Minimally **I**nvasive **N**euroendoscopic **U**ltra-Early **T**argeted ICH **E**vacuation (MINUTE)

Protocol Training

Study Chairs:

J Mocco, MD, Professor of Neurosurgery, Mount Sinai Medical School, New York

Magdy Selim, MD, PhD, Professor of Neurology, Harvard Medical School, Boston

Sharon Yeatts, PhD, Professor of Biostatistics, Medical University of South Carolina

Sponsored by NINDS (Grant PAR-24-101)

Last updated: 4/23/2026

MINUTE Leadership

Icahn School of Medicine at Mount Sinai

MPI: J Mocco, MD

Site Role: Administrative contact, subaward contracting (main sites), enrollment.

Medical University of South Carolina

MPI: Sharon Yeatts, PhD

Site Role: Data maintenance, monitoring and computing, statistical support.

Beth Israel Deaconess Medical Center

MPI: Magdy Selim, MD

Site Role: Enrollment.

University of Cincinnati (StrokeNet National Coordinating Center)

Co-I: Joe Broderick, MD

Site Role: NCC interaction, Operational guidance, enrollment.

University of Cincinnati (StrokeNet National Coordinating Center)

NCC PI: Pooja Khatri, MD

Site Role: Coordination of subsites, per-patient reimbursement tracking, enrollment.

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MINUTE Study Organization

StrokeNet National Coordinating Center(U Cincinnati)

Dr. Joe Broderick, NCC Co-I

Dr. Pooja Khatri, NCC PI

Iris Davis, co-Director

Cristina Francois, NCC Project Manager

StrokeNet Data Management Center(MUSC)

Jessica Griffin, Director of Trial Operations

Jocelyn Craven, StrokeNet Program Manager

Susanna Steinmuller, Data Manager

Jordan Stallings, Data Manager

Laura Kowalski, Site Data Monitoring Manager

Akash Roy, Assistant Professor of Biostatistics

Mount Sinai Neurosurgery Academic Research Organization (ARO)

Sukaina Davdani, Research Director

Ally Qi, Clinical Trials Manager

Sarah Torres, Senior Grants & Contracts Specialist

NIH/NINDS

Scott Janis, Scientific Program Director

Sean McCarthy, Program Official

Core Lab Imaging (U Cincinnati)

Dr. Vivek Khandwala

Dr. Achala Vagal

Siobhan McDermott (Imaging Core CRP)

Independent Medical Safety Monitor (University of Texas Health Science Center)

Dr. Justin R. Mascitelli

Berry Consultant

Dr. Kert Viele

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MINUTE Timeline

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Protocol Training

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Trial Design

Design

Prospective, multi-center, randomized, controlled, blinded-assessor

Study Population

Up to 55 U.S. sites,
300 patients,
Adults **18–80** with spontaneous BGH ≥ 20ml

Cohorts

<8h vs **8–16h** from onset to randomization

Study Arms

SCUBA evacuation
vs
standard medical management

Participant Duration

12 months

Study Period

5 years with estimated 3.5 years of study recruitment

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Study Objectives & Endpoints

	Primary	Secondary
Objective	To **evaluate the utility** of early/ultra-early SCUBA evacuation in patients with BGH and LKW-to-randomization time **≤16h**, and to determine whether SCUBA warrants further **efficacy study** in either **<8h or 8-16h** cohorts.	To evaluate the **safety** of early/ultra-early **hematoma evacuation** using the minimally invasive endoscopic **SCUBA** technique.
Safety Endpoints	30-day all-cause **mortality**	1. **Symptomatic rebleeding** after evacuation 2. **CNS infection** attributed to surgery
Efficacy Endpoints	**UW-mRS** at 180 days	1. Successful **clot removal** with ≤ 10 mL remaining on the post-evacuation CT scan **2. ICH volume** on the 24-hr CT scan **3. Peri-cavity edema** (PCE) on the 24-hr CT scan

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Key Inclusion Criteria

1. Age ≥ 18 and ≤ 80 years
2. Non-traumatic, spontaneous, supratentorial, non-thalamic, **BGH of volume ≥ 20 mL**, as determined by the treating physician using ABC/2 method
3. **NIHSS ≥ 6** at presentation
4. Computed Tomography Angiography (**CTA**) or Magnetic Resonance Angiography (**MRA**) is performed and **does not show an underlying vascular lesion**
5. **Pre-ICH mRS 0-2**
6. Informed consent from patient or legally authorized representative (LAR) to participate in the trial, wherein patient/LAR's stated wishes are to pursue lifesaving therapies as opposed to early withdrawal of care (explicitly explained as <7 days following ictus)
7. The treating physician anticipates that **surgery can be initiated <120 min** from randomization
8. Randomization **within 16 hours from LKW** and **within 2 hours of arrival** to the randomizing center.

