ATACH-II
Antihypertensive Treatment of Cerebral Hemorrhage

Volume 1, Issue 10 | August 2014

Greetings from the Principal Investigator

Dear ATACH-II Colleagues:

As the summer is almost over, it was greatly encouraging to see an increase in enrollment in the months of July and August compared to the slower enrollment in the previous months of May and June. Additionally, thank you all for your outstanding cooperation and participation in the all-site calls that were conducted in July and August. The five major topics that were discussed and the excellent suggestions and comments from the participating investigators are summarized and included in this newsletter. All-site calls with the remaining countries are in progress and we look forward to hearing from each one of you. We are always glad to answer any questions that you may have and provide support if needed.

Again, we are counting on greater commitment from all of you toward reaching our goal of enrolling an average of 40 subjects per month.

Thank you again for your hard work and continued commitment to the ATACH-II study!

Warmest regards,

Adnan I. Qureshi, M.D.

Inside This Issue...

- ATACH-II Leaderboards
- Winners of the ATACH-II Challenge
- Member Bio
- Hematoma Volume Measurement
- Insights and Updates from the All Site Calls
- Recent DSMB Meetings
- Recent Investigators Meetings
- Dr. Qureshi's Visit to China
- Dear Logan
- Article for Additional Reading
- Friendly Reminders
- 2015 Investigators Meeting
- Contact Information

Clinical Coordinating Center
Zeenat Qureshi Stroke Research Center
University of Minnesota
925 Delaware Street SE Suite 300
Minneapolis, MN 55414
Phone: (612) 625-6974 | Fax: (612) 625-7950
www.atach2.com

UNIVERSITY OF MINNESOTA

ATACH-II Site Leaderboard as of August 31, 2014

Rank	Site Name	Country	No.	Principal Investigator(s)	Primary Study Coordinator
1	National Cerebral and Cardiovascular Center	Japan	53	Toyoda, Kazunori	Hirase, Kanae
2	Beijing Tiantan Hospital	China	43	Wang, Yongjun	Ding, Zeyu
3	Kobe City Medical Center General Hospital	Japan	33	Sakai, Nobuyuki	Okitsu, Miyuki
4	Toranomon Hospital	Japan	24	Hara, Takayuki	Matsukami, Mihoko
5	Columbia University	USA	24	Agarwal, Sachin	Falo, Cristina
6	The First People's Hospital of Taizhou	China	21	Wang, Zhimin	Ying, Jiangxian
7	Abington Memorial Hospital	USA	21	Shah, Qaisar	Jonczak, Karin
8	National Taiwan University Hospital	Taiwan	18	Jeng, Jiann-Shing	Lin, Wei-Chi
9	New Jersey Neuroscience Institute, JFK Medical Center	USA	18	Kirmani, Jawad	Porbeni, Charles
10	St. Cloud Hospital	USA	17	Suri, M. Fareed K	Freese, Melissa
	Total Enrolled = 612				

International Leaderboard as of August 31, 2014

Rank	Country	Enrollments	Sites Released to Enroll
1	United States	279	52
2	Japan	173	12
3	China	89	5
4	Taiwan	56	9
5	South Korea	11	3
6	Germany	4	8

Winners of the Summer ATACH-II Training Challenge

Dear ATACH-ll Team:

Following are the first five sites to complete the training of the new Residents and Fellows: Congratulations!!

- University of Pennsylvania, on July 01, 2014
- Hennepin County Medical Center, Minnesota, on July 03, 2014
- UCSD Stroke Center, California, on July 11, 2014
- Yale New Haven Stroke Center, Connecticut, on July 11, 2014
- Regions Hospital – Minnesota, on July 17, 2014

We greatly appreciate your commitment to the ATACH-II trial.

A Special mention to the National Taiwan University Hospital, Taipei, Taiwan for enrolling the 600th Subject. We are getting closer to the half way mark!

Getting to Know the ATACH-II Team - Congratulate Ms. Dale Gamble

Ms. Dale Gamble - ATACH-II Project Coordinator

Ms. Dale Gamble - ATACH-II Project Coordinator at Mayo Clinic, Jacksonville, Florida was nominated by the Principal Investigator Dr. William Freeman for the *Dedicated ATACH-II Team/ Member Award.*

Where did you grow up?
Jacksonville, Florida

What is the best advice you've ever received?
Just do it!

If you could travel anywhere, where would you like to go? I would like to go anywhere with family, food, and fun.

How did you become interested in clinical research? After college I was introduced to a Clinical Trials Manager and learning about their position and career path sparked an interest ☺

What is one of your favorite habits? Waking up early on Saturdays and going to the beach with my daughter.

Do you like to plan things out in detail or be spontaneous? A little of both (but more detail oriented).

Key Enrollment Information for ATACH-II

www.atach2.com

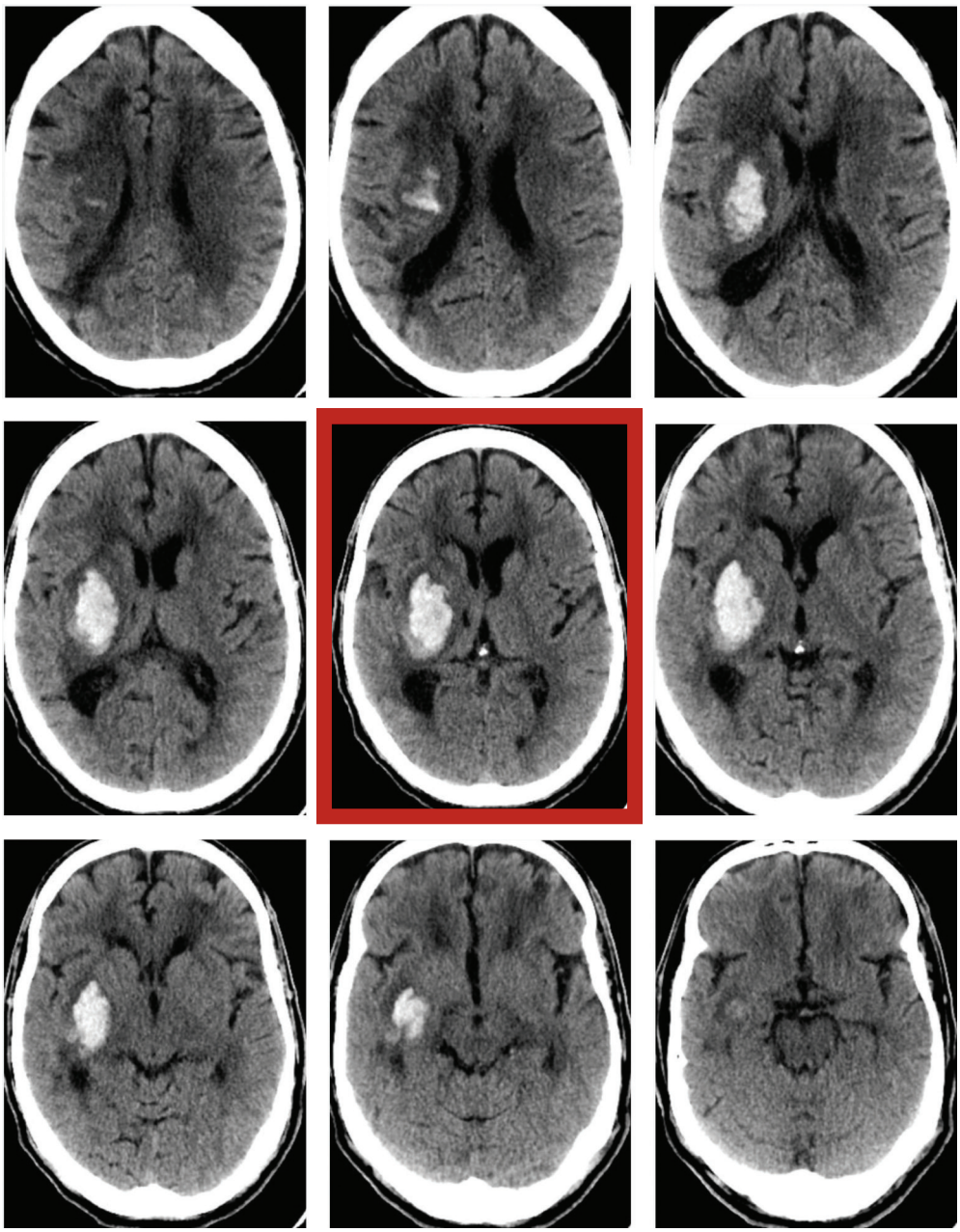
24-Hour Toll Free Hotline: 1-855-870-7205 *or* 952-225-0779
Tell the operator: I have a question regarding the ATACH-II Clinical Study

