PI and Coordinator Webinar

July 23, 2019

ARCADIA

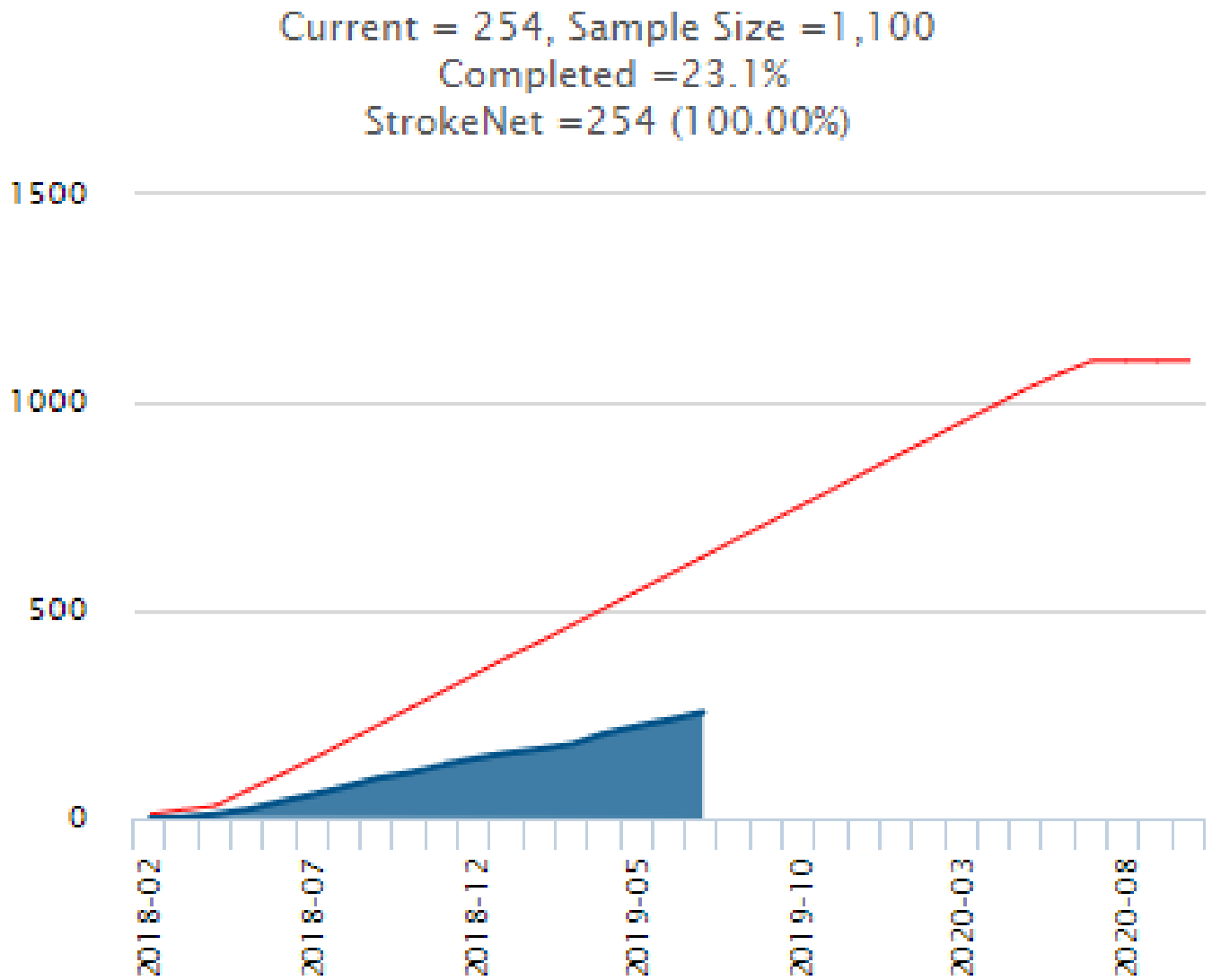
NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Study Sites

- 120 sites actively enrolling
- 21 other sites actively working on being released to enroll
- 120 sites have consented at least one subject
  - 1047 total consents
  - Since July 15th

Intercoastal Medical Group - Hyde Park, Sarasota, FL
United Hospital, St. Paul, MN
Baylor College of Medicine Medical Center, Houston, TX
Sharp Grossmont Hospital, La Mesa, CA
OSU Wexner Medical Center, Columbus, OH
Yale New Haven Hospital, New Haven, CT

ARCADIA



- More sites
- Continued efforts at every site to try to identify every possible patient
- Efforts to randomize eligible patients

ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Eligible not yet Randomized
N = 41

Banner University Medical Center - Tucson Campus, Tucson, AZ
Cleveland Clinic, Cleveland, OH
Grady Memorial Hospital, Atlanta, GA
Greenville Hospital System, Greenville, SC
Harborview Medical Center, Seattle, WA
Henry Ford Hospital, Detroit, MI
Hospital of the University of Pennsylvania, Philadelphia, PA
Intermountain Medical Center, Murray, UT
Long Beach Memorial Medical Center, Long Beach, CA
Los Angeles County + USC Medical Center, Los Angeles, CA
Mayo Clinic Saint Marys Campus, Rochester, MN
McLaren Flint, Flint, MI
Montefiore Medical Center, Bronx, NY

North Shore University Hospital, Manhasset, NY
North Shore University Hospital, Manhasset, NY
NYP Weill Cornell Medical Center, New York, NY
OU Medical Center, Oklahoma City, OK
OU Medical Center, Oklahoma City, OK
OU Medical Center, Oklahoma City, OK
OU Medical Center, Oklahoma City, OK
Rhode Island Hospital, Providence, RI
St. Louis University Hospital, St. Louis, MO
Stanford University Medical Center, Stanford, CA
Tufts Medical Center, Boston, MA
Tufts Medical Center, Boston, MA
UCSD Medical Center - Hillcrest Hospital, San Diego, CA

University of Alabama Hospital, Birmingham, AL
University of Illinois Hospital, Chicago, IL
University of Kansas Hospital, Kansas City, KS
University of Kansas Hospital, Kansas City, KS
University of Kentucky Hospital, Lexington, KY
University of Louisville Hospital, Louisville, KY
University of Michigan University Hospital, Ann Arbor, MI
University of Minnesota Medical Center Hospital, Minneapolis, MN
University of Mississippi Medical Center, Jackson, MS
University of Wisconsin University Hospital, Madison, WI
UPMC Presbyterian Hospital, Pittsburgh, PA
Vanderbilt University Hospital, Nashville, TN
Yale New Haven Hospital, New Haven, CT
Yale New Haven Hospital, New Haven, CT
Yale New Haven Hospital, New Haven, CT

ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

ARCADIA Heroes

- Lots of new (and our dedicated existing) coordinators (and PIs) trying hard to help identify and consent patients
- Susan Hetzel - University of Mississippi Medical Center has enrolled 5 subjects this month – the site was released to enroll 5/20. She consented 3 subjects in one week!

