Minnesota
SPOKE SPLASH
Neurological Emergencies Treatment Trials

The Minnesota NETT Hub: 9 years and more

Michelle Biros, MD MS
Minnesota NETT Hub PI

The NETT research network will be entering its 10th year in spring of 2016. For the last 9 years, we have been an active and energetic Hub within the network. Our last year promises to continue the excitement of engaging in some of the best designed, most relevant clinical trials of neurological emergencies.

Since its inception, NETT has pushed boundaries in terms of new creative study designs, challenging clinical questions conducted in emergent conditions and smooth efficient operations and rapid deployment of multicenter clinical trials. We have studied stroke, traumatic brain injury, pre-hospital seizures management, status seizures, intracranial hemorrhages, and transient ischemic attacks. Along the way the NETT has become recognized as a leader in the conduct of ethical research under high pressure and critical circumstances, and has added to the medical literature on appropriate application of exception from informed consent. Our NETT has served as a model for the creation of other broad research networks, and has provided a prototype for the concept of economies of scale for the completion of complex clinical trials.

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Our Minnesota NETT Hub has done amazing things in creating a very strong local and regional network. Since we began nine years ago, we have been very active contributors to all NETT trials (ALIAS, RAMPART, ProTECT III, SHINE, POINT, ATACH-2 , soon to launch ESETT, and various supplemental biomarker studies) and have included many academic and community institutions within our network (UMMC, Fairview Southdale, Mayo – St Mary's, Abbott Northwestern, Ridgeview – Waconia and Two Twelve, HCMC, Regions, North, United, Kansas City Medical Center, Essentia – St. Mary's Duluth, Essentia - Fargo, Masonic Children's). It has been a pleasure developing these research relationships, and exciting to connect with regional researchers of like mind to help develop new and better management options for patients with neurological emergencies.

The next year proves to be equally exciting. We continue with SHINE and POINT and will soon be launching ESETT. In addition, a number of studies that will address spinal cord injury, pre-hospital stroke interventions, and traumatic brain injury are in the works from the national NETT. We will keep you informed and gauge your interest in these various studies as their final protocols evolve.

The NIH has informed us that with the next five-year cycle of funding for the NETT will morph into a different sort of research network. It will still be managed by the National Institute for Neurological Disease and Stroke but will also work with the National Heart, Lung and Blood Institute. The pathologies we will study will include not only neurological emergencies but also broader aspects of acute emergent resuscitation. The funding mechanism for the new network will also likely be different with more direct NIH contracting with institutions. Once the finalized description of the new network is provided, we will approach our current spoke institutions and discuss their ability and interest in continuing our network collaboration through the University of Minnesota Hub.

It is clear that the University of Minnesota NETT Hub and its Spokes have a lot to be proud of and a lot to look forward to. We thank all of our participating institutions and investigators, their research coordinators, their study nurses, research assistants and their interested research clinicians for all of the delightful interactions and collaborations that we have developed. We will contact each of you soon for visits to outline our accomplishments in more detail and describe our hopes for the future of our regional network.

We offer our most sincere gratitude for your help in making the Minnesota NETT so successful and for your assistance in helping to create new and better management strategies for our acutely ill and injured patients. ■

Announcements

Kathleen Miller, BSN, CCRC
MINNESOTA HUB MANAGER

Hello everyone, and thank you for your contributions to a productive year with research studies. Minnesota continues to be a leader with the POINT study and climbing the ladder in our standings with SHINE. The ATACH-II study will close out in early 2016 at several sites in Minnesota as well.

NETT hopes to build on its success with the RAMPART trial by undertaking ESETT (Established Status Epilepticus Treatment Trial) in 2015. This study will take place in the Emergency Department under Exception From Informed Consent (EFIC) regulations. Welcome to our new investigators from HCMC, University of Minnesota: UMMC, Masonic, Southdale, and Regions and Mayo. Spoke recruitment is still open for this study. Please contact me (mill4109@umn.edu) if you are interested in ESETT. ■

Staffing Updates

Coordinators can provide their expertise for studies and help you with regulatory questions, assist with training new personnel and generally help you navigate DCR (Data Clarification Requests), WEBDCU and as needed we provide enrollment support to spokes.

Our goal is to visit each spoke at least once a year or have a conference call with research team members. Don't hesitate to invite us to attend a staff meeting to answer questions or meet your staff.

ESETT Study Coordinator: Abbey Staugaitis, RN (staug002@umn.edu)

If you have an interest in learning more about ESETT, we are happy to meet with you and/or your team on site.

ON CALL Staffing: to keep our sites enrollment ready 24/7, we rely on our regular staff and a group of select coordinators.

Amanda Weller, RN, joined our team in October to work with StrokeNet and NETT. She managed to score two POINT enrollments and one SHINE enrollment within 5 days!

Justin Eklund is an evening and weekend on call staff. His day job is coordinating cancer studies but enjoys emergency medicine studies with a background as an EMT.

Michelle Lambert, RN takes call for us weekends and evenings also. She works full time at HCMC and has many years of Emergency Department and cardiology experience. ■

ESETT: The Basics

Established Status Epilepticus Treatment Trial

The primary objective of ESETT is to determine the most effective and/or the least effective treatment of benzodiazepine-refractory SE among patients 2 or older.

