Emboli Testing in the Outpatient Neurology Clinic

John J. Volpi, MD
Co-Director, Eddy Scurlock Stroke Center

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Outline

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- Patient flow in evaluation of PFO/cryptogenic stroke
- Cases
  - The unexpected embolus
  - Deciding on medical management in complex cases
  - Asymptomatic carotid stenosis, stay the course?

Stroke work-up for PFO

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- Three step process for evaluation of stroke
  - Tissue based diagnosis
  - Vessel evaluation
  - Emboli source

Cryptogenic Stroke vs ESUS (embolic stroke of undetermined source)?

Stroke work-up

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- Tissue based diagnosis
  - Step 1: MRI imaging
    - If negative MRI, not sufficient evidence for stroke, proceed to medical management only
    - If positive MRI, does the tissue suggest ***chronic*** small vessel disease? If so, treat with medical management only
    - Note: isolated acute infarcts of any size and any location without chronic associated ischemia are potentially from emboli

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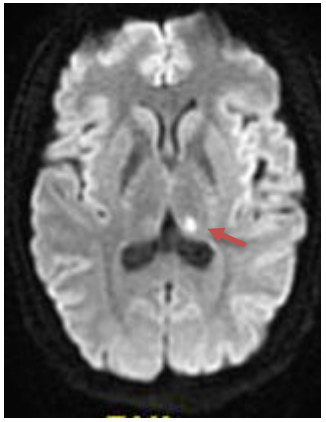

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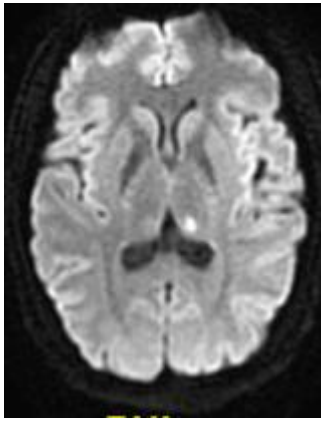
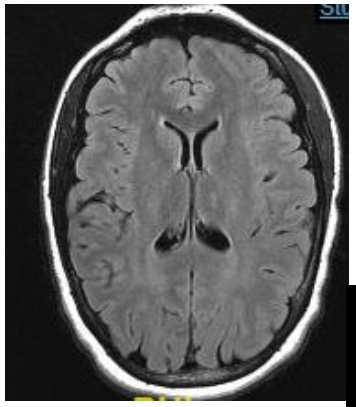
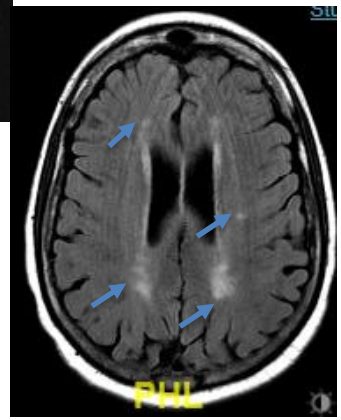




Patient A



Patient B

Stroke work-up

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- Vessel evaluation
  - Step 2: MRA/CTA/Doppler imaging
    - If vessel stenosis or significant athero, that is the etiology, proceed to medical management only
    - Consider other disease of vessel other than atherosclerosis:
      - Dissection
      - Reversible cerebral vasoconstriction syndrome
      - Moyamoya
      - Microangiopathic disease (TTP)
      - Vasculitis
    - Unlike PFO Emboli, these causes typically produce multiple regions of ischemia

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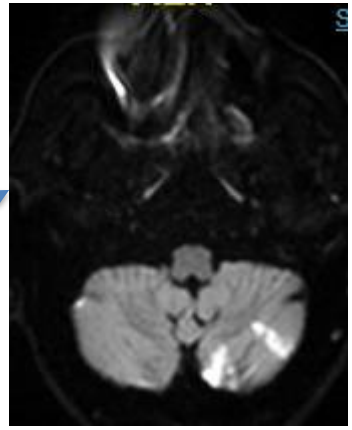