To randomize: http://dcu.musc.edu/ctms/

Special thanks to Mushtaq Qureshi for his imaging expertise and contributions to this project.

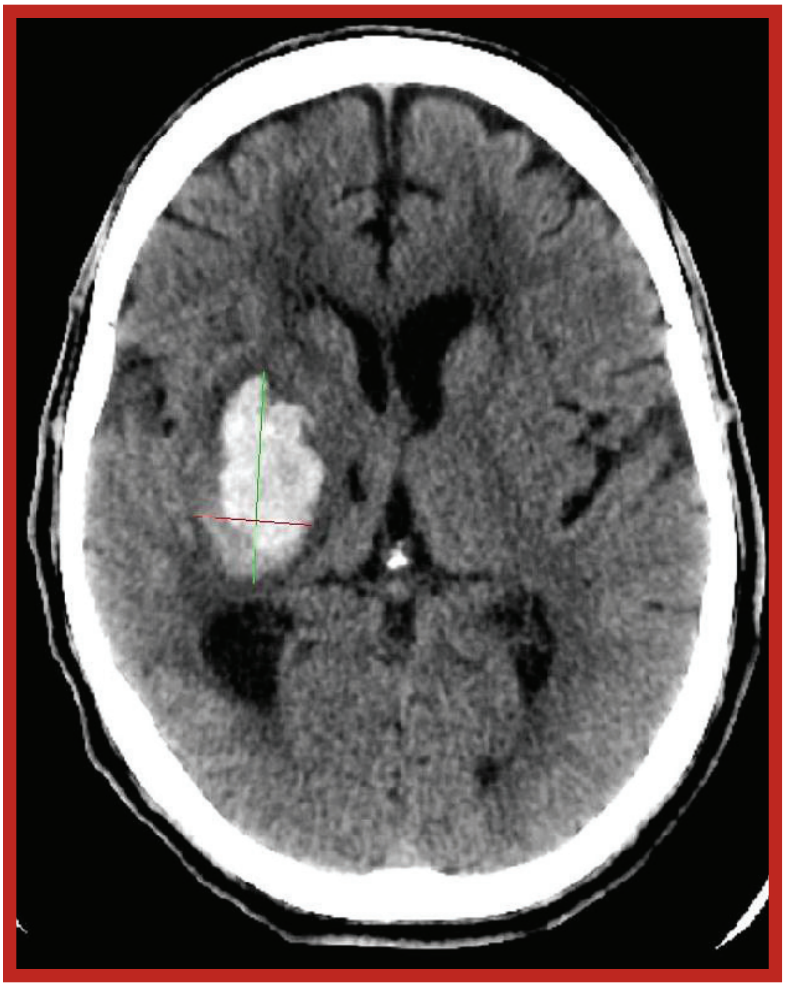
Measuring Hematoma Volumes Using the ABC/2 Method

Here are 9 slices from a head CT showing a right-sided intraparenchymal hematoma, which appears white or light grey on the images. The ventricles appear black. The hematoma is compressing the right lateral ventricle but is not inside it.



To measure the hematoma volume using the ABC/2 method, pick the slice showing the largest area of the hematoma. Find the measuring tool that is part of the imaging software so that the measurement is proportional to the image size (try right-click).

