



# NEWSLETTER

APRIL 2022 | VOLUME 1 | ISSUE 1



## FASTEST

EVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

### Message from Dr. Broderick



We are excited to kick off the monthly FASTEST Newsletter as enrollment starts and sites are coming online. The FASTEST trial is critically important to find the first medical treatment

for spontaneous ICH. Recombinant Factor FVIIa is easy to mix up and administer but enrolling patients within 2 hours from last known well is a big challenge. However, we did this before in the NINDS tPA trial for acute ischemic stroke which changed stroke treatment throughout the world, and we have the opportunity to do this again. The newsletter will highlight our successes, challenges, and investigator teams throughout the world while also keeping our FASTEST investigators up-to-date with the latest science surrounding treatment of acute ICH.

**Joseph Broderick, MD**  
 Director NIH StrokeNet  
 Director UC Gardner  
 Neuroscience Institute

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## Please join us for the FASTEST Monthly Webinar

**Wednesday April 20<sup>th</sup>  
2:00-3:00 pm EST**

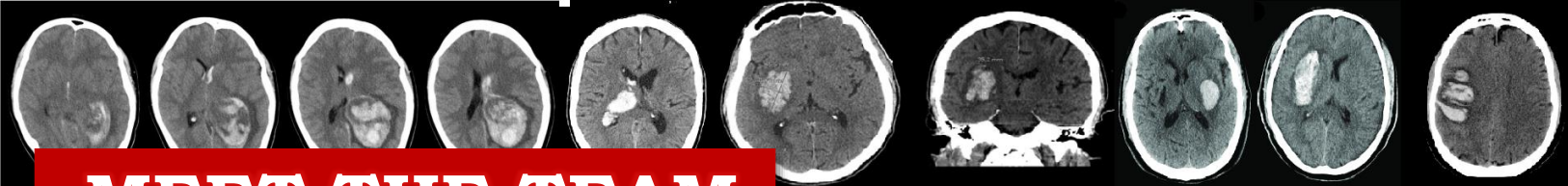
- Dr. Ritvij Bowry, MD from Memorial Hermann Hospital-Texas Medical Center will be discussing his study on ICH Enlargement.
- Patti Bratina, RN will shed light on how to leverage the MSU alert system via EMS to identify possible patients when the MSU isn't operating.

### Zoom:

<https://ucincinnati.zoom.us/j/96899791261?pwd=d1VtcEppL0RoTkFxQTV1WW54SERaZz09>

**To join Zoom Meeting** -- Meeting ID: 968 9979 1261  
 Passcode: 710245 or call in. To find your local number, go to  
<https://ucincinnati.zoom.us/j/96899791261?pwd=d1VtcEppL0RoTkFxQTV1WW54SERaZz09>

Prior presentations and slides are available at,  
<https://www.nihstrokenet.org/fastest/webinars>



# MEET THE TEAM

## Protocol Investigators



**Joseph Broderick, MD**  
Protocol Director / Lead  
Principal Investigator (LPI)  
University of Cincinnati



**James Grotta, MD**  
Memorial Hermann  
Hospital Texas Medical  
Center Houston



**Andrew Naidech, MD, MSPH**  
Northwestern Memorial Hospital  
Northwestern University  
Chicago, IL



**Jordan Elm, PhD**  
Medical University of  
South Carolina  
Charleston, SC

## NIH StrokeNet National Coordinating Center (NCC) - University of Cincinnati



**Pooja Khatri, MD**  
NCC PI  
University of Cincinnati



**Julie Denlinger, BSN, RN**  
Prime Project Manager (PPM)  
University of Cincinnati



**Emily Stinson, MS**  
NCC Project Manager  
University of Cincinnati



**Syed Quadri MD**  
NCC Project Manager  
University of Cincinnati

## NCC Central Pharmacy



**Noor Sabagha, PharmD, MPH**  
NCC Central Pharmacy  
University of Cincinnati



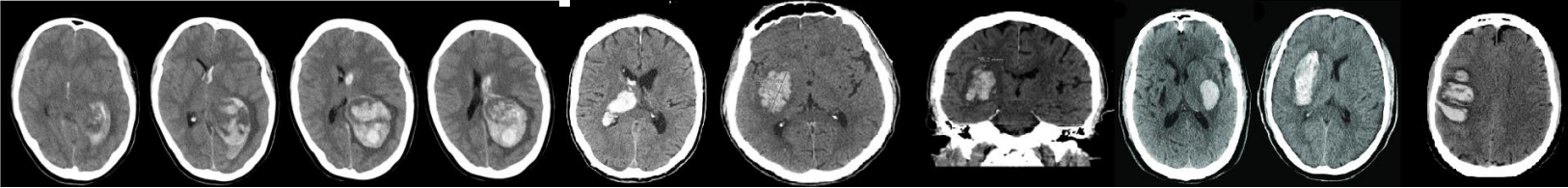
**Brittany Dornheggen CPhT II**  
NCC Central Pharmacy  
University of Cincinnati



**Chris Unger PharmD**  
NCC Central Pharmacy  
University of Cincinnati



**Kandis Harris Rhodes CphT**  
NCC Central Pharmacy  
University of Cincinnati



## StrokeNet National Data Management Center (NDMC)

### Medical University of South Carolina



**Jocelyn Anderson, MPH**

WebDCU™ Data Manager  
Medical University of South Carolina



**Jama Olsen, MPA**

StrokeNet NDMC Site Monitoring Manager  
Medical University of South Carolina



**Evan Tomaschek, RN, MPH**

FASTEST Trial WebDCU™ Data Manager  
Medical University of South Carolina

## FASTEST Imaging Core Lab (ICL)



**Lily Wang, MD, MPH**

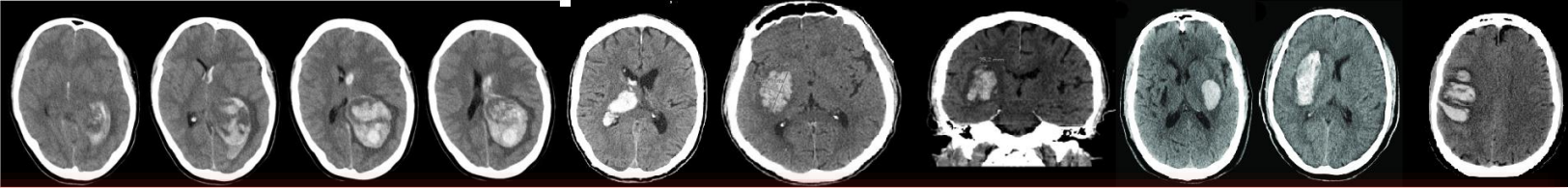
FASTEST Imaging Core  
University of Cincinnati



**Janice Carrozzella, MSN,  
CNP, RT(R), CCRA**

FASTEST Imaging Core  
University of Cincinnati





## **FASTEST International Investigators**



**Darisuh Dowlatshahi, MD, PhD**  
The Ottawa Hospital  
Ottawa Hospital Research Institute  
University of Ottawa



**Philip Bath, MD**  
Nottingham City Hospital  
Head, Division of Clinical Neuroscience  
University of Nottingham



**Thorsten Steiner, MD, PhD**  
Frankfurt Höchst, Germany.  
Klinikum Frankfurt Hoechst  
and Heidelberg University  
Hospital



**Carlos Molina, MD**  
Hospital Universitari Vall d'Hebron  
Barcelona, Spain



**Kazunori Toyoda, MD, PhD**  
National Cerebral and Cardiovascular Center  
Osaka, Japan

## **FASTEST International CROs**



**Joanne Lambley**  
Canadian CRO Collaborator  
Ottawa Hospital Research Institute  
University of Ottawa, Canada



**Mayumi Fukuda-Doi, MD, MPH**  
Japanese CRO Collaborator  
National Cerebral and Cardiovascular Center  
Osaka, Japan



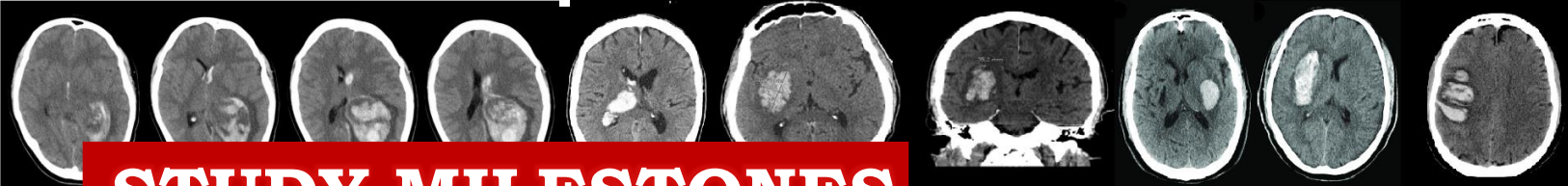
**Diana Salein, MD, PhD**  
EU/UK CRO Collaborator  
Research Coordinating Center  
Europe



**Sohei YOSHIMURA, MD, MPH**  
Japanese CRO Collaborator  
National Cerebral and Cardiovascular Center  
Osaka, Japan



**Megumi Hatano**  
Japanese CRO Collaborator  
National Cerebral and Cardiovascular Center  
Osaka, Japan



## STUDY MILESTONES

Total Sites Released to Enroll: **10** (6 USA, 2 Germany, 1 Japan, 1 Canadian)

Total Randomization = **7**

- US Randomizations: **5**,
- International randomizations: **2** (2 Canadian)

Randomization this month = **1**

Total Screen Failures = **20**

Subjects Randomized by MSU = **0**

Subjects Terminated Early = **0**

eConsent Used = **0**

Remote Consent Used = **0**

## CALENDAR OF EVENTS

Upcoming Advarra EFIC Panel meeting dates - **April 11th and 25th May 9th and 23<sup>rd</sup>**

Upcoming *FASTEST* Monthly Webinar: **Wednesday April 20<sup>th</sup> 2:00-3:00 pm EST**

QUESTION  
CORNER

## FAQs

**Q: Who do I reach out to if I have questions about EFIC?**

**A:** Please reach out to FASTEST Project Manager Emily Stinson at [stinsoey@ucmail.uc.edu](mailto:stinsoey@ucmail.uc.edu) or Julie Denlinger Denlinger at [denlinjk@ucmail.uc.edu](mailto:denlinjk@ucmail.uc.edu)

**Q: Who can help me if I have questions about the Advarra CIRBI application?**

**A:** Please reach out to Advarra service support representative Kyle Naylor at [Kyle.Naylor@advarra.com](mailto:Kyle.Naylor@advarra.com)

**Q: If I have questions about the FASTEST Informed Consent template who can help me?**

**A:** For US sites please reach out to FASTEST Project Manager Emily Stinson [stinsoey@ucmail.uc.edu](mailto:stinsoey@ucmail.uc.edu) or Advarra FASTEST service representative Kyle Naylor [Kyle.Naylor@advarra.com](mailto:Kyle.Naylor@advarra.com). For OUS sites please reach out to your FASTEST CRO representative or FASTEST Project Manager Julie Denlinger [denlinjk@ucmail.uc.edu](mailto:denlinjk@ucmail.uc.edu)

**Q: Who at my site is required to do imaging training and who can help me if I have questions about the FASTEST required Imaging Training?**

**A:** Certification is required for investigators and sub investigators who will determine eligibility as a responsibility on the DOA. Please reach out to Julie Denlinger [denlinjk@ucmail.uc.edu](mailto:denlinjk@ucmail.uc.edu) if you have questions or need assistance with this training.





# New Sites... Welcome Aboard!

The following new sites were **released to enroll** in the *FASTEST* study during the month of April



**Grady Memorial Hospital,  
Atlanta, GA**

Site PI:  
Digvijaya Navalkele, M.D., MPH



**National Cerebral and  
Cardiovascular Center,  
Osaka, Japan**



# Congratulations on First Enrollment!



University of Cincinnati Medical Center Team

PSC: Stephanie Thomas  
Site PI: Joseph Broderick, MD  
Pooja Khatri MD

UC San Diego Health



UC San Diego Medical Center, Hillcrest Team

PSC: Karen Rapp, R.N., B.S.N., C.C.R.C. & TERI McQuaid  
Site PI: Thomas M. Hemmen, M.D., Ph.D.  
Brett Meyer, MD



# SHOUT OUTS!!

Congratulations to all our US sites that have completed their EFIC reports and gained Advarra full study approval. Advarra shared that the FASTEST sites reviewed have been strong! Well done!

Recently, two of our US sites, received extra recognition for their EFIC community consultation efforts from Advarra. We would like to extend a special acknowledgment to the teams at **UC Irvine (UCI)**, under **Dr. Shah** and **PSC Julia Fong** and **Kaiser Permanente Los Angeles Medical Center**, under **Dr. Sangha** and **PSC Vanessa Audea**. The Advarra reviewer described both sites' efforts as "excellent". **AMAZING WORK!**

**Thank you** to the sites preparing for readiness:

- **Kaiser Permanente**
- **Central DuPage**
- **VCU**

**Thank you** to sites that have completed EFIC Plans and preparing to begin EFIC activities:

- **Thomas Jefferson**
- **Mass General**
- **Regions**

**Thank you** to sites that have submitted to Advarra for CIRB review:

- **Northwestern**

**Thank you** for sites preparing for Advarra submission:

- **UMASS**
- **Stony Brook NY**
- **North Shore**



## Top Enrolling Site

Congratulations to **Memorial Hermann Hospital-Texas Medical Center** for being the highest enrolling site in the study.

**Subjects enrolled = 3!!**

## Congratulations to the Enrolling Sites This Month!

1. Memorial Hermann Hospital Texas Medical Center      2 Subjects



## Hemorrhage Enlargement Is More Frequent in the First 2 Hours: A Prehospital Mobile Stroke Unit Study

Ritvij Bowry, Stephanie A. Parker, Patti Bratina, Noopur Singh, Jose-Miguel Yamal, Suja S. Rajan, Asha P. Jacob, Kenny Phan, Alexandra Czap and James C. Grotta

Originally published 4 Apr 2022 / <https://doi.org/10.1161/STROKEAHA.121.037591> / Stroke.2022;0:STROKEAHA.121.037591

**Background:** Hematoma enlargement (HE) after intracerebral hemorrhage (ICH) is a therapeutic target for improving outcomes. Hemostatic therapies to prevent HE may be more effective the earlier they are attempted. An understanding of HE in first 1 to 2 hours specifically in the prehospital setting would help guide future treatment interventions in this time frame and setting.

**Methods:** Patients with spontaneous ICH within 4 hours of symptom onset were prospectively evaluated between May 2014 and April 2020 as a prespecified substudy within a multicenter trial of prehospital mobile stroke unit versus standard management. Baseline computed tomography scans obtained <1, 1 to 2, and 2 to 4 hours postsymptom onset on the mobile stroke unit in the prehospital setting were compared with computed tomography scans repeated 1 hour later and at 24 hours in the hospital. HE was defined as >6 mL if baseline ICH volume was <20 mL and 33% increase if baseline volume >20 mL. The association between time from symptom onset to baseline computed tomography (hours) and HE was investigated using Wilcoxon rank-sum test when time was treated as a continuous variable and using Fisher exact test when time was categorized. Kruskal-Wallis and Wilcoxon rank-sum tests evaluated differences in baseline volumes and HE. Univariable and multivariable logistic regression analyses were conducted to identify factors associated with HE and variable selection was performed using cross-validated L1-regularized (Lasso regression). This study adhered to STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology) for cohort studies.

**Results:** One hundred thirty-nine patients were included. There was no difference between baseline ICH volumes obtained <1 hour (n=43) versus 1 to 2 hour (n=51) versus >2 hours (n=45) from symptom onset (median [interquartile range], 13 mL [6-24] versus 14 mL [6-30] versus 12 mL [4-19]; P=0.65). However, within the same 3 time epochs, initial hematoma growth (volume/time from onset) was greater with earlier baseline scanning (median [interquartile range], 17 mL/hour [9-35] versus 9 mL/hour [5-23]) versus 4 mL/hour [2-7]; P<0.001). Forty-nine patients had repeat scans 1 hour after baseline imaging

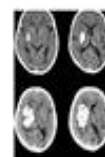
(median, 2.3 hours [interquartile range, 1.9-3.1] after symptom onset). Eight patients (16%) had HE during that 1-hour interval; all of these occurred in patients with baseline imaging within 2 hours of onset (5/18=28% with baseline imaging within 1 hour, 3/18=17% within 1-2 hour, 0/13=0% >2 hours; P=0.02). HE did not occur between the scans repeated at 1 hour and 24 hours. No association between baseline variables and HE was detected in multivariable analyses.

**Conclusions:** HE in the next hour occurs in 28% of ICH patients with baseline imaging within the first hour after symptom onset, and in 17% of those with baseline imaging between 1 and 2 hours. These patients would be a target for ultraearly hemostatic intervention.

Hemorrhage enlargement is more frequent in the first two hours:  
A Pre-hospital Mobile Stroke Unit Study



Reducing hematoma enlargement after ICH can improve outcomes



Earlier identification of hematoma enlargement could help guide earlier treatment



Patients with spontaneous ICH within 4 hours of symptom onset were evaluated on a mobile stroke unit in the pre-hospital setting

Baseline CT scans obtained within <1, 1-2 and 2-4 hours after symptoms were compared with CT scans repeated 1 hour later



Early hematoma growth was greater within 2 hours of symptom onset

\*\* 28% patients within 1 hour of symptoms

\*\* 17% patients between 1-2 hours

Patient with ICH within 2 hours would be a target for ultra-early hemostatic interventions





# HELPFUL REMINDERS & TIPS

## For Project Managers and Study Teams

- **HELPFUL Tip** We would like to share a few of the tactics **UC Irvine** used, that proved very successful in canvassing deep into their community and reaching key demographic communities. UCI worked with their Public Health division, that had great penetration and contacts into the community. They reached community members using a variety of media, print and radio, and in a variety of languages. The team went to community markets and events to meet and talk to community members. Their efforts embodied the goals of EFIC to inform the community and allow the community to dialog with the team. We would be happy to share their examples with other sites. **Sites can view EFIC events, from other sites, in WebDCU, and can generate ideas for your own community events!**
- **As you are completing EFIC events, please complete the CC and PD forms in WebDCU™.** The updated EFIC Forms Resource Guide is available in WebDCU™ (in the Toolbox under Project Documents) and is a very helpful tool for completing these forms. The FASTEST webinar from March 16<sup>th</sup>, 2021 (available at <https://www.nihstrokenet.org/fastest/webinars>) can provide additional tips. If you have questions in completing the forms, please feel free to reach out to the NCC. The NCC is also happy to review the forms and provide guidance and feedback along the way to ensure completeness.
- **US Manual of Procedures v1:** Finalized version of the US MOP v1 has been distributed to all the sites but can also be found in the WebDCU Tool Box: <https://webdcu.musc.edu/nett/ViewRecord.asp?theFormID=1015&theRecordID=109>

## From the **FASTEST** Central Pharmacy Team

- **Study Drug Shipment:** The Central Pharmacy will ship FASTEST study drugs few days prior to the readiness call. *FASTEST* IP will be shipped refrigerated. The initial study drug shipment will contain a total of two study drug kits to sites with one enrolling location (ED or MSU) and four study drug kits to sites that have two enrolling locations (ED+MSU) or 2 Eds
- **For the US sites:** Please upload the following regulatory documents into WebDCU for your site pharmacy to receive IP:
  - Institutional Pharmacy License
  - Institutional Drug Destruction Policy/SOP
  - Clinical Site Drug Shipping Address, Phone Number, and Contact Person
  - Adding Pharmacy Personnel to WebDCU DOA

# STUDY CONTACTS & USEFUL INFO

For any study related queries or help please reach out to **FASTEST** Project managers

**International Sites:** Julie Denlinger ([denlinjk@ucmail.uc.edu](mailto:denlinjk@ucmail.uc.edu))

**United States Sites:** Emily Stinson ([stinsoey@ucmail.uc.edu](mailto:stinsoey@ucmail.uc.edu))

Syed Quadri ([quadrisd@ucmail.uc.edu](mailto:quadrisd@ucmail.uc.edu))

For more information regarding the **FASTES** study please visit : <https://www.nihstrokenet.org/fastest/home>

For prior **FASTES** Presentations and Webinars slides and recordings visit: <https://www.nihstrokenet.org/fastest/webinars>

For more information regarding the StrokeNet Trials please visit: <https://www.nihstrokenet.org/>