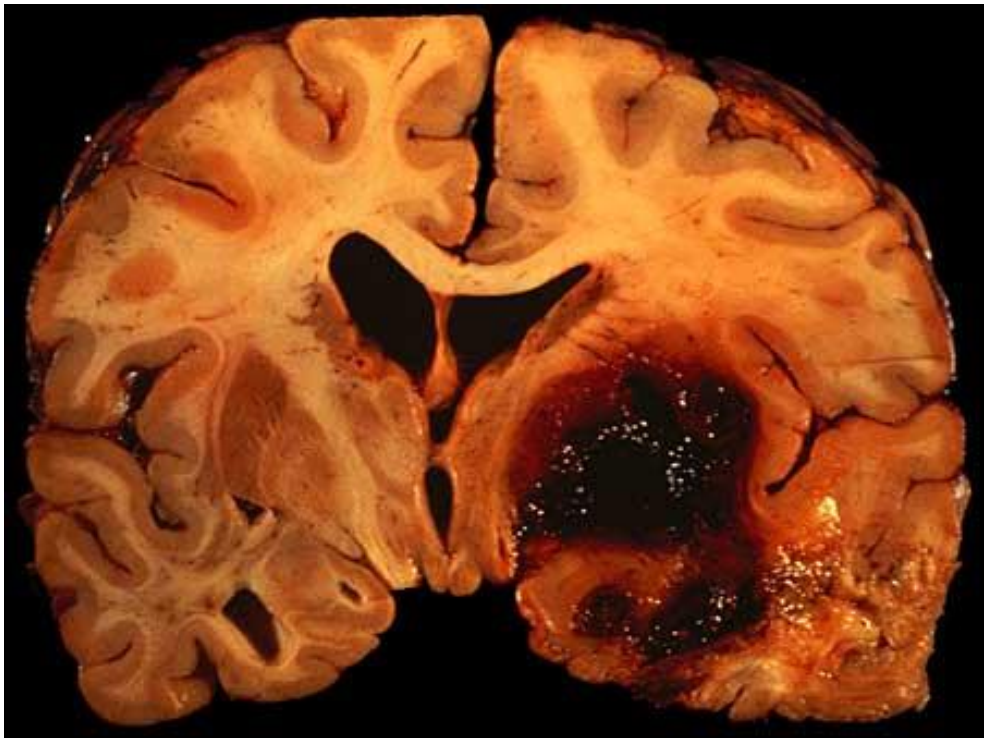
RUSH UNIVERSITY MEDICAL CENTER

The management of ICH when to operate when not to?

Rush Center for
Neuroendovascular surgery

Intracranial Hemorrhage

- High Incidence
  - Accounts for 10-15% of all strokes[1,2,5]
  - 80,000 cases in US; 2 million WW[2,5]
  - Incidence doubles for African-Americans and Asians [1,2,3]
- High Mortality/Morbidity
  - 30-day mortality ~50% with majority dead in first 2 days[3]
  - Substantial disability; only 20% of survivors live independently at 6 months[3]
- 45% of all ICH has a ventricular component (IVH) [7]

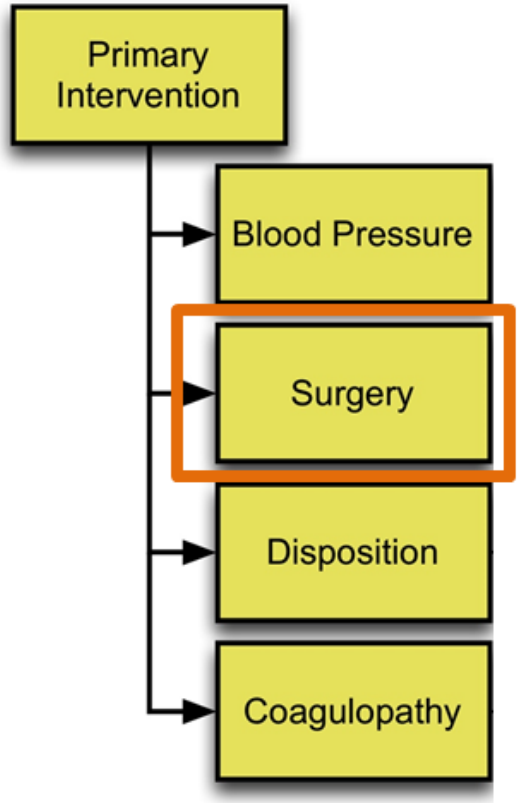


Source:
[1] Qureshi AI, Tuhrim S, Broderick JP, Batjer HH, Hondo H, Hanley DF. Spontaneous intracerebral hemorrhage. N Engl J Med. 2001;344:1450-1460. doi:10.1056/NEJM200105103441907.
[2] Qureshi AI, Mendelow AD, Hanley DF. Intracerebral haemorrhage. Lancet. 2009;373(9675):1632-1644. doi:10.1016/S0140-6736(09)60371-8.
[3] Broderick JP, Adams HP Jr, Barsan W, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: A Statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. Stroke. 1999;30:905-915. doi:10.1161/01.STR.30.4.905.
[4] Thrift AG, Geoffrey DA, McNeil JJ. Epidemiology of intracerebral hemorrhage. Epidemiol Rev. 1995;17(2):361-381.
[5] Towfighi A, Greenberg SM, Rosand J. Treatment and prevention of primary intracerebral hemorrhage. Semin Neurol. 2005;25(4):445-452
[6] Sahni R, Weinberger J. Management of intracerebral hemorrhage. Vasc Health Risk Manag. 2007;3(5):701-709.
[7] Morgenstern LB, Hemphill JC III, Andersen C, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: A Guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2010;41:2108-2129, published online before print July 22 2010. doi:10.1161/STR.0b013e3181ec611b.

Intraventricular hemorrhage

- Intraventricular and intracerebral hemorrhage have a morbidity and mortality rate of 50-80%
- Animal models have demonstrated that in IVH intracranial pressure control is important but to the change in neurological outcome, removal of IVH is important
- IVH has been shown to increase tissue inflammation and the more of the blood removed, the more decrease in inflammatory factors

Role of Surgery



Location	Surgery urgently:
Cerebellum	• Declining neuro exam • Size > 3 cm, or • Compressive effects brainstem, or • hydrocephalus
Lobar	ICH causing mass effect/herniation in severely affected but salvageable patient and as a life-saving measure

V. Procedures/Surgery

Craniotomy for Posterior Fossa Hemorrhage

- Deterioration can occur quickly in cerebellar hemorrhage
  - Obstructive hydrocephalus
  - Mass effect on brainstem
- Nonrandomized studies suggest that patients with cerebellar hemorrhage that is:
  - > 3 cm in diameter
  - Associated with brainstem compression
  - Associated with hydrocephalus

  have better outcomes with surgical decompression
- Attempting to control ICP via means other than hematoma evacuation is not recommended and may be harmful

How about treatment of supratentorial intracranial hemorrhage?

V. Procedures/Surgery

Craniectomy for ICH

- Potential of decompressive craniectomy (DC) to improve outcomes has not been well studied.

- STITCH trial suggests improved outcomes with DC in patients with:
  - Coma (GCS < 8)
  - Significant midline shift
  - Large hematomas
  - ICP that did not normalize with medical management

- Systematic review suggests that DC with hematoma evacuation might be safe and improve outcomes.

Intraparenchymal hemorrhage

- STICH trial
  - Randomized prospective study looking at effectiveness of early surgery (within 24 hours of randomization) versus initial medical therapy
  - STICH trial did not show significant difference in outcome between surgical arm and medical therapy
  - Subgroup analysis showed that superficial hemorrhages (< 2 cm from the surface) benefited from evacuation

Intraparenchymal hemorrhage

- STICH showed us that evacuation of deeper hemorrhages through craniotomy was not more beneficial than conservative measures

- Subgroup analysis showed that superficial hemorrhages (< 2 cm from the surface) benefited from evacuation

How about evacuation through less invasive methods has not been tested?

MISTIE II Trial

Medical Management + Clot Drainage Catheter With tPA vs. Medical Management Alone

- **Inclusion**: Spontaneous, supratentorial Intracerebral Hemorrhage ≥ 20ml, with a GCS ≤ 14 or a NIHSS ≥ 6.
- **n** = 96 patients randomized
- **Therapy**: 1 mg of tPA administered via drainage catheter every 8 hours for up to 72 hours (3 days)