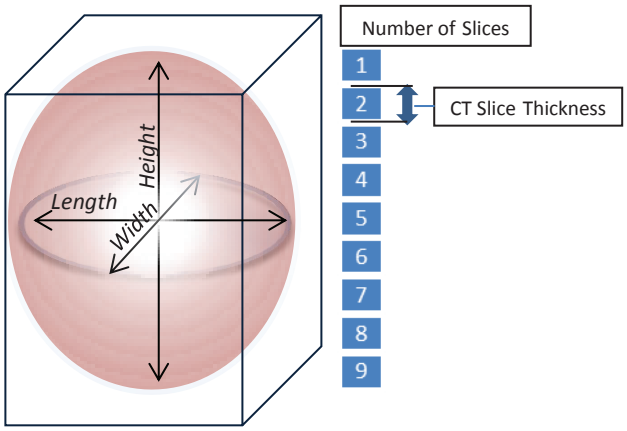
Hematoma Volume Measurement



Measure the hematoma using the longest part going one way (shown as a green line on the image at left), and then the widest part going perpendicular to that (shown as a red line on this image). Usually you can point and click to place each end of the line, and delete it if you want to afterward. Remember that you may need to convert from millimeters to centimeters to get the "cc" or cubic centimeter volume.

To get the height, since you can't see it directly, count the number of CT slices on which the hematoma is visible and multiply it by the slice thickness.

Measuring a hematoma using the rapid ABC/2 method is based on simplified mathematical principles for finding the volume of an elliptical object by measuring the volume of a cube that might be drawn tightly around it and dividing by two.



Example: if…

A = Length = 46.5 mm or 4.7* cm
B = Width = 25.5 mm or 2.6 cm
C = Height = 9 slices x 5.0 mm slice thickness**
= 45 mm or 4.5 cm

A X **B** X **C** / 2 = **4.7** x **2.6** x **4.5** / **2** = 55.0/2 = **27.5*cc**

** It is acceptable to round decimal places. When close to 60 cc total volume, be more exacting for decisions about enrollment.*
*** Check the slice thickness used for the CT images being examined. It should be noted somewhere on the images, often on the opening panel.*

ATACH-II: Insights and Updates from the All-Site Calls

1. Recruitment on your own:

A sole investigator can enroll a subject quickly and easily using the rapid randomization CRF and any computer with internet access, or the mobile APP on a cell phone. Remember that the attestation statement on the CRF still requires a careful check of inclusion/exclusion criteria. The randomization CRF can be completed in very little time, and should be submitted before the eligibility CRF to insure rapid enrollment and assignment of a treatment group within the 4.5-hour time window from symptom onset. All other data, including the eligibility CRF, can be submitted up to 5 days later. Some important things needed by team members making use of this feature are a good understanding of the protocol, ATACH-II WebDCU™ user access and password, randomization training certificate upload (randomization training can be completed in about 6 minutes), and allowances on the DOA log for consent and randomization of subjects. Pre-made order sets and nursing awareness packets for just-in-time training are very helpful toward ensuring protocol compliance after randomization. Team contact information and the hotline number should be readily available to hospital staff as well as team members.

When sites are well-trained, the simplicity and close adherence to standard of care in the ATACH-II trial has allowed for good success with this process at several sites, including Abington, Stanford, Valley Baptist, Columbia, and St. Cloud. At St. Cloud Hospital, Dr. Fareed Suri and Melissa Freese have been especially successful in implementing this process.

"Here at St. Cloud Hospital in St. Cloud, MN, in the research binders that we have located in the emergency department, we include only the consents and the baseline data report forms. The providers are responsible for getting the consents signed and providing the baseline data. The following day after enrollment the study coordinator then collects the binder and begins abstraction of the remaining data. We have 99.9% of our medical record electronically, so this makes it easy to pull data needed for blood pressures, GCS, medication administration, etc. If the patient arrives from an outside facility the paperwork from the facility is still on the patient's chart or it gets scanned into the electronic medical record within 24 hours. Our providers are also very good about documenting the NIHSS, size of hemorrhage, and other elements in their H&P and progress notes. Overall this process works very well for our team." By Melissa Freese, BSN, RN, CNRN, Stroke Care Specialist, St. Cloud Hospital, MN.

2. Off-site Recruitment Strategies:

Off-site enrollment processes including the use of telemedicine are a topic of interest to many sites. Investigators expressing interest have been put in touch with some of our key investigators already contributing to developments in this area. A working group is being established and our first teleconference devoted to this topic will be held in early October. Any sites interested will be invited to join in these discussions. If you are interested please contact Kathy France at: kafrance@umn.edu

ATACH-II: Insights and Updates from the All-Site Calls *(continued)*

3. Keeping up with new Screening Log:

The Data and Safety Monitoring Board that met on May 6, 2014 suggested that the investigators encourage the enrollment of more subjects with baseline GCS < 15, and are interested to know hematoma volumes for subjects enrolled versus those screened out of the trial. Under the tight enrollment window, it is also unknown how closely hematoma volume correlates to baseline GCS. To this end, the investigators should collect data to determine whether sites are turning away otherwise eligible patients with GCS < 15. In order to address this concern, the ATACH-II trial Screening Log was revised to document the GCS score and the hematoma volume. All sites are required to routinely document the hematoma volume and the GCS scores for all subjects who are screened for this trial. The study practice had been that if a potential subject met an exclusion criterion, then that subject was not screened for the remaining inclusion/exclusion criteria. With the new process, hematoma volume and GCS scores will be documented on the screening log for all screened subjects, regardless of why they may be excluded.

4. Consent in Anticipation:

If consent was obtained from a potential subject in anticipation that the subject will meet the inclusion/exclusion criteria and then they aren't enrolled because study requirements couldn't be met just before randomization, always retain the signed consent form and all relevant information for these subjects.

5. Hematoma Volume Assessment:

Thanks to everyone who has been entering hematoma volume measurements in to the screen failure logs to help meet our DSMB request. For those of you still learning, we hope that the section of this flyer devoted to this topic, also available for future training under "Project Documents" in ATACH-II WebDCU™, will be helpful.

Recent DSMB Meetings

May 6, 2014
DSMB had no safety concerns and recommended that the study continue as planned.

November 1, 2013
The DSMB recommended to NINDS that clevidipine not be allowed as an alternative to nicardipine for the ATACH-II trial.

October 6, 2013
DSMB had no safety concerns and recommended the study continue.

April 22, 2013
DSMB reviewed the safety and overall progress of the trial: found everything to be satisfactory and recommended the study proceed as planned.

The next DSMB meeting will be on December 16, 2014.

Recent ATACH-II Investigators Meetings

Investigators Meeting at the University of Alberta, Canada on May 29, 2014

Dr. Qureshi in China, July 2014

Dear Logan -
Letters about Imaging Procedure

Dear Logan,
I have been hearing a soft buzzing sound in my ear for the past couple of days, do you have any idea what may be causing it?

-Joe Friend

Dear Joe,
I am sorry to hear about the buzz in your ear. If I had to take a guess, I would assume all the buzz is being caused by talks of the data freeze coming up shortly. Due to the data freeze, it is important that everyone attempts to get their images to the CCC so that they may be entered. Hopefully when all of the images are turned in, the buzzing will subside. Please send the images to the following address:

Attention: **Logan Brau**
Dinnaken Office Building
925 Delaware Street SE, Suite 300
Minneapolis, MN 55414

- Logan

Article for Additional Reading

JVIN | Journal of Vascular and Interventional Neurology
OFFICIAL JOURNAL OF THE ZEENAT QURESHI STROKE INSTITUTE

Interpretation and Implementation of Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial (INTERACT II)

Adnan I Qureshi, MD*, Yuko Y Palesch, PhD, Renee Martin, PhD, Kazunori Toyoda, MD, PhD, Haruko Yamamoto, MD, PhD, Yongjun Wang, MD, Yilong Wang, MD, PhD, Chung Y Hsu, MD, Byung-Woo Yoon, MD, PhD, Thorsten Steiner, MD, Kenneth Butcher, MD, Daniel F Hanley, MD, and Jose I Suarez, MD

For a copy of the above journal article go to: http://jvin.org/journal/index.php/jvin

Friendly Reminders...

Form 05 Re-visited-

On Form 05, Question 10 captures the vital signs and nicardipine infusion rate from randomization until 24 hours post randomization. Please enter the vital signs and infusion rate in each row of Question 10 corresponding to the time from randomization in Column A. There is no need to complete Column I (Start Time) and Column J (End Time) because after Form 05 is saved in WebDCU™, those data items will automatically populate based on the time of randomization entered on Form 33. If the time of randomization is changed on Form 33, please contact Cassidy Conner (connerc@musc.edu) to update the start/end times in Columns I & J.

Regulatory Issues-

In order to remain compliant with the U.S. government's Code of Federal Regulations and ICH-GCP Guidelines, documentation verifying IRB renewal, Informed Consent approval and an active IRB Federal-wide Assurance (IRB FWA) must be kept current from the date sites are released to screen and enroll subjects into the ATACH-II Trial until site discontinuation or the end of the trial (whichever comes first). Local IRB renewals must take place at a *minimum* of every 365 days at all participating domestic and international sites.

Domestic sites' designated study team member(s) and international CRO representatives should be vigilant with the monitoring of upcoming expirations for the IRB FWA, IRB renewals and Informed Consent approvals and be mindful of the local IRBs' required time frames for renewal submissions. If lapses in any of these IRB approvals occur, the site will be placed on temporary Enrollment Hold until the proper documentation is uploaded and approved in WebDCU™.

The WebDCU™ system may be used to assist with the monitoring of upcoming expirations. Automated email notifications are generated by the database at 90 days, 60 days, 30 days, and 7 days prior to the expiration of required essential and regulatory documents; notifications of expired documents are also generated. These notifications are sent to site regulatory coordinators, primary study coordinators, and CRO representatives. In addition to the automated email notifications, the "Reg Doc Site Summary" (accessed by clicking on the Regulatory Document tab) provides a snapshot of the expiration dates of essential documents and the submission status of regulatory documents for each active study team member. For CROs that manage multiple sites, the filter and sort tools can be applied to the "Reg Doc Status Report" (also accessed by clicking on the Regulatory Document tab) to produce a list of each site's essential/regulatory approval periods.

For questions or assistance with the management and/or submission of essential/regulatory documents, please contact the following:

Domestic sites: NETT CCC at 734-232-2142 or ATACHII-TRIAL@UMICH.EDU
International CROs: Kristen Clasen, clasen@musc.edu

ATACH-II
2015 Investigators' Meeting

Save the Date

Saturday, January 24 2015
Starting at - 1:00 PM

Ending Sunday, January 25 2015

At - 12:00 PM

(Venue to be announced at a later date)

The Latest Contact Information for ATACH-II

Don't hesitate to reach out to us - we are here to help you!

Need help with an enrollment or other ATACH-II emergency?

Call the Toll Free Hotline at: 1-855-870-7205 *or* 952-225-0779

and you will be routed through a list of qualified individuals to ensure you're connected with a core team member who is available to help you immediately.

General Questions? Contact Kathy France at 612-625-6974 or kafrance@umn.edu

Contract or Reimbursement Questions? Contact Emily Abbott at 612-625-0551 or eiabbott@umn.edu

WebDCU questions? Contact Cassidy Conner at 843-876-1105 or connerc@musc.edu

Questions for the NETT CCC at 734-232-2142 **or** ATACHII-TRIAL@UMICH.EDU

To avoid delay in receipt of study drug, please email requests for additional drug to atachstudydrug@gmail.com

UNIVERSITY OF MINNESOTA

Clinical Coordinating Center
Zeenat Qureshi Stroke Research Center
University of Minnesota
925 Delaware Street SE Suite 300
Minneapolis, MN 55414
Phone: (612) 625-6974 | Fax: (612) 625-7950

MUSC
MEDICAL UNIVERSITY of SOUTH CAROLINA

Statistical and Data Coordinating Center
Medical University of South Carolina
Data Coordination Unit
Department of Public Health Sciences
135 Cannon Street, Suite 303
MSC 835 Charleston, SC 29425-8350
Phone: (843) 876-1919 | Fax: (843) 876-1923

Funded by NIH through grants U01NS062091 and R01NS061861; The content is solely the responsibility of the authors and does not necessarily represent the official views of NINDS or NIH.