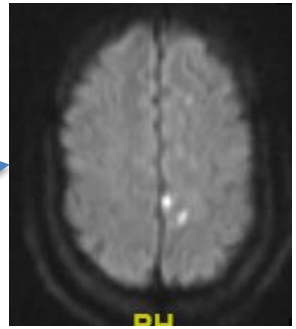

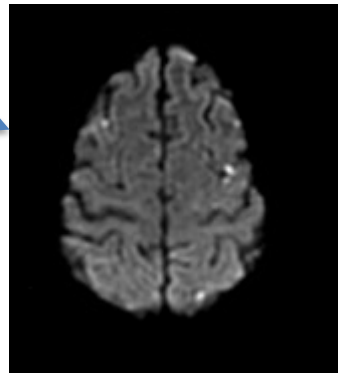

Stroke work-up

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- Emboli source testing
  - No “one size fits all” approach
  - consider major medical conditions, such as cancer, DVT, PE
  - Evaluate for cardiac abnormalities with echocardiographic testing
  - Consider occult atrial fibrillation
- In general, a normal EKG is a strong predictor of a possible PFO etiology

Comparison

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Comparison of transthoracic echocardiography using second harmonic imaging, transcranial Doppler and transesophageal echocardiography for the detection of patent foramen ovale in stroke patients

Geraud Souteyrand, Pascal Motreff, Jean-René Lusson, Raphaël Rodriguez, Etienne Geoffroy, Claire Dauphin, Jean-Yves Boire, Dominique Lamaison, Jean Cassagnes

Eur Heart Journal – Cardiovascular imaging, March 2006
107 consecutive patients, 82 cryptogenic stroke

Table 1 Results with Valsalva manoeuvre

	Transthoracic echocardiography	Transcranial Doppler	Transesophageal echocardiography
Small shunt	2	7	3
Medium shunt	15	17	22
Large shunt	21	24	17
Total	38	48	42
Wilcoxon test	p=0.004	p=0.015	

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All patients who were TEE+ were TCD+, and all TCD- were TEE-, but some TCD+ were TEE-

Data from my lab

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- Our TCD lab receives distinct referrals for PFO evaluations from a stroke neurologist in a population of stroke patients (my patients) and from a headache specialist who sees migraine patients with aura.
- We asked the question in our lab's last 2 years, what size shunt was observed in these 2 populations.
- Our hypothesis that there should be no difference.

PFO shunt in Migraine vs CVA

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- 51 patients referred to the lab
- For statistical purposes, we reassigned the typical 1 to 4 grade into 2 categories: high grade = more than 10 bubbles, or low grade = less than 10 bubbles.
- Migraine, n = 24, 18 high grade, 6 low grade
- CVA, n = 27, 2 high grade, 25 low grade
- $p<0.0001$ for patients with migraine having a higher grade shunt than CVA patients.
- Suggests possibly a different pathophysiology.
- *~92% of Cryptogenic CVA were low/medium*

Similar Results

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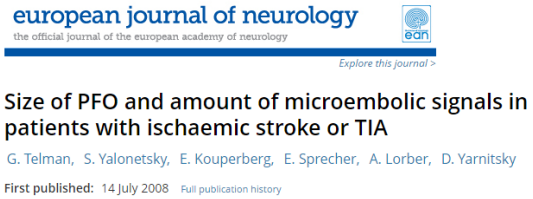

- Study comparing TCD to TEE shunt grades, but it has important data on cryptogenic patient PFO size.
- The study found that TEE and TCD, had similar grades of shunt volume.
- Interestingly, though, in these modalities, large shunts were present in 14.4% of TEE and 21.1% of TCD.
- Meaning that ***80-85% of cryptogenic stroke patients in this series also had a small to medium size shunt***.

