

Modern Management of Intracerebral Hemorrhage

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Goals

1. Know what to expect
2. Emergent medical management
3. Is my patient a surgical candidate?
4. Minimally invasive surgical management

The Stats

1. Spontaneous ICH accounts for 15% of all strokes
2. Major cause of morbidity and mortality especially in the first 48hrs
3. Early neurologic deterioration within 48hrs;
30 day mortality 47%

Complications

1. Hematoma expansion
2. Intraventricular hemorrhage
3. Perihematomal edema
4. Hypertention
5. Hydrocephalus
6. Seizures
7. Hyperglycemia
8. Venous emboli
9. Fever

Presentation

- **Headache**
- **Nausea and Vomiting**
- Sudden loss of consciousness or change in consciousness
- Sudden focal weakness or other focal neurologic symptom
- HTN

Suspect
ICH!!!



What caused these ICHs?

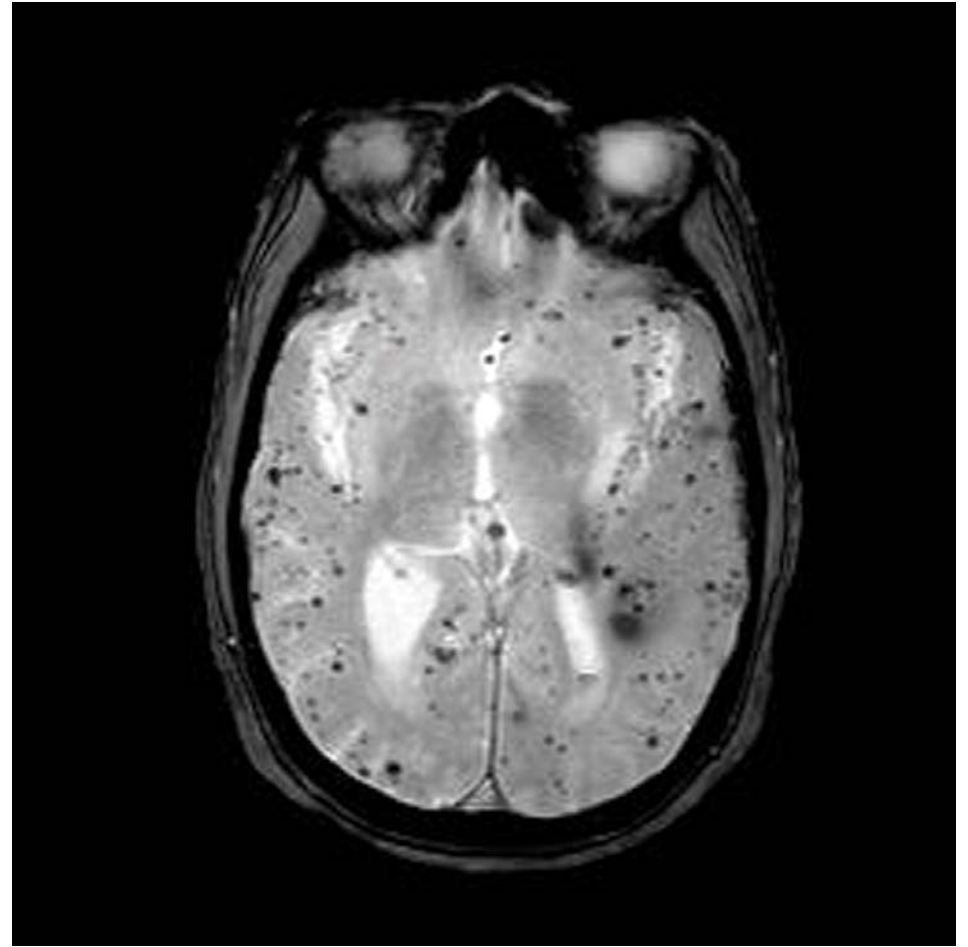
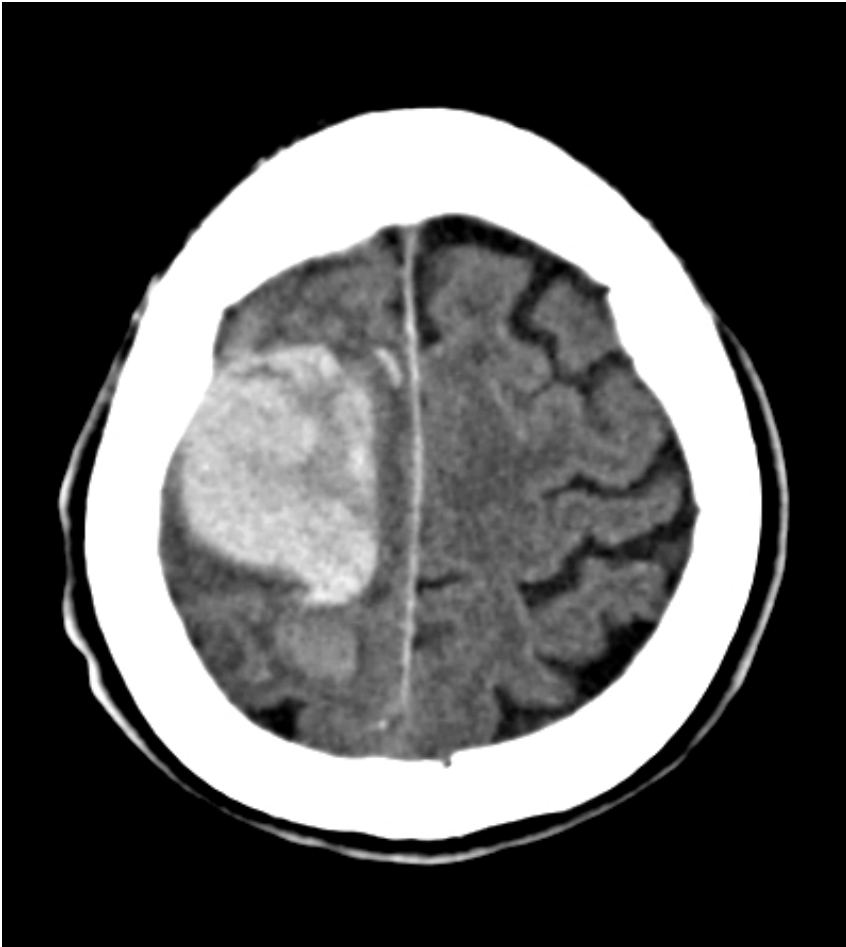


Etiology

Primary ICH:

HTN or amyloid angiopathy (80%)

What caused this ICH?



Etiology

Secondary ICH:

Blood dyscrasias, liver, renal disease, malignancy, medications

Anticoagulants, antiplatelets

Drug abuse: cocaine, sympathomimetic

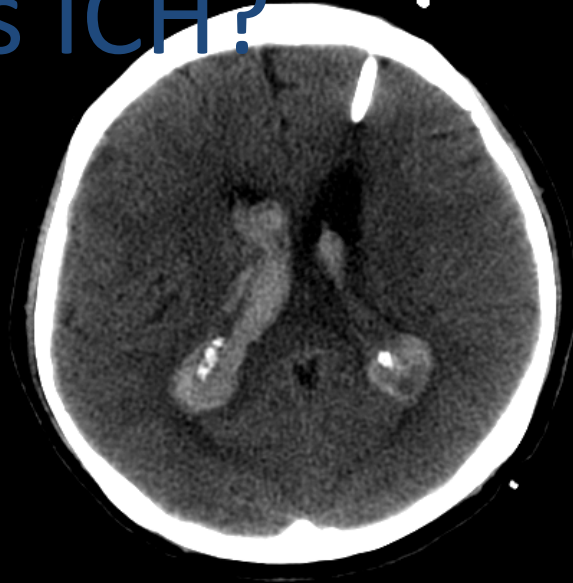
vascular malformations (AVM, cav mal)

tumors (melanoma, choriocarcinoma, renal carcinoma, thyroid carcinoma)

hemorrhagic transformation of an ischemic stroke

venous sinus thrombosis

What caused this ICH?



Acute Management

1. *Stat CT head noncontrast*
2. SBP 100-140
3. Reversing medications?
4. Hypertonic saline, mannitol
5. ICP < 20mmHg, CPP 50-70

Acute Management

6. Seizure prophylaxis: Is NO longer recommended:
 - prophylactic dilantin independent