The primary outcome is clinical cessation of status epilepticus, without recurrent seizures, or use of additional anti-seizure medications within 60 minutes of the start of study drug infusion. Clinical cessation of SE consists of absence of clinical seizures and improving responsiveness.

Population: Patients 2 years or older (no upper age limit) witnessed to have a clinically apparent seizure who continue to have seizure activity in the ED after having received an adequate dose of benzodiazepines (first-line agents)
(diazepam 10 mg IV, lorazepam 4 mg IV, or midazolam10mg IV or IM for subjects above 40 kg, and diazepam 0.3mg/kg IV, lorazepam 0.1 mg/kg IV or midazolam 0.3mg/kg IV or IM for subjects between 10-40 kg)

Intervention: Subjects will be enrolled under EFIC guidelines by ED staff and administered 1 of the following study drugs by IV infusion over 10 minutes: fosphenytoin (Cerebyx), levetiracetam (Keppra), or valproic acid (Depakote)- (second-line agents). Subjects ar obsereved for an additional 10 minutes after the end of study drug infusion. At that point, physicians can select additional anti-seizure medications (Third-line agents) as necessary, or continue to observe the subject and assess for improved responsiveness through the remaining 60 minutes post-study drug infusion.

Consent: Subjects are enrolled under Emergency Research Exception From Informed Consent (EFIC) guidelines. Research personnel will obtain consent for continued participation from the subject OR Legally Authorized Representative as soon as possible after enrollment.

Study Participation: From the start of study drug infusion through hospital discharge.

IRB submissions will require community consultation. Our research team led by Dr. Biros attended numerous events and locations to obtain public opinion from the general public and this patient population. ■

We are happy to provide your spoke with the community consultation results to use for your submission.

ESETT

Investigator HOTLINE: 1-855-ESETT-PI (373-8874)

-Inclusion Criteria-

- Seizing for >5 minutes
- Continued/recurring now despite adequate benzo
- Last dose of benzos given >5 minutes ago
- Last dose of benzos given <30 minutes ago
- Age ≥ 2 years

-Exclusion Criteria-

- **Known** pregnancy, severe metabolic/liver/renal disease
- **Known** allergy or contraindication to:

  phenytoin (Dilantin), fosphenytoin (Cerebyx), levetiracetam (Keppra), or valproic acid (Depakote)
- **For this episode** of status epilepticus already...

  given intravenous 2nd line anticonvulsant or

  non-benzo sedatives with anticonvulsant properties (propofol, etomidate, ketamine, etc) or

  endotracheally intubated
- Status epilepticus thought to be caused by:

  hypoglycemia < 50 mg/dL

  hyperglycemia > 400 mg/dL

  acute traumatic brain injury

  cardiac arrest/post anoxia
- Prisoner
- Opt-out identification declining ESETT

POINT

Platelet Oriented Inhibition in New TIA and minor ischemic stroke

POINT Study Lead Coordinator: Abbey Staugaitis, RN (staug002@umn.edu)

Abbey coordinates the work done at all sites and runs interference as needed to get your questions answered. Her usual work schedule is Tuesday to Friday.

The POINT study aims for 90 enrollments/month to meet the NIH milestone in February. Minnesota made great contributions in November with 5 enrollments. Please help us capture all potential enrollments. We have consistently been among the top four enrolling NETT Hubs since the study started in 2010. Thank you!

POINT Study tip: if the 90 day research visit cannot be conducted in person, a telephone visit is acceptable. Please be sure to document the visit in WebDCU.

Reminder: track biomarker samples when they go to your lab for storage before shipping. Also make sure you get a tracking number when they are shipped and save with your study records. ■

SHINE

Stroke Hyperglycemia Insulin Network Effort

SHINE Study Lead Coordinator: Julie Scherber, RN (sche0245@umn.edu)

Julie manages all patients enrolled at HCMC and UMMC (currently our only active spokes). She is expert with issues that arise during study participation. Her usual work schedule is half days Monday – Friday. The study passed the 50% enrollment target in early November. The goal is 1400 within 2- 3 years.

The study is still recruiting a limited number of sites. Please let us know if you have interest in pursuing this study. ■

NETT NewsFlash

December 2015

Enrollment Update:
As of 12-22-15 at 9:51a (EST)

Arizona	52	8	
Cincinnati	149	19	<5
Emory	80	85	<5
HFH	52	5	
Kentucky	51	38	<5
Maryland	42	9	
Mass General	44	10	
Minnesota	134	11	
NYP	56	87	
Ohio State	4 *(16 Emmes)*	56	<5
OHSU	54	6	<5
Pittsburgh	21	35	
SUNY Downstate	59 *(25 Emmes)*	14	
Stanford	110	27	<5
Temple	73	28	
Texas	94	35	<5
UCLA	3 *(30 Emmes)*	10	
UCSF	70	11	<5
UPenn	258	24	
VCU	12	<5	
Wayne State	145	14	
Wisconsin	76	12	
PECARN (ESETT only)	-	-	<5
Emmes and OUS (POINT only)	1654	-	-
Ancillary Sites (SHINE only)	-	184	-
TOTAL	3293	728	9

POINT Primary Drug recipient: If there is a change of staff in this role, ***update the Spoke Team Member Table AND the Project Spoke Table*** to reflect this change and to ensure drug resupply is not interrupted.

HAPPY HOLIDAYS

NETT Network
Contact Us: nett-contact@umich.edu (734) 232-2142 Website: http://nett.umich.edu

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