Septal Embolism

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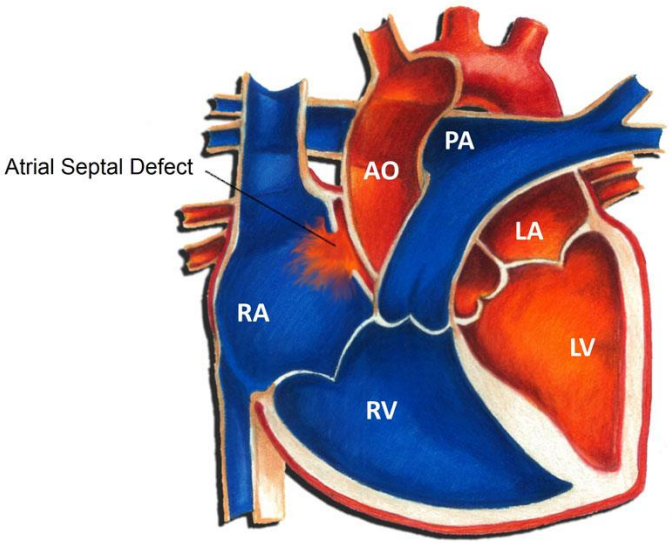
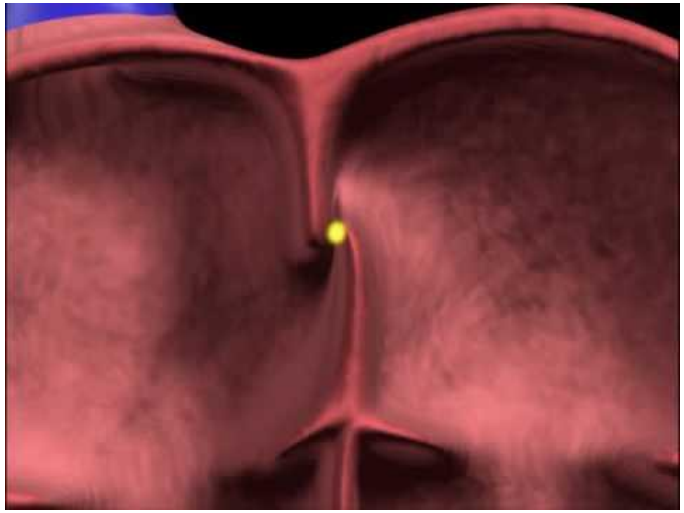
In CVA patients, might the clot form in the septum itself?





In migraine, might the phenomenon be from an admixture of blood?

Recent Trials

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- Size of PFO
  - Large vs small PFO showed no difference in recurrent stroke rates in both the RESPECT and REDUCE trials
  - CLOSE trial only included large PFOs

Cryptogenic Stroke Work up

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- Real risk of false negative with TTE bubble
- Almost no utility to TEE in hospital for patients with normal TTE/EKG and TEE remains with a risk of false negative especially in a patient with stroke related disability (aphasia/weakness).
- You have time, no need to urgently close a PFO.
- Consider a loop recorder, think about the case, postpone the bubble for 1st f/u visit

Cryptogenic Stroke Work up

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- I advocate for:
  - In hospital TTE without bubble or if you feel compelled to do bubble, recognize that a negative result is not the end of the road.
  - Outpatient TCD bubble about 1 month post d/c, combined with heart monitor data follow up
  - If TCD bubble +, then I d/w patient pros and cons of closure.
  - For patients who opt for closure, I refer to cardiology and let them coordinate TEE to avoid interobserver error/technical concerns

Case 1

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- 67 year old woman referred for headache and scintillating scatomas in 2014.
- She had lifelong migraines but vision changes were new.
- Referred to me, and MRI shown.
- PCP had already ordered MRA and it was normal.
- Main concern for her was that she had chronic headaches.

Case 1

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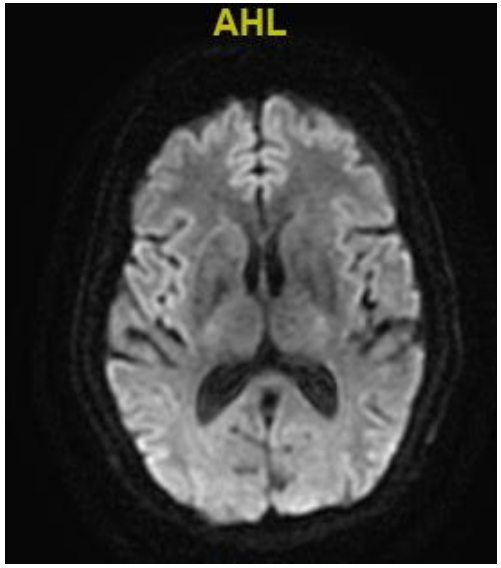

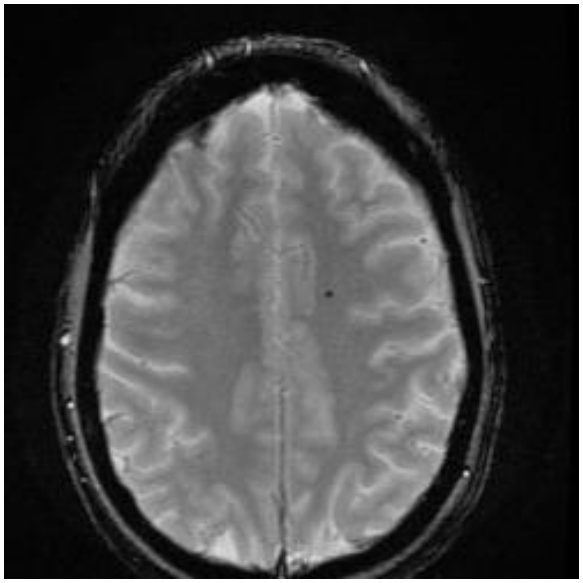

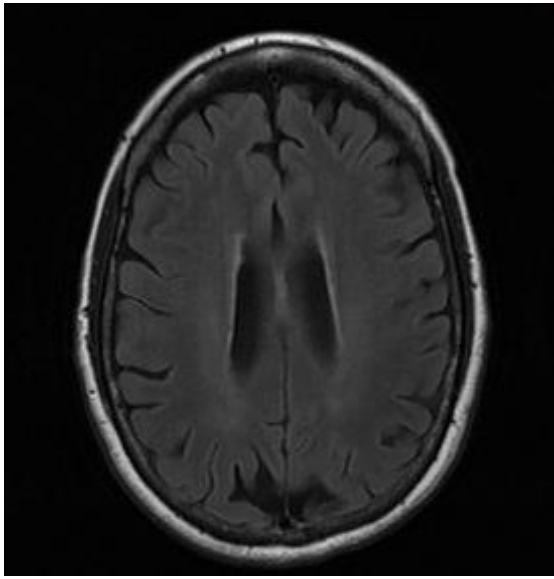

TCD

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- Even necessary?
- I had some concern for PFO (migraine/?TIA), but she had no real ischemia. Some concern for RCVS, but age was atypical for both.

TCD

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- TCD done: ***+spontaneous emboli***
- Communicated back to PCP and we coordinated hypercoag w/u and she was found with +APL antibodies

Management

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- APL+ without PE/DVT and no definite stroke, but +emboli
  - Reasonable to use antiplatelet
  - Is anticoagulation a better choice or overkill?
  - Started clopidogrel
- Next steps?
  - I should have followed up with TCD, but she did not return to follow up. No stroke symptoms.
  - She was primarily concerned with HA and sought care with her long time HA specialist

Follow up

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- Prior events 2014, then in
- March 2016 has mid frontal severe HA
- MRI/MRA/MRV all normal
- April 2016 acute LMCA ischemic stroke
- Found with intracardiac thrombus on echo
- Started on DOAC, and then follow up TCD no emboli.
- 2017 MV clot (no CVA), required surgery, switched to enoxaparin q12.

Thoughts

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- Once TCD +, in retrospect, I should have followed her more closely with routine TCD and prolonged monitoring q 6months.
- Any change in medications is also a good opportunity for re-monitoring
- Non-focal symptoms in a high risk patient may represent micro-emboli
- Scatomas may have come from ischemic ON

Case 2

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- In 2015, 65 y/o man with PhD noted cognitive decline.
- Prior to this he was known to have longstanding Sjogren's disease, was on plaquenil for decades, off it for many years, then on azathioprine in 2016.
- Cognitive eval unremarkable: neuropsych ok but below expected education, MRI neg

Case 2

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- mid 2018 stops azathioprine due to anemia and low WBC
- Notes splinter hemorrhages around 8/2018, started on apixaban by rheumatologist
- Heme eval shows no specific clotting issues, continue apixaban.
- Remains with anemia, Hgb 9s, and EGD + gastritis