DCU Slides - Faria

ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

ICF v5 vs. v6 (F245 vs. F246)

- If your site has not yet been approved to use ICF v6, it should be left blank for now.
- You should re-consent all active subjects once you receive ICF v6 approval.

What happens when you are unable to re-consent subject due to LTFU, withdrawal of consent, or moved to EOS?

No.	Item Description	Data Value
Q01	Informed consent form version *Derived by WebDCU*	Version 6
Q02	Signed informed consent obtained	(•) No ( ) Yes, signed by subject ( ) Yes, signed by Legally Authorized Representative
Q03	Informed consent form language	
Q04	Other language specify	
Q05	Date informed consent was signed	
Q06	Signed informed consent form file upload *PDF file only*	
Q09	Subject consented to additional blood collection for biobank	
Q07	Reason subject was unable to consent	
Q08	Reason signed informed consent not obtained	explain reason here *(200 char.)*
GC	General comments	*(250 char.)*
	Signed informed consent form review	
Q10	Review result	( ) Not uploaded yet ( ) Review pending ( ) Rejected ( ) Accepted
Q11	Reason for review rejection	
Q12	Reviewed by	
Q13	Reviewed on	

Secure File Upload: Browse... Upload File

Save Record Cancel Edit

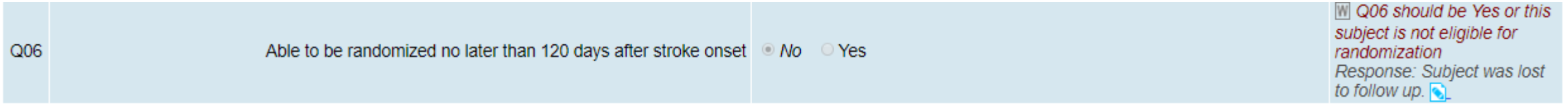
-Mark Q02 as no
-Explain why in Q08

ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Subject LTFU prior to randomization

- In order to document this in WebDCU™ , please do the following:
  - Edit **F101 Q06** 'Able to be randomized no later than 120 days after stroke onset' to 'No'
  - This will generate a warning on the right hand side, which needs to be addressed. Click on the blue pencil icon to respond to the warning and provide an explanation. Responding to the warning will also allow you to save and submit the CRF.



Q06	Able to be randomized no later than 120 days after stroke onset	◉ *No* ○ Yes	*Q06 should be Yes or this subject is not eligible for randomization* *Response: Subject was lost to follow up.*

  - Due to Q06 now being an eligibility violation on F101, **F126 Q12** 'Eligible for randomization' should be 'No'
  - Please **do not** mark LTFU subjects as 'consent withdrawn' on F126 End of Study

ARCADIA

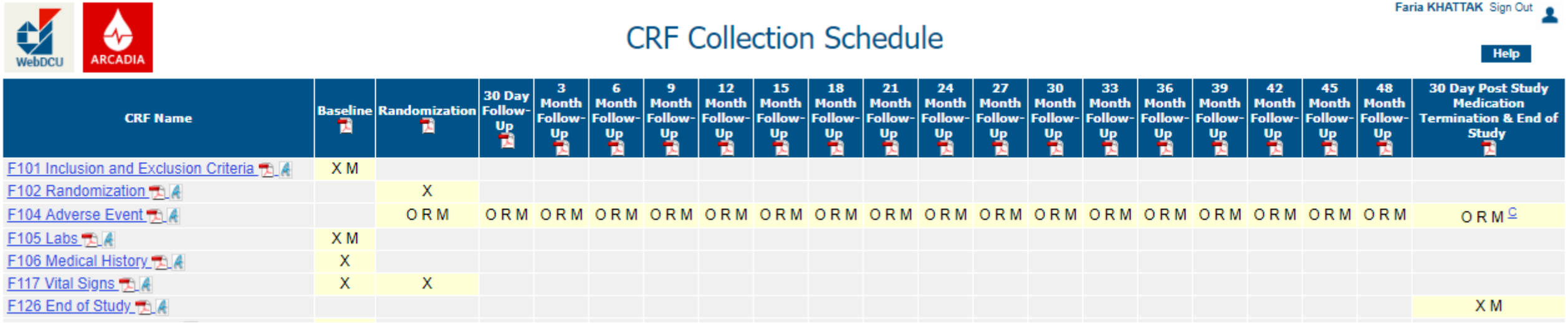
NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Documenting Eligibility Violations on F101

- Similar to documenting a subject as LTFU prior to randomization, we use F101 to document other eligibility violations that occur prior to randomization
  - Atrial fibrillation detected
  - Indication for anticoagulant therapy
  - Indication for antiplatelet agent
  - Etc.
- Update the answer to the F101 question relevant to your findings
- Please make sure to always respond to the warning and save and submit the CRF
  - Warnings can trigger on any CRF and the data will show as outstanding until the CRF has been submitted.
  - Please provide sufficient explanation to avoid DCRs/queries for clarification
    - Ex: In response to a warning for 'Able to be randomized no later than 120 days after stroke onset' please do not respond with 'unable to be randomized'/'not eligible'. Instead, you need to explain *WHY*
    - Similarly, for 'specify' fields such as 'Consent withdrawn, specify' on EOS, please explain *WHY* the subject withdrew consent, do not restate that consent was withdrawn or this will need to be queried.

New Study Book Format

- The study book is no longer posted under Project Documents.
- To find the new study book, go to [Project Setup] -> [CRF Collection Schedule]. There are CRF packets for each visit uploaded under the visit name.



WebDCU ARCADIA

Faria KHATTAK Sign Out

Help

CRF Collection Schedule

CRF Name	Baseline	Randomization	30 Day Follow-Up	3 Month Follow-Up	6 Month Follow-Up	9 Month Follow-Up	12 Month Follow-Up	15 Month Follow-Up	18 Month Follow-Up	21 Month Follow-Up	24 Month Follow-Up	27 Month Follow-Up	30 Month Follow-Up	33 Month Follow-Up	36 Month Follow-Up	39 Month Follow-Up	42 Month Follow-Up	45 Month Follow-Up	48 Month Follow-Up	30 Day Post Study Medication Termination & End of Study
F101 Inclusion and Exclusion Criteria	X M																			
F102 Randomization		X																		
F104 Adverse Event		O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M	O R M C
F105 Labs	X M																			
F106 Medical History	X																			
F117 Vital Signs	X	X																		
F126 End of Study																				X M

ARCADIA

NIH StrokeNet PREVENTION | TREATMENT | RECOVERY

Who to Contact?