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Key Exclusion Criteria

1. **Suspected secondary cause for the ICH**, such as an underlying vascular malformation (cavernous malformation, arteriovenous malformation, etc.), aneurysm, neoplasm, hemorrhagic transformation of an underlying ischemic infarct; or venous infarct
2. Infratentorial or thalamic hemorrhage
3. Midbrain extension/involvement
4. Coagulopathy defined as international normalized ratio (**INR**) > 1.4
5. Elevated activated Partial Thromboplastin Time (**aPTT**) > 40 s
6. Concurrent use of direct oral anticoagulants or low molecular weight heparin at ICH onset
7. Known hereditary or acquired hemorrhagic diathesis or coagulation factor deficiency
8. Platelet count <100 x 103 cells/mm3, or known platelet dysfunction (reversal of coagulopathy is not allowed)
9. **GCS score <7** at presentation
10. Evidence of active infection indicated by **fever ≥100.7 °F** and/or open draining wound at the time of enrollment

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Key Exclusion Criteria

11. Any comorbid disease or condition expected to compromise survival or ability to complete follow-up assessments through 365 days
12. Intraventricular extension of the hemorrhage is visually estimated to involve > 50% of either of the lateral ventricles
13. Pregnancy (women of childbearing potential must have a negative pregnancy test to participate)
14. Based on investigator's judgment, the patient does not have the necessary mental capacity to participate or is unwilling to comply with the protocol follow-up schedule
15. **Current participation in another interventional (drug or device) trial**
16. Pre-existing Do Not Resuscitate (**DNR**)/Do Not Intubate (**DNI**) status
17. History of **severe dementia**