Case 2

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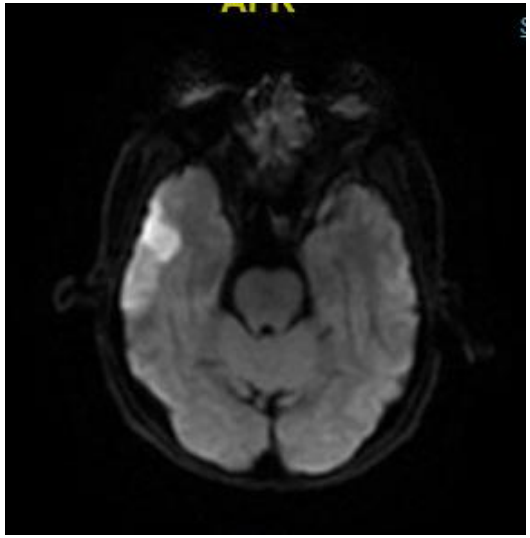
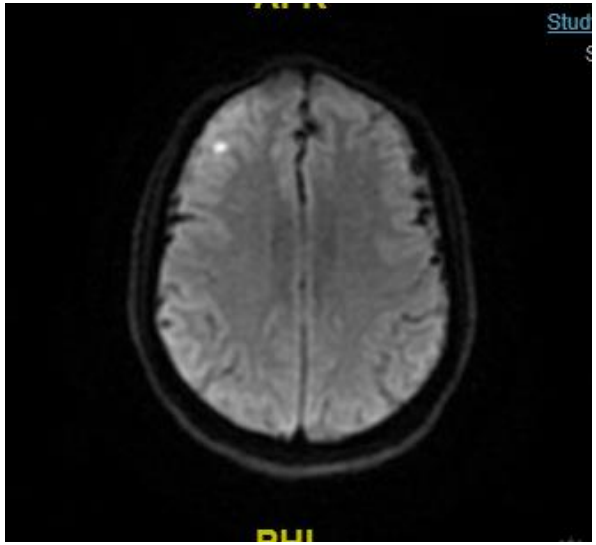
- Seems stable, but MRI repeated for further evaluation of cognitive decline in 2018.
- Results shown:





Case 2

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- Sees me in January 2019
- What to do?
  - Ddx
    - Ongoing emboli despite DOAC?
    - Demyelination?

Case 2

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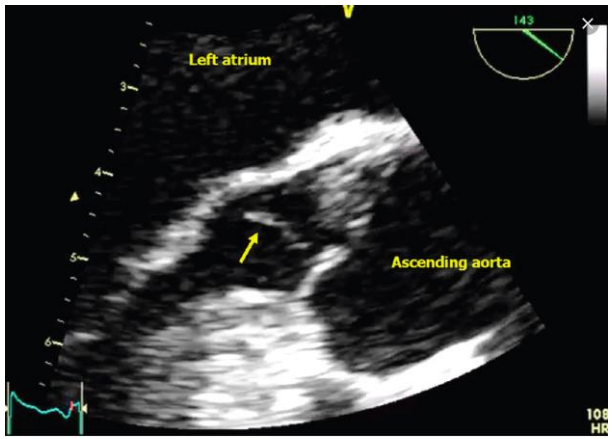
- MRI w/wo repeated, stable
- MR Spectroscopy c/w ischemia
- TCD negative for ongoing microemboli
- LP +VDRL, otherwise ok
- Echo +Lambl's Excrescences



Plan

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- ID consult
- Likely will change apixaban to enoxaparin or coumadin
- Follow up MRI/TCD/CBC
- Also has DM/HLD and needs optimization

Case 3

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- 76 year old woman, HTN/HLD (not on statin)
- Asymptomatic RICA CEA in 2016
- Routine screening carotid Doppler in 2017:
- Right ICA: 50-69%
- Left ICA: 80-90%
- Referred by cardiologist for carotid stent.
- Upset re: prior CEA restenosis and not interested in redo CEA or CEA on the left

Case 3

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- Discussed at length with patient pros and cons of elective stenting of the carotid for asymptomatic disease and limitations of data in women and CREST data on stenting in patients over 70.
- She fully understood but felt “torn” between cardiologist recommendation to intervene and my recommendation to consider medical management.

Case 3

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- TCD offered as risk stratification:
- BHI: Right MCA = 1.9
- BHI: Left MCA =1.6
- No microemboli
- Normal intracranial flow

Case 3

- Agreed to medical management and close observation.
- Now almost 2 years later, no symptoms, all TCD and CUS remain stable.
- Able to tolerate low dose statin + PCSK9
- LDL 168 initially, low dose stain →108, now on statin + PCSK9→ 17

Final Thoughts

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- Emboli are rare in an outpatient setting but should be taken seriously when present.
- TCD follow up during changes in therapy can be a tool for assessing response to therapy.
- Helpful in risk stratification in complex cases.

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