Stroke Hyperglycemia Insulin Network Effort Trial Newsletter

August 2015 – Volume 3, Issue 4

IN THIS ISSUE

As summer comes to a close, we write to provide updates on the SHINE trial and share information that we think may be useful to our study teams. First, we would like to welcome four new enrolling sites: Mount Sinai, Miami Valley Hospital (spoke of OSU), Tufts MC (spoke of MGH), and University of Iowa. This now completes our site initiation phase for SHINE. We are excited to have our full cohort of sites up and running.

We are encouraging all sites to follow us on social media (@SHINE_TRIAL on Twitter) and to download our SHINE App for your front line teams who are screening potential SHINE subjects. There are currently 48 Twitter followers and our App has been downloaded 105 times! Many of you got bonus points for being early adopters.

In this issue of the newsletter, we have included best practices on reducing stroke mimics. This will be one of our areas of focus moving forward. We recognize that maximizing recruitment and minimizing stroke mimics is a delicate balance. Several of our sites have hit the sweet spot for this.

Finally, we want to update you on our most recent SHINE DSMB meeting that took place in June 2015. The DSMB recommended for the trial to continue as planned. As a team, we will also strive to make improvements in retention and data quality as they recommended. It is a pleasure to present your successes to our DSMB. As always, we welcome the input of our teams on any issues or ideas related to SHINE. Thanks again for all of your hard work.

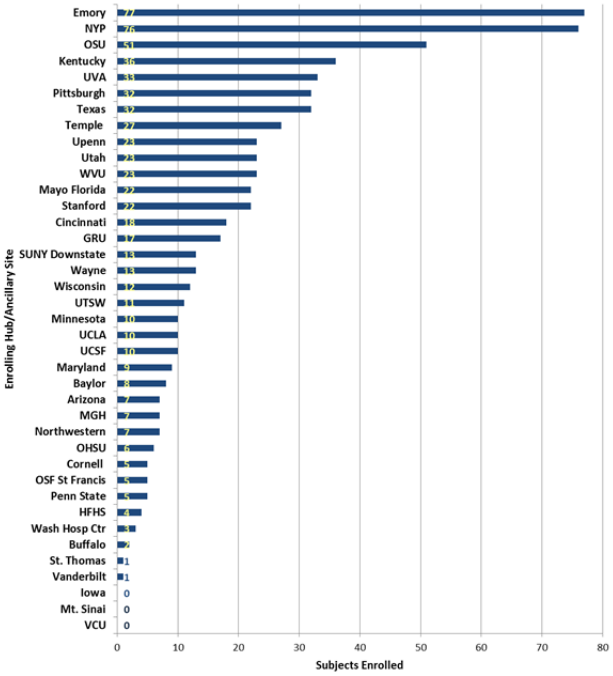
Karen C. Johnston, MD, MSc, SHINE Administrative PI
On behalf of the SHINE Team

SHINE Bravo Zulu Award

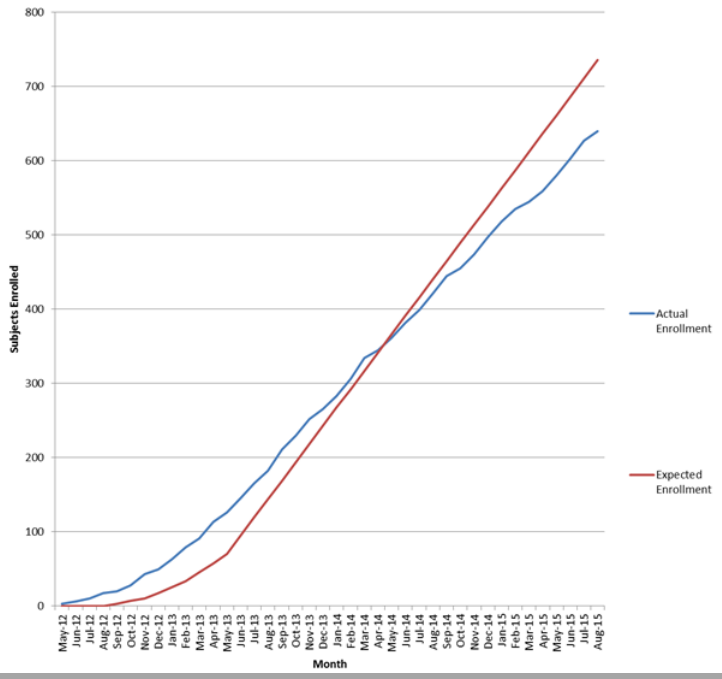
Our sincere congratulations to our SHINE study team at **Stanford University**, this quarter's recipient of the SHINE Bravo Zulu flag. The Bravo Zulu flag is traditionally used by US naval forces to publically recognize a job especially well done.

The SHINE study team at Stanford is led by **Dr. Karen Hirsch,** SHINE PI, **Dr. Jim Quinn**, NETT PI, **Carine Ho**, SHINE primary study coordinator, and **Rosen Mann**, NETT PM**.** We have all learned from their successes in maintaining a low rate of mimics, being proactive in updating screening based on changes in practice and through sharing their model on use of StrokeNet resources to support SHINE. On top of that, Stanford has enrolled 22 subjects in the trial and has a perfect rate of retention. Many thanks for all of your efforts!

SHINE Enrollment by Site—Apr 2012– Aug 2015

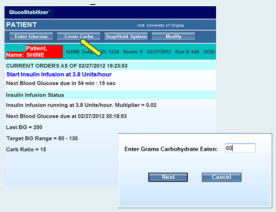


SHINE Enrollment—Actual vs Expected—Apr 2012– Aug 2015



Improving Protocol Adherence

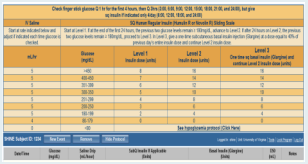
Meal Insulin Dosing



One of the most common deviations in the intervention group is incorrectly entering meal consumption estimates. As a reminder, ONLY **30** or **60** should be entered in the 'Cover Carbs' function of GlucoStabilizer. Any entry other than 30 or 60 will result in the wrong dose recommendation for meal coverage.

Level Changes in the Control Group

Level changes in the control group allow for more aggressive SQ insulin dosing for patients that are not in target. At 24 and 48 hours from randomization, review the 2 latest glucose levels. If



both are ≥180mg/dL, advance to the next level. Work with your nursing team to ensure the correct level on the sliding scale is referenced at each dosing time (06:00, 12:00, 18:00, 24:00). As a reminder, Level 3 also includes a one-time dose of Lantus/glargine to be given as close as possible to 48 hours from randomization.

Late Glucose Checks

In general, there is an association between late glucose checks and hypoglycemia. There is a +/- 15 minute window for regularly scheduled glucose checks. The window for glucose checks during an episode of hypoglycemia is +/-5 minutes. The protocol adherence team regularly monitors the timing of glucose checks and will be working with sites that have higher rates of late checks.

If your study team has tips or resources that have helped to maximize protocol adherence related to any of the topics above, we would like to be able to share with other sites. Please send any study resources that you have developed to Amy Fansler (acf7h@virginia.edu).

NIHSS at 90 Days

The 90 day visit for SHINE was designed to be completed as an in-person visit. The NIHSS assessment for SHINE is required to be completed in person, so in order for us to have all of the 90 day outcomes for all subjects, this visit has to take place in person.

While we do have the backup option of obtaining the mRS and other outcomes by phone if a study team is otherwise unable to complete in person – and please note that we absolutely want you to capture by phone if there is not another option or you have concerns that the visit might fall through— to the extent possible, we would like to have this visit done in person for all subjects.

Our SHINE sites are overall doing a very nice job with retention, and the DSMB recently has challenged us to do even better. Thank you for making follow up a top priority.

New SHINE Sites

The SHINE team would like to extend a warm welcome to four new sites during the last quarter. We are excited to have them on board!

Mount Sinai

Tufts Medical Center

University of Iowa Hospitals & Clinics

Miami Valley Hospital
Premier Health Partners

Stroke Mimics - Best Practices

Differentiating between acute ischemic stroke and a stroke mimic can be challenging. Our priority in SHINE is to minimize the likelihood of enrolling a stroke mimic into the trial. The current stroke mimic rate for the trial is 5% with a goal of reducing the rate as low as possible.

We offer the following tips and best practices for improving diagnostic accuracy of ischemic stroke - including situations where stroke mimics should be strongly considered.

- **Patients with a history of migraine headaches, particularly migraine with aura** - If headache, complex visual disturbance, or marching/evolving symptoms are present at onset, consider migrainous basis for focal deficits.
- **History of prior stroke**— If symptoms of current event are similar to those from the previous stroke, then consider reactivation of the old stroke symptoms if there is concurrent infection or other toxic metabolic disturbance evident at the time of diagnosis.
- **Unwitnessed symptom onset** - Look for history of epilepsy and examine for tongue biting, urinary/bladder incontinence, or other post-seizure sequelea as a post-ictal (Todd's) paralysis deficit may be a stroke mimic.
- **Younger than usual patient without significant stroke risk factors** - variable, inconsistent, and distractible deficits are uncommon in acute ischemic stroke and should raise the possibility of a functional disorder (conversion disorder).
- **Stroke consults on nights/weekends** – In academic centers these are times when housestaff are primarily responsible for acute stroke diagnosis and may have less oversight from more experienced vascular neurologists to confirm the diagnosis.

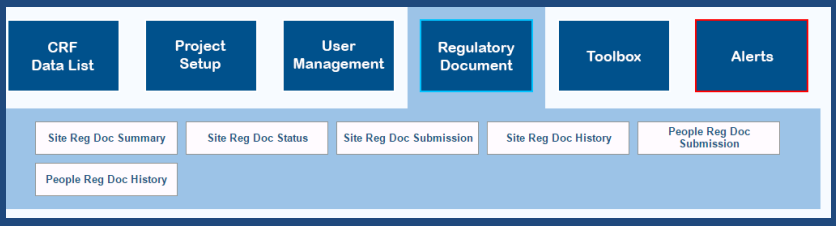
These are common stroke mimics that at times can be reconciled using best clinical judgement. Other times, utilization of **brain MRI with DWI** can be leveraged to improve diagnostic accuracy. In cases where DWI is indicated, a 'fast brain' protocol can reduce scan time to <5 minutes and reduce the likelihood of delaying enrollment after hospital arrival.

We encourage sites to use their best clinical judgement when determining eligibility for SHINE. As a reminder, a SHINE PI is available 24/7 on the study hotline to help consider this and other inclusion and exclusion criteria.

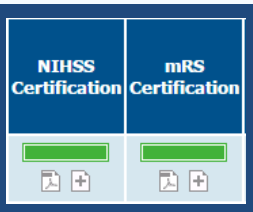
Kevin Barrett, MD
SHINE Recruitment PI

Frequently Asked Questions
New WebDCU SHINE Regulatory Database

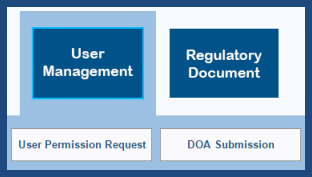
Q: How can I submit regulatory documents?
A: Follow the steps below.



- From the main menu page, click on [Regulatory Document] then [Site Reg Doc Status].
- This will display a table view of the documents required at your site as well as the submission status of each document.
- To upload a new document, click on the link and this will take you to [Reg Doc Submission].
- If there are any existing documents available for selection, they will be listed.
- If there are no existing document available, or none that you would like to select, click on the 'upload new file' link, browse for the document, and then click upload.
- Enter the required information, and then click 'Save Record.'
- The document will then be in a pending status until the Trial Project Manager verifies the information and approves/accepts the document



Q: Where can I find the electronic Delegation of Authority (eDOA) log?
A: In order to locate the DOA log, please login into WebDCU-SHINE, click on the [User Management] tab and click on [DOA submission]. Then click on the blue # link to the left and choose which site you'd like to edit. Lastly, click edit on the top right hand corner of the page



For more FAQs related to the updated SHINE Regulatory database, visit the study website www.shinetrial.com.

I-SPOT
Insights on Selected Procoagulation markers and Outcomes in stroke Trial

Total Enrollment: 81
I-SPOT Sites: 44

Because I-SPOT enrollments happen infrequently it may be easy to forget a step. Please review the collection and processing instructions found on the NETT website: https://nett.umich.edu/clinical-trials/shine/i-spot and always use the step by step checklist from the collection kit.

Hannah Reimer
I-SPOT Project Manager

New SHINE Resources

Check out the study website to review newly updated resources for SHINE. These include:

- **SAE narrative templates for Stroke and Hemorrhage**—These new templates highlight key details that we would like to see in SAEs related to stroke and hemorrhage and also provide guidance on event naming.
- **Control group timing spreadsheet**—This is a tool to auto-calculate the timing of the glucose checks in the control group. Our thanks to Laura Buchwalder from Ohio State's Wexner MC for her efforts to develop one of these tools!

Congratulations to July's SHINE Recognition System Winners!

The winner of BOTH divisions for the Recognition system is The **University of Arizona**! Banner University Medical Center—Tucson Campus won the individual site division and Arizona wins the NETT HUB division. Great job Arizona!

Katrina van de Bruinhorst,
SHINE Recruitment Specialist

Emory & Columbia—#1 Enrolling SHINE Sites

Congratulations to the Emory/Grady & Columbia teams who have been alternating in the lead for enrollments for all of August! Emory currently has 77 enrollments and Columbia has 76 enrollments to date. Our thanks to the entire team for your outstanding efforts to screen and enroll in the SHINE trial.

Who to contact

Protocol questions – Amy Fansler – (434) 982-6027 or acf7h@virginia.edu
Budget & contracts questions - Amy Fansler – (434) 982-6027 or acf7h@virginia.edu
Recruitment – Katrina van de Bruinhorst – (214) 648-9248 or katrina.vandebruinhorst@utsouthwestern.edu
General education and training – Joy Pinkerton – (734) 232-2138 or joypink@umich.edu
I-SPOT questions – Hannah Reimer – 215-707-5483 or hreimer@temple.edu
Laptop questions – Amy Fansler – (434) 982-6027 or acf7h@virginia.edu
Regulatory & site readiness – Arthi Ramakrishnan – (734) 936-2454 or arthrama@umich.edu
WebDCU support – Kavita Patel – (843) 876-1167 or pateka@musc.edu

24 hour emergency contacts:
SHINE Study Hotline – 800-915-7320
WebDCU Emergency Randomization Hotline – 1-866-450-2016
I-SPOT Study Hotline – 774-234-7768