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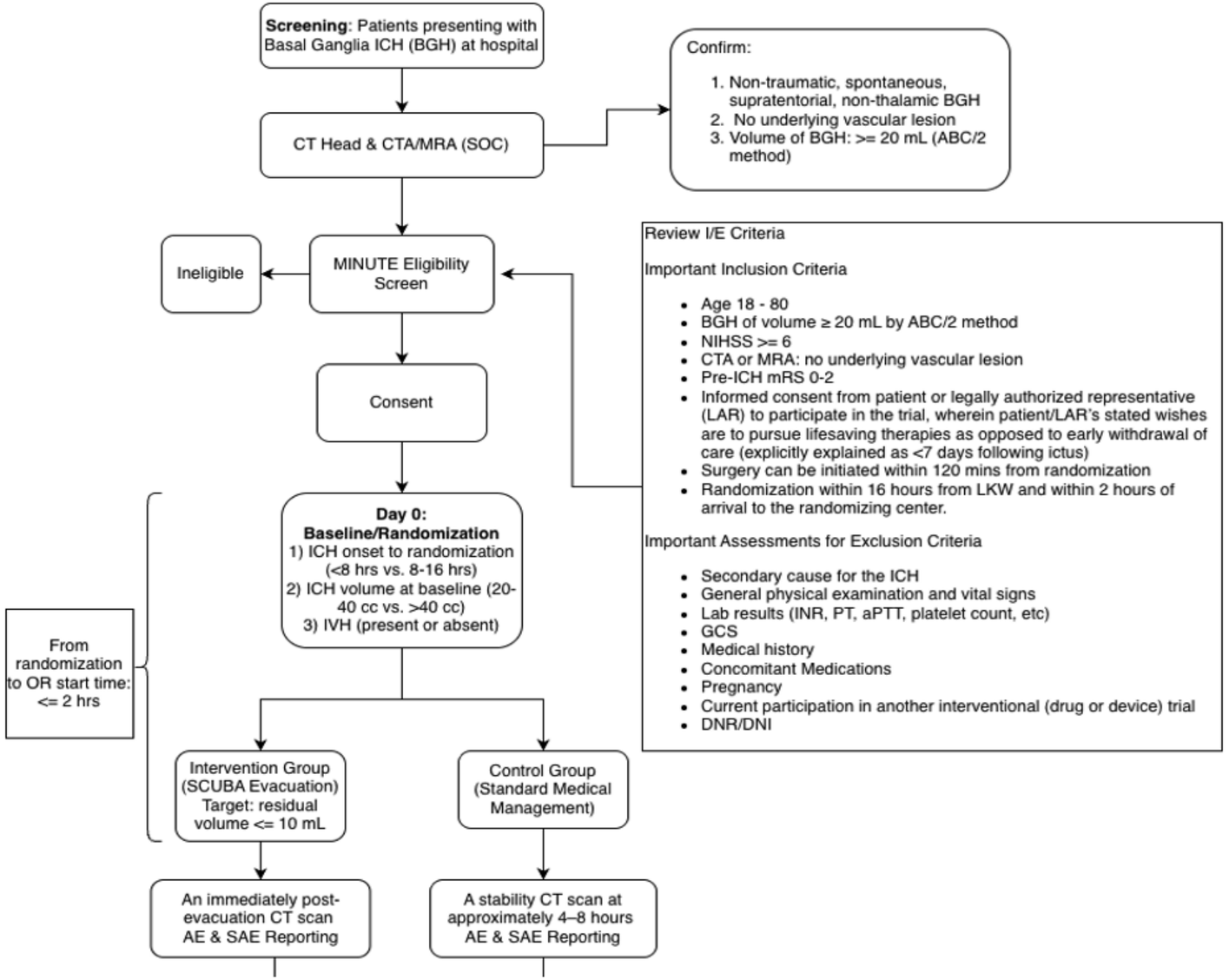
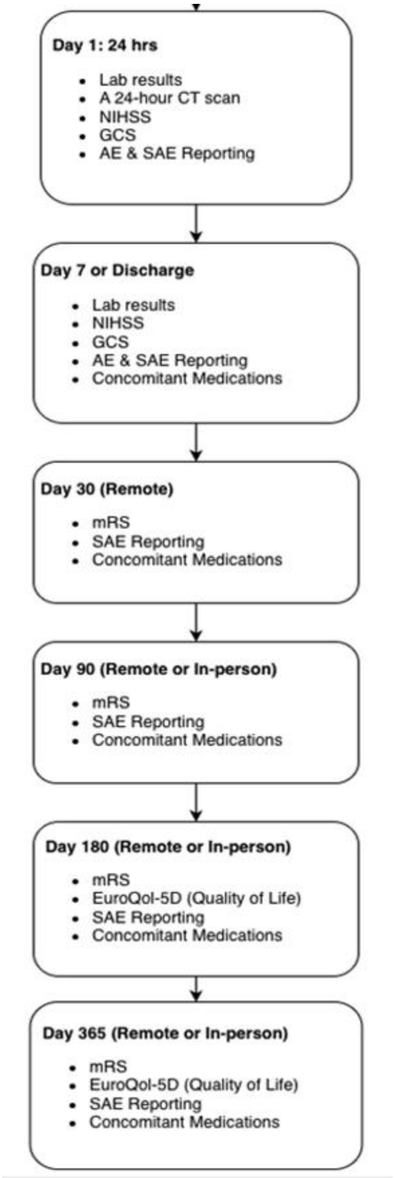
Study Workflow

Note: The whole enrollment process is less than or equal to 16 hours from ICH onset or LKW.



Study Workflow



Schedule of Activities (SOA)

Procedures	Baseline	Day 0 Baseline	Day 1, 24 ± 6 hours after Randomization	Day 7 or Discharge*	Day 30 ± 7 days	Day 90 ± 30 days	Day 180 ± 30 days	Day 365 ± 30 days
Inclusion/Exclusion Criteria	X							
Demographics	X							
Medical History	X							
Prior Medication Review	X							
Pregnancy Test	X							
Review of Standard-of-Care Labs (CBC and Coagulation Panel)	X		X	X				
Diagnostic CT (ICH location and volume, determined by ABC/2)	X	X^	X					
Diagnostic Pre-Operative CTA or MRA	X							
Informed Consent	X							
Randomization		X						
Endoscopic Evacuation of the Hematoma#		X						
National Institutes of Health Stroke Scale (NIHSS)	X		X	X				
Glasgow Coma Scale (GCS)	X		X	X				
Modified Rankin Scale (mRS)	X				X	X	X	X
EuroQol-5D Quality of Life							X	X
Adverse Events		X	X	X				
Serious Adverse Events		X	X	X	X	X	X	X
Concomitant Medications		X	X	X	X	X	X	X