Intraparenchymal hemorrhage treated with minimally invasive therapy

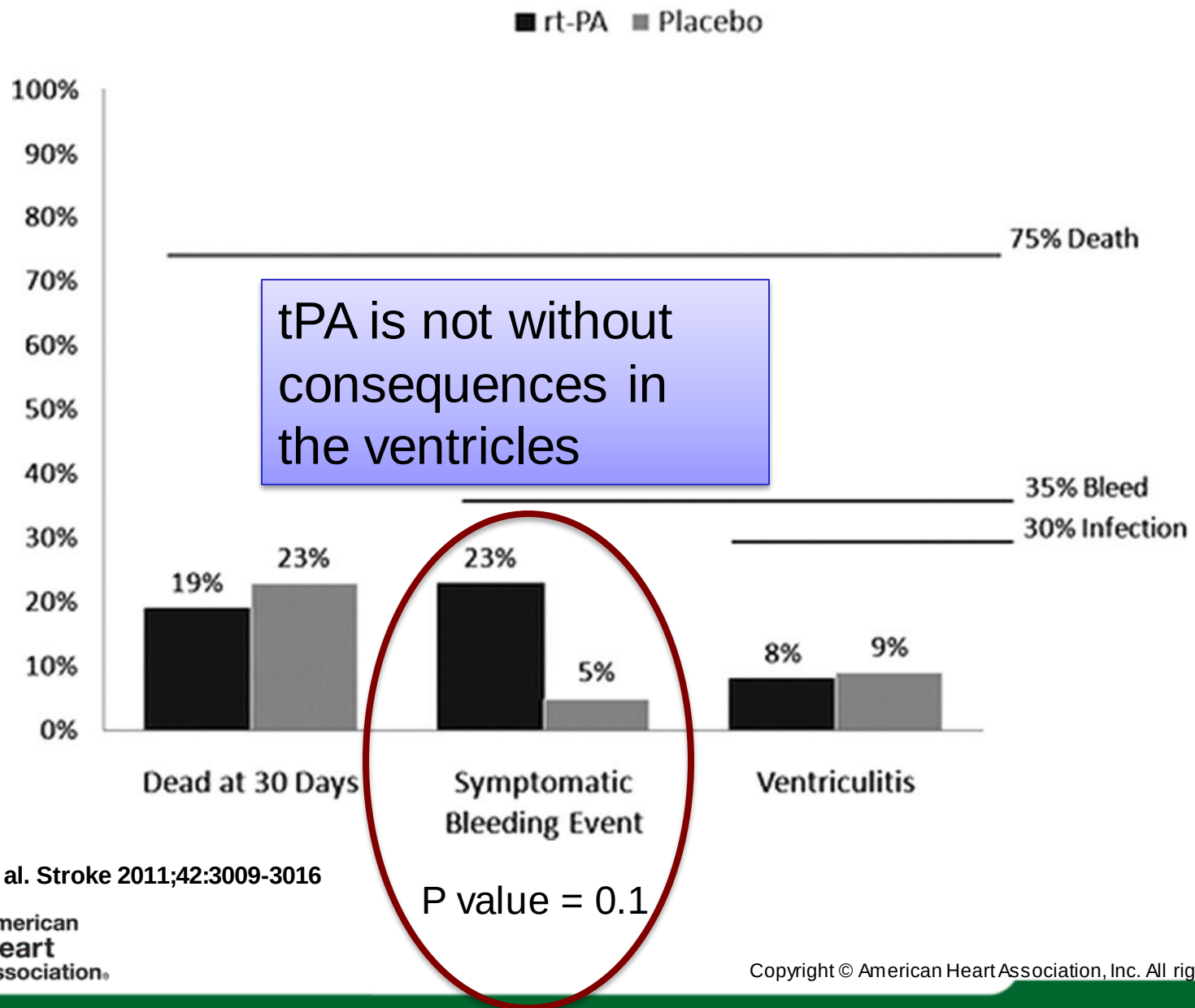
- MISTIE II

Conclusions: Minimally invasive surgery plus rt-PA enhances survivor functional outcomes for independence. MISTIE treatment may benefit ICH patients because effective removal occurs and there appears to be limited tissue injury. These clinically significant benefits should be tested in a Phase III trial. These results could lead to a major change in practice. Now, the majority of ICH patients do not undergo surgical removal of the ICH.

CLEAR II Trial
EVD + tPA vs. EVD + placebo

- **Inclusion**: small supratentorial ICH (≤ 30 ml) with massive IVH with an EVD already placed for treatment of obstructive hydrocephalus, per standard of care
  - Median ICH volume: 7.5 ml
  - Median IVH volume: 52.7 ml
- **n** = 48 patients randomized
- **Therapy**: Subjects were randomized to receive either 3 mg of rtPA or 3 ml of normal saline injected via the EVD into the ventricular spaces every 12 hours until clot resolution.
  - **10.2 ± 8 days in ICU for rtPA and 12.7 ± 8.4 days in ICU for placebo**

CLEAR II Outcomes



Naff N et al. Stroke 2011;42:3009-3016

American Heart Association.

Intraventricular hemorrhage

- t-PA group underwent earlier removal of EVD catheters due to clot obstruction and there were less exchanging of EVD catheters due to clot obstruction
- There was also clinical improvement by an increase in GCS scores at 4 days in t-PA group
- This was an initial safety study and not designed to assess long-term functional outcome.
- CLEAR III trial is a current ongoing trial that will assess functional performance in a 90 to 180-day time frame

Clinical Conclusions

- MISTIE II and CLEAR II show positive trend of evacuating clot in patients with ICH / IVH to reduce mass effect and hemotoxicity.
- Both trials show trends toward better outcomes if the clot burden can be reduced quickly
- Thrombolysis is not without consequence in terms of bleeding events and ICU stay days.

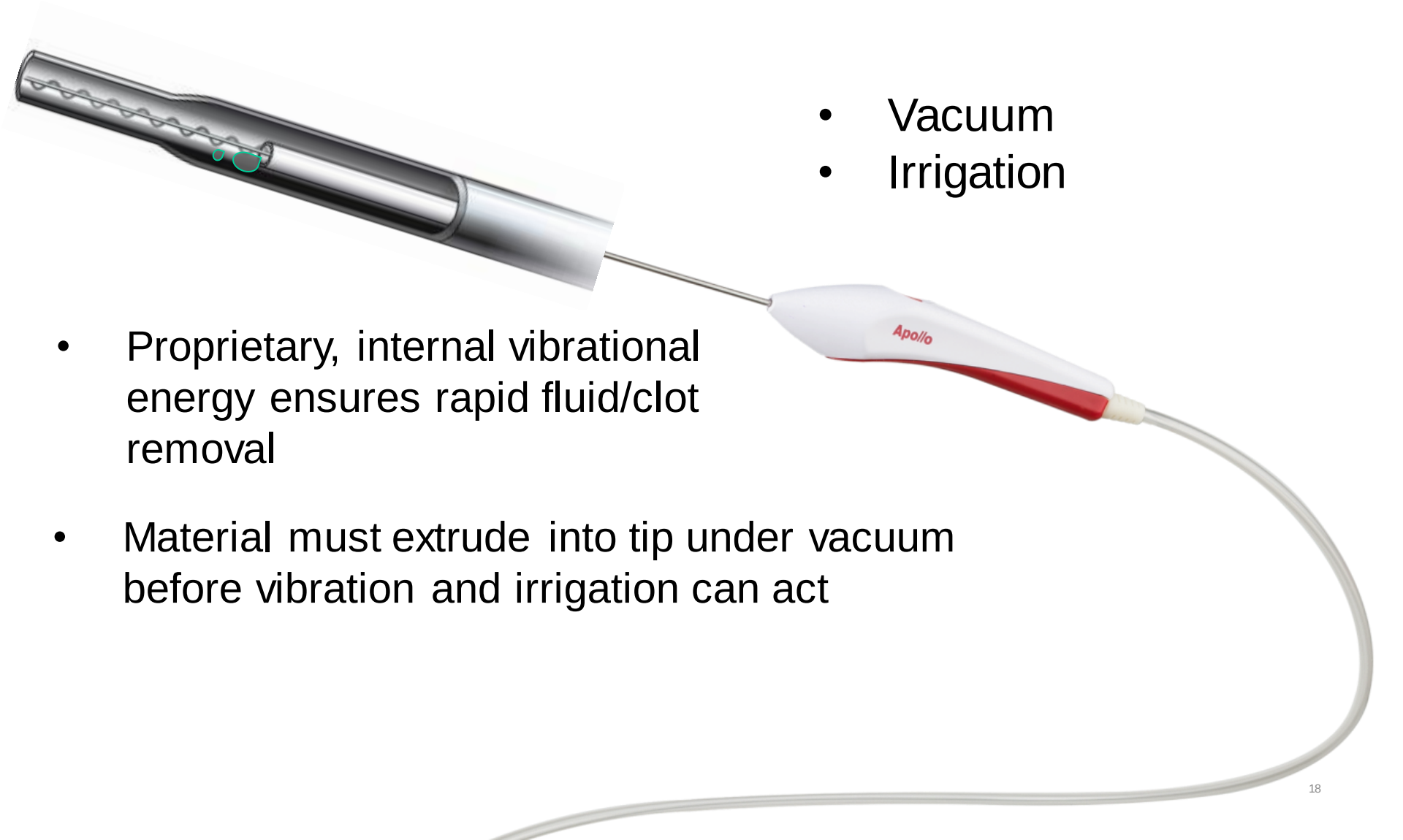
Apollo

A minimally invasive device that is primarily indicated for intraventricular hemorrhage but its use in intraparenchymal hemorrhages might have a role in the future

The Apollo™ System

- Dedicated hardware components deliver
  - Vacuum, irrigation, vibrational energy
- All components physician controllable, precise, and gentle
- Compatible neuroendoscope enables:
  - Fluid/clot vs. brain differentiation
  - Hemostasis confirmation

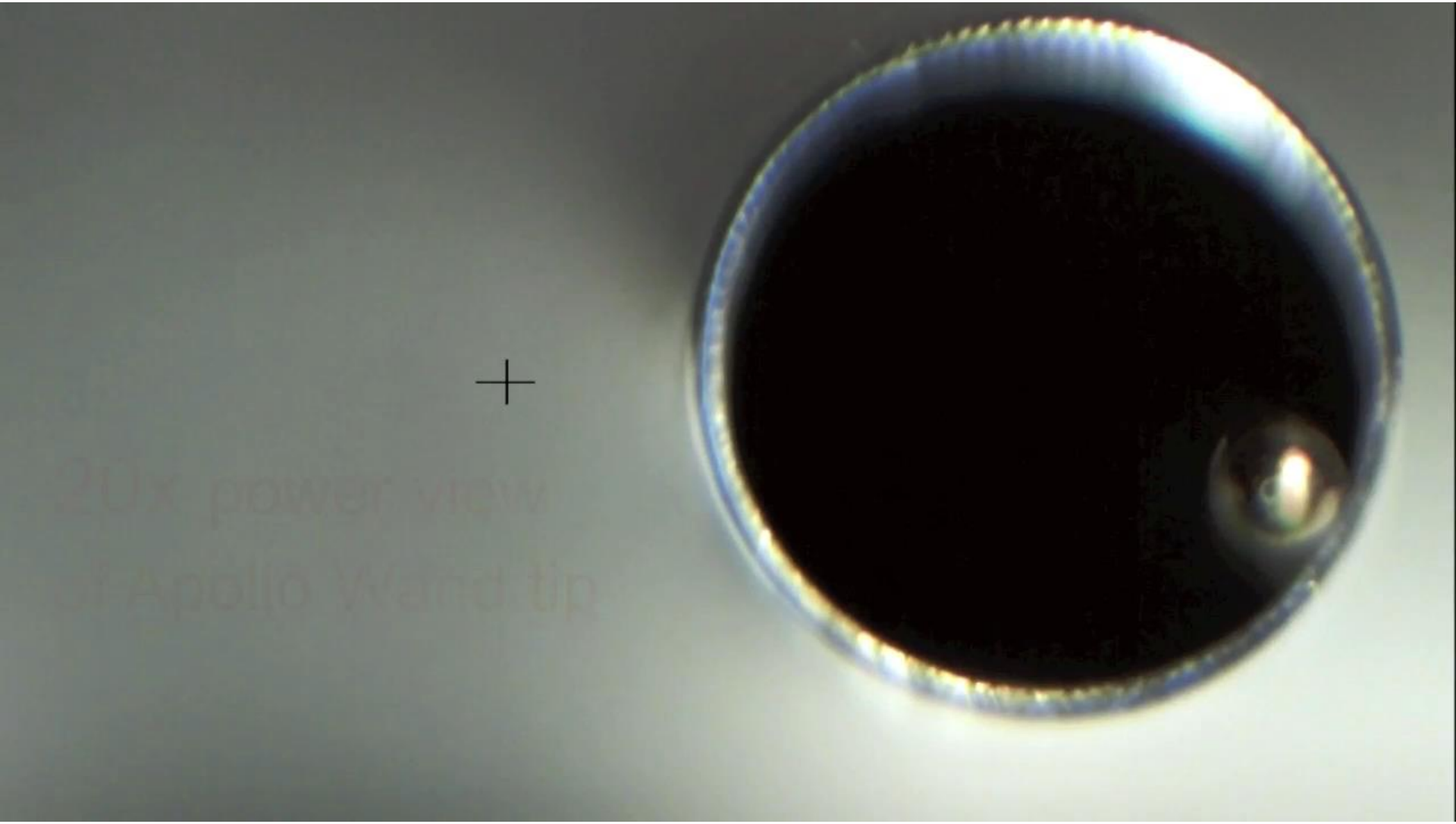
The Apollo™ System Wand



- Vacuum
- Irrigation

- Proprietary, internal vibrational energy ensures rapid fluid/clot removal

- Material must extrude into tip under vacuum before vibration and irrigation can act

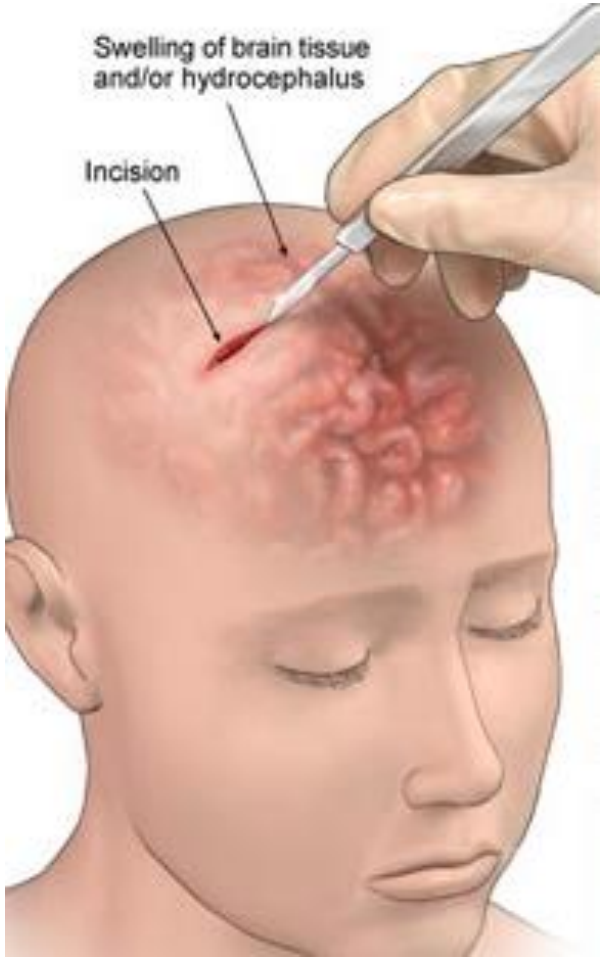


Rush Medical Center

Adjunctive Technologies

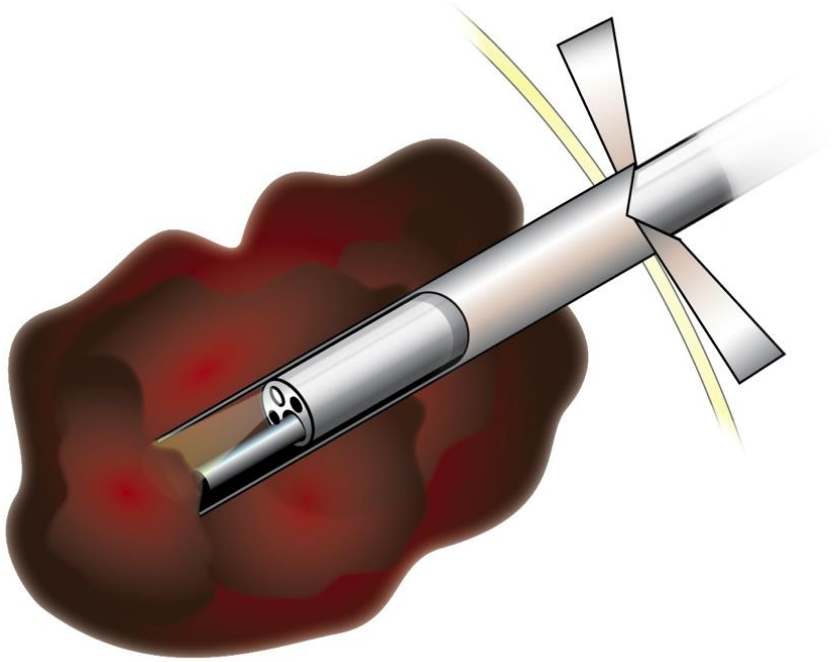
- Access
  - Burr Hole, mini-craniotomy
  - 19F Peel away sheath
- Neuronavigation: Trans-dural Ultrasound, Stealth
- Direct Visualization: Storz Neuroendoscope
- Location: OR

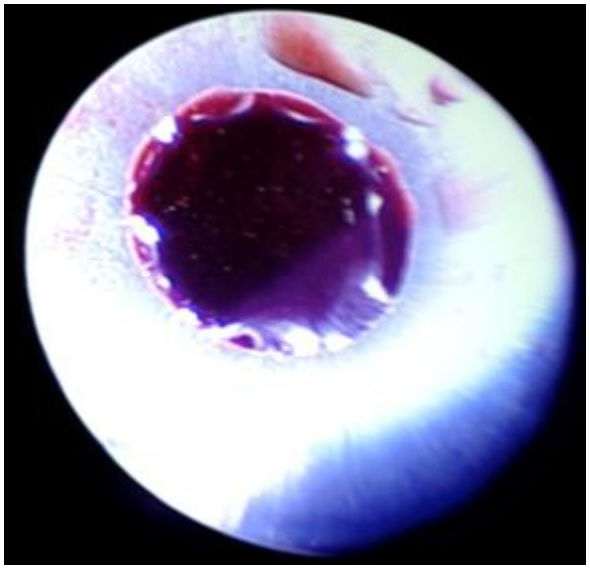
Apollo case

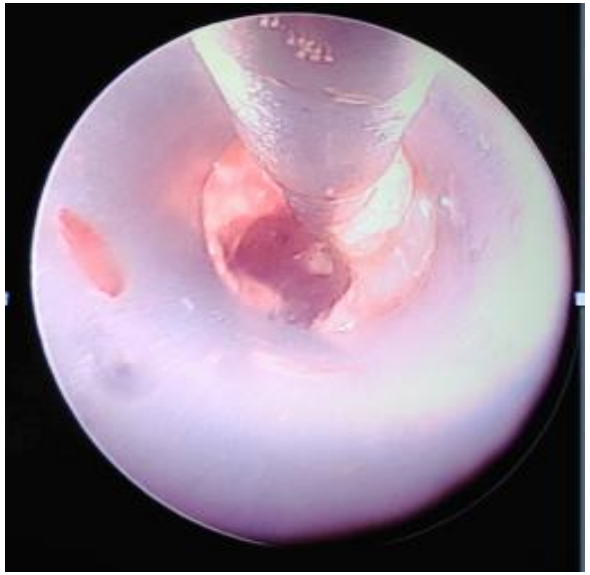


Procedure: Endoscopy

- Important to create a working space within the sheath away from clot at tip





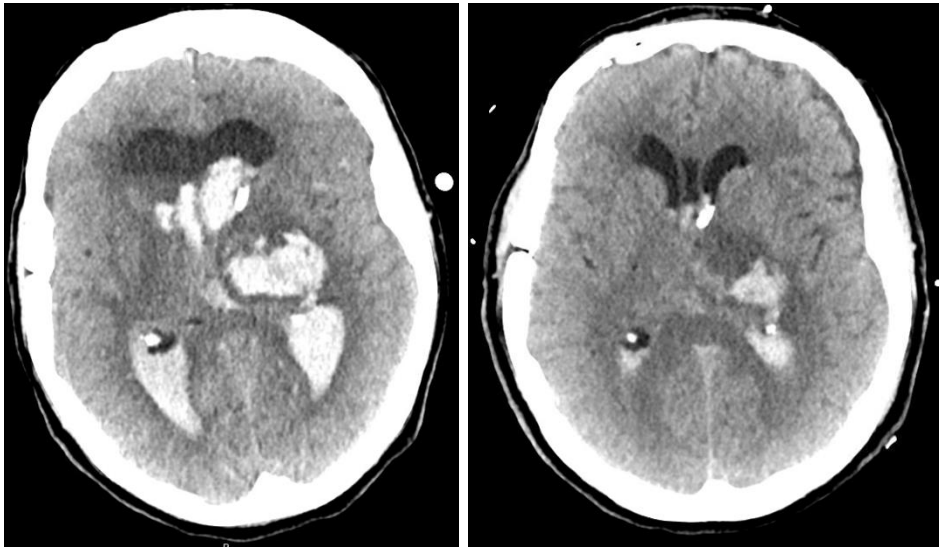


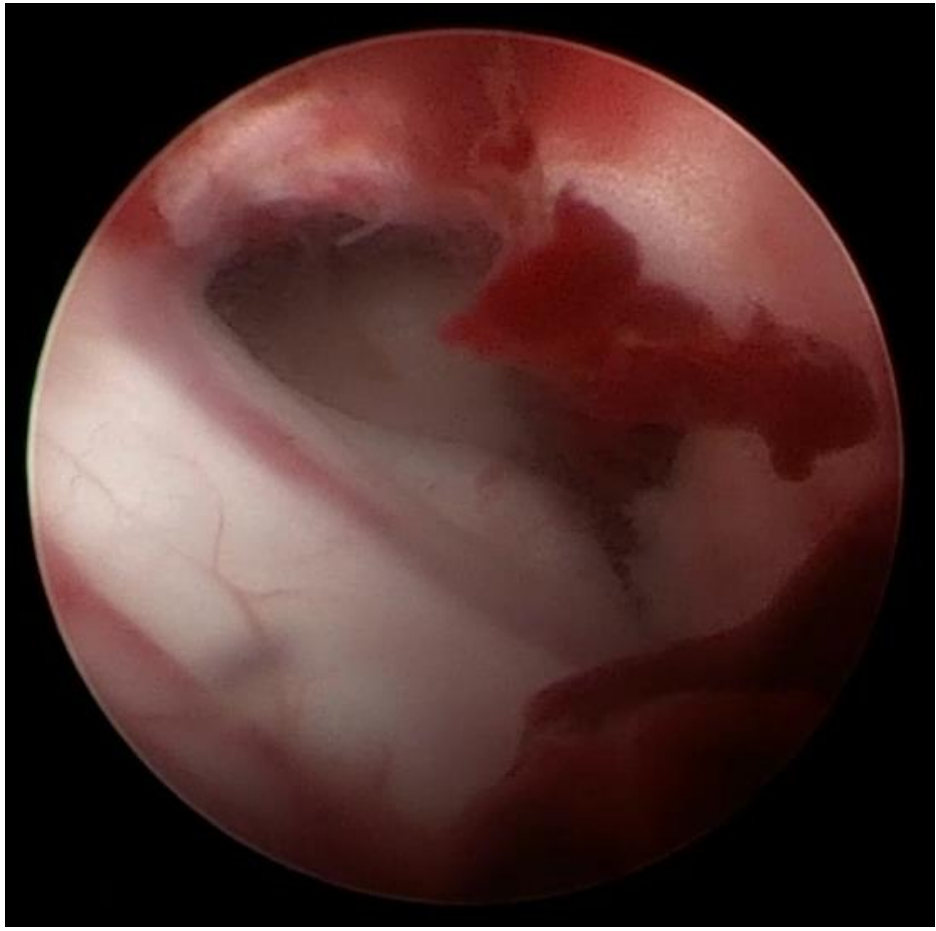
- Evacuate the hematoma until tissue differentiation is seen.
- Exit sheath later in case.

Setup: Room Orientation

- Apollo™ System near patient's head, behind physician
- Endoscopy tower and neuronavigation at patient's feet
- If using intraop CT, need short drapes, minimize other equipment near head

PRE POST





51y F found unresponsive at home

- Exam
  - GCS 4T
  - Intubated
  - Pupils 2mm, non-reactive
  - Localizing lt UE
- CT: Lt BG ICH/ IVH
- OR: Apollo aspiration

- 49y M woke up w HA, emesis
  - Exam:
    - GCS 7T
    - Intubated
    - Localizing in all extremities
  - CT head:
    - Rt caudate ICH w IVH
  - OR:
    - Apollo aspiration
  - Permanent Shunt: None

PRE

POST

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- 53y F found unresponsive
  - GCS 8 at OSH, there decompensated to 4T
  - Exam:
    - GCS 4T
    - Intubated
    - Pupils 3mm, sluggish
    - Localizes rt UE
  - CT: pan IVH
  - OR: Apollo aspiration
  - Permanent Shunt: Yes

PRE

POST

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- 56y M presented with confusion, rt sided weakness
  - Exam:
    - GCS 14
    - Dysarthric
    - Plegic on Rt
  - CT: lt thalamic ICH/ IVH
  - OR: Apollo aspiration
  - Permanent Shunt: None

PRE

POST

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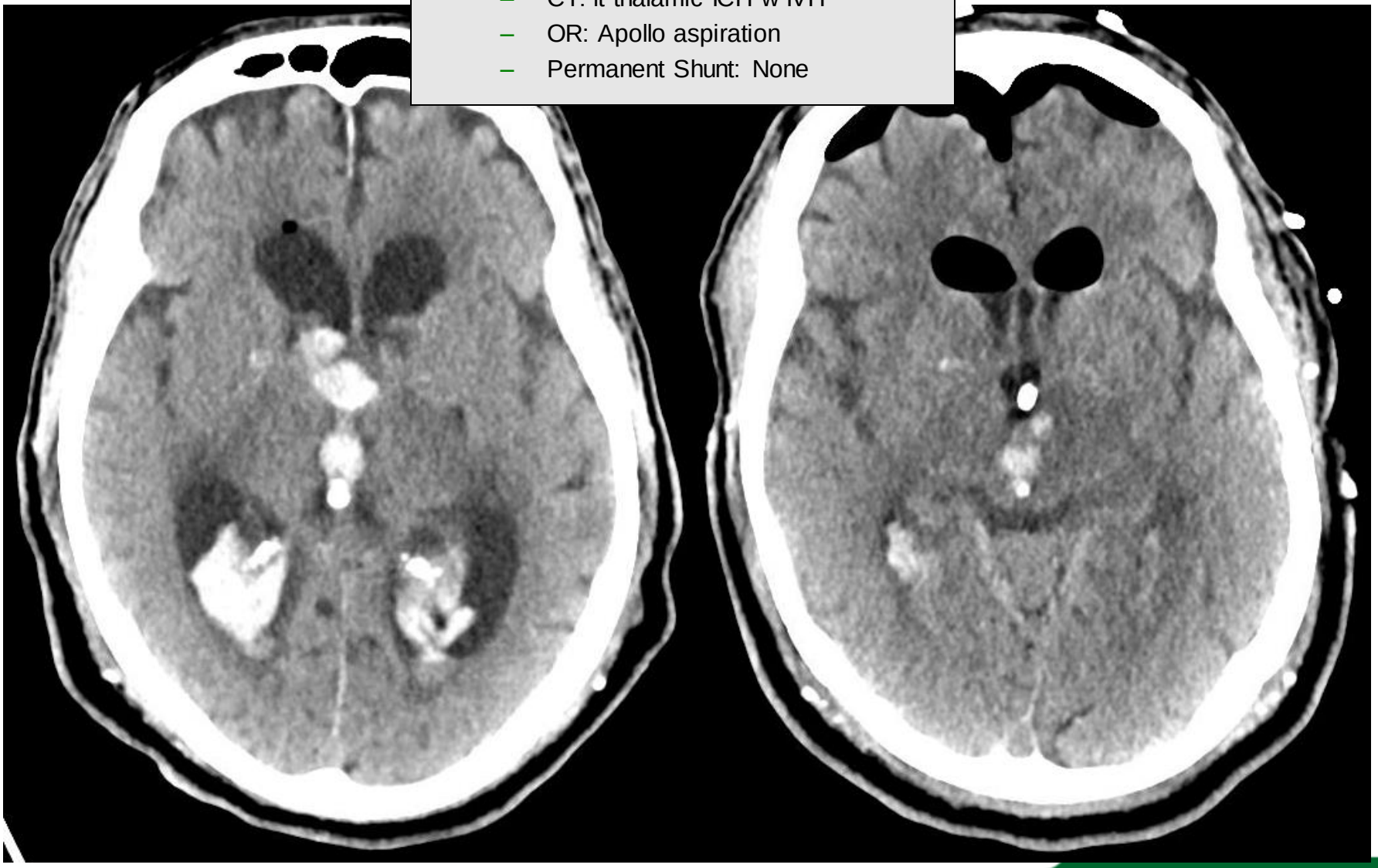
- 76y M found unresponsive
  - Exam
    - GCS 3T
    - Eyes closed to painful stimuli
    - No movement of extremities
  - CT: lt thalamic ICH w IVH
  - OR: Apollo aspiration
  - Permanent Shunt: None

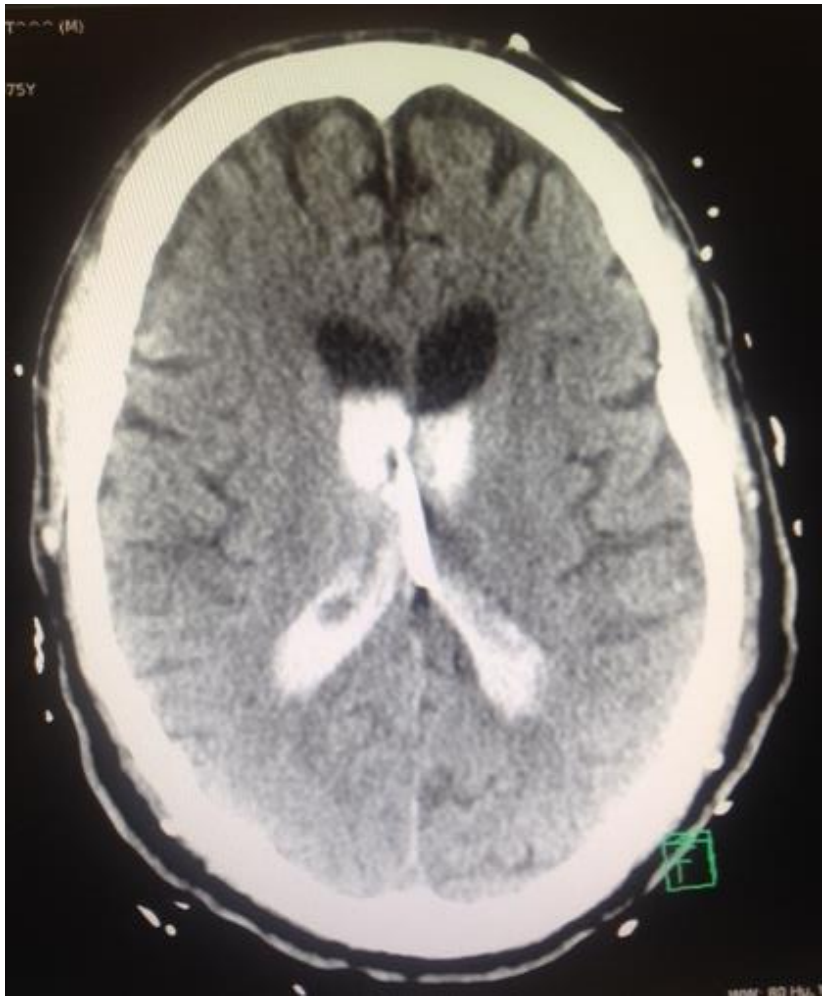
PRE

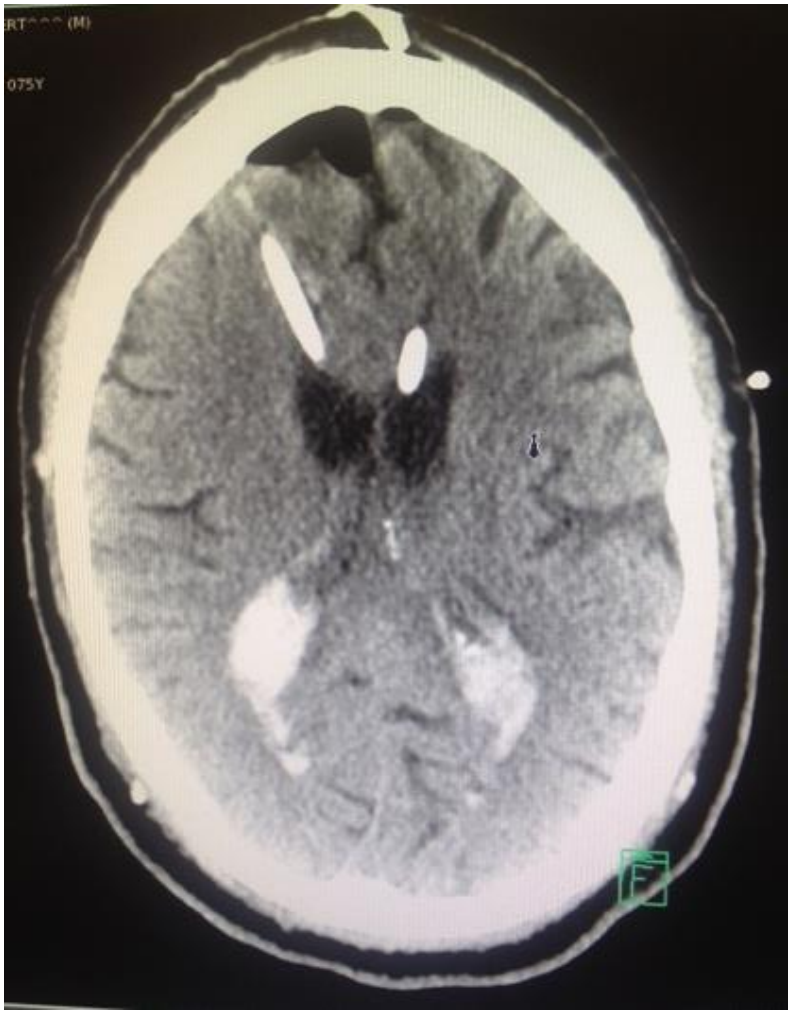
POST



Bilateral Casted Ventricles

Surgical Goal: Bilateral ventricular aspiration to clear IVH

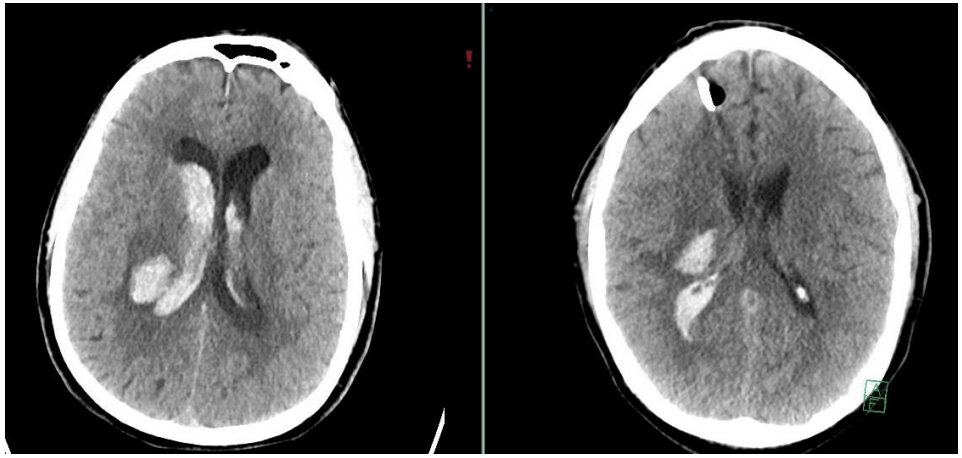


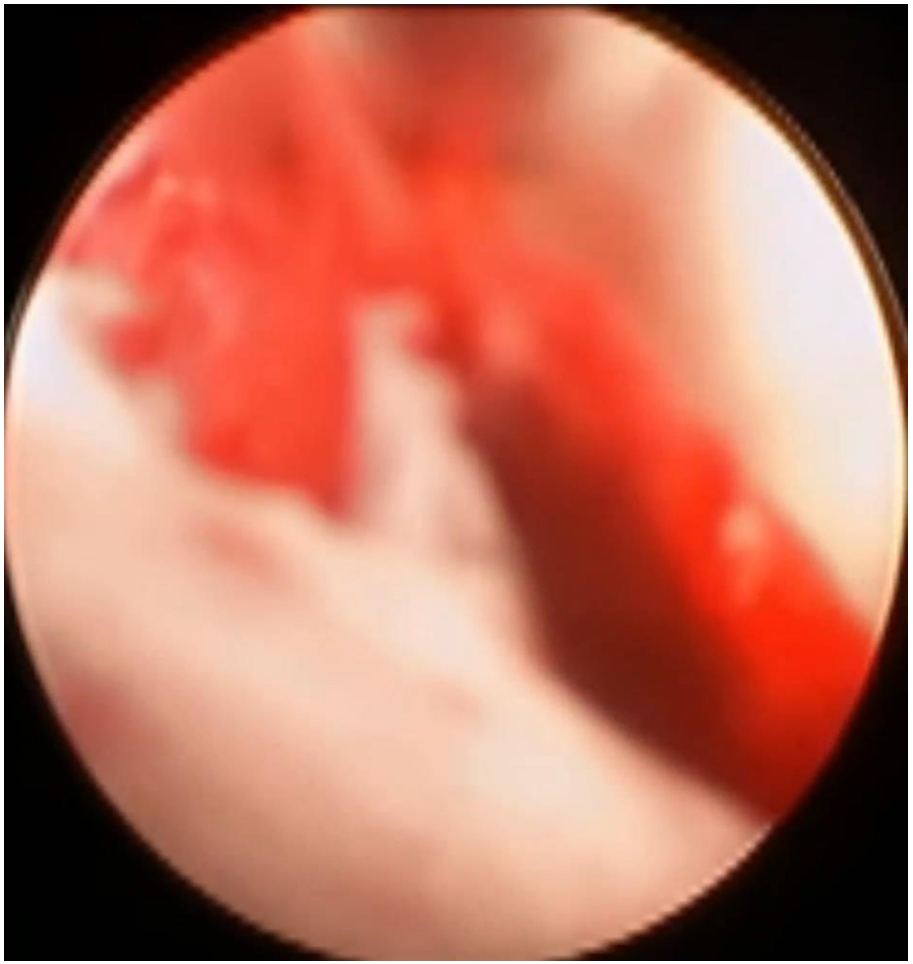


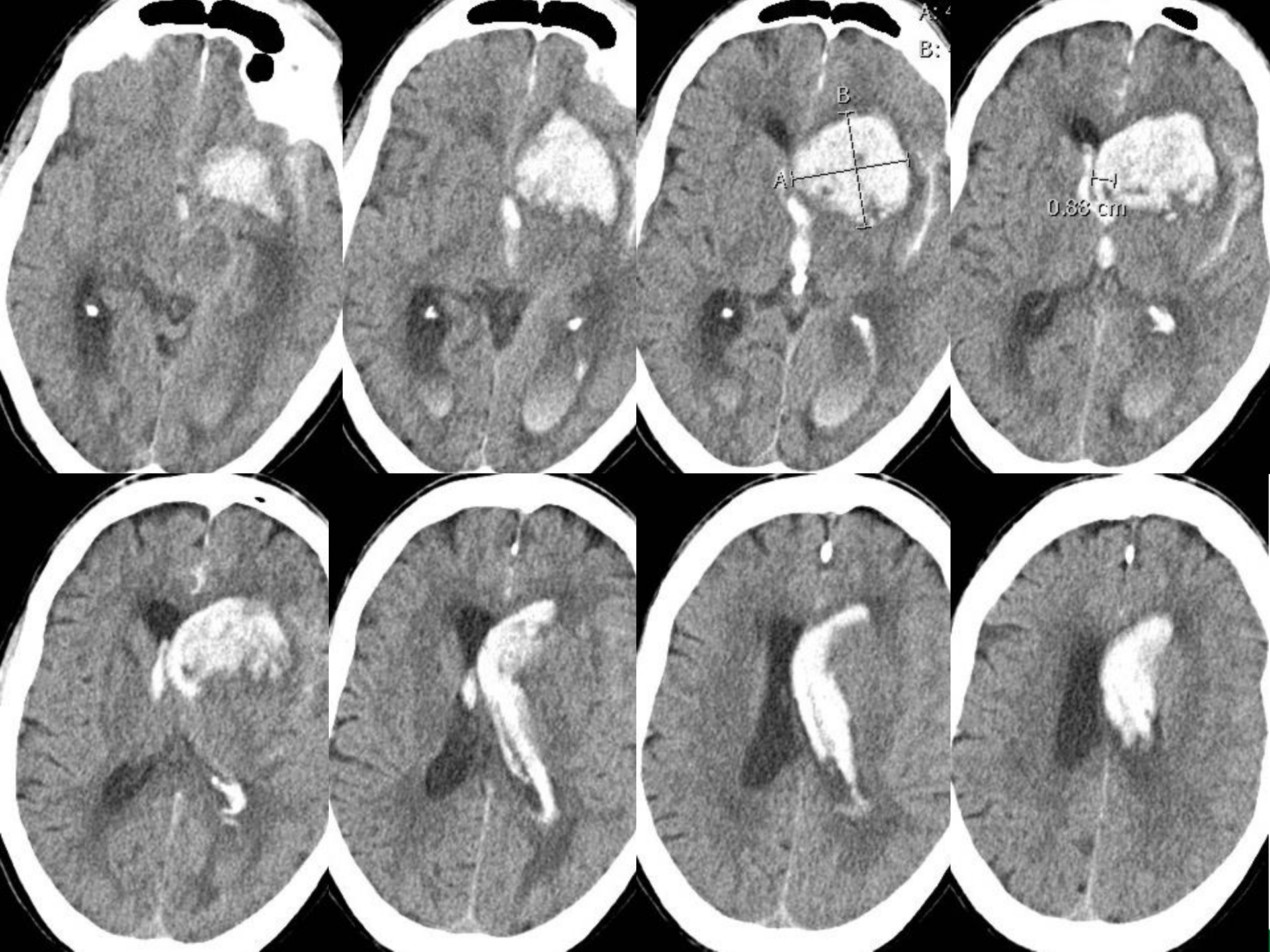
Surgical goal : Clear Frontal Horn and Foramen of Monro

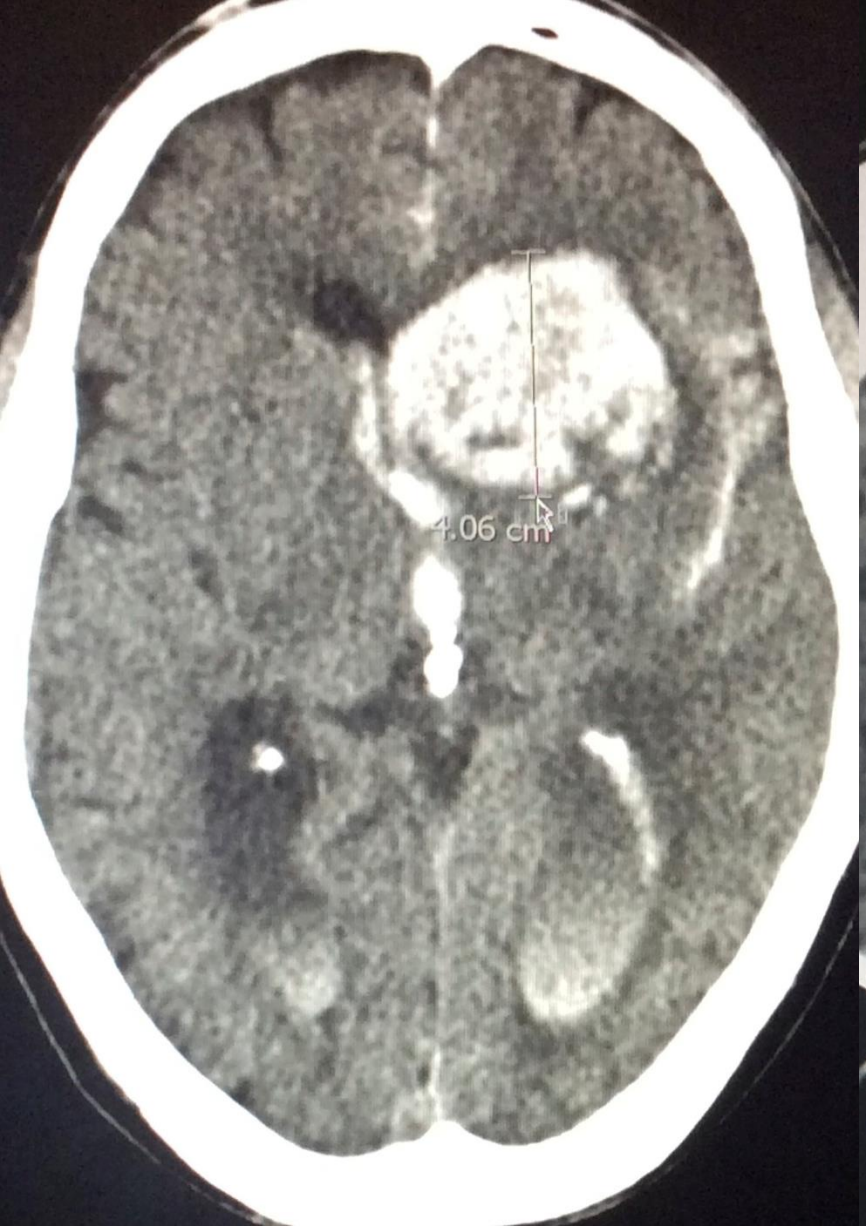
Pre

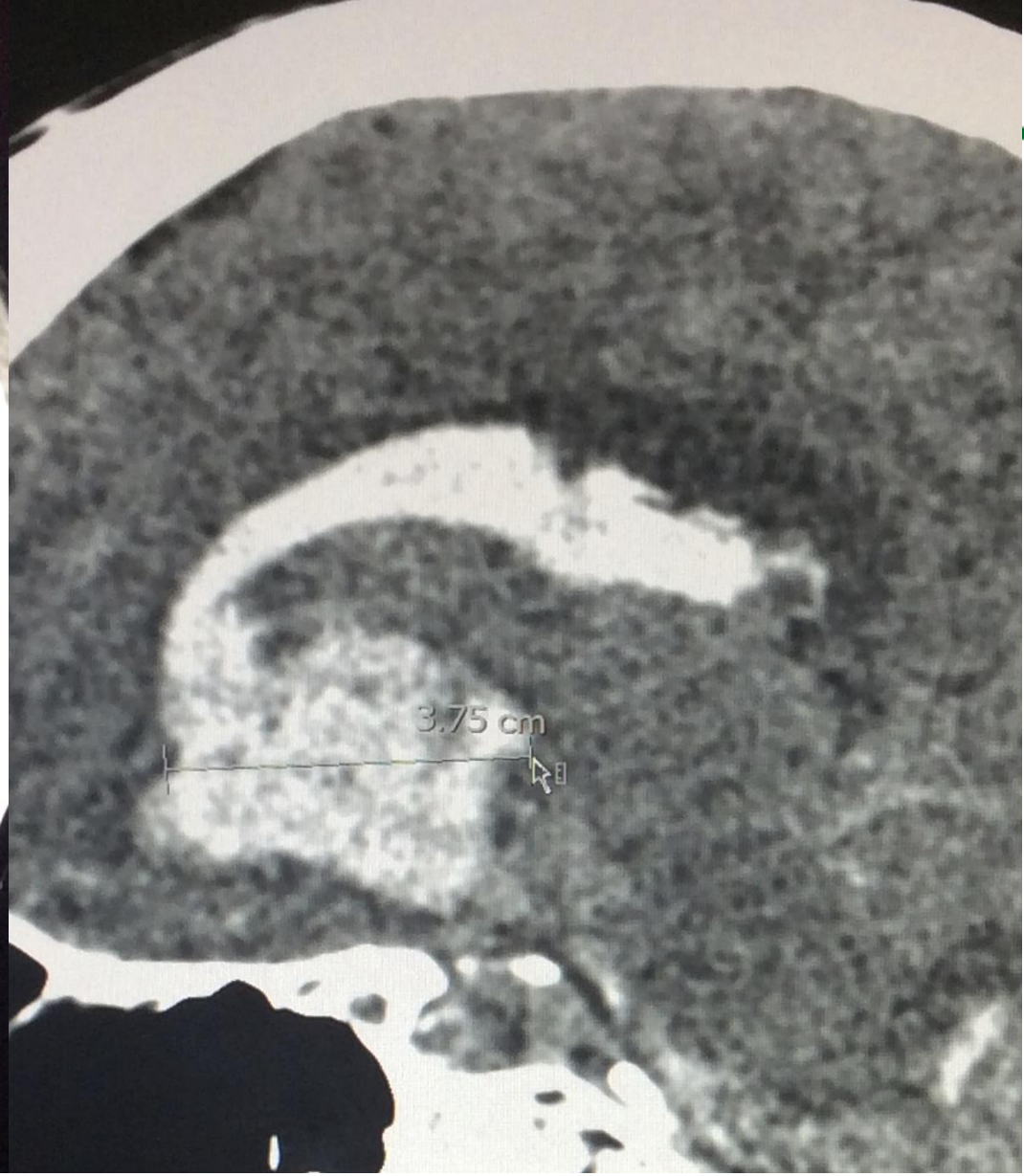
Post

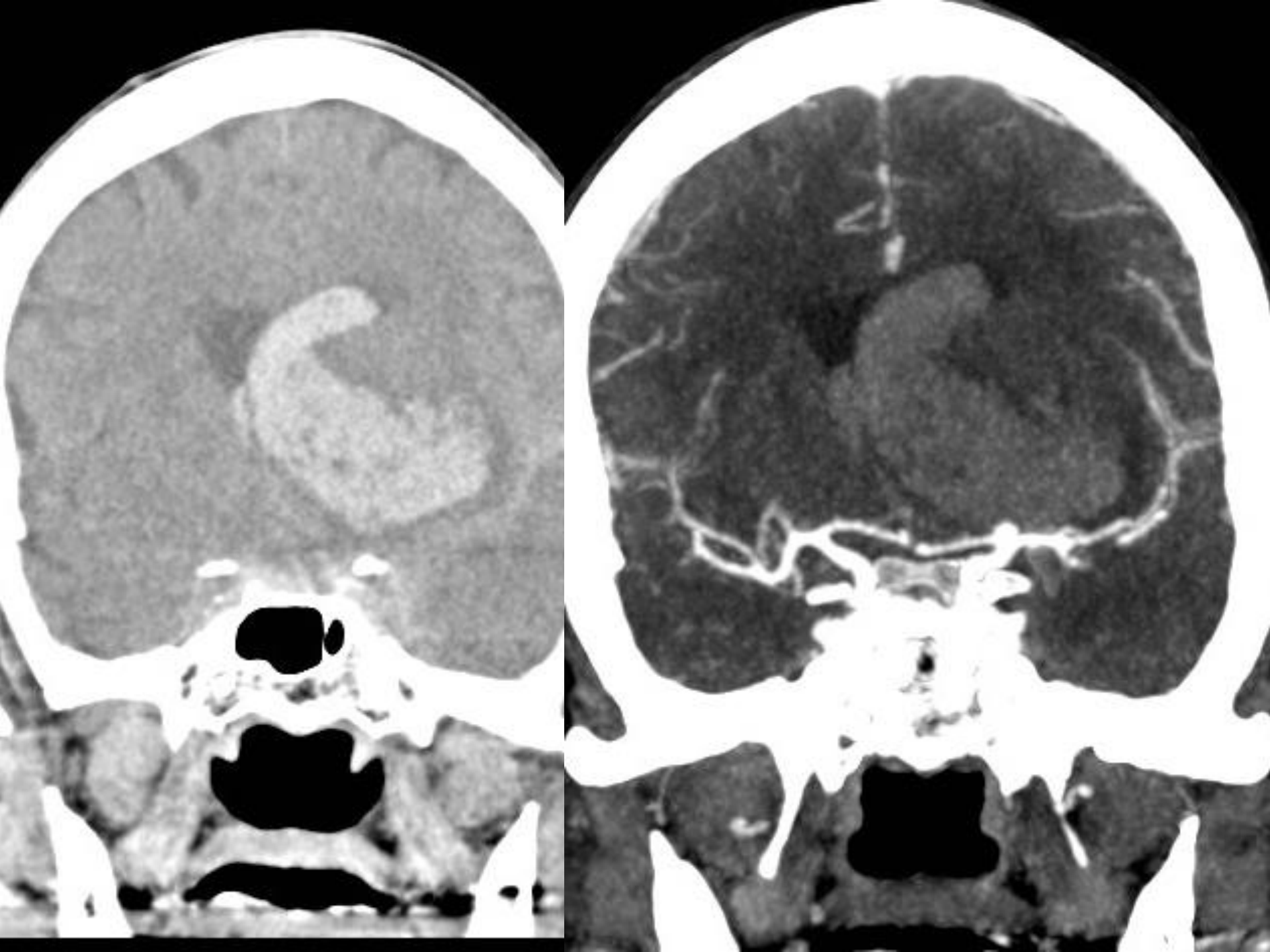


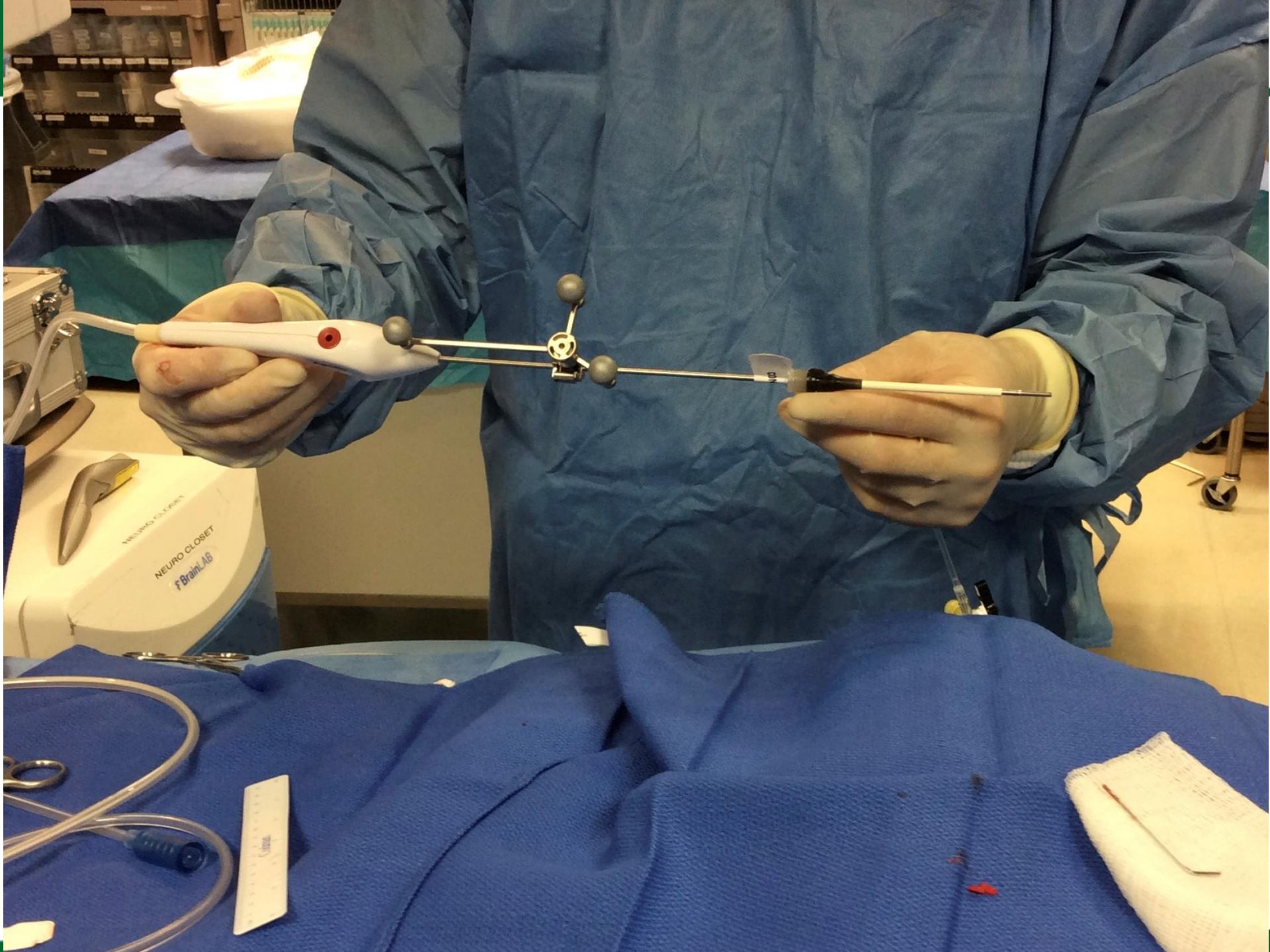


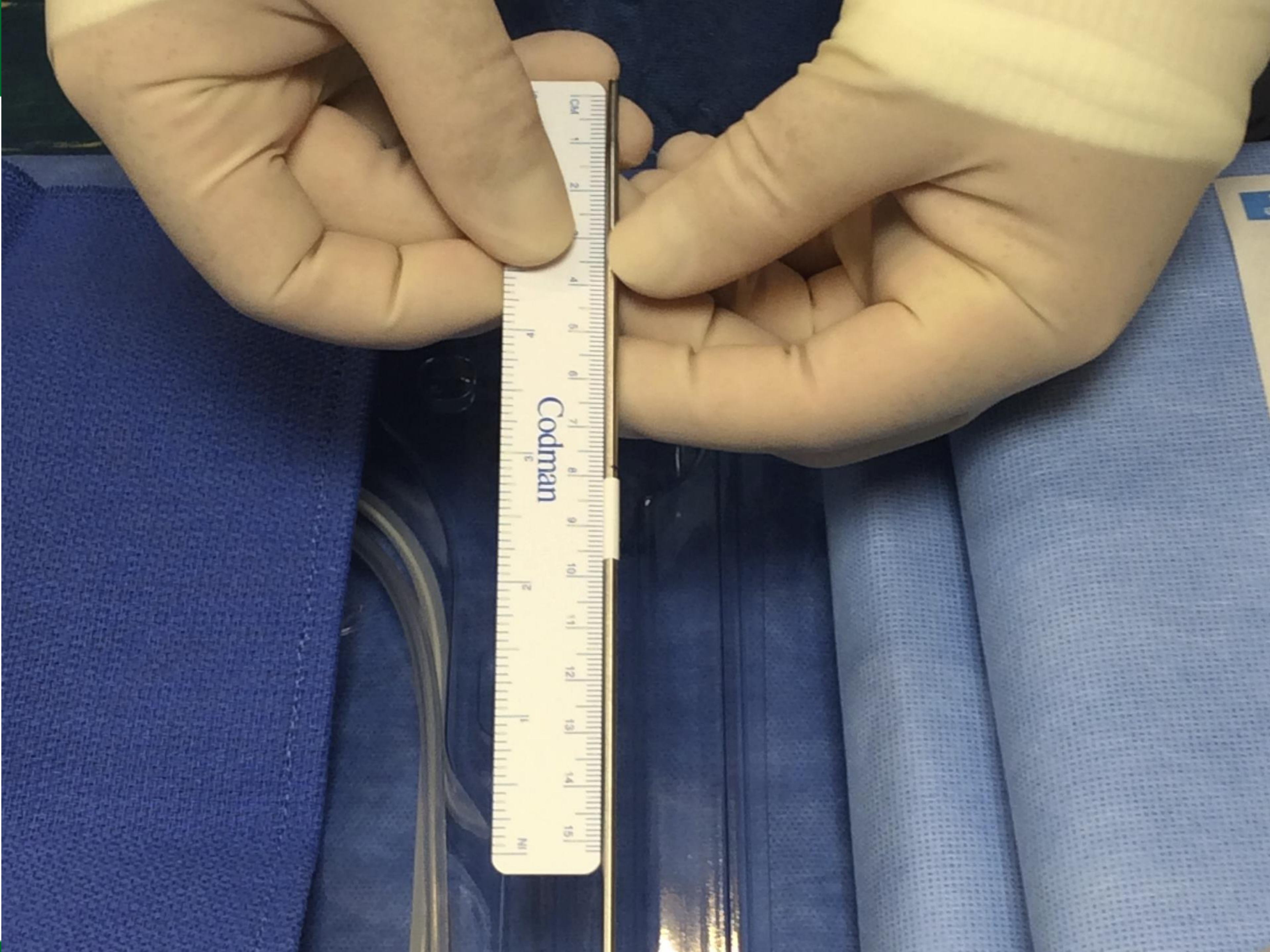

B
A
0.83 cm


4.06 cm


3.75 cm



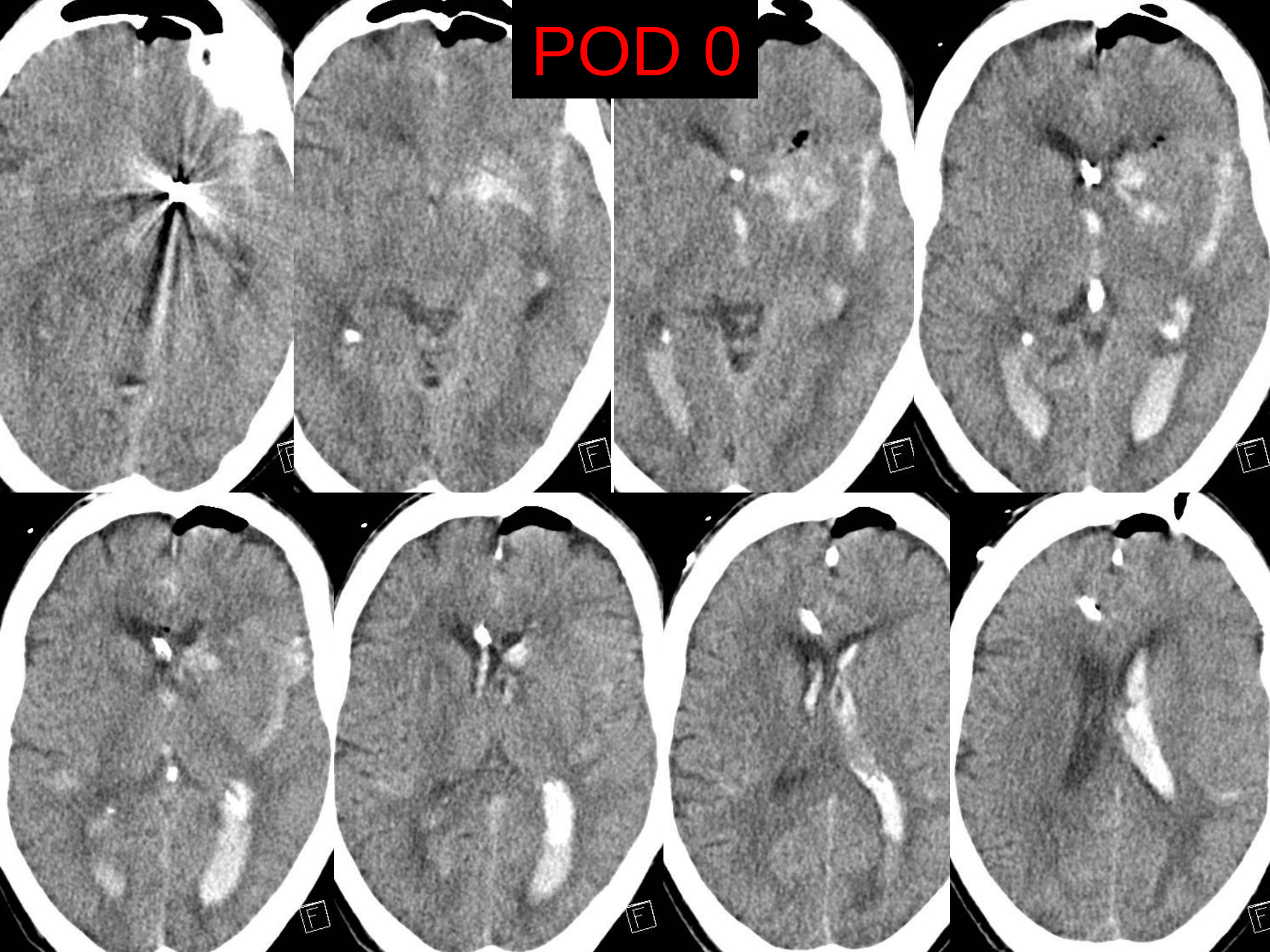

NEURO CLOSET
BrainLAB

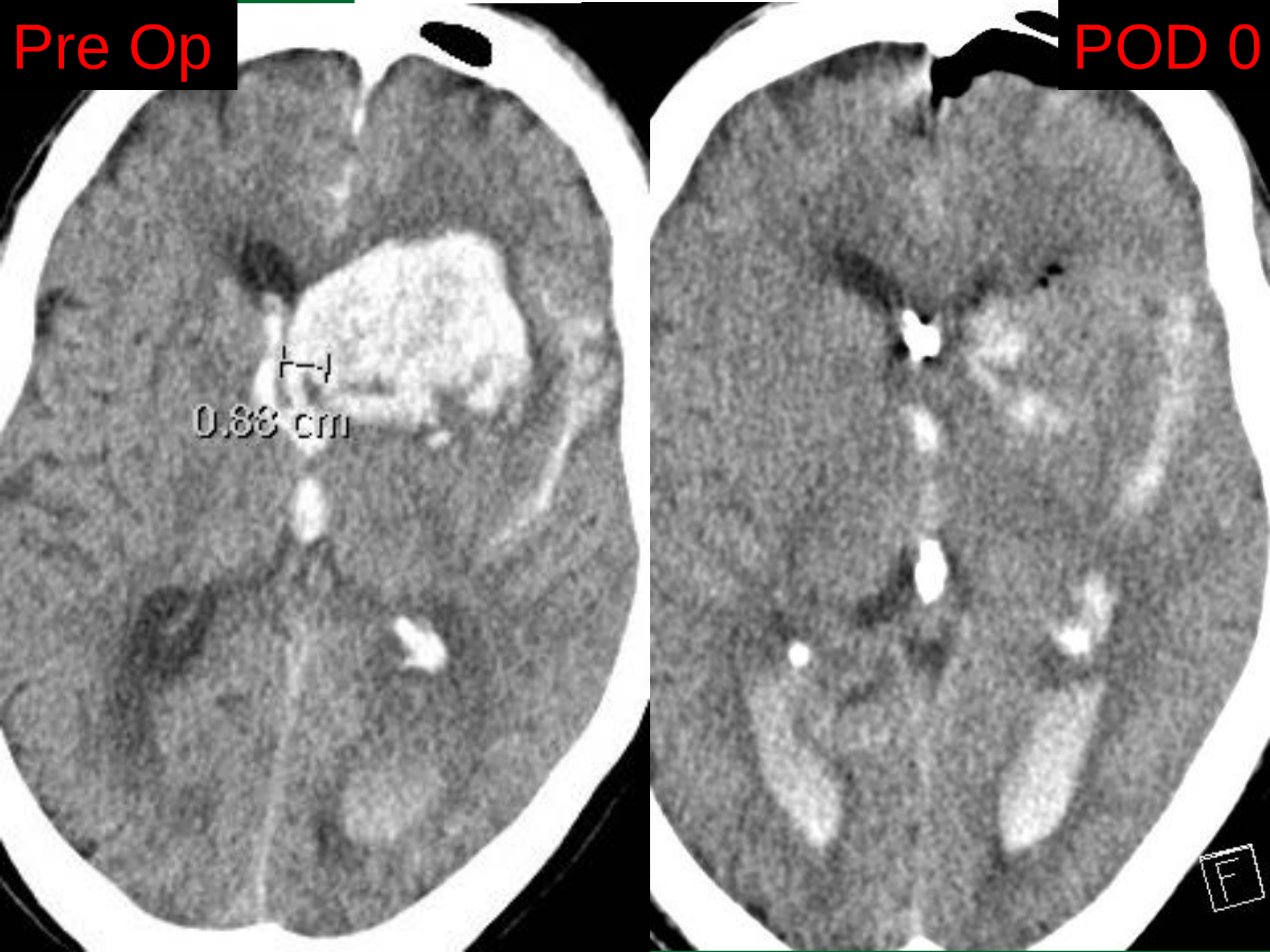

CM
Codman


BRAINLAB


400 ml
300 ml
200 ml
100 ml


Apollo™ System
02:50

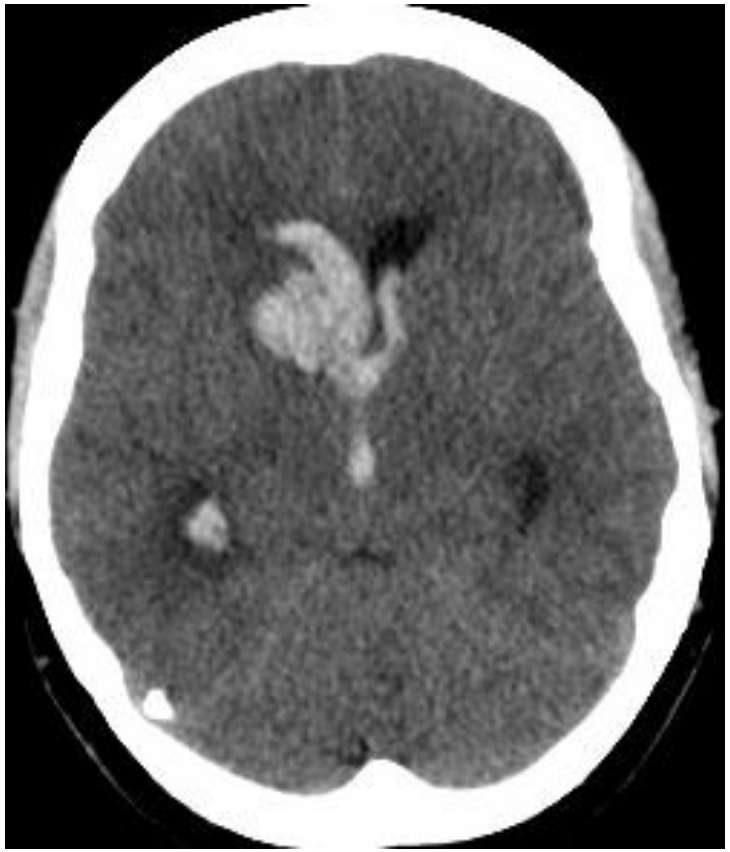

POD 0


Pre Op
0.88 cm
POD 0


POD 6

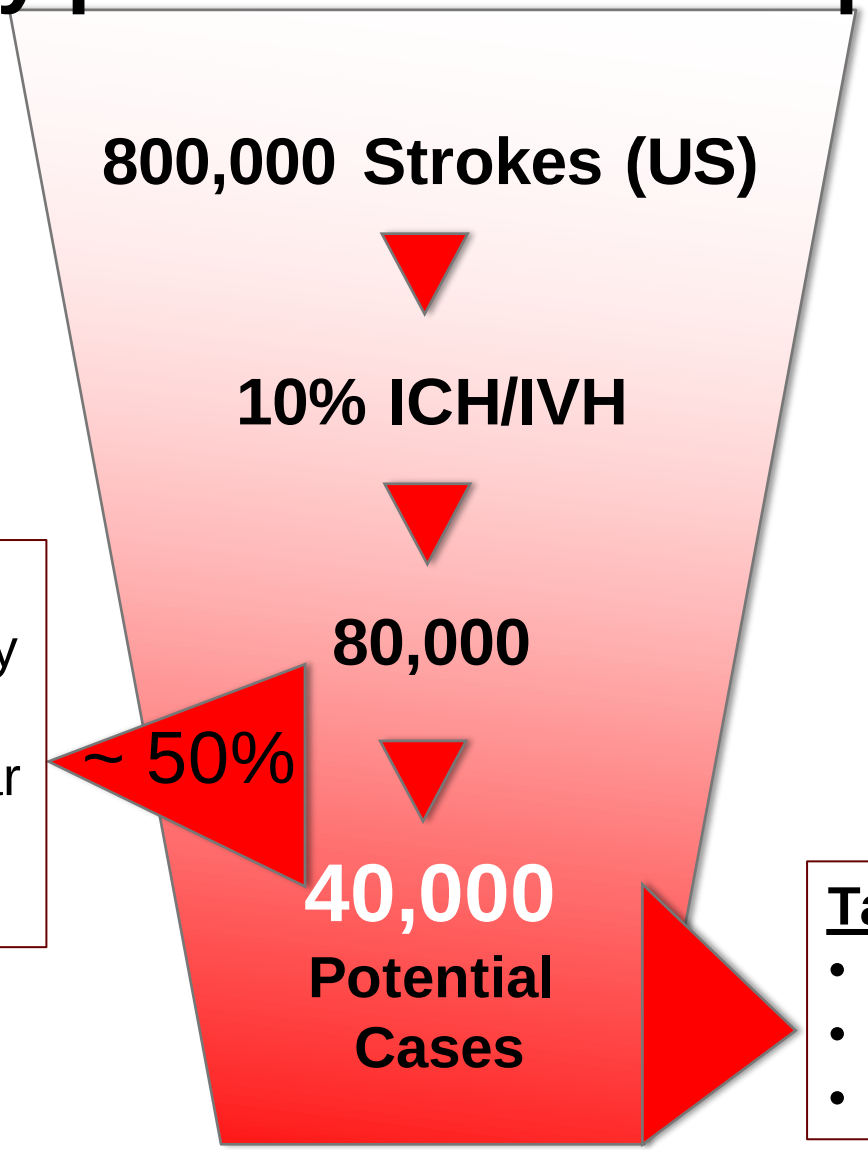
Why do we care about ICH?

NEUROLOGICAL INJURY AFTER ICH



- Stage 1: Mechanical Disruption
  - Immediate mechanical destruction of neurons
- Stage 2: Local Ischemia
  - Adjacent brain suffers ischemia from pressure
- Stage 3: Hemotoxicity
  - Hours, days even weeks after hemorrhage
  - Direct toxic effects of blood product degradation on surround brain tissue

How many patients can be helped in USA?



Not Targets:
- Acute mortality
- < 20 cc clot
- Amyloid, Lobar
- Subdural
- Subtentorial

Target:
- Anterior, Ventricular
- Hypertensive
- > 20 cc clot

ICH TREATMENT

- Removal of blood products could improve outcomes
  - Relieve local ischemia
  - Remove hemotoxic material
- Must be accomplished without any additional injury to the adjacent normal brain

Apollo Randomized Clinical Trials

- **US INVEST**
  - **Phase II, Randomized, Controlled Trial of Minimally INVasive Endoscopic Surgical Treatment with Apollo versus Medical Management for Supratentorial Intracerebral Hemorrhage (ICH)**
    - **Physician investigator-sponsored IDE**

Design INVEST

- Study Design:
  - Prospective, randomized, multi-centered trial that will enroll 222 patients at up to 30 US centers
  - Allowing for 10% lost to follow-up

*Concurrent registry for patients treated with Apollo MIES at INVEST sites who do not qualify for the trial

Objective

- To provide an initial assessment of the safety and efficacy of minimally invasive endoscopic surgery with Apollo for the evacuation of intra-cerebral hemorrhage (ICH)

Patient Population

- Stable patients with moderate to large (20-80cc) supratentorial ICH
  - with a significant baseline neurological deficit
  - good pre-hemorrhage neurological status

Randomization

- Patients will be randomized to either minimally invasive endoscopic evacuation with the Apollo system or best medical management (1:1)

Primary Endpoints

- Primary Efficacy Outcome: mRS $\leq$ 3 @ 180 days
- Primary Safety Outcome: Mortality @ 30 days

RUSH UNIVERSITY MEDICAL CENTER

Rush Center for Neuroendovascular surgery

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