NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

FEBUARY 2023 | VOLUME 2 | ISSUE 2

FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Naidech

Q: *What's the fastest enrolling trial in the history of the NIH StrokeNet?*

A: *FASTEST, which has enrolled nearly a patient per day in December 2022 and January 2023. More than 100 patients have been enrolled from nearly 70 sites in Japan, the US, Canada, Britain, Spain, and Germany.*

Congratulations to sites that have enrolled, and especially our leading sites for enrollment National Cerebral and Cardiovascular Center, Osaka, Japan; Foothills Medical Centre, Calgary, Canada; Memorial Hermann Texas Medical Center, Houston, Texas and Kobe City Medical Center General Hospital, Kobe, Japan.

Andrew M Naidech, MD MSPH

Professor
Northwestern University
Feinberg School of Medicine
Department of Neurology
Physician Informatics Director,
Northwestern Memorial Healthcare

Please join us for the *FASTEST* Monthly Webinar

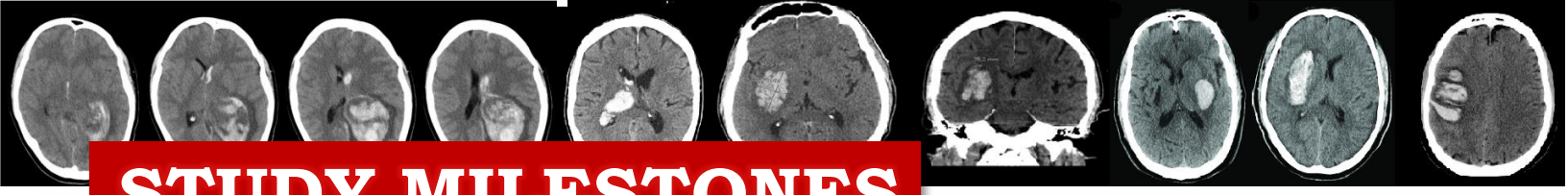
Wednesday June 22nd, 2:30-3:30 pm EST

- Dr. Sun from Queen's Medical Center, Honolulu, HI will be presenting a case, first patient to enroll using e-consent.
- Dr. Broderick will be discussing the Rankin Focused Assessment (RFA) tool and a case on ICH volume measurement.
- Subject and LAR consenting procedures will be discussed in detail.
- Study updates and announcement of the trial wide awards for recruitment.

Join Zoom Meeting

https://nam11.safelinks.protection.outlook.com/?url=https%3A%2F%2Fucincinnati.zoom.us%2Fj%2F95768343105%3Fpwd%3DZjYwZ0tNakxsN01qMmhPOE15N21Jdz09&data=05%7C01%7Cquadrisd%40ucmail.uc.edu%7C7b2505f4647443dd6b2e08da7ec1eb4c%7Cf5222e6c5fc648eb8f0373db18203b63%7C1%7C0%7C637961668587750683%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=40q90l8dB9QtZj9P5aZ0BeWkvzCsNx1WgQL9cFmISHQ%3D&reserved=0

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



STUDY MILESTONES

Total Sites Released to Enroll: **56** (**28** USA, **28** OUS: **4** Germany, **14** Japan, **4** Spain, **5** Canadian, **1** UK)

Total MSUs Released to Enroll: **7** (**6** US and **1** OUS)

Total Randomization = **109**

- US Randomizations: **33**,
- International randomizations: **76** (**14** Canadian, **7** Germany, **50** Japan, **5** Spain)

Randomization last month = **26**
Total Screen Failures = **365**
Subjects Randomized by MSU = **2**
Subjects Terminated Early = **0**
eConsent Used = **2**
Remote Consent Used = **1**

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinar: **Wednesday, February 15th @ 2:00 pm EST**

FASTEST study team office hours: **Monday, February 13th and 27th @ 2:00 pm EST**

ISC 2023 MEET-UP INVITE

Dear *FASTEST* site PIs and PSCs,

Just a reminder, on behalf of the NIH StrokeNet leadership teams and the *PIs of all the current StrokeNet trials* you are invited:

When: Wednesday, 8-February 2023
Time: 6:30-9:00 pm
Where: The Omni Dallas Hotel, 555 S Lamar Street, Trinity 5-6

There will be a light buffet provided, with an informal program beginning promptly at 7:45pm. Unfortunately, space is limited, so we are unable to accommodate guests outside of StrokeNet. We want to make sure that we have room enough for everyone who has worked so hard to ensure the success of the StrokeNet. Please join us as we recognize teams and individuals for their efforts in recruitment and retention, and for contributions to the Network, both large and small.

IMPORTANT NOTE

This is a very important communication and trial update please read carefully for instructions.

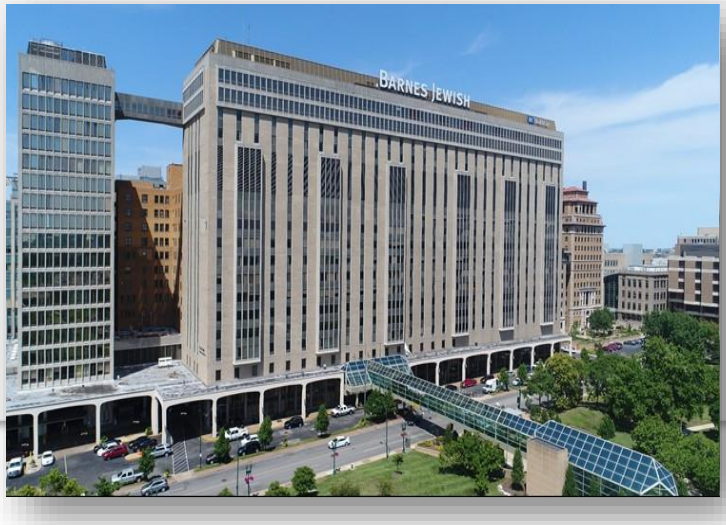
Use of the Rankin Focused Assessment (RFA) is required by the protocol (4.9 ssessments for Efficacy, Page 19). When assessing mRS for follow up visits at day 30 thru day 180 all investigators should be using the Rankin Focused Assessment Tool as per the study protocol. We have recently added the **Rankin Focused Assessment (RFA)** tool to the WebDCU Toolbox. We are specifically asking for the investigator to fill out the tool and **add it to the subject binder once complete.** WebDCU is in the process of updating the CRF **F144 Modified Rankin Scale** to add a check box that will ask if the RFA was used for each assessment.

New Sites... Welcome Aboard!

The following new sites were **released to enroll** in the *FASTEST* study during the last month.

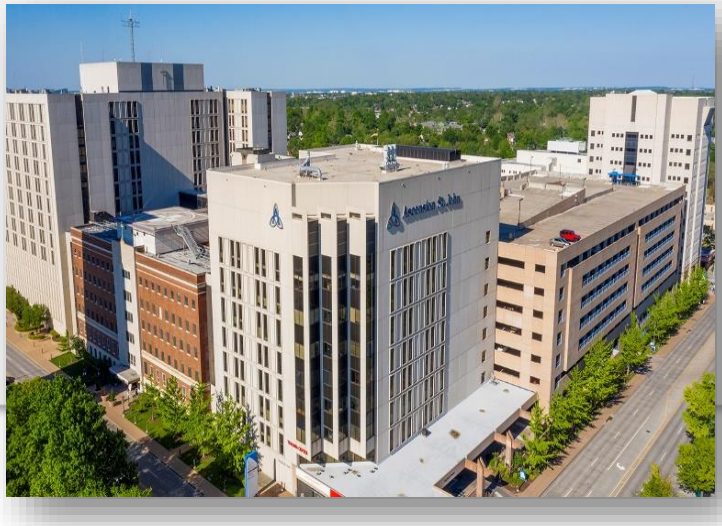
Girona University Hospital, Girona, Spain

Site PI:
Yolanda SILVA, MD, PhD



Barnes Jewish Hospital, St. Louis, MO

Site PI:
Peter D Panagos, MD



St. John Medical Center, Tulsa, OK

Site PI:
Errol L. Gordon, MD

Congratulations on First Enrollment!!

Congratulations to Dr. Peter D Panagos and his team at the Barnes Jewish Hospital, St. Louis, MO for enrolling their first subject in *FASTEST*.

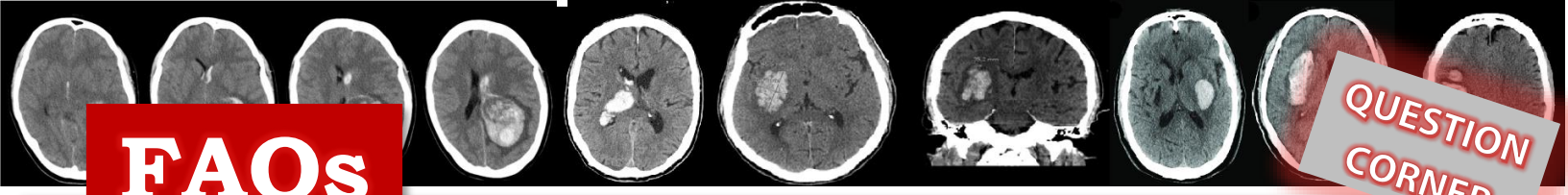
Congratulations to Dr. Hauke SCHNEIDER and his team at the University Hospital Augsburg, Augsburg, Germany for enrolling their first subject in *FASTEST*.

Congratulations to Dr. William HICKS and his team at the Riverside Methodist Hospital, Columbus, OH for enrolling their first subject in *FASTEST*.

Congratulations to Dr. Houman KHOSRAVANI and his team at the Sunnybrook Health Sciences Center, Toronto, ON, Canada for enrolling their first subject in *FASTEST*.

Congratulations to Dr. Christian NOLTE and his team at the Charite University Medicine Berlin, Berlin, Germany for enrolling their first subject in *FASTEST*.

Congratulations to Dr. Harish SHOWNKEEN and his team at the Central DuPage Hospital, Winfield, IL for enrolling their first subject in *FASTEST*.



FAQs

QUESTION CORNER

Q: In WebDCU, once I click [Save Record] on a CRF, I see a link in the top right that says [Submit CRF]. What is the difference?
A: Data is not considered complete until you click [Submit CRF]. As you enter data, you are working on a draft of the CRF. You may edit and save as often as you like.
Also, if required data is missing or other rule violation is found (e.g. entering a future date), you will receive a small pop-up window in the middle of your screen listing your errors. You must fix these errors before you can save the form. Once the errors and violations have been addressed, click on [Submit CRF] at the top right-hand corner of the page. Data clarification requests (DCRs) also require that the CRF is submitted before the Data Manager or Monitor is able to close the DCR.

Q: Can the baseline troponin be a "point of care" troponin? This is what is ordered and resulted for most of our stroke alert patients.
A: Yes, the baseline troponin is usually the "point of care" troponin done for stroke patients and is reported in F105-Laboratory Tests.

Q: Can we use the GCS from the ER staff?
A: Yes, as long as the GCS from the ER staff (licensed physician or nurse) is recorded in your EMR notes.

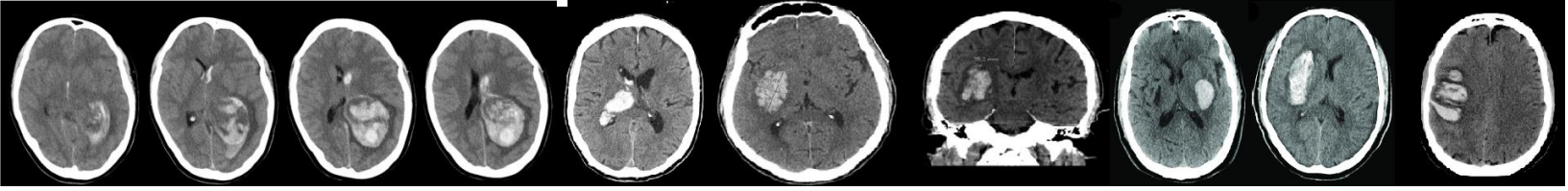
Q: If the data (ex. NIHSS, mRS, GCS etc.) is recorded in our EMR, you won't be expecting the hard copy NIHSS form to be in our subject binder, correct?
A: Please refer to the FASTEST Data Collection Guidelines on page 3. As per the guidelines especially the first two points (as below), the eCRFs should serve as the source document and can be used for site monitor review.

- Unless otherwise indicated, data can be directly entered into eCRFs, whereby the eCRF becomes the source document. A general comment should indicate that the eCRF is the source document to assist site monitors and reduce data clarification requests.
- eCRFs should be completed utilizing documentation from the legal medical record or other source data, whether it is paper or electronic. These source documents should be retained for site monitor review.

Q: If site fail to utilize the lowest kit number during the randomization, will that cause any queries when the research staff completes the enrolment form in WebDCU?
A: No, you will not get queries in WebDCU for not using the lowest kit number.

Q: Can we use estimated weight to calculate the IP dose?
A: Actual weight is preferred, but estimated weight **is acceptable.** Estimated body weight is appropriate to use for dosage determination, especially since we can't always wait for a stroke patient to be weighed. However, to ensure that there is no overdose and to calculate the dose check **we do need the sites to report the subject's actual weight** in the WebDCU. This can be done at any time during their hospitalization.

Q: Does the "rounding" rules apply to the drug dose? The patient's weight was 52.8, but we used the line for 51-52 kg for the dosing. It ended up being a 0.1 difference in dose. (The syringe only gives .5 marking, so it was hard to gauge the 0.1 anyway).
A: Yes, as explained above, **the rounding rule can be applied to the drug dose.** Estimated weight is appropriate to use, especially since we can't always wait for a stroke patient to be weighed. But since in this current example the weight of the patient was 52.8 (almost 53), it should have been rounded off as 53 kg. However, using 52 kg will not be of any harm to the patient or the study. As emphasized above, **we do require the study team to eventually enter the actual weight for the patient.**



Q: if we have a subject that needs 2 syringes, how do the other sites handle that. Do they try to put them into one syringe before doing the bolus, or do they just remove the first one and then attach the second one after the first is done.

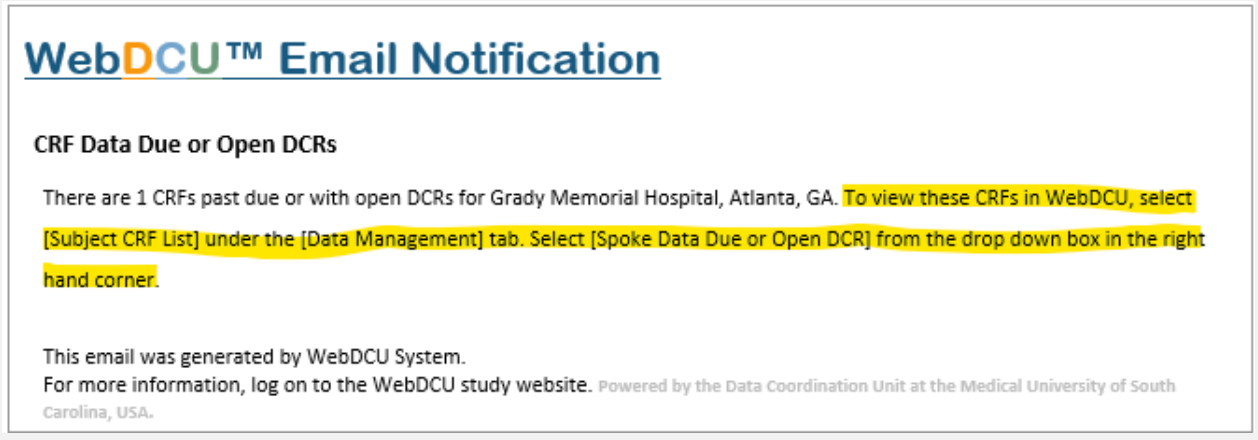
A: The two syringes issue has been confusing for some sites. We are recommending that sites use the two histidine diluent syringes for mixing the drug only. Once the vial is reconstituted with the histidine, we recommend that the histidine syringe be removed, and the actual dose of drug be drawn up with a single 10ml syringe from the site's local inventory. So, say a patient needed 8.2ml of drug, they would reconstitute the two vials with the histidine syringes, remove the histidine syringes, and then use a single 10ml syringe to draw up 5ml from one vial and 3.2ml from another. This is advantageous because you only need one syringe for the dose, and the 10ml syringes are marked in 0.2ml increments so it is easier to draw up a specific dose.

Q: Do we also report AE and what is the timeline to report the Non-serious AEs?

A: All non-serious adverse events observed by the investigator or reported by the participant will be recorded from the time of randomization through **Day 4.** Kindly make note that these non-serious adverse events need to be reported in WebDCU™ within **5 days** of the site investigator's awareness of the event.

Q: My site received a WebDCU email notifying us that we have data overdue and/or open DCRs. How do I find these in the database?

A: You can get to these quickly by following the directions in the email notification:



WebDCU™ Email Notification

CRF Data Due or Open DCRs

There are 1 CRFs past due or with open DCRs for Grady Memorial Hospital, Atlanta, GA. To view these CRFs in WebDCU, select [Subject CRF List] under the [Data Management] tab. Select [Spoke Data Due or Open DCR] from the drop down box in the right hand corner.

This email was generated by WebDCU System.
For more information, log on to the WebDCU study website. Powered by the Data Coordination Unit at the Medical University of South Carolina, USA.

Likewise, the email notification for overdue visits also includes directions on how to find a list of which subjects are overdue in WebDCU.

Please send in your questions and we will address them accordingly and share with others in the next Newsletter.

SHOUT OUTS!!

Congratulations to all our US sites that have completed their EFIC reports and gained Advarra full study approval.

Thank you to the sites recently released to enroll for their hard work

1. **Washington University Barnes Jewish**
2. **Assention St. Johns**
3. **Girona University Hospital, Spain**
4. **Vancouver General Hospital, Canada**

Thank you to the sites that have gotten CIRB/REB/EC approval and preparing for readiness

1. **Mayo Clinic**
2. **Providence St. Vincent**
3. **Regions MC**
4. **St. Joseph MC**
5. **Thomas Jefferson**
6. **University of Alabama**
7. **Mt. Sinai West**

Top Enrolling Site

Congratulations to **National Cerebral and Cardiovascular Center, Osaka, Japan** for being the highest enrolling sites in the study.

Subjects enrolled = 15!!

Congratulations to the December Enrolling Sites!

National Cerebral and Cardiovascular Center, Osaka, Japan	**3 Subjects**
Memorial Hermann Texas Medical Center, Houston, TX	**2 Subjects**
Kobe City Medical Center General Hospital, Kobe, Japan	**2 Subjects**
Iwate Prefectural Central Hospital, Morioka, Japan	**3 Subjects**
Vall d'Hebron Hospital, Barcelona, Spain	**1 Subjects**
Kagoshima City Hospital, Kagoshima, Japan	**2 Subjects**
Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA	**1 Subject**
Niigata City General Hospital, Niigata, Japan	**2 Subjects**
Barnes Jewish Hospital, St. Louis, MO	**1 Subject**
Toledo Hospital, Toledo, OH	**1 Subject**
University Hospital Augsburg, Augsburg, Germany	**1 Subject**
Sunnybrook Health Sciences Center, Toronto, ON, Canada	**1 Subject**
Central DuPage Hospital, Winfield, IL	**1 Subject**
Grady Memorial Hospital, Atlanta, GA	**1 Subject**
Riverside Methodist Hospital, Columbus, OH	**1 Subject**
Tubingen University Hospital, Tubingen, Germany	**1 Subject**
Charite University Medicine Berlin, Berlin, Germany	**1 Subject**
University Hospital Augsburg, Augsburg, Germany	**1 Subject**

SCIENCE CORNER

RESEARCH ARTICLE OF THE MONTH

Using Noncontrast Computed Tomography to Improve Prediction of Intracerebral Hemorrhage Expansion

Andrea Morotti , MD; Gregoire Boulouis , MD, PhD; Jawed Nawabi , MD; Qi Li , MD, PhD; Andreas Charidimou , MD, PhD; Marco Pasi , MD, PhD; Frieder Schlunk, MD; Ashkan Shoamanesh , MD; Aristeidis H. Katsanos , MD; Federico Mazzacane , MD; Giorgio Busto, MD; Francesco Arba , MD, PhD; Laura Brancaleoni , MD; Sebastiano Giacomozzi , MD; Luigi Simonetti , MD; Andrew D. Warren , BS; Michele Laudisi , MD; Anna Cavallini , MD; Edip M. Gurol , MD, MSc; Anand Viswanathan , MD, PhD; Andrea Zini , MD; Ilaria Casetta , MD, PhD;Enrico Fainardi , MD, PhD; Steven M. Greenberg , MD, PhD; Alessandro Padovani, MD, PhD; Jonathan Rosand , MD, MSc; Joshua N. Goldstein , MD, PhD

Originally published 9 Jan 2023 I https://doi.org/10.1161/STROKEAHA.122.041302 I Stroke. 2023;54:567–574

Background:

Noncontrast computed tomography hypodensities are a validated predictor of hematoma expansion (HE) in intracerebral hemorrhage and a possible alternative to the computed tomography angiography (CTA) spot sign but their added value to available prediction models remains unclear. We investigated whether the inclusion of hypodensities improves prediction of HE and compared their added value over the spot sign.

Methods:

Retrospective analysis of patients admitted for primary spontaneous intracerebral hemorrhage at the following 8 university hospitals in Boston, US (1994–2015, prospective), Hamilton, Canada (2010–2016, retrospective), Berlin, Germany (2014–2019, retrospective), Chongqing, China (2011–2015, retrospective), Pavia, Italy (2017–2019, prospective), Ferrara, Italy (2010–2019, retrospective), Brescia, Italy (2020–2021, retrospective), and Bologna, Italy (2015–2019, retrospective). Predictors of HE (hematoma growth >6 mL and/or >33% from baseline to follow-up imaging) were explored with logistic regression. We compared the discrimination of a simple prediction model for HE based on 4 predictors (antitplatelet and anticoagulant treatment, baseline intracerebral hemorrhage volume, and onset-to-imaging time) before and after the inclusion of noncontrast computed tomography hypodensities, using receiver operating characteristic curve and De Long test for area under the curve comparison.

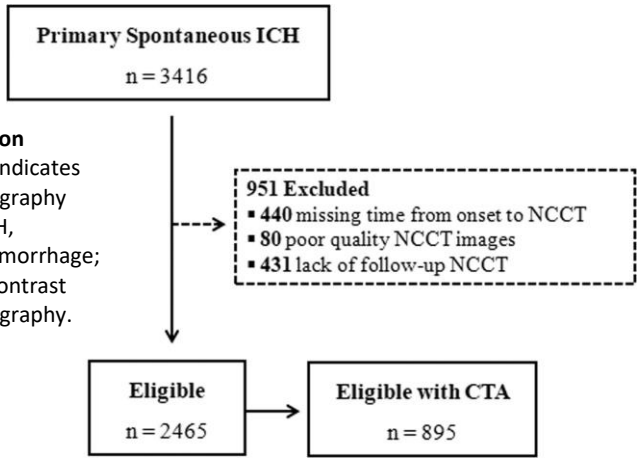


Figure 1. Selection flowchart. CTA indicates computed tomography angiography; ICH, intracerebral hemorrhage; and NCCT, noncontrast computed tomography.

Results:

A total of 2465 subjects were included, of whom 664 (26.9%) had HE and 1085 (44.0%) had hypodensities. Hypodensities were independently associated with HE after adjustment for confounders in logistic regression (odds ratio, 3.11 [95% CI, 2.55–3.80]; P<0.001). The inclusion of noncontrast computed tomography hypodensities improved the discrimination of the 4 predictors model (area under the curve, 0.67 [95% CI, 0.64–0.69] versus 0.71 [95% CI, 0.69–0.74]; P=0.025). In the subgroup of patients with a CTA available (n=895, 36.3%), the added value of hypodensities remained statistically significant (area under the curve, 0.68 [95% CI, 0.64–0.73] versus 0.74 [95% CI, 0.70–0.78]; P=0.041) whereas the addition of the CTA spot sign did not provide significant discrimination improvement (area under the curve, 0.74 [95% CI, 0.70–0.78]).

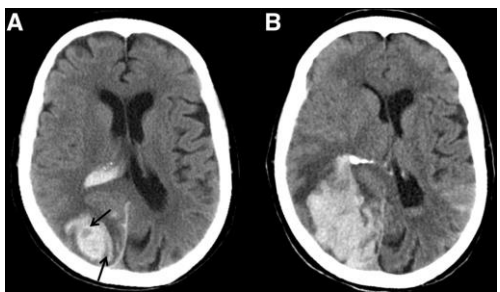


Figure 2. Noncontrast computed tomography (NCCT) hypodensities and hematoma expansion. A, Lobar intracerebral hemorrhage (ICH) with 29 mL baseline ICH volume and multiple hypodensities (black arrows). **B**, Follow-up NCCT showing hematoma expansion to 56 mL ICH volume. **C**, Deep ICH with 21 mL baseline ICH volume and intrahematoma hypodensity (black arrow). **D**, Follow-up NCCT showing hematoma expansion to 93 mL ICH volume.

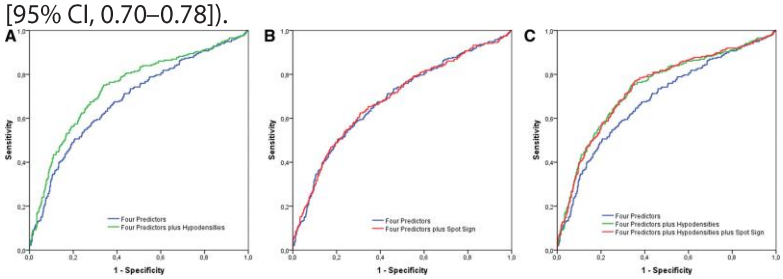
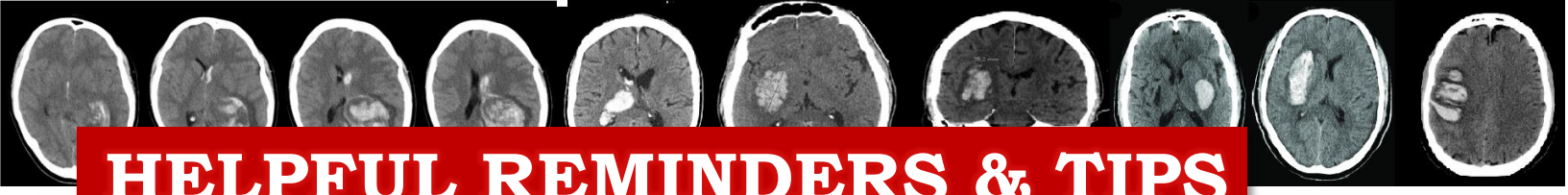


Figure 4. ROC curves for the predicted probability of hematoma expansion in patients with CTA (n=895). A, 4 predictors: AUC, 0.68; 95% CI, 0.64 to 0.73; 4 predictors plus hypodensities: AUC, 0.74; 95% CI, 0.70 to 0.78. **B**, 4 predictors: AUC, 0.68; 95% CI, 0.64 to 0.73; 4 predictors plus spot sign: AUC, 0.69; 95% CI, 0.65 to 0.73. **C**, 4 predictors: AUC, 0.68; 95% CI, 0.64 to 0.73; 4 predictors plus hypodensities: AUC, 0.74; 95% CI, 0.70 to 0.78; 4 predictors plus hypodensities plus spot sign: AUC, 0.74;, 95% CI, 0.70 to 0.78. AUC indicates area under the curve; CTA, computed tomography angiography; and ROC, receiver operating characteristic curves.

Conclusions:

Non-contrast computed tomography hypodensities provided a significant added value in the prediction of HE and appear a valuable alternative to the CTA spot sign. Our findings might inform future studies and suggest the possibility to stratify the risk of HE with good discrimination without CTA.



HELPFUL REMINDERS & TIPS

For Project Managers and Study Teams

- **WHAT IS NEW IN THE TOOLBOX?**
  - We have recently added the **Rankin Focused Assessment (RFA) tool** to the WebDCU Toolbox. We are specifically asking for the investigator to fill out the tool and add it to the subject binder once complete.
  - Pharmacy TERF Example Filled out form has been added to the FASTEST toolbox in WEbDCU.

- **Follow-up labs and imaging:** The follow-up non-contrast CT of the head and Serum troponin need to be obtained at **24±6 hours from stroke onset/last known well** as per the study Table of Events.

- **Pharmacy documents in Toolbox:** Any documents that are pharmacy/drug related will be categorized as "pharmacy" in the toolbox starting on/before **2/1/2023**.

- **Adding new study members:** Please update your DOA logs and upload the training documents to WebDCU as soon as you add a new study member to your FASTEST study team. All sites currently released to enroll kindly make sure your DOAS are up to date.

- **CRF Completion within 24 hours:** We would like to emphasize all sites on the timely completion of the case report forms (CRFs) **within 24 hours** of the visit (Baseline, 1-hour, 24-hour, Day 4/ Discharge). For the follow-up visits (Day 30, Day 90, Day 180, and End of study) which have a window of ±14 days please fill out the CRS as soon as the follow up visit has been completed.

- **Clarification regarding Emerald Temp Loggers:** We would like to clarify the misperception among sites receiving the Emerald loggers from StrokeNet NCC for their MSUs and EDs that the NCC is not responsible to track or note any temperature excursions. We are ONLY providing technical assistance to set up the loggers for the respective sites. Like any other trial, **it is the sole responsibility of the site to note any temperature excursions** and inform us duly so that NOVO can be informed accordingly.

- **Syncing & Accessing Data from the Cloud:** Kindly ask the MSU staff to sync the Temp loggers regularly so that the data can be uploaded to the cloud. **You can download the PDF of the monthly temp log from the cloud for study records and internal or external audits.** No need to fill out a temp log manually. If the PSC or the MSU staff having any issues with the device kindly notify FASTEST Project Manager, Syed Quadri quadrisd@ucmail.uc.edu to further assist you with troubleshooting the device.

- **Requesting 48 hrs recording from the data logger:** We are asking all sites receiving the Emerald loggers to send us a 48 hrs recording/data after placing the device in the MSU or ED and before moving the study drug. This is to make sure that the temp. logger is set up properly and recording the data. Once we give approval you can move the drug to the MSU or ED.

- **Screen failure logs: Please update the screen failure logs in WebDCU screen failure data is very important to the study. As you are aware we will be reimbursing the sites for their screen failures.**

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

- While the IP has a wide temperature range and could be stored either refrigerated OR room temperature, we highly encourage sites to **choose one range** and **keep this range for the duration of the trial**.

- **Temperature excursion and monitoring: Please be very vigilant about temperature excursion and temperature monitoring documentation.**

INTERNATIONAL SITE OF THE MONTH

Girona University Hospital, Girona, Spain

The Josep Trueta University Hospital (Catalan: Hospital Universitari de Girona Doctor Josep Trueta, Spanish: Hospital Universitario Doctor Josep Trueta) is a public hospital in the city of Girona in Catalonia. It was opened on 13 April 1956 in honor of the one of the most internationally renowned Catalan surgeon, Dr. Josep Trueta with the intention to give care to Social Security Beneficiaries, ie people without economic resources. In 2006 the Hospital Universitari de Girona Doctor Josep Trueta de Girona commemorated the 50th anniversary.

It is one the leading Spanish center for biomedical research. The Dr. Josep Trueta Foundation who promotes, development and dissemination biomedical research to improve the prevention, diagnosis, and treatment of diseases. It develops a great scientific activity through the nine research institutes integrated in the hospital. One of these research institutes is the IDIBGi (Institute of Biomedical Research of Girona Dr. Josep Trueta). The fundamental orientation of the research activities they develop is to respond to the health problems of citizens from the field of biomedical research.

Site PI:

Yolanda Silva, MD, PhD

Dr. Silva is the Head of Studies at the Girona University Hospital Dr. Josep Trueta. She is the lead member of the Cerebrovascular Pathology Research group, a multidisciplinary group with a consolidated track record of more than 20 years in translational research in acute stroke. The different lines of research of the group aim to identify new biomarkers and therapeutic targets for the management of cerebrovascular pathology.

STUDY CONTACTS & USEFUL INFO

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

International Sites: **Syed Quadri** (quadrisd@ucmail.uc.edu)

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

FASTEST Clinical Hotline: 1-855-429-7050

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

For prior ***FASTEST*** 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/

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY