



# ARCADIA



**Atrial Cardiopathy and Antithrombotic Drugs In Prevention After Cryptogenic Stroke**

**Webinar: December's Webinar has been cancelled**

**Next Month: January 26, 2021**

**ARCADIA Virtual Investigator Meeting**

**January 26, 2021**

**1p - 4p EST, 12a - 3p CST, 11a - 2 p MT, 10a - 1p PT**



## **MILESTONES**



**Congratulations to Wake Forest for the 550th randomization. Halfway there!**

**Congratulations to Hamilton General. Our 1st Canadian consent!**

**Randomized = 555    November Randomizations = 17**

**Consents = 2089    November Consents = 59**

**Congratulations to ARCADIA National PI Hooman Kamel on being awarded the American Heart Association's Joseph A. Vita Award, given by the editors of the AHA journals for transformative impact in the field by a mid-career investigator. We are lucky to have you as a colleague!**

## **CALM Lab Update**

The CALM Lab Director, Janey, is retiring. We wish her the best and all of our thanks to helping us with this vital component of the study. See the back page for new contact information.

### **Shipping Information:**

**Christmas Week: The CALM lab will be closed 12/24 & 12/25. Ship samples to arrive by 12/23.**

**New Year's Week: The CALM lab will be closed 12/31 & 1/1. Ship samples to arrive by 12/29.**

**Any samples that are sent during the lab closures will be damaged when the personnel return.**

**When requesting lab supplies, please send email to CALM@columbia.edu. Do not send via fax. You may receive a reply email that you will have to confirm by clicking on "To APPROVE the message..."**

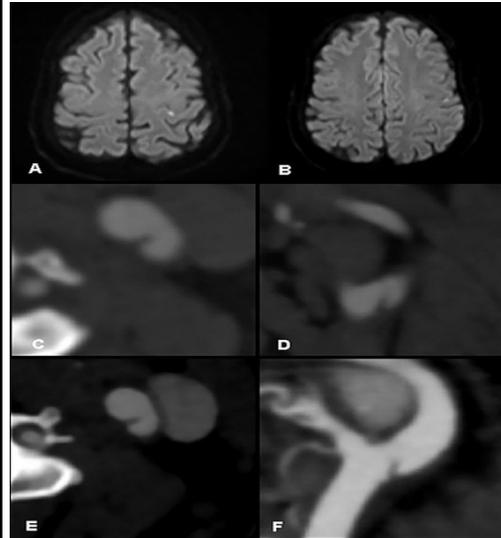
*From all of us in the ARCADIA Team*

*We wish you a safe and happy Holiday Season and many blessings in the New Year!*

## FAQ

**Question:** One of my colleagues has a patient with recent stroke who has a carotid web. Is this patient eligible for ARCADIA?

**Answer:** Yes! While carotid webs have been proposed as a potential mechanism of cryptogenic stroke, they are not an exclusion for ARCADIA since the association remains less well-established than other stroke mechanisms, like paroxysmal atrial fibrillation. Carotid webs are shelf-like projections into the lumen of the proximal cervical internal carotid artery without evidence of calcification; they are characterized by intimal fibromuscular dysplasia. Although, they may cause flow abnormalities that could lead to embolization of fibrin-based clots, optimal management remains uncertain. Like other possible causes of cryptogenic stroke or ESUS (think PFO, cancer), patients with a web can be included in ARCADIA if the treating physicians do not think an anticoagulant or antiplatelet is specifically indicated. Because ARCADIA focuses on those who *do* have atrial cardiopathy (i.e., a “positive” finding), it is less concerning that they have other causes for which management is uncertain.



For a terrific review of carotid webs and stroke, see this recent paper, from which this figure is taken:

Mac Grory B, Emmer BJ, Roosendaal SD, Zagzag D, Yaghi S, Nossek E. Carotid web: an occult mechanism of embolic stroke. *J Neurol Neurosurg Psychiatry*. 2020 Dec;91(12):1283-1289.

Young, otherwise healthy woman presenting with cryptogenic ischaemic stroke in the left MCA territory (A, B). CTA demonstrated a carotid web in the left internal carotid artery visible as a septum on axial imaging (C) and as a protruding shelf-like lesion on sagittal imaging (D). Follow-up imaging performed 11 months after the index event revealed no change in conformation of the web on axial imaging (E). Oblique sagittal imaging (F) was also obtained on this occasion. CTA, CT angiography; MCA, middle cerebral artery.

## Updates/Reminders/Tips

- Con-med CRF warning “Date last assessed” - when completing each follow up visit, the subject’s medications must be re-assessed. Update column “G” with date that the visit was completed and medications assessed. If you are unable to re-assess the medications then the warning can be dismissed by entering an explanation.
- Please remember to review the subject’s medications and compare to the prohibited medication list. We do not want subject’s withdrawing after randomization due to medications they have been on long term. Also there may be risks that the subject’s PCP and/or neurologist need to review and monitor.
- If your consented subject did not qualify for randomization, please enter the EOS CRF as soon as possible.

## SPOTLIGHT ON SITES

### November Top Randomizing Sites

#### November Top Consenting Sites

**Emory University Hospital - 4**

**Emory University Hospital**

**2 randomizations!**

**Welcome Aboard - We’re Happy you joined our ARCADIA Team!**

**Lahey Hospital & Medical Center - Burlington, MA**

**Allegheny General Hospital - Pittsburgh, PA**

**Cooper University Hospital - Camden, NJ**

## SCIENCE CORNER

### Left atrial fibrosis on cardiac MRI and atrial fibrillation

In a substudy of the Atrial Fibrillation Detected by Continuous ECG Monitoring (LOOP) study (NCT02036450), left atrial fibrosis ascertained by late gadolinium enhancement on cardiac MRI was associated with incident atrial fibrillation (AF) as detected by continuous long-term monitoring. Investigators obtained cardiac MRI in 68 patients age  $\geq 70$  years with risk factors for stroke. All patients received an implantable loop recorder and were continuously monitored for AF. Over a median of 41 months, AF episodes  $\geq 6$  min were detected in 32 patients (47%), and AF episodes lasting  $\geq 5.5$  hours occurred in 16 patients (24%). Left atrial volumes and function, and the extent of left atrial late gadolinium enhancement, were all independently associated with incident AF, after adjusting for sex, age, and comorbidities. Left atrial fibrosis increased the risk of AF  $\geq 6$  min by 40% (hazard ratio 1.40, 95% CI 1.03 to 1.89) and AF  $\geq 5.5$  hours by approximately 60% (HR 1.63, 95% CI 1.11 to 2.40) per 10 cm<sup>2</sup> increase. Left atrial fibrosis was significantly associated with a high burden of AF. The addition of left atrial fibrosis to a multivariable risk prediction model for incident AF significantly increased the predictive value, as well. These findings suggest that atrial cardiomyopathy, such as left atrial fibrosis assessed by cardiac MRI, may predict AF in patients at risk of stroke. The role of cardiac MRI in predicting risk of AF remains undetermined, but it is likely that left atrial fibrosis could be another marker of atrial cardiomyopathy. Further research is needed to determine whether left atrial fibrosis, like the markers being tested in ARCADIA, might predict a response to anticoagulant therapy.

Legend: Representative images showing different amounts of left atrial late gadolinium enhancement (LA LGE) as specified on next to the images presented in **A, D, and G**. Segmentations of the images are shown in **B, E, and H** and corresponding 3-dimensional reconstructions in **C, F, and I**. **Blue** indicates no enhancement and **colors grading from white to red** indicate enhancement.

Reference: Bertelsen L, Diederichsen SZ, Haugan KJ, et al. Left Atrial Late Gadolinium Enhancement is Associated With Incident Atrial Fibrillation as Detected by Continuous Monitoring With Implantable Loop Recorders. JACC Cardiovasc Imaging. 2020;13(8):1690-1700.

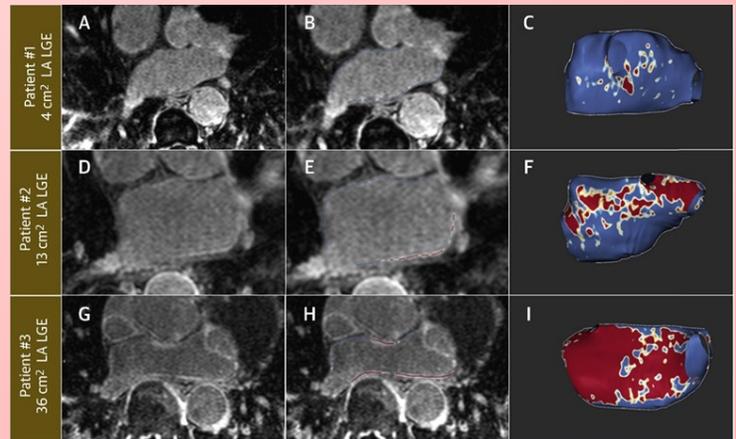


Figure 1. Representative Images of LA LGE

## WebDCU Reminders

### F104 Adverse Event Reporting

In WebDCU, Form 104 Adverse Event is used to report serious adverse events, clinical outcomes, and adverse events of special interest. Aside from the baseline visit, F104 is posted at each visit. It is an optional form that should only be completed if a subject experiences an SAE, clinical outcome, or adverse event of special interest, in which case it must be submitted in WebDCU within 24 hours of the first knowledge of the event. This is because there are time-sensitive safety reporting requirements based on the review of the Medical Safety Monitor. Submitting the form occurs after saving the CRF and, if necessary, addressing any issues. The safety review process cannot begin until the CRF is submitted, not just saved.

### F244, F245, F246, F247 Informed Consent CRFs for Versions 4, 5, 6 & 7

Please continue to work with your subjects to resolve any outstanding informed consent issues noted with WebDCU queries. Reach out to Site Monitoring Manager, Aaron Perlmutter, perlmutt@musc.edu, with any questions.

### Direct Data Entering

If you enter subject data directly into WebDCU while speaking to the subject on the phone, you would need to add a general comment that says, "direct data entry". Otherwise, the site monitor will ask you for the source document.

## ARCADIA Contacts

**ARCADIA@ucmail.uc.edu**

**24/7 Hotline: (833) 427-2234 if unable to reach please call (206) 535-1229**

**For an emergency that requires knowing whether patient is taking apixaban (Eliquis) or aspirin**

### Principal Investigators

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### Culture corner

Finally, at the end of one of the most challenging years most of us have ever faced, comes Christmas. Interestingly, some of the traditions of the Christmas celebration find their roots in ancient Greek history, beliefs, and customs. In December, for instance, the ancient Greeks celebrated the birth of Dionysus, calling him "Savior" and divine "infant." According to Greek mythology, his mother was a mortal woman, Semele, and his father was Zeus, the king of the Gods. The priest of Dionysus held a pastoral staff as did the Good Shepherd. On December 30, ancient Greeks commemorated his rebirth.

One of the most well-known customs throughout the Christian world is Christmas carols. These also have roots in ancient Greece. Homer, during his stay on the island of Samos, along with a group of children composed the carols. In ancient Greece, carols symbolized joy, wealth and peace, and children sang the carols only in the homes of the rich. Children would go from house to house, holding an olive or a laurel branch adorned with wool, symbol of health and beauty, and different fruits.

The children then hung the branch on the door of their homes, where it remained for the rest of the year. Ancient Greeks also used to decorate temples with trees as a divine offering. Now the Christmas tree, adorned first with fruits and later with clothes and other household objects, symbolizes the rejoicing for the birth of Jesus Christ.

And Santa Claus? Perhaps his sleigh and reindeer derive from Helios, the god and personification of the sun, who travelled in a chariot pulled across the sky by horses.



Figure: Image of Helios in his chariot, from Dome of the entrance hall of the Széchenyi Bath, Budapest, Northern Hungary