Srikala Appana at NDMC
appana@musc.edu
When to contact: If you have WebDCU-related DOA/regulatory database questions, Informed Consent Remote Monitoring questions, or Site Monitoring questions

Faria Khattak at NDMC
khattak@musc.edu
When to contact: Any other WebDCU-related or CRF-related questions

Patty Hutto at NDMC
huttoja@musc.edu
When to contact: Any other WebDCU-related or CRF-related questions

NOTE: Please refer to the Data Collection Guidelines posted in [Project Documents] under [Toolbox] in WebDCU™, or email Faria or Patty for CRF related questions

Regulatory Updates Slide - Emily

ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Regulatory Updates:

- **Amendment progress for the v6, v3 consents**.
  - 70 + sites have been sent current versions of the consent template
  - Some sites will remain on the v2 Pregnant Partner consent.
  - Please upload the approval letter sent with your approved ICD to the 4.1 space holder in WebDCU. The Prime Approval letter for the 4.1 should not be uploaded.
  - Please upload your updated consents to WebDCU as soon as possible
  - WebDCU will be archiving the v5 space holders soon
  - Translations will be sent to the site once received, please upload to WebDCU as soon as possible
  - Reach out to the NCC for a short form if needed

Loss to Follow Up Slides - Pam

ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Lost-to-Follow Participants

Preparations to decrease loss to follow up begins at screening

- *Screen efficiently*
  - *If the patient has a history of "no shows", known social issues, and/or non-compliance, consider not consenting*
- *Develop a relationship with the patient*
  - *After consent, send birthday cards, holiday cards, etc…*
- *Provide a list of all study visits and windows for those visits*
  - *This should also contain detailed instructions for the visits and site contact information*
  - *Send visit reminder postcards or emails; Reminder visit calls*
- *Consenting*
  - *Educate the patient thoroughly regarding the study visits and their commitment*
    - *Why it's important to complete the study visits*
  - *Obtain a contact sheet after completing consent*
    - *Email address(es)*
    - *Friends & Family numbers (Children/Siblings/Neighbors)*
    - *Work numbers*
    - *Emergency contacts*

When Lost-to-Follow Up Occurs

- *Check your facility's EMR; we have permission in consent to consult EMR for outcomes*
- *Consider seeing patient at another scheduled visit at the facility*
- *Call emergency contacts or friends/ family members from contact sheet*
- *Standard letter x3 followed by a registered letter (signature required) if needed*
- *Try calling participant from a non-facility number*
- *Visit their home*
- *Social Media – only to search, not contact*
  - *FaceBook*
  - *Instagram*
  - *Twitter*
- *Search internet*
  - *Google People*
  - *Social Security Death Index*

ARCADIA Subject Scheduler

ARCADIA Patient Visit Scheduler Subject Name _____

Visit	Timepoint	Visit Date	Window Allowance	Visit Window		Special Instructions
Date of Randomization		07/22/19				
Follow Up Visit 1	Day 30	08/21/19	7 days +/-	08/14/19	08/28/19	
Follow Up Visit 2	Day 90	10/20/19	5 day +/-	10/15/19	10/25/19	
Follow Up Visit 3	Day 180 / 6 months	01/18/20	5 day +/-	01/13/20	01/23/20	
Follow Up Visit 4	Day 270 / 9 month	04/17/20	5 day +/-	04/12/20	04/22/20	
Follow Up Visit 5	Day 360 / 12 months	07/16/20	5 day +/-	07/11/20	07/21/20	
Med Resupply visit 5b	Day 450 / 15 months	10/14/20	5 day +/-	10/09/20	10/19/20	Add specific site instructions, i.e....
Follow Up Visit 6	Day 540 / 18 months	01/12/21	5 day +/-	01/07/21	01/17/21	1. It's very important to keep your scheduled appointments
Med Resupply visit 6b	Day 630 / 21 months	04/12/21	5 day +/-	04/07/21	04/17/21	
Follow Up Visit 7	Day 720 / 24 months	07/11/21	5 day +/-	07/06/21	07/16/21	2. Please bring your study drug bottles to each visit
Med Resupply visit 7b	Day 810 / 27 months	10/09/21	5 day +/-	10/04/21	10/14/21	
Follow Up Visit 8	Day 900 / 30 months	01/07/22	5 day +/-	01/02/22	01/12/22	3. Please let us know if you have any emergency room or hospital visits
Med Resupply visit 8b	Day 990 / 33 months	04/07/22	5 day +/-	04/02/22	04/12/22	
Follow Up Visit 9	Day 1080 / 36 months	07/06/22	5 day +/-	07/01/22	07/11/22	
Med Resupply visit 9b	Day 1170 / 39 months	10/04/22	5 day +/-	09/29/22	10/09/22	
Follow Up Visit 10	Day 1260 / 42 months	01/02/23	5 day +/-	12/28/22	01/07/23	
Med Resupply visit 10b	Day 1350 / 45 months	04/02/23	5 day +/-	03/28/23	04/07/23	
Follow Up Visit 11	Day 1440 / 48 months	07/01/23	5 day +/-	06/26/23	07/06/23	
Close Out Visit	30 days after end of study		7 days +/-			

