Welcome!

The Minnesota Spoke Splash is the monthly newsletter of the Minnesota NETT Hub. If you know of others who should receive this newsletter directly, if you would like to change your email subscription, or if you have comments or suggestions, please submit them to Marinda Bland (blan0181@umn.edu).

Why Research Networks Matter

Michelle Biros, MD, MS
Minnesota NETT Hub PI

It has been over 15 years since the FDA approved a medical intervention for acute ischemic stroke, and there has been no new medical treatment for traumatic brain injury for at least 30 years. The results of several large ongoing stroke trials were presented last month at the 2013 International Stroke Conference. These studies looked at medical, intravascular, and surgical treatment of ischemic and hemorrhagic stroke and well as TIA's. Among these many trials, thousands of patients and millions of dollars were involved. Unfortunately, most of these trials had negative outcomes, despite years of trying.

The National Institute of Neurological Disorders and Stroke (NINDS) has invested in stroke research for almost forty years, determined to support the discovery of new treatments. The need for protocol support, regulatory review and oversight, data management, and stringent recruitment criteria have proved daunting to many individual investigators. In addition, the relative rarity of these conditions prolong the enrollment phase if a powerful enough number of subjects is to be recruited; many recent clinical trials have taken up to 10 years to complete.

Continued on page 2
To improve the efficiency of research logistics and the likelihood of robust and rapid enrollment, NINDS has endorsed the concept of research networks that can capitalize on economy of scale and reduced redundancy of expensive services. Research networks also have the advantage of bringing together like-minded individuals who all share the same goal of advancing patient care in devastating conditions. Networks provide a testing ground for possible projects; the shared expertise of their components help keep the protocols practical and also help hasten the “go/no go” decision about a complex medical research trial. The NINDS has made a commitment to prioritize funding of networks. The reality of the current economics of research makes such networks the best bet for answers to complex research problems.

The Neurological Emergencies Treatment Trials (NETT) is only one of several networks sponsored by NINDS. Unlike most other neuro-based networks, the NETT focuses on the acute phase of treating neurological emergencies, and NETT is the only supported neurological network that has addressed pre-hospital care of these conditions. The NETT is comprised of 17 academic Hub sites, each with several “Spokes”, which are medical facilities, systems and institutions where patients are recruited into research trials.

Nationally, research networks provide a cost effective method of obtaining important answers in a rapid manner. Locally, network benefits also include advancing reach involvement and sophistication, developing effective communications and collaborations between many different medical disciplines, and of course offering our patients the opportunity to participate in research that otherwise would not be available to them.

At the 2012 Minnesota Stroke meeting, our Hub presented findings of additional benefit to research and network participation. The poster we presented is included on the next page.

GRANT ANNOUNCEMENT

NINDS Stroke Trials Network - Regional Coordinating Stroke Centers (U10)

The University of Minnesota intends to submit a grant for this Stroke Trials Network. The deadline is May 15, 2013. We hope that we can count on your support and interest in participating in this new Network. Our understanding is that new stroke trials will be directed toward through this network. You can expect a phone call or email from Mustapha Ezzeddine or Michelle Biros very soon. Or if you prefer, please send us an email to let us know of your interest: mlil4109@umn.edu.

Legislative Update from the MDH for Acute Stroke Care Systems

Legislation has passed through two legislative committees without opposition. AHA has spearheaded this effort to ask for permission for MDH to certify Minnesota Hospitals as Acute Stroke Capable if they meet certain standards. Stroke Centers that have already been certified by TJO are exempt from this process and automatically granted this status.

In addition, the legislation will provide EMS with the authority to develop stroke transport policies.
The Benefits From Research Participation
Michelle Biros, MD, MS; Kathleen Miller, BSN, CCRC; Kathy France, PHN, CCRC/CCRA; Corey Sargent, MA, NREMT-P, CCRC

Neurological Emergency Treatment Trials

The NETT Research Network
The Neurological Emergency Treatment Trials (NETT) is a NINDS funded research network that includes 17 academic “Hub” centers. The Hubs provide local infrastructure and administrative support for NETT studies, all of which are interventional and aimed at some aspect of emergency medical care. Each Hub works with “Spokes”, which are local institutions where patients are enrolled into NETT studies.

The Minnesota NETT Hub
The Minnesota Hub is housed at the University of Minnesota and its Co-PIs are from the Departments of Emergency Medicine and Neurology. The Minnesota Hub has 11 Spokes, each of which participate in some or all of the NETT studies (Table 1).

Minnesota NETT Hub Success
In its five year existence, the NETT and the Minnesota Hub have successfully implemented 5 research studies.

Table 1: Spoke ED Census Spoke-Hub Relationship
<table>
<thead>
<tr>
<th>Spoke</th>
<th>ED Census</th>
<th>Spoke-Hub Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCMC (Level 1)</td>
<td>101,000</td>
<td>NETT Direct</td>
</tr>
<tr>
<td>Regions (Level 1)</td>
<td>70,881</td>
<td>NETT Oversight</td>
</tr>
<tr>
<td>North Memorial (Level 3)</td>
<td>74,140</td>
<td>Blended</td>
</tr>
<tr>
<td>United</td>
<td>45,355</td>
<td>NETT Direct</td>
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<tr>
<td>Mercy</td>
<td>57,167</td>
<td>Blended</td>
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<tr>
<td>Abbott-Northwestern</td>
<td>44,660</td>
<td>NETT Direct</td>
</tr>
<tr>
<td>Ridgeview</td>
<td>20,998</td>
<td>NETT Direct</td>
</tr>
<tr>
<td>UVMC - Fairview</td>
<td>48,157</td>
<td>NETT Direct</td>
</tr>
<tr>
<td>Fairview Southdale</td>
<td>43,602</td>
<td>NETT Direct</td>
</tr>
<tr>
<td>Essentia - Duluth</td>
<td>42,000</td>
<td>NETT Oversight</td>
</tr>
</tbody>
</table>

Unanticipated Benefits of Research
As research studies are conducted at our Spokes, we observed some unanticipated beneficial “side effects” of study participation. These include benefits to patients, caregivers, local institutions, clinicians and other health professionals.

Patient Benefits
- Perceived (or real) extra personal attention, “caring”.
- Better understanding of diagnosis because of the required details of the consent process.
- Resources provided during research follow-up calls.
- Extra vigilance with lab results, and observing for neurologic worsening.
- Patient advocacy with patient care teams because of contact between the patient and research team.
- Additional and prolonged follow-up with patients.
- Added care without added cost (when above Standard of Care).
- Better adherence to medication regimens.
- Extra teaching by the research team to further patient understanding of diagnosis, treatment, and recovery.

Caregiver-Family Benefits
- Long term follow-up provides encouragement with injury recovery progress.
- Research visit quality of life assessments can provide more insight into stroke / injury deficits.
- Monthly to annual follow-ups are done.
- Long term resource for families to ask “What is normal?”
- Research team is not part of the “hierarchy” of medical providers; families feel more comfortable with questions.
- The relationship with the research team allows identification of potential contacts as needed.

Health Care Professional Benefits
- Focused care for the patient population involved in the study.
- Increased awareness of similar research findings related to the patient population.
- Recognition for contributions to the medical sciences.
- Well vetted research protocols.
- Opportunities for professional exchanges with practitioners locally and from other U.S. regions and countries.
- Opportunities for side research studies.

Institutional Benefits
- Training/standardization of assessments by research and medical care teams (may improve quality of care).
- Documentation expectations improved.
- Attention to more details with patient follow-up (such as additional QOL assessments, etc.)
- Longer term patient follow-up and QOL assessments than may otherwise be possible.
- Feedback from research team to the medical team related to patient status between clinic visits.
- Recognition nationally for research participation.
- Hospitals can be among early adopters of new research / treatment concepts and technologies.
- Ability to “test drive” new patient care technologies.
- Protocols can drive change and standardization with other high profile centers.
- Protocols may provide opportunities to drive improved patient care management guidelines based on best evidence. “Best Practices”
- Patient feedback regarding medical care can be obtained by neutral observers (research team)
- Promote cross collaboration for research (neurology and emergency medicine), which can have long term clinical benefits.
- Medication adherence and issues can be consistently monitored during research follow-up.

Summary
Availability of a regional research infrastructure such as the Minnesota NETT Hub provides resources to supplement local Spoke research capabilities.

In addition to providing input related to the study question, research involvement has unanticipated patient, professional and institutional benefits.
ProTECT

Progesterone for the Treatment of Traumatic Brain Injury

Lessons learned from ProTECT Monitor Visits

One thing that we have noticed is that the NETT continues to refine its monitoring standards with each visit. In other words, the bar continues to rise for all of us as the NETT matures with the challenges of each study. Regions Hospital had an extended monitor visit March 4-7 for ProTECT due to its high enrollment. They were complimented for the QA processes they have implemented to ensure quality data collection and follow through.

Reminders and suggestions:

1) Clinical Standards: the sponsor’s expectation that neurosurgery follows the Clinical Guidelines set forth in the protocol. For example, the protocol specifies Dilantin use over newer agents. This takes vigilance by PIs and Study Coordinators to make sure it is followed. Also, EVDs need to remain closed unless the ICP is greater than 20.

2) Nursing documentation and cooperation is vital in this study: CPP is the “driver” in this study and needs to be verified hourly in the electronic medical record (or it is lost forever). Tapering errors are common in the last 24 hours unless research staff stays in communication with nursing staff when the rate needs to change.

3) Consents: Reminder that when the patient is deemed competent to sign their own consent (6 month visit), that an additional entry is made on the Informed Consent Log.

4) Verbal Information: reminder that if a lab result needed to screen eligibility (such as an ETOH level or pregnancy test) is first given verbally and later posted to the medical record, to make sure that it is documented and kept in the patient study book. The timing of lab results is closely reviewed for protocol deviations.

ProTECT Minnesota Spokes Enrollment Summary

<table>
<thead>
<tr>
<th>Spoke</th>
<th>Active</th>
<th>Enrollments</th>
</tr>
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<tr>
<td>Hennepin County Medical Center</td>
<td>09/03/2010</td>
<td>14</td>
</tr>
<tr>
<td>Regions Hospital</td>
<td>11/04/2010</td>
<td>47</td>
</tr>
<tr>
<td>North Memorial Medical Center</td>
<td>09/02/2011</td>
<td>6</td>
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ProTECT National Hub Enrollment Ranking

<table>
<thead>
<tr>
<th>Rank</th>
<th>Hub</th>
<th>Enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cincinnati, Emory</td>
<td>74</td>
</tr>
<tr>
<td>3</td>
<td>Arizona</td>
<td>72</td>
</tr>
<tr>
<td>4</td>
<td>Minnesota, Stanford</td>
<td>67</td>
</tr>
<tr>
<td>6</td>
<td>Texas</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>Total Enrollment Nationwide: 713</td>
<td>Enrollment Goal: 1140</td>
</tr>
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</table>
Platelet-Oriented Inhibition in New TIA and minor ischemic stroke Trial

The optional ancillary biomarker study is available at all of our sites now. This involves one blood draw as close to the time of randomization as possible. It is not a requirement for patients to participate in the study. POINT Study will be locking data on 3/15/2013. Please make sure all DCR's have been addressed by this Friday. They are planning to do an interim analysis for the DSMB.

### POINT Minnesota Spoke Enrollment Summary

<table>
<thead>
<tr>
<th>Spoke</th>
<th>Active</th>
<th>Enrollment</th>
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<tr>
<td>Hennepin County Medical Center</td>
<td>June 2010</td>
<td>17</td>
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<tr>
<td>UMMC - Fairview</td>
<td>November 2010</td>
<td>10</td>
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<tr>
<td>Fairview Southdale Hospital</td>
<td>July 2010</td>
<td>7</td>
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<tr>
<td>Regions Hospital</td>
<td>January 2012</td>
<td>24</td>
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<tr>
<td>Ridgeview Medical Center</td>
<td>February 2012</td>
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### POINT National Hub Enrollment Ranking

<table>
<thead>
<tr>
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<th>Hub</th>
<th>Total Enrollments Nationwide: 1343</th>
<th>Total Enrollment Goal: 4150</th>
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<tr>
<td>1</td>
<td>UPenn</td>
<td>119</td>
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<td>2</td>
<td>Wayne State</td>
<td>73</td>
<td></td>
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<tr>
<td>3</td>
<td><strong>Minnesota</strong></td>
<td><strong>59</strong></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Cincinnati</td>
<td>54</td>
<td></td>
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<tr>
<td>5</td>
<td>Texas</td>
<td>42</td>
<td></td>
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We are looking forward to HCMC becoming an active site in the coming week. Prospective sites that utilize paper order sets for research may find it easier and faster to get started without the EPIC order set delays we have encountered at our 2 sites. If you would like examples of paper or EPIC order sets, please let us know.

We now have IRB approval for Version 2.0 at UMMC, which lifted the restriction of randomization within 3 hours of ED arrival. We expect that this will improve enrollment as patients are eligible within 12 hours of stroke onset or last known well if they are hyperglycemic during the first 12 hours of stroke.

Reminder: Drip and ship patients are potential candidates as well as new inpatient strokes.

### SHINE Minnesota Spoke Enrollment Summary

<table>
<thead>
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<th>Spoke</th>
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<td>UMMC - Fairview</td>
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### SHINE National Hub Enrollment Ranking

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<th>Total Enrollment Nationwide: 99</th>
<th>Total Enrollment Goal: 1400</th>
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<tr>
<td>Rank</td>
<td>Hub</td>
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<tr>
<td>--------</td>
<td>--------------------------</td>
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<tr>
<td>1</td>
<td>Emory</td>
</tr>
<tr>
<td>2</td>
<td>NYP</td>
</tr>
<tr>
<td>3</td>
<td>Kentucky</td>
</tr>
<tr>
<td>5</td>
<td>Texas, Temple</td>
</tr>
<tr>
<td>7</td>
<td>Cincinnati, Ohio State</td>
</tr>
<tr>
<td>9</td>
<td>Minnesota, Wayne, Wisconsin</td>
</tr>
<tr>
<td>12</td>
<td>Stanford, Pittsburgh, Maryland, UCSF, UPenn</td>
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</tbody>
</table>
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Ridgview Medical Center
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University of Minnesota Medical Center
Hennepin County Medical Center

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