Only for the SCUBA surgical arm
^In the medical management arm: stability CT scan 4-8 hours after randomization; in the SCUBA surgical arm: CT scan immediately post-evacuation
* Visit performed on Day 7 or on the day of discharge, whichever comes first

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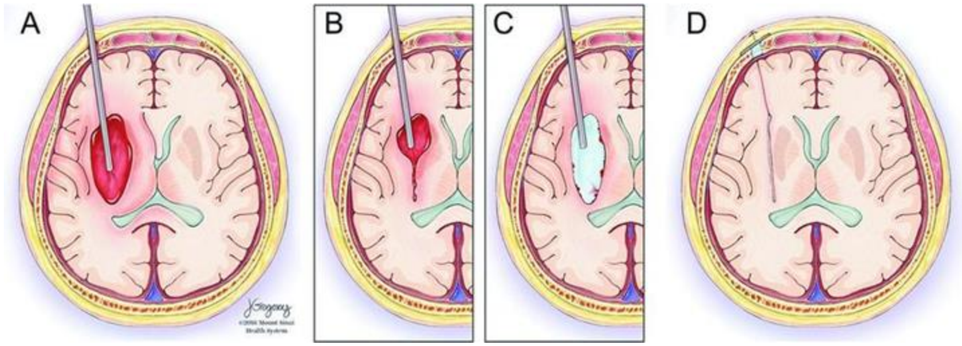
Intervention: SCUBA



SCUBA: *Stereotactic Cerebral Underwater Blood Aspiration*

- Goal: ≤10ml residual hematoma on post-op CT
- **It's a surgical technique and is not device specific.** FDA exemption letter available.
- Multiple different evacuation devices have been used in SCUBA cases, such as *Apollo* (Penumbra), *Artemis* (Penumbra), *Myriad* (NICO), and standard endoscopic tools (Storz).
- SCUBA avoids traditional craniotomy and emphasizes minimal brain and soft tissue disruption.

Image credits: Kellner CP, Chartrain AG, Nistal DA, et al, The Stereotactic Intracerebral Hemorrhage Underwater Blood Aspiration (SCUBA) technique for minimally invasive endoscopic intracerebral hemorrhage evacuation, Journal of NeuroInterventional Surgery 2018;10:771-776.

Concomitant Medications

- The use of **low molecular weight fractionated and unfractionated heparin** for deep vein thrombosis and the use of **aspirin** as clinically indicated for an underlying condition are permitted **48 hours** after surgery, as long as repeat imaging assures ICH stability.
- The use of other **antithrombotic agents**, such as warfarin, direct oral anticoagulants, antiplatelet agents, and IIb/IIIa inhibitors should be avoided as much as possible for 7 days after surgery.
- **Intraventricular thrombolytics is not allowed**.

Surgical Leadership Committee (SLC) & Surgical Training Center

Committee Composition:

- The SLC consists of 3–5 experienced neurosurgeons; initially Drs. Mocco, Kellner, and Shigematsu will form the leadership team.

Clinical & Surgical Expertise:

- All SLC members are fully trained neurosurgeons with extensive experience in intracerebral hemorrhage (ICH) care and endoscopic ICH evacuation.

24/7 Surgical Support:

- SLC members jointly staff a round-the-clock hotline providing pre-operative planning support and intra-operative tele-proctoring.

Training & Education:

- The SLC will livestream ~20 endoscopic ICH evacuations annually from Mount Sinai using HIPAA-compliant technology and conduct one-day training courses and 3D model practice sessions.

Leadership & Membership:

- Surgeons from participating centers may join the SLC after submitting >7 cases; Dr. Kellner will lead the SLC throughout MINUTE, with membership rotating as needed once the committee reaches five members.

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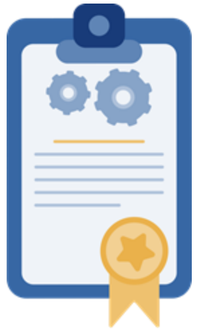
Control Arm: Standard Medical Management



- Standard medical management per AHA ASA ICH guidelines for management of spontaneous ICH

2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association

Citation: Greenberg SM, Ziai WC, Cordonnier C, Dowlatshahi D, Francis B, Goldstein JN, Hemphill JC 3rd, Johnson R, Keigher KM, Mack WJ, Mocco J, Newton EJ, Ruff IM, Sansing LH, Schulman S, Selim MH, Sheth KN, Sprigg N, Sunnerhagen KS; American Heart Association/American Stroke Association. 2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2022 Jul;53(7):e282-e361. doi: 10.1161/STR.0000000000000407. Epub 2022 May 17. PMID: 35579034.

Link: https://pubmed.ncbi.nlm.nih.gov/35579034/

Outcomes & Follow-up

Primary:

- UW-mRS at Day 180
- Mortality (Day 30)

Secondary:

- Successful clot removal with ≤10 mL remaining on the post-evacuation CT scan;
- ICH volume on the 24-hour CT scan; and
- Peri-cavity edema (PCE) on the 24-hour CT scan

Follow-up:

Day 1, 7, 30, 90, 180, 365

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Statistical Considerations

- Sample size: 300 patients, powered for UW-mRS improvement ≥0.1

- Bayesian adaptive design: interim analyses for adaptive enrichment to determine optimal time window
  - if low probability that SCUBA has a clinically meaningful effect in a given time window, enrollment in that window will be discontinued
  - first interim after the first 100 patients have been randomized
  - subsequent interims occur after every additional 50 patients have been randomized

- Final analysis will be conducted when all patients have completed the 180-day follow-up period.
- Possible decisions based on a posterior probability of superiority > 0.9
  - recommend both windows
  - recommend either ultra early or early window
  - recommend neither

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Primary Staff Roles and Responsibilities

Principal Investigator	Surgical Co-PI	Primary Coordinator

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Site PI Responsibilities

Overall Study Responsibility

The investigator is responsible for patient selection, evaluation, protocol adherence, data collection, and overall study conduct in compliance with regulations and IRB requirements.

Delegation with Accountability

Although tasks may be delegated to qualified study staff, the investigator retains full responsibility for study execution and oversight.

Surgical PI & Primary Study Coordinator

The investigator must designate a surgical PI & a primary study coordinator to support the administrative and surgical operational aspects of the study.

Informed Consent & Protocol Compliance

The investigator ensures informed consent is obtained before enrollment and that all procedures follow the approved protocol.

Staff Qualifications & Documentation

The investigator must ensure study personnel are qualified and trained, maintain confidentiality, and keep delegation of authority logs and training records accurate.

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Surgical PI Responsibilities

Site Surgical Leadership

- Serve as the designated neurosurgical lead for the study at the site and oversee all SCUBA procedures.

Required Training

- Attend and successfully complete the mandatory SCUBA surgical training requirements prior to site activation.

Procedure Oversight

- Ensure the SCUBA procedure is performed correctly and consistently for all participants randomized to the SCUBA arm.

Protocol Compliance

- Confirm adherence to the surgical protocol, study procedures, and applicable guidelines during pre-operative, intra-operative, and post-operative care.

Quality & Accountability

- Act as the primary surgical point of contact for training, procedural questions, and surgical quality assurance in coordination with study leadership.

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Primary Coordinator Responsibilities

Study Operations Support

- Manage day-to-day study activities at the site and support the PI and Surgical PI in study execution.

Participant Coordination

- Coordinate screening, enrollment, scheduling of study visits, procedures, and follow-up assessments.

Regulatory & Documentation

- Maintain regulatory binders, ensure informed consent documentation is complete, and support IRB submissions and approvals.

Data Management

- Ensure timely and accurate data entry, respond to data queries, and track protocol deviations and adverse events.

Communication & Compliance

- Serve as the primary liaison between the site and study leadership, NDMC, and monitors, and ensure staff training and protocol adherence.

