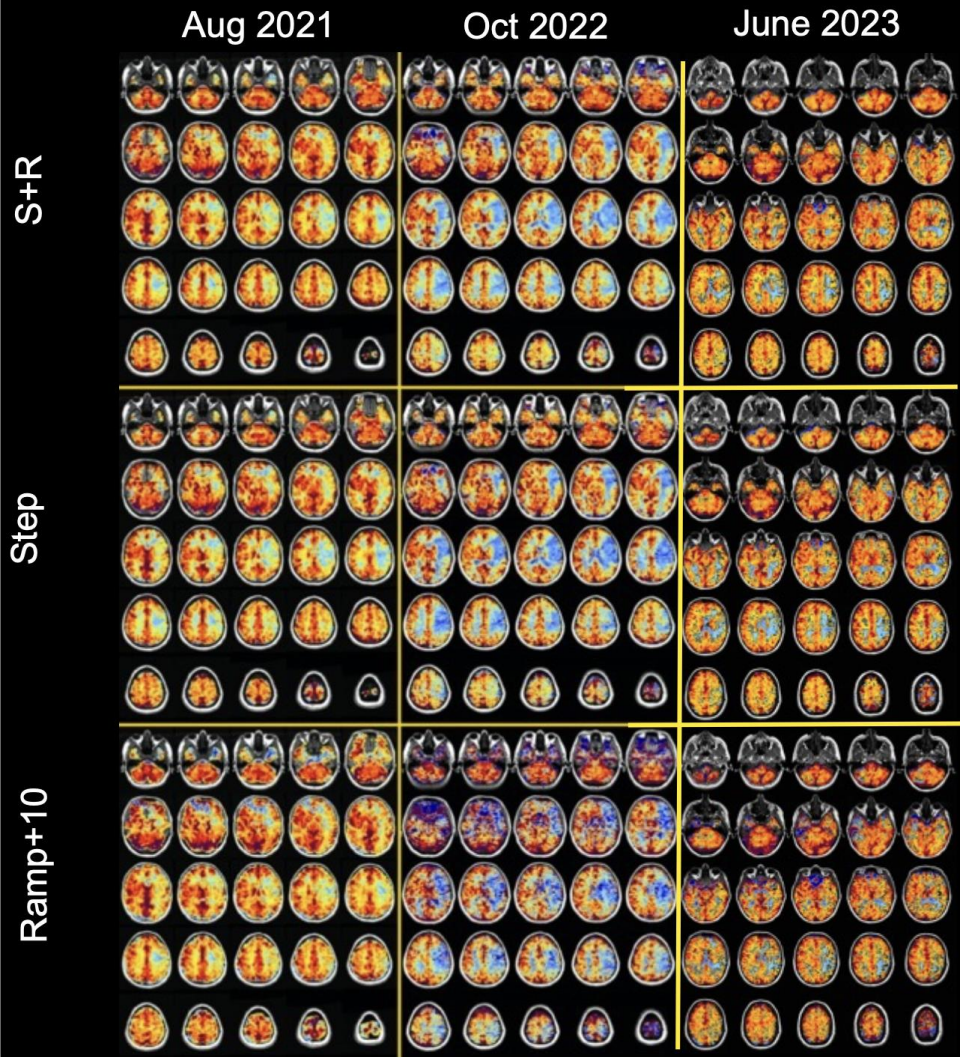


Oct 2022



June 2023





2021: Baseline

2022: 1-yr post-stenting

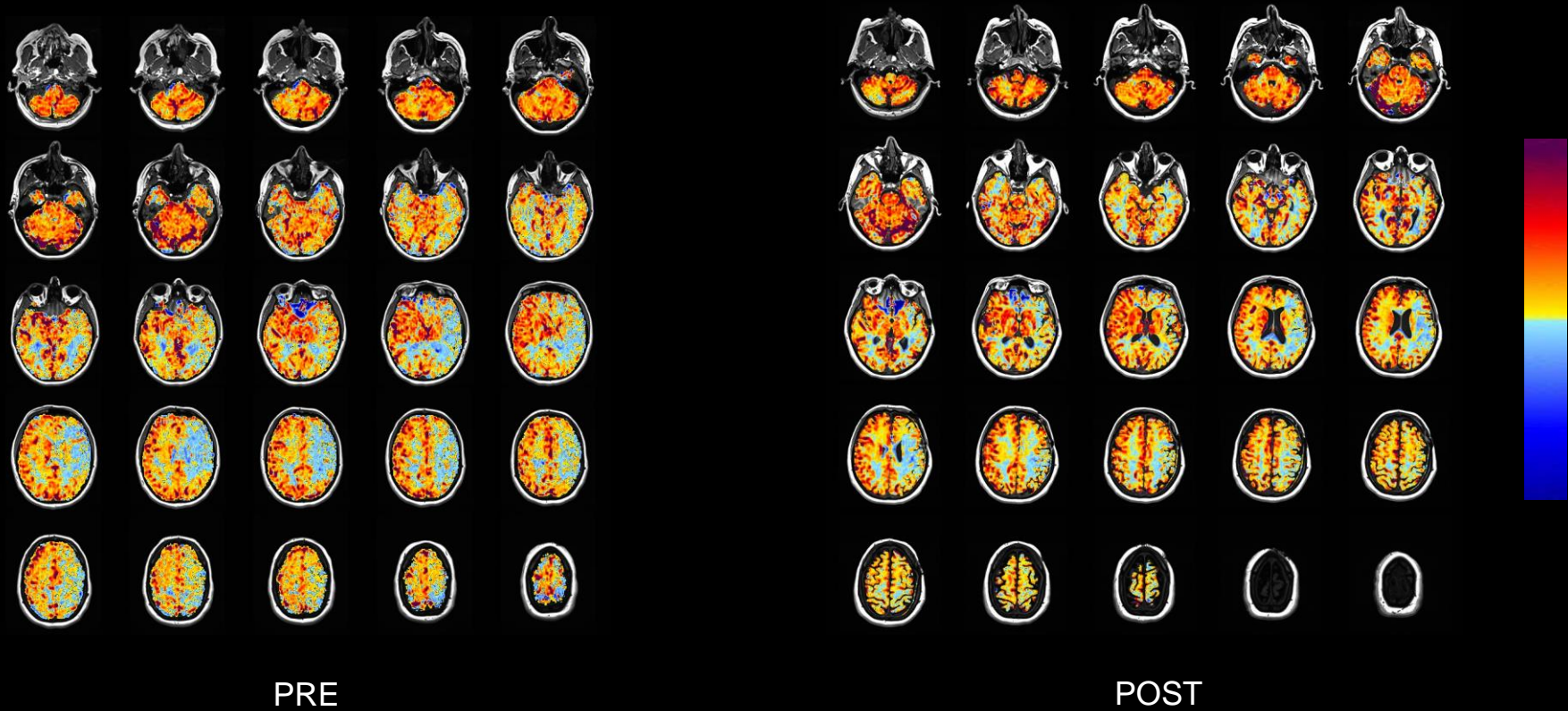
2023: Post angioplasty A1

Temporary clinical improvement after each procedure

- Temporary clinical improvement after each endovascular flow augmentation treatment
- But recurrent hemodynamic symptoms, headache, and 'brain fog'.
- BOLD CVR:
 - Worsening cerebrovascular reserve
- Offered EC-IC bypass surgery

- ECA was occluded:
 - Radial graft for cervical ICA to M2 high-flow bypass
- Target SBP 90-110 mm Hg
- No complications
- Improvement of symptoms
- Gradual reduction in caliber of the graft on follow-up but remains patent
- Improvement of BOLD CVR:

CVR Step+Ramp Pre & 3-month Post EC-IC bypass



Management of MMA steno-occlusive disease

Extracranial

- Symptomatic ICA stenosis 70-99%:
 - Revascularization with CEA/CAS , irrespective of stroke mechanism
- Symptomatic vertebrobasilar artery stenosis:
 - Medical management: antiplatelets + risk factors (*VIST, VAST, SAMMPRIS, VISSIT, CAVATAS*)
 - *VERiTAS: hemodynamic impairment: higher stroke risk -> subtotal angioplasty?*
- Symptomatic ICAO with hemodynamic impairment on imaging:
 - Medical management: antiplatelets, risk factors, optimize perfusion
 - COSS trial (¹⁵O-PET): no benefit of EC-IC bypass over medical treatment alone

Management of MCA steno-occlusive disease

Intracranial

- Regardless of the stroke mechanism:
 - Aggressive medical management (DAPT 90 days, risk factors)
 - SAMMPRIS/WEAVE/WOVEN/CASSISS/WICAD: medical management > intracranial stenting
 - No selection based on hemodynamic compromise
- Expert consensus:
 - Consider angioplasty +/- stenting >7 days post-event **as rescue therapy** in >70% symptomatic stenosis after failed medical management, especially if hemodynamic impairment

Symptomatic ICA or MCA occlusion

- CMOSS: patient selection based on hypoperfusion on CTP: MTT >4 s, CBF < 0.95:
 - 30-day stroke/death: 6.2% after EC-IC bypass, 1.8% with MM
 - >30-day to 2-year ipsilateral stroke: 2.0% after EC-IC bypass, 10.3% with MM
 - At 7 years: 11% after bypass, 20% with MM (RR 0.57; 95%CI: 0.33-0.97)
 - Age <56: improved outcomes

- Efficacy of revascularization procedures for **selected patients based on hemodynamic impairment** needs to be assessed and quantified because of the **high stroke risk despite medical management**
- E.g. in a combined diagnostic-therapeutic trial
 - Optimal imaging technique -> optimal patient selection
 - Reduction of revascularization (peri-)procedural risks
 - Longer follow up

Decision-making when there is limited evidence

Multidisciplinary setting:

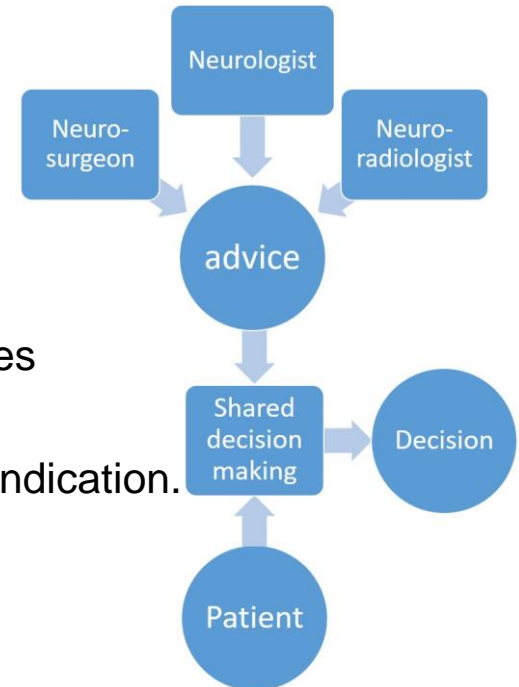
- Cerebrovascular Neurosurgery
- Vascular Neurology
- Diagnostic Neuroradiology
- Interventional Neuroradiology
- Neuropsychology

Chronic steno-occlusive disease

Predominantly:

- Moyamoya arteriopathy
- Atherosclerotic steno-occlusive disease

- Interdisciplinary pre-discussion
- Comprehensive clinic visits by relevant specialists
- Integration of guidelines, expert consensus, patient preferences
- Standard imaging: arterial wall imaging, BOLD CVR. DSA by indication.
- Neuropsychology assessment pre and post surgery
- Patient satisfaction¹:
 - 247 visits over 15 months
 - Response rate 92%
 - 98.5% (very) satisfied: provided information, patient communication
 - 72% preferred a multidisciplinary over a single-physician visit



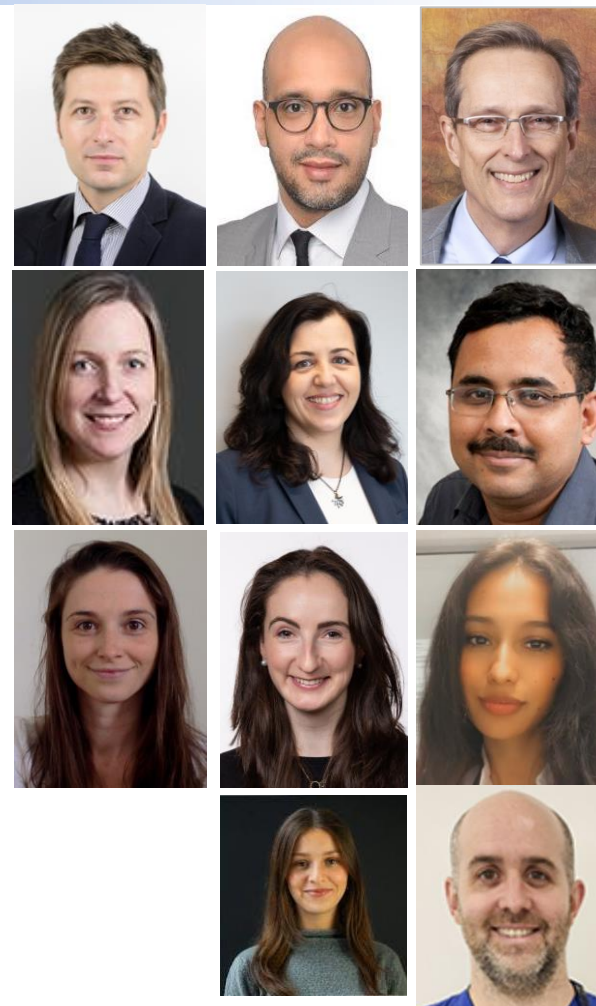
¹Janssen et al, submitted

- Hemodynamic stroke is challenging
- Recognize and ask for hemodynamic signs and symptoms: high stroke risk
- Identify the underlying pathology, e.g. with vessel wall imaging
- Assess the cerebrovascular reserve to identify high-stroke risk, e.g. with BOLD CVR
- Main treatment remains medical management
 - Avoid triggers, hydration, blood pressure, anemia
 - Atherosclerosis: CV risk factors, antiplatelets to prevent progression
- Revascularization interventions: open surgery or endovascular
 - Currently in highly selected patients
 - Multidisciplinary approach
 - Need a better understanding of their long-term efficacy and peri-procedural risks
 - Future: optimal selection of patients who benefit

Acknowledgement

- Ivan Radovanovic, cerebrovascular neurosurgeon
- Hugo Andrade, cerebrovascular neurosurgeon
- David Mikulis, neuroradiologist
- Andrea Para, neuroradiologist
- Federico Carpani, stroke neurologist
- Melanie Cohn, clinical neuropsychologist
- Lashmi Venkatraghavan, neuro-anesthesiologist
- Helena Janssen, stroke neurologist & PhD student
- Roisin O’Cearbhill, neuroradiology fellow
- Daniela Gallego Moyano, med student
- Noa Chazot, research student

- *The INR team, Stroke Neurology Team,
Diagnostic Neuroradiology Team*



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.

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