NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

SEPTEMBER 2022 | VOLUME 1 | ISSUE 6

FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Toyoda

Intracerebral hemorrhage (ICH) is much more devastating than ischemic stroke. Nevertheless, the impact of acute therapy for ICH lags far behind that for acute ischemic stroke. An established therapeutic strategy for acute ICH analogous to reperfusion therapy for acute ischemic stroke has not been established. In the nationwide registry of the Japan Stroke Data Bank, functional outcomes improved for ischemic stroke patients over the past 20 years after age adjustment but did not improve for ICH patients. The lack of an established strategy might be an essential reason for the difference. Recombinant factor VIIa (rFVIIa) is a promising agent that can fill the gap of the therapeutic strategies between ischemic stroke and ICH. How wonderful if rFVIIa is widely used globally for acute ICH patients as a standard therapy like rtPA!

Kazunori Toyoda, MD, PhD
Deputy Director General of the Hospital,
Chair, Department of Stroke and Cerebrovascular Diseases,
National Cerebral and Cardiovascular Center, Suita, Osaka, JAPAN
FATEST Japanese National PI

Please join us for the *FASTEST* Monthly Webinar

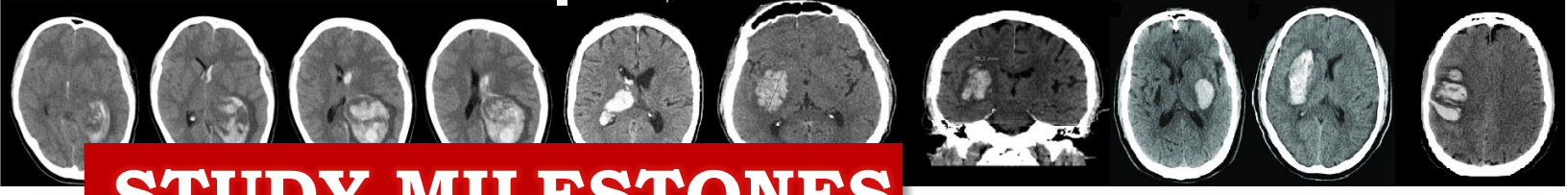
Wednesday September 21ST, 2:00-3:00 pm EST

- Dr. Digvijaya Navalkele from Grady Memorial Hospital, Emory University will be presenting their recent case and sharing their experience of first enrollment at their center.

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

Meeting ID: 957 6834 3105
Passcode: 111641

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



STUDY MILESTONES

Total Sites Released to Enroll: **38** (**18** USA, **3** Germany, **12** Japan, **1** Spain, **3** Canadian, **1** UK)

Total Randomization = **23**

- US Randomizations: **10**,
- International randomizations: **13** (5 Canadian, 3 Germany, 3 Japan, 2 Spain)

Randomization this month (last 30 days) = **7**

Total Screen Failures = **81**

Subjects Randomized by MSU = **1**

Subjects Terminated Early = **0**

eConsent Used = **0**

Remote Consent Used = **0**

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinar: **Wednesday, September 21st @ 2:00-3:00 pm EST**

FASTEST study team office hours: **Monday, September 19th @ 2:00 pm EST**

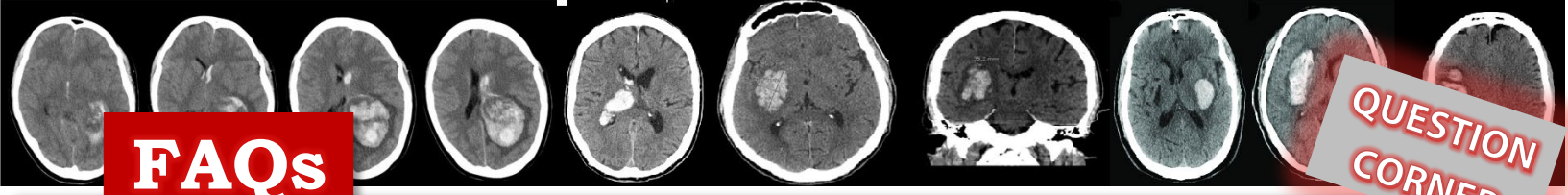
FASTEST Investigator's Meeting: **Monday November 7th , 2022 @ 2:00 - 4:00 pm EST**

Important Update

During our July meeting with the DSMB the status of site activation was of concern. The DSMB is asking that all sites that have an approved EFIC plan, complete their EFIC activities and be activated by the end of this year, 2022.

Emily Stinson stinsoey@ucmail.uc.edu NCC Project Manager is the point of contact for EFIC. Please reach out to her for assistance if your site has not completed the EFIC process. The FASTEST study team is committed to help all remaining sites finish with EFIC and get open for enrollment as soon as possible.

Please reach out us for guidance and updates.



FAQs

QUESTION CORNER

Q: Are there any issues using glass versus plastic syringes (electrostatic properties of glass versus plastic)?
A: The histidine syringes provided in the kit are glass syringe provided by Novo and the package insert allow to utilize the Lure-Lock plastic syringe for administration if needed.

Q: If the kits are stored in a 10C fridge, how long would it take to come to room temperature?
A: Novo recommends the rule of thumb of 15 minutes (thaw time) for the refrigerated study drug. Therefore, we recommend sites to store IP at room temperature if possible, if not, we recommend that site pull the kit from fridge as soon as they have a potential patient to allow for "thaw time". The kits can be put back in the fridge if the patient deemed not eligible AND the kit is still sealed.

Q: There is hematoma expansion/growth in our patient without clinically significant neurological deterioration/ worsening (24 hrs. NIHSS unchanged from baseline NIHSS?
A: Hematoma expansion/growth without clinically significant neurological deterioration/worsening should be documented as non-serious AE. This is similar to how we document the rise in troponin levels without clinically significant deterioration as non-serious AE.

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: Can we use our own temp. monitoring logs?
A: All areas where study drug is stored (including MSUs) must be monitored continuously for temperature excursions and the temperature monitoring system, at a minimum, must provide a daily minimum and maximum temperature. Sites may use their own institution-specific or electronic study drug temperature monitoring log to document temperature readings if such temperature log is deemed equivalent. The original Study Drug Temperature Log must be filed in the master file at the site and available for monitoring visits.

Q: Who can compound the study drug?
A: Trained Pharmacy staff, physicians (PI AND Sub-I) and trained Coordinators with a **medical license** including drug compounding within their scope of practice can compound and prepare study drug for administration. There is no need to delegate this responsibility on the DoA and should be a study team determination. Training on compounding study drug video can be found in the WebDCU training campus under the FASTEST project WebDCU™ Campus - Training Center (musc.edu).

Q: What is the timeline to report SAEs?
A: All SAEs must be reported in WebDCU™ within **24 hours** of site investigator's awareness of the event and must be followed for the duration of the study follow-up or until resolution, whichever comes first. Kindly note that all SAEs will be recorded from the time of randomization through **Day 90**. However, mortality is reported through end of study **(day 180).** Kindly remember that Death due to the natural history of ICH will be recorded as a non-related SAE. Additionally, all serious but known complications of ICH (i.e., malignant brain edema) will be recorded as non-related SAEs. Please refer to our study MOP sent to all the participating sites earlier.

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

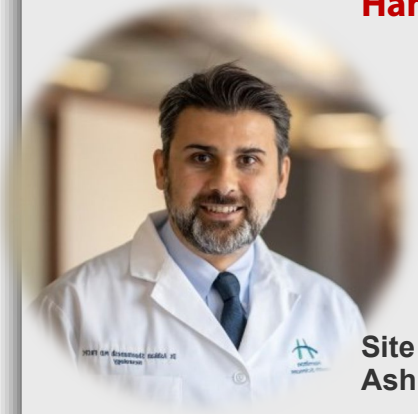
New Sites... Welcome Aboard!

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

Queens Medical Centre, Nottingham, United Kingdom

Site PI:
Ganesh Subramanian, FRCP

Hamilton General Hospital, Hamilton, ON, Canada



Site PI:
Ashkan Shoamanesh, MD

The Queen's Medical Center, Honolulu, HI

Site PI:
Chung-Huan Sun, MD

New Sites... Welcome Aboard!

University of Utah Healthcare, Salt Lake City, UT

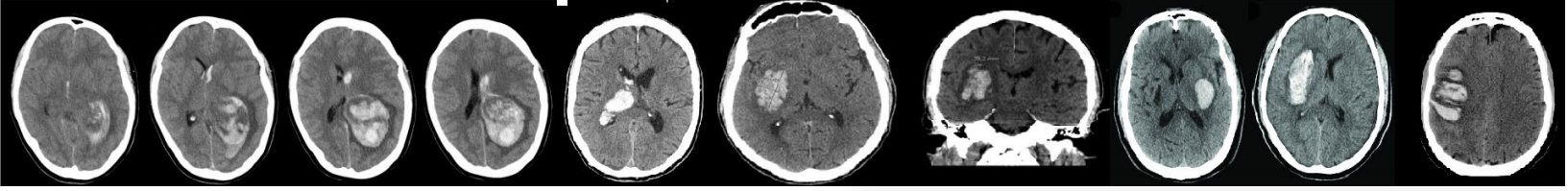
Site PI:
Ramesh Grandhi, MD, MS

Central DuPage Hospital, Winfield, IL

Site PI:
Harish N. Showkeen, MD

M Health Fairview Southdale Hospital, Edina, MN

Site PI:
Christopher Streib, MD

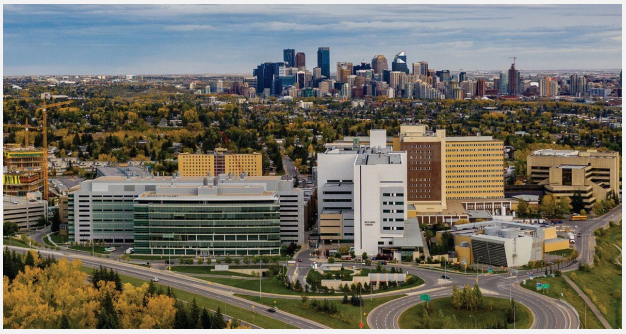


University of Minnesota Medical Center Hospital, Minneapolis, MN

Site PI:
Christopher Streib, MD

Congratulations on First

Congratulations Dr. Kazunori Toyoda and team at the National Cerebral and Cardiovascular Center, Osaka, Japan for enrolling their first subject in *FASTEST*.



Congratulations Dr. Demchuk and team at the University of Calgary - Foothills Medical Centre, Calgary, AB, Canada for enrolling their first subject in *FASTEST*.

Congratulations Dr. Digvijaya Navalkele and team at the Grady Memorial Hospital, Atlanta, GA for enrolling their first subject in *FASTEST*.

Congratulations Dr. Teruyuki Hirano and team at the Kyorin University Hospital, Tokyo, Japan for enrolling their first subject in *FASTEST*.

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.

1. **Central DuPage**
2. **University of Utah**
3. **Memorial City**
4. **The Queens MC**
5. **University of Minnesota**
6. **M Health Fairview Southdale**

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

1. **Providence St. Vincent**

Thank you for the sites preparing for Advarra CIRB submission:

1. **North Shore**
2. **Prima Health**
3. **Cedar Sinai**
4. **Ohio Health (OSU, Riverside, Mt. Carmel)**
5. **Promedica Toledo, OH**

Thank you for sites scheduled for Readniness Calls

1. **Mills Peninsula**

Top Enrolling Site

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

Subjects enrolled = 5!!

Congratulations to the Enrolling Sites Past Month (30 days)!

University of Calgary - Foothills Medical Centre, Calgary, AB, Canada	**3 Subjects**
Kyorin University Hospital, Tokyo, Japan	**1 Subject**
Grady Memorial Hospital, Atlanta, GA	**1 Subject**
National Cerebral and Cardiovascular Center, Osaka, Japan	**1 Subject**
Vall d'Hebron Hospital, Barcelona, Spain	**1 Subject**

Looking forward to 1st Enrollment from UK!

SCIENCE CORNER

RESEARCH ARTICLE OF THE MONTH

Mechanism of Spontaneous Intracerebral Hemorrhage Formation: An Anatomical Specimens-Based Study

Radosław Rzepliński, Mikołaj Sługocki, Sylwia Tarka, Michał Tomaszewski, Michał Kucewicz, Krzysztof Karczewski, Paweł Krajewski, Jerzy Małachowski and Bogdan Ciszek

Originally published 8 Sep 2022/ https://doi.org/10.1161/STROKEAHA.122.040143 / Stroke. 2022;0:10.1161/ STROKEAHA.122.040143

Background: Despite advances in understanding various risk and prognostic factors, spontaneous intracerebral hemorrhage is connected to very high morbidity and mortality, while the therapy is mainly supportive. Understanding of the pathophysiology of initial hematoma expansion is limited due to insufficient clinical data and lack of a suitable animal model

Methods: We injected 40 anatomic specimens of the basal ganglia with contrast medium, scanned them with a micro-computed tomography scanner and analyzed the results of radiological studies, direct and histological examinations.

Results: In 9 cases, micro-computed tomography and histological examinations revealed contrast medium extravasations mimicking intracerebral hematomas. The artificial hematomas spread both proximally and distally along the ruptured perforator and its branches in the perivascular spaces and detached the branches from the adjacent neural tissue leading to destruction of the tissue and secondary extravasations. Moreover, some contrast extravasations skipped to the perivascular spaces of unruptured perforators, created further extravasation sites and aggravated the expansion of the artificial hematoma. There was no subarachnoid extension of any artificial hematoma.

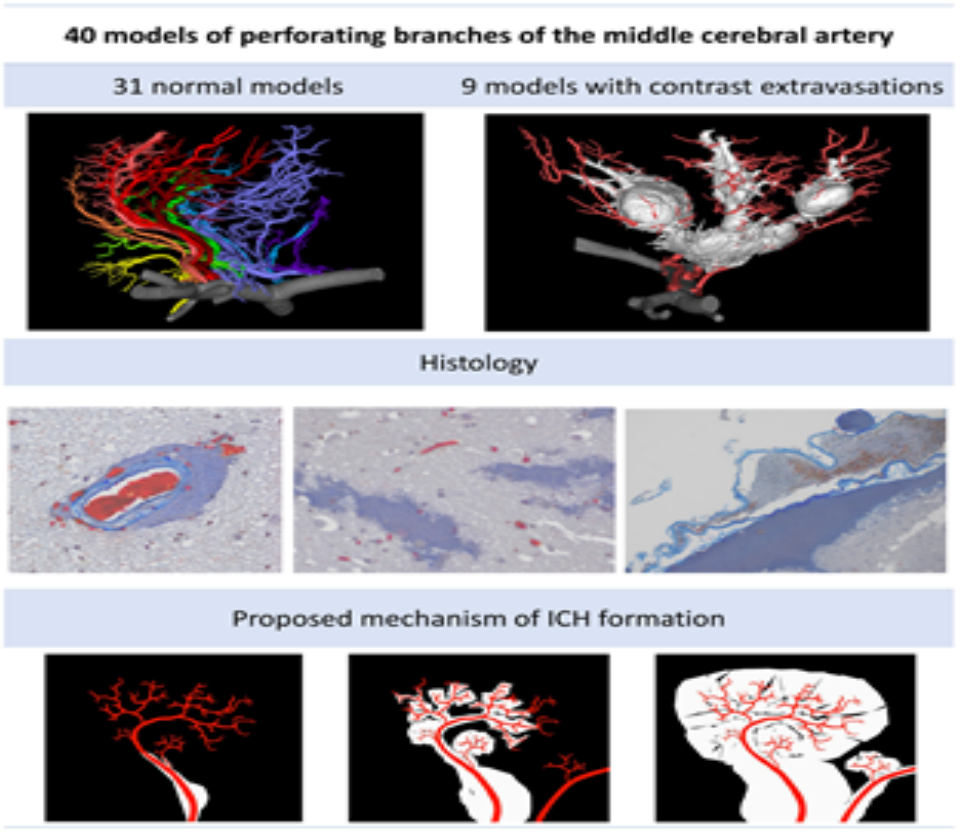
Conclusions: We postulate that a forming basal ganglia intracerebral hematoma spreads initially in the perivascular space, detaches the branches from the neural tissue and causes secondary bleeding. It can also skip to the perivascular space of a nearby perforator. The proposed mechanism of hematoma initiation and formation explains extent of damage to the neural tissue, variability of growth in time and space, creation of secondary bleeding sites, and limited usefulness of surgical interventions. The model is reproducible, the extent of the artificial hematoma can be easily controlled, the rupture sites of the perforating arteries can be determined, and preparation of the model does not require specialized, expensive equipment apart from the micro-computed tomography

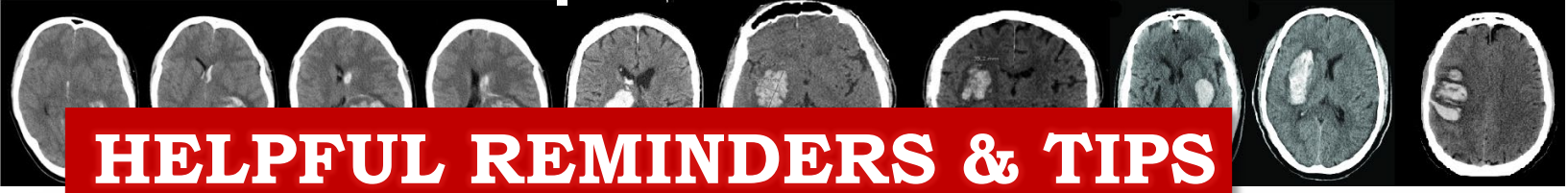
Mechanism of spontaneous intracerebral hemorrhage formation: an anatomical specimens-based study

R. Rzepliński et al. 2022

MEDICAL UNIVERSITY OF WARSAW

Military University of Technology





HELPFUL REMINDERS & TIPS

For Project Managers and Study Teams

- **Updating DoA's and 1572:** For sites updating their DoA's especially if adding or removing sub-investigators. Please remember that you must update these changes in box six of the 1572 and have the PI re-sign the updated form and re-upload to WebDCU.

- Newly approved study wide documents available in the Tool Box in WebDCU

  - **Condensed Radio advertisement** less than 60 sec. Can be used for sites still working on EFIC public disclosures. **REMINDER:** All radio advertisements recordings need to be submitted for CIRB approval prior to ad running.

  - **Consent conversation script**- This is **NOT** a consent document but a script of a conversation that can be used to help explain EFIC and emergency consent to LAR's and/or subjects.

- **Screen failure logs: Please update the screen failure logs in WebDCU screen failure data is very important to the study**.

- **CTA Amendments:** Please make sure the amended CTA's have been returned to UC for execution.

- eICD templates are being sent to CIRB approved sites that have the amended CTA's fully executed.

- **Uploading of documents:** Please remember to pull approval letters and CIRB approved documents from the CIRBI portal and upload them to WebDCU. It is the sites responsibility to keep their site documents updated and uploaded to WebDCU. If you have questions about where to upload your documents please reach out to Emily Stinson stinsoey@ucmail.uc.edu

- **Study team office hours:** Please join the FASTEST study team office hours. Calendar invites have been sent out. This is an informal meeting to answer questions and provide additional training and support. We will meet biweekly on **Monday's at 2pm EST each month.** We highly recommend that you attend regularly as we plan to touch on many topics. We especially encourage new study coordinators to join to help get acclimated to FASTEST as well as spend time collaborating with different FASTEST study sites.

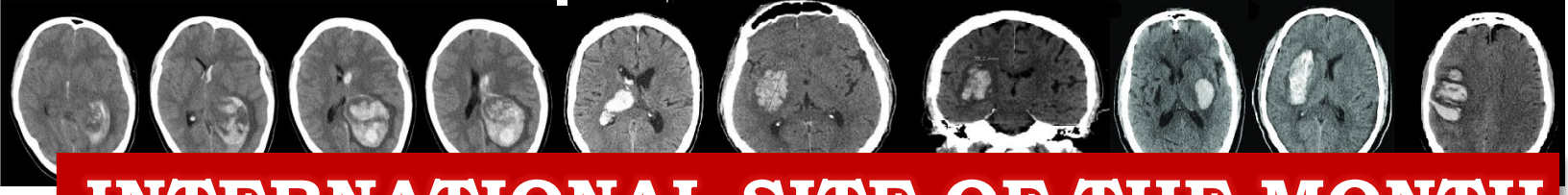
- **As you are completing EFIC events, please complete the CC and PD forms in WebDCU™**. The updated EFIC Forms Resource Guide is available in WebDCU™ (in the Toolbox under Project Documents) and is a very helpful tool for completing these forms. The FASTEST webinar from March 16th, 2021 (available at 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.

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.**

- Please make sure to disseminate this newsletter to you site pharmacist/s too as it may contain helpful information regarding drug compounding, storage, accountability, etc.



INTERNATIONAL SITE OF THE MONTH

University of Calgary - Foothills Medical Centre, Calgary, AB, Canada

Foothills Medical Centre (FMC) is the largest hospital in the province of Alberta and is located in the city of Calgary. It is one of Canada's most recognized medical facilities and one of the leading research and teaching hospitals. Foothills Medical Centre provides advanced healthcare services to over two million people from Calgary, and surrounding regions including southern Alberta, southeastern British Columbia, and southern Saskatchewan.

FMC includes the University of Calgary Cumming School of Medicine, Hotchkiss Brain Institute, and the Tom Baker Cancer Centre which is a leading center in Alberta for cancer treatment and research. FMC boasts the world's first and most powerful movable MRI machine, which was introduced in January 2009. In addition, the world's first robotic surgery to remove a brain tumor was performed on a patient at the FMC, which also created a landmark in Canadian medical history.

Site PI:

Andrew M. Demchuk, MD

Dr. Andrew Demchuk is a Professor in the Department of Clinical Neurosciences for the Cumming School of Medicine, University of Calgary. He is also Director of the Calgary Stroke Program, Alberta Health Services.

Dr. Demchuk's primary research interests focus on vascular imaging, where he is trying to establish target populations for new stroke treatments by selecting patients based on imaging tests performed in the emergency setting.

In addition to his research and clinical activities, Dr. Demchuk is a member on a number of local, national, and international committees. He is the past board chair for the Heart and Stroke Foundation of Alberta, NWT, and Nunavut and member of the Board of Directors of the Canadian Stroke Consortium. He is currently a member of the Scientific Committee of the European Stroke Conference.

Throughout his career he has received a number of awards, including the Michael S. Pessin Stroke Leadership Prize from the American Academy of Neurology (2003), and the A Keith W Brownell Neurology Teaching Award for resident teaching (2006). He currently holds a scholar award from the Alberta Heritage Foundation for Medical Research (AHFMR).

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/

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