Required Study Trainings

- Standard Trainings:
  - Protocol (quiz + webinar or slides)
  - Coordinator (quiz + slides)
  - ABC/2 Method (slides + attestation)
  - Core Lab (individual site training)
- Certifications:
  - mRS – WebDCU Campus
  - NIHSS – WebDCU Campus
- For **Site Neurosurgeons** Only:
  - In-person surgical training (attestation/approval form)
  - Five Educational modules: (attestation)
  - Case submissions: 4 non-trial cases (approval form)

- Additional Resources:
  - AHA ASA ICH Medical Management Recommendations Guidelines
  - Randomization in WebDCU – WebDCU Campus
  - E-consenting in REDCap – WebDCU Campus
  - EuroQol-5D Quality of Life – Website Guide & WebDCU Campus Under STEP
  - Viz AI Introduction – WebDCU Campus
  - Adverse Event Reporting Workflow - WebDCU Tools
  - Angio-Suite Introduction - WebDCU Campus

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Safety Monitoring Plan

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Safety Monitoring

- Independent Safety Monitor + DSMB oversight
  - Anticipated **semi-annual DSMB meetings**
- AE/SAE assessment through **1 year**
- **Interim 30-day mortality monitoring**: every 30 consecutive evacuation subjects have had the opportunity to complete the 30-day period

General safety monitoring:

- The primary safety endpoint is **30-day all-cause mortality**.
- The secondary safety endpoints include:
  i. **Symptomatic rebleeding** into the cavitary lesion after evacuation resulting in **residual hematoma volume >10 mL** and worsening of neurological status (defined as an increase in pre-evacuation **NIHSS ≥4** points or a decrease in **GCS ≥2** points which cannot be attributed to any other cause such as infection, seizures, sedation, or worsening edema) within 30 days; and
  ii. **CNS infection** attributed to surgery.

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List of Anticipated Adverse Events

Adverse Events Related to the Procedure (surgery + anesthesia)

- Skin infection at the surgery site
- Swelling/edema at the surgery site
- CNS infection
- CSF leak
- Rebleeding/Hematoma expansion
- Scar formation, skin irritation or itching at the surgery site
- Ischemic stroke

Adverse Events Related to Anesthesia

- Sore throat after intubation
- Allergic reaction (rash, hives, flushing, headache, fever, and trouble breathing.
- Malignant hyperthermia (very rare)
- Myocardial infarction

Adverse Events Related to Imaging (CT/CTA or DSA)

- Allergic reaction including flushing, nausea/vomiting, skin rash, anaphylaxis, difficulty breathing after CTA
- Worsening renal functions after CTA (Contrast Induced Nephropathy)
- Ischemic stroke - DSA
- Contrast injection site complications

**Note, CTA/DSA are SOC and are not part of study-specific procedures*

Adverse Events Related to ICH/Condition

- Worsening neurological status
- Brain edema/swelling
- Hematoma expansion
- Seizure
- Worsening renal functions
- Respiratory and urinary tract infection
- Cardiac arrhythmias
- DVT/PE
- ARDS
- Death
- Ischemic stroke
- Myocardial infarction
- Anemia,
- Electrolyte disturbances,
- Fever
- Confusion or altered mental status

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Adverse Event Reporting Timelines

Reporting Timeline	**SAE**	**AE**
Within **24 hours***	1. Unanticipated or 2. At least possibly related to the procedure	
Within **3** business days*	1. Not unanticipated and are 2. Unrelated, or unlikely to be related to the procedure	
Within **5** business days*		Non-serious
* The investigator's first knowledge of the event		

Thank you! 👏 😊

Thank you for your time! Please take the protocol training quiz in REDCap. Here's the link: https://redcap.link/minuteprotocolquiz.

- By completing this quiz, you are confirming you have attended the training webinar or reviewed the training slide deck.
- You must answer at least 12 out of 14 questions correctly to receive a passing score. A PDF will be generated at the conclusion of this test and sent to the email address entered below.
- That PDF must be uploaded to WebDCU to document your training.
- A separate attestation form is not required for protocol or coordinator training.
- If you can't make it to the webinar, the recording will be posted on WebDCU Training Campus. Please watch the recording and complete the REDCap quiz.

Email Ally Qi, ally.qi@mountsinai.org if you have any questions regarding this material.

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