Add Site contact information

ARCADIA

NIH StrokeNet PREVENTION | TREATMENT | RECOVERY

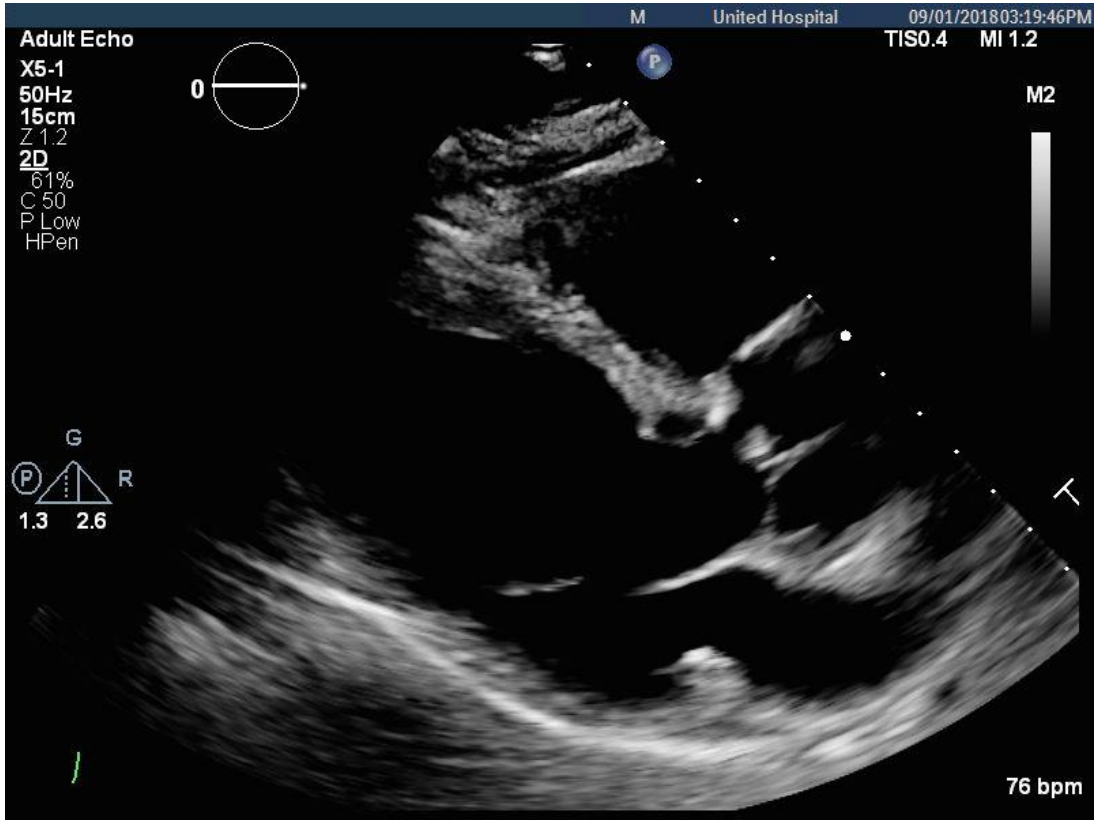
ECHO Slides - Marco

ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

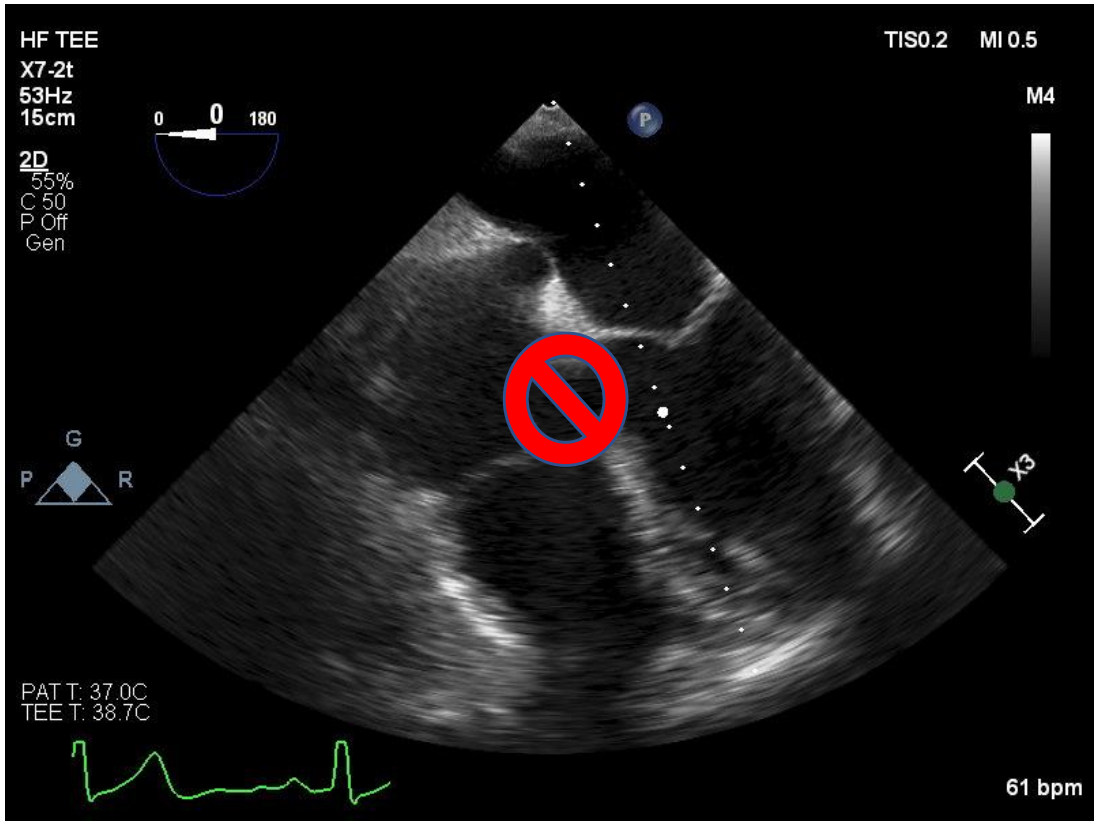
Transthoracic Echocardiogram (TTE)

THE ONE WE WANT



Transesophageal Echocardiogram (TEE)

THE ONE WE DO NOT WANT

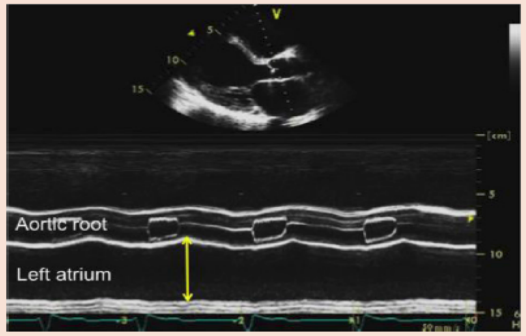
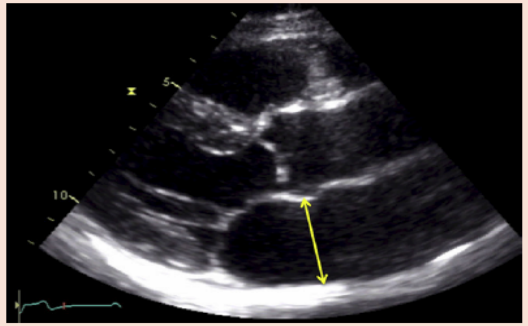


ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Transthoracic Echocardiogram – Left atrial diameter

Table 11 Recommendations for the echocardiographic assessment of LA size

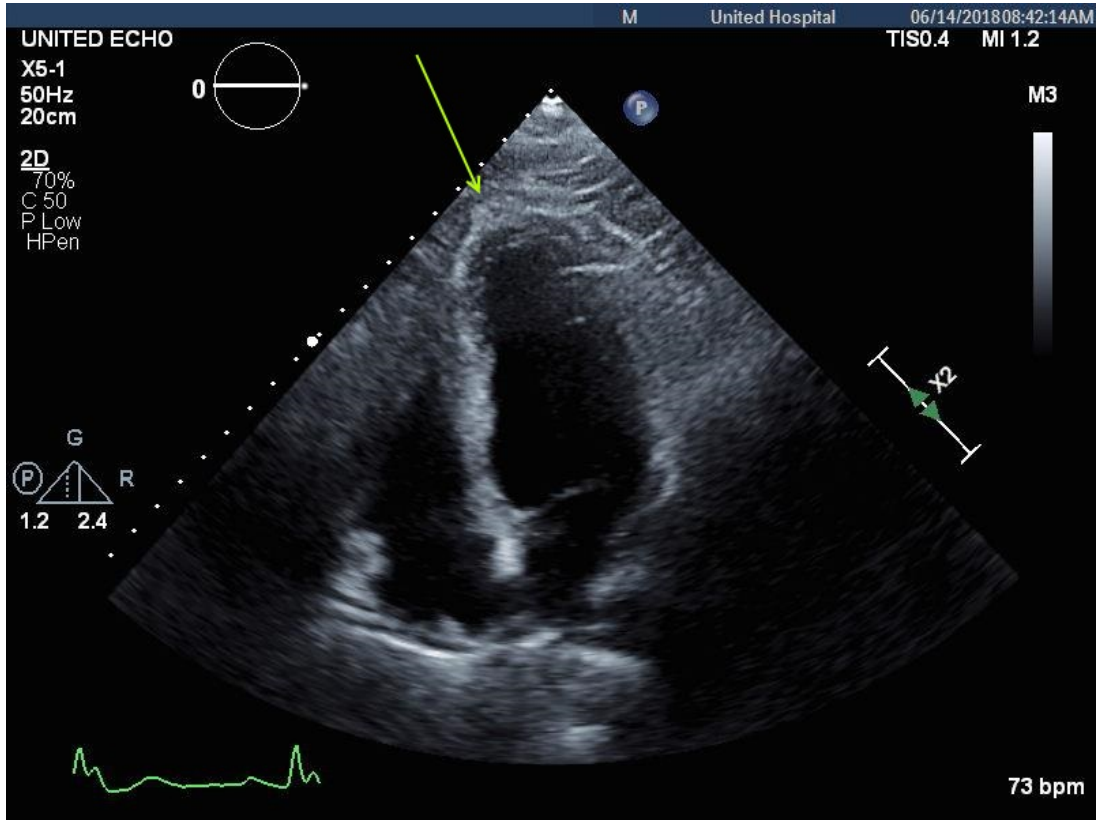
Parameter and method	Echocardiographic imaging	Advantages	Limitations
Internal linear dimensions. The anteroposterior diameter of the left atrium can be measured in the parasternal long-axis view perpendicular to the aortic root long axis, and measured at the level of the aortic sinuses by using the leading-edge to leading-edge convention.	M-mode tracing 	• Reproducible • High temporal resolution • Wealth of published data	Single dimension not representative of actual LA size (particularly in dilated atria)
	2D-guided linear measurements 	• Facilitates orientation perpendicular to LA posterior wall	• Lower frame rates than in M-mode • Single dimension only

ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

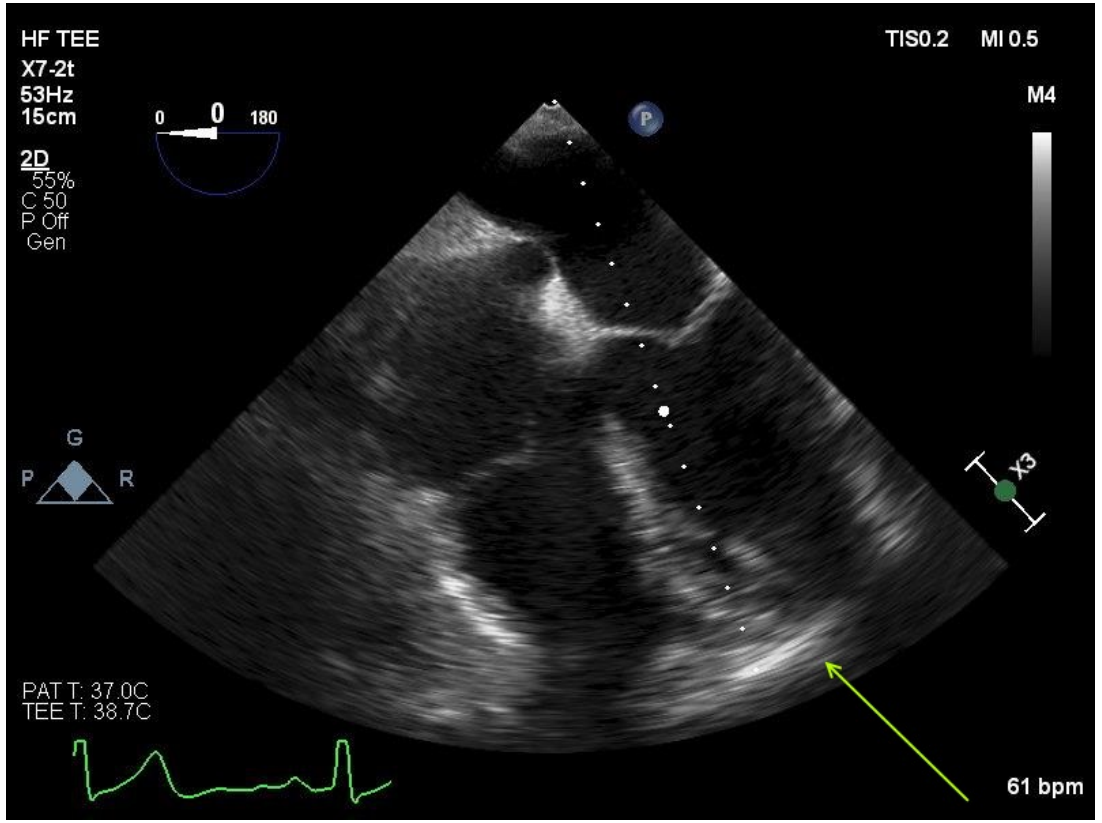
Transthoracic Echocardiogram (TTE)

The cardiac apex is UP



Transesophageal Echocardiogram (TEE)

The cardiac apex is DOWN



ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

ARCADIA cases

Shashank Shekhar MD, MS

Site PI

University of Mississippi Medical Center

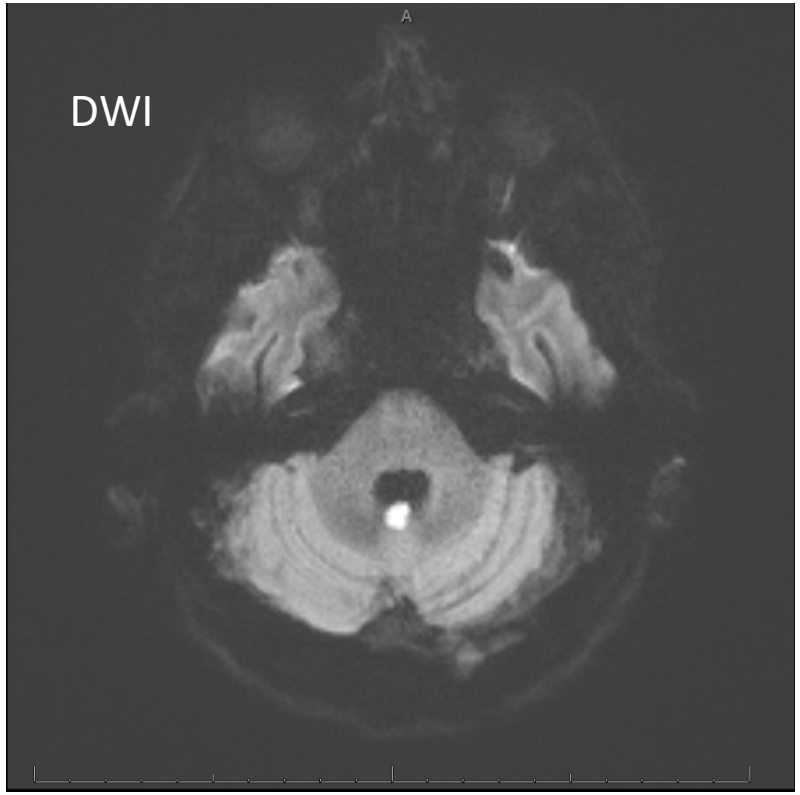
Jackson, MS

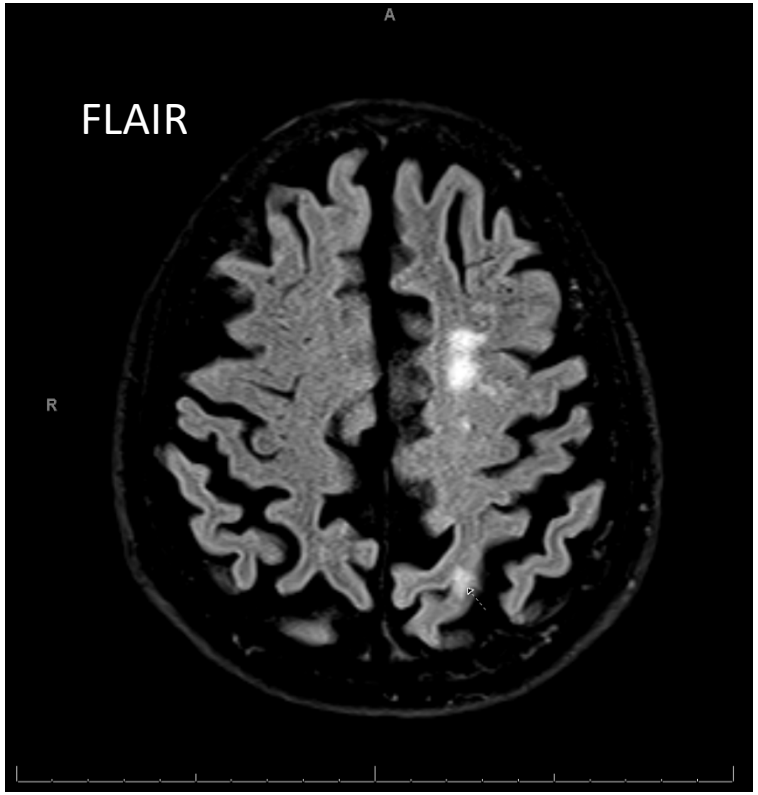
NIH StrokeNet

PREVENTION | TREATMENT | RECOVERY

Case #1

- 79 yo African American female presents with acute onset gait instability. MRI reveals acute DWI lesion in the cerebellar vermis >1cm and multiple cortical lesions on FLAIR.



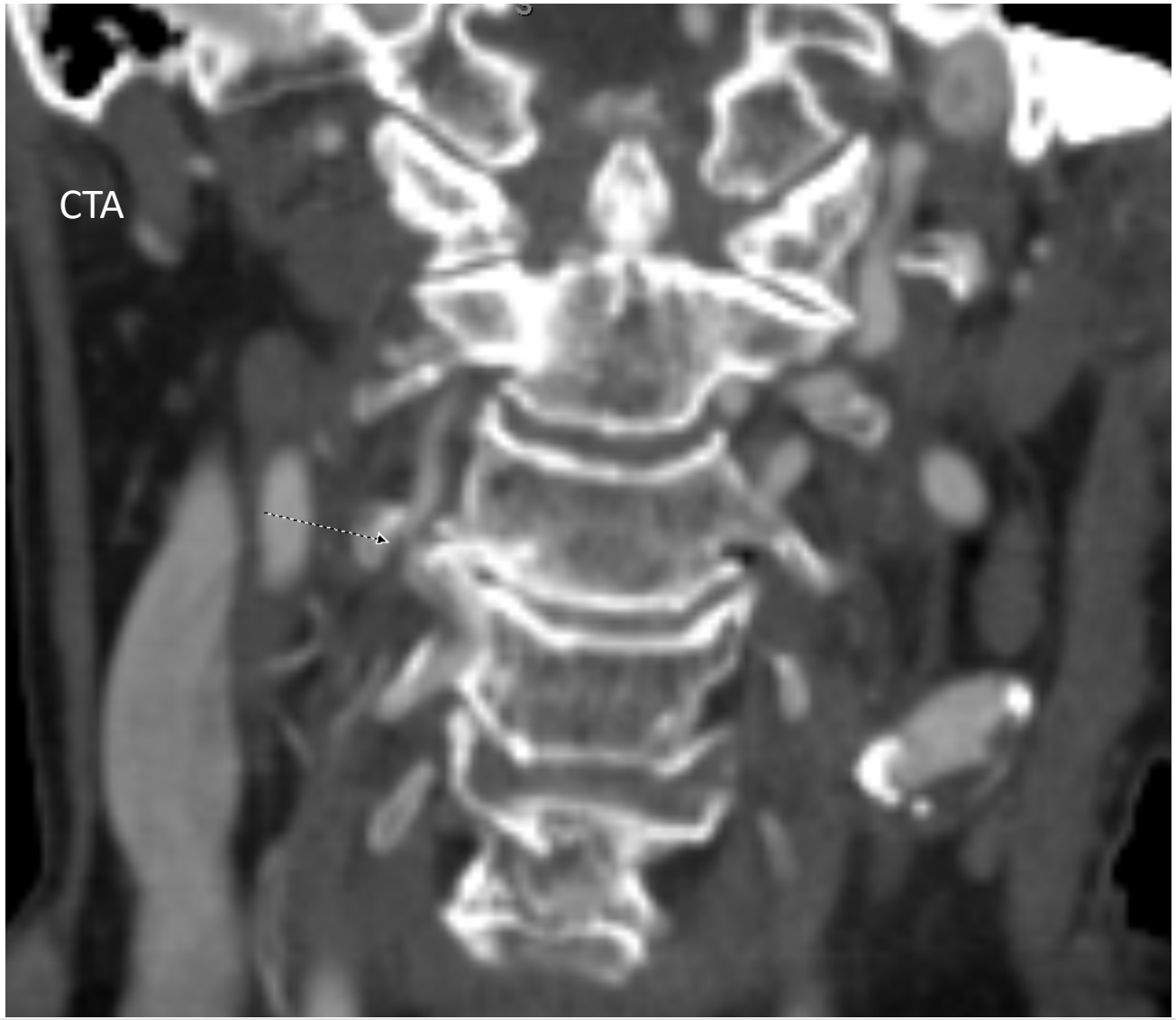


ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

CTA of head and neck

- Right vertebral artery:- hypoplastic with focal moderate to severe stenosis (>50% stenosis) at C3-C4 from uncovertebral osteophytes (arrow).
- Lt vert unremarkable.
- Rest of work up unremarkable.



ARCADIA

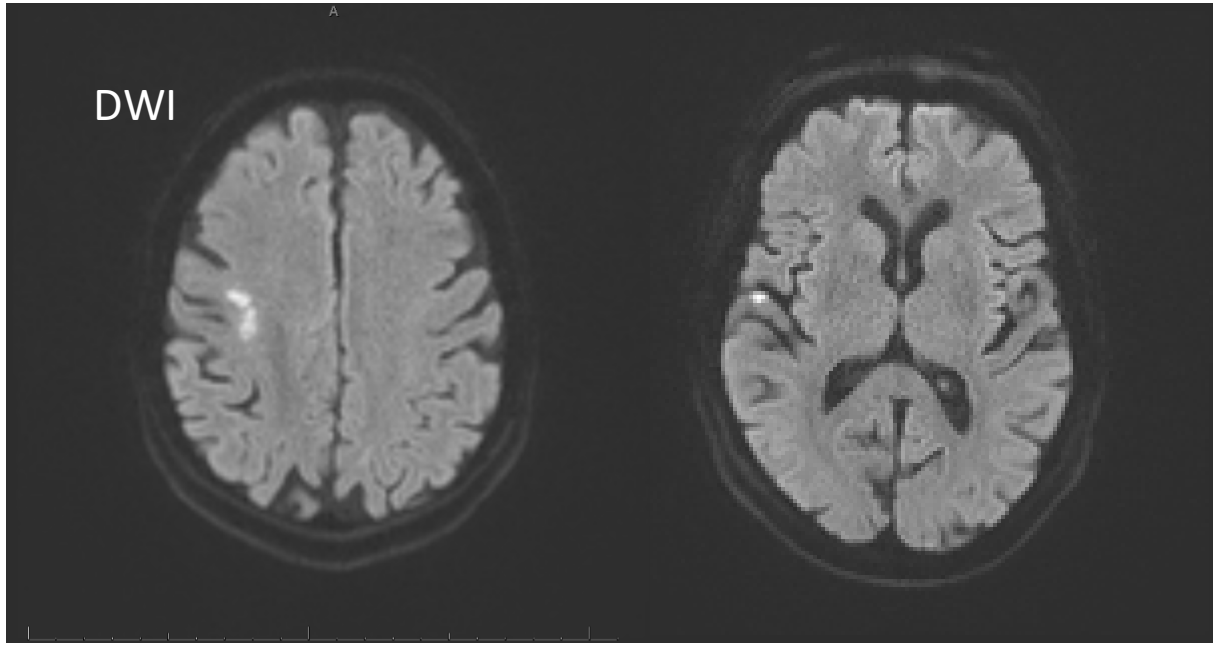
NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

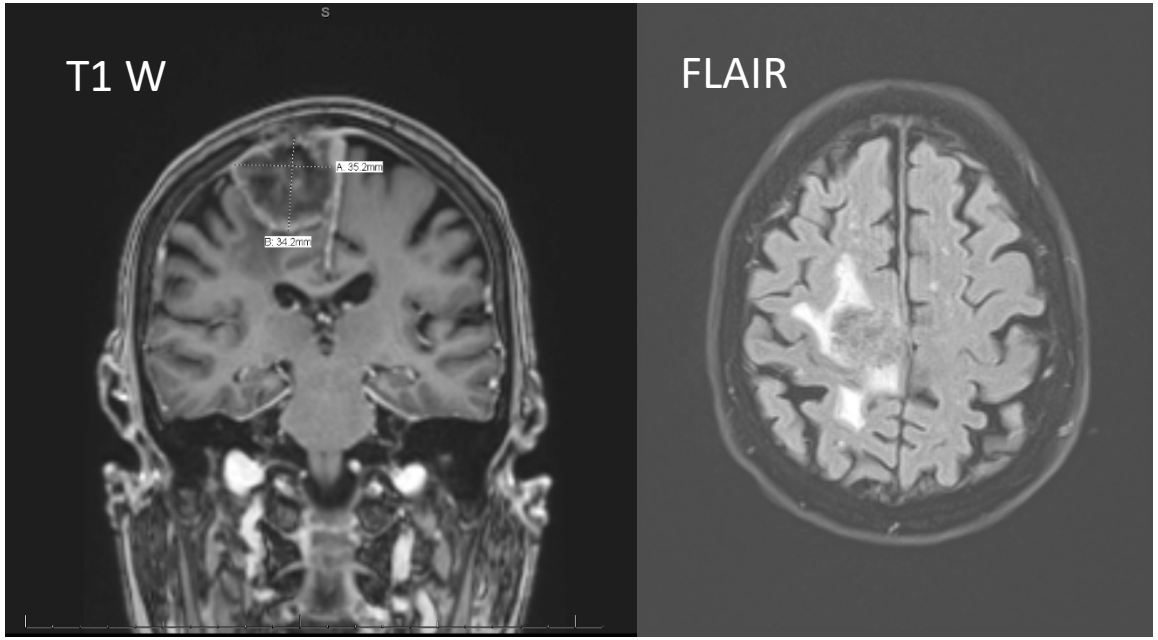
Q: Would you consent this patient if no other exclusions?

- Answer: Yes, even though the non-dominant vertebral artery is significantly stenotic, it is believed to be due to external compression from osteophytes and not due to intrinsic atherosclerotic disease and thus unlikely to be related etiology.

Case #2

- 93 yo Caucasian female with HTN, DM, presents with left hemibody weakness, CTH shows heavily calcified extra-axial mass with mild surrounding edema. MRI shows DWI embolic appearing lesions in right MCA territory. Patient lives independently. No contraindications for study.





ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Q: Will this patient be eligible for consenting?

- Answer: Yes.

ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Literature Update Slides - Mitch

Literature update

- Ntaios G et al. Carotid plaques and detection of atrial fibrillation in ESUS. Neurology 2019; 92:e2644-2652.
- Background: Substenotic plaque (i.e., carotid plaque <50%) may be a cause of ESUS. If so, then patients with ipsilateral substenotic plaque should be ***LESS LIKELY*** to have AF detected during follow-up.
- Hypothesis: Patients with ESUS with substenotic plaque are less likely to have AF detected during follow up.

ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Literature update

- Retrospective analysis
- 777 patients from 3 different registries (Lausanne, Athens, Larissa)
- Follow up 2642 patient-years (mean 3.4 years per patient)
- Primary outcome: detection of AF; no systematic monitoring for AF

Ntaios G et al. Neurology 2019; 92:e2644-2652.

ARCADIA

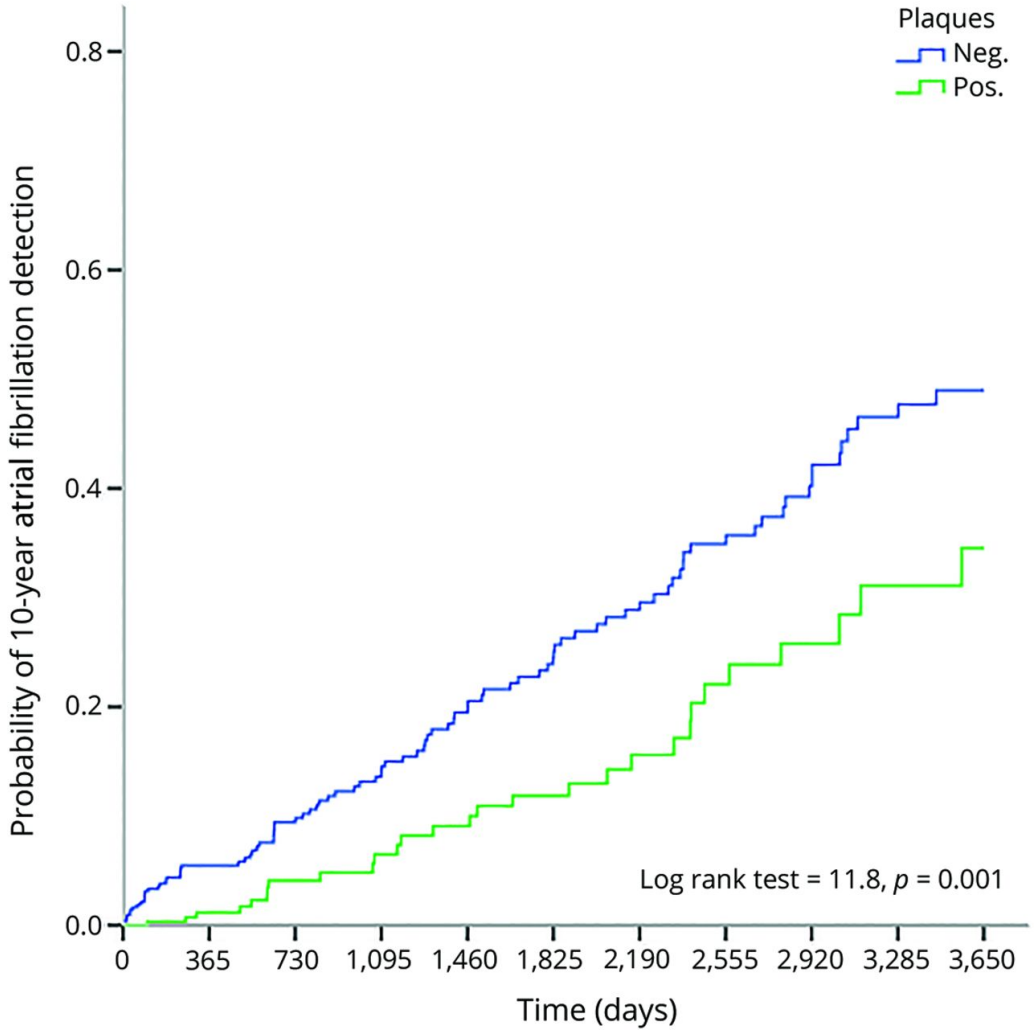
NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Literature update

- Retrospective analysis
- 777 patients from 3 different registries (Lausanne, Athens, Larissa)
- Follow up 2642 patient-years (mean 3.4 years per patient)
- Primary outcome: detection of AF; no systematic monitoring for AF
- Results:
  - 38.6% of patients (n=341) had an ipsilateral substenotic plaque
  - The detection rate was 8.5% in patients with substenotic plaque vs 19.0% in patients without substenotic plaque.
  - After adjusting for other factors, presence of plaque associated with ~50 likelihood of detecting AF (adj HR 0.57, 95%CI 0.34-0.96).

Ntaios G et al. Neurology 2019; 92:e2644-2652.

Ten-year cumulative probability of atrial fibrillation detection in embolic stroke of undetermined source patients with and without nonstenotic carotid plaques ipsilateral to the index stroke



George Ntaios et al. Neurology 2019;92:e2644-e2652

AMERICAN ACADEMY OF NEUROLOGY

Literature update

- Potential implications:
  - Substenotic plaque may be causally associated with ESUS
  - The finding of substenotic plaque may be a reason to pursue more or less aggressive monitoring for AF (i.e., look less hard in those without the plaque)
  - Patients with substentoic plaque may similarly be less likely to have atrial cardiopathy
- Limitations
  - The incidence of AF detection is high even in those *with* substenotic plaque (~9% over 3 years).
  - Study was retrospective
  - No systematic monitoring for AF or uniform detection protocol (i.e., based on clinical detection)
  - Patients did not have intracranial imaging for “pragmatic reasons”: may not have all had ESUS

Ntaios G et al. Neurology 2019; 92:e2644-2652.

Open mike…

Feel free to reach out!

- 24-hour telephone hotline
  - Please use it for any urgent questions
  - Eligibility, randomization, unblinding, etc
- 1-877-427-2234 (1-877-4AR-CADI): useful to save in your cell phone
- The hotline automatically calls the four PIs in succession
  - Please let it ring
  - And call back if no luck—one of us will pick up!
- Please email arcadia@ucmail.uc.edu with non-urgent questions

ARCADIA

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY