



SPRING 2021

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Pathways to a Cure

The CAA Newsletter

MESSAGE FROM THE DIRECTOR

We continue to expand our search for markers that lead to bleeding strokes with the goal of providing breakthrough therapies and preventative measures. In this edition of Pathways to a Cure, we are thrilled to introduce a new study by Dr. Susanne van Veluw. This new study will use an injected dye, called Dotarem, that could pave a pathway for us to detect leakages in the blood vessels of the brain before bleeding. Please see the adjacent section "Vessel Enhancement Study" for more information on this research study.

In this edition, we also highlight the amazing work our research fellows have continued around the globe. We greatly appreciate our previous fellows who have worked with us here at the J. Philip Kistler Stroke Research Center (JPK). It has been a win-win affair to have our fellows because they bring a tremendous amount of talent and creativity to our team and are able to take back the training that they've received here at JPK to their countries to continue working on Cerebral Amyloid Angiopathy (CAA) research with other CAA communities around the world.

Lastly, we want to express our gratitude to the CAA patients who have generously donated their brains for research and to their families. It is the truest sign of our patients' generosity for them to donate a part of their body to this important scientific and medical cause. Brain donation is one of the most effective ways for a person with CAA to help the next person in the same boat. We hope we can pay it forward by providing research updates to previous donor families as well as the broader CAA community.

Sincerely,
Steve Greenberg, MD, PhD



VESSEL ENHANCEMENT STUDY

The aim of this study is to look for subtle leakage from small blood vessels in the brain of individuals with CAA. Patients with CAA are at risk of developing bleeds in the brain, because of the accumulation of the toxic protein amyloid in the walls of small blood vessels. With this study we hope to be able to identify those affected blood vessels that are likely to bleed in the future, at an early stage.

In this study, we will obtain MRI scans after the injection of a contrast agent called Dotarem. With this method we will be able to find those vessels in the brain that are leaky. This optional sub-study is part of an existing project, and patients meeting study criteria will be able to choose if they want to participate.

This project is led by Dr. Susanne van Veluw, an investigator within the MGH CAA Research Program. Her lab seeks to understand what happens to blood vessels in the brain of patients with CAA before they start to become fragile and bleed. Using novel neuroimaging techniques, brain tissue samples, and experimental models of the disease, her lab aims to discover previously unknown pathophysiological mechanisms that may someday provide targets for new therapies.

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- Vessel Enhancement Study

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Interview with Dr. Susanne van Veluw



Is Dotarem safe?

Dotarem is a Gadolinium-based contrast agent and considered safe. Before enrollment in the study, we will ask participants a few questions about their general health and kidney function, as individuals with impaired kidney function will not be able to clear this agent from their body as quickly as healthy individuals would. Research staff will provide each participant with more detailed information regarding safety.

If leakage is seen on my brain scan what could that mean for future studies and treatments?

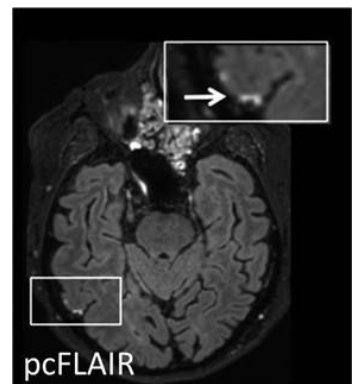
The technique that we are using in this sub-study is a sensitive method that can pick up even the subtlest of blood vessel leakage in the brain. We have reasons to believe that this form of subtle leakage occurs to blood vessels that are affected by amyloid proteins in CAA but haven't bled yet. This study will be one of the first in the world to investigate this form of blood vessel injury in patients with CAA. Future secondary prevention studies may use this imaging technique to identify patients that may benefit from treatment. Moreover, we will learn a great deal about the relationship between this type of leakage and other prominent bleeding markers that are frequently identified on MRI scans of patients with CAA.

If leakage is seen on my brain scan, does this mean I am more likely to have a stroke, brain bleed or dementia?

We do not know yet. This sub-study is our first attempt to study patterns of brain blood vessel leakage in patients with CAA. If the results are encouraging, we will likely design a follow-up study to determine whether patients with leakage on their MRI scans are at increased risk of developing bleeding strokes or dementia.

The photo on the right is an example of a 'leaky' blood vessel on an MRI scan of a patient with mild cognitive impairment injected with a contrast agent. (pcFLAIR = post-contrast Fluid Attenuated Inversion Recovery). Adapted from Freeze et al. AJNR Am J Neuroradiol 2017.

This is an exciting opportunity in our research community! If you are interested in learning more about this study, please contact study coordinator Christopher Kwon at 617-724-2829.





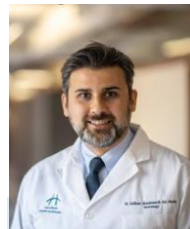
PREVIOUS JPK FELLOWS SPOTLIGHT



Name: Dr. Andreas Charidimou, MD, PhD

Location: Boston, Massachusetts

Research: Dr. Charidimou is currently completing specialty training as a Neurology Resident at Boston University Medical Center (PGY2). He continues in the CAA field, which is his passion, through ongoing collaborations with Dr. Steve Greenberg and Dr. Anand Viswanathan. One of his ongoing projects is the International CAA Association Boston Criteria Study Group which is an international effort to refine and improve the diagnostic criteria for CAA. He continues to work on further validating cortical superficial siderosis as the strongest marker for future brain hemorrhage and overall prognosis. He will also be involved with the Framingham Heart Study at Boston Medical Center. There he will study brain MRI markers of small vessel disease over time and collaborate with the JPK stroke research team to conduct other studies.



Name: Dr. Ashkan Shoamanesh, MD, PhD

Location: Ontario, Canada

Research: Dr. Ashkan Shoamanesh is currently working in Ontario, Canada on several CAA trials. He is the principal investigator of a trial which is accessing optimal antithrombotic treatment in intracerebral hemorrhage (ICH) survivors with atrial fibrillation (Afib) at over 300 sites in 20 countries.

Dr. Shoamanesh is also involved in a trial that is assessing the effects of statin continuation compared with discontinuation for the primary outcome of recurrent intracerebral hemorrhage (ICH) in patients with lobar ICH. He is also the founding chair of the Canadian Hemorrhagic Stroke Trials Initiative which is a Canada-centric multidisciplinary network filled with investigators devoted to bettering the lives of hemorrhagic stroke survivors.



Name: Dr. Marco Pasi, MD, PhD

Location: Lille, France

Research: Dr. Pasi currently investigates the role of CAA-related MRI markers that may be useful to better define the long-term prognosis of ICH survivors. He is particularly interested in cognitive decline and neuropsychiatric symptoms after a spontaneous ICH.



Name: Dr. Nicolas Raposo, MD, PhD

Location: Toulouse, France

Research: Dr. Raposo is working at Hospital Pierre Paul-Riquet and Toulouse University Hospital in Toulouse, France. He is working on imaging markers of CAA and the risk of ICH and dementia in CAA.

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Summer 2021 Brain Donation Webinar

When patients who have participated in CAA research make the decision for brain donation, they complete a chain of research data. This final link gives researchers the ability to examine the brain microscopically which is often the “missing link” in our research studies. In many ways this is the greatest contribution a patient and family can make toward aiding the fight against CAA.

Since the start of our CAA Brain Donation program, we have received a substantial number of autopsies. In an attempt to report back what we have learned so far and to show our appreciation for these generous donations, we are excited to announce that we will be hosting a Virtual Brain Donation Information Webinar on July 7, 2021 between 7-8PM (EST). This 1 hour webinar will be led by Dr. Susanne van Veluw, Dr. Steven Greenberg, and Dr. Matthew Frosch, all lead experts in the CAA research field. Attendees will have the opportunity to ask questions to the panelists in an (anonymous) moderated Q&A session. If you are interested in attending this virtual webinar you can register on our website at angiopathy.org or by contacting our research coordinator Mr. Christopher Kwon directly at YIKWON@mgh.harvard.edu.

Looking to support CAA Research?

Many patients and families have lent their time and heartfelt dedication to finding a cure for CAA by helping raise funds for our clinical research program. The CAA Research Team at MGH encourages your interest in hosting a charity event or fundraising among friends, family and colleagues, and appreciate the efforts you have already made to this end!

If you would like to learn more about how to support CAA research at MGH, please visit this link:

<https://giving.massgeneral.org/crowdfunding-community-fundraising/>

Individual donations can also be mailed to:

MGH Development Office c/o Elizabeth Barberio
125 Nashua Street, Suite 540 Boston, MA 02114

*Please make checks payable to Mass General Hospital, memo #1200-028184

CAA Brain Donation Webinar Contact:

If there are any difficulties accessing the link, please contact clinical research coordinator, Christopher Kwon at YIKWON@mgh.harvard.edu or by calling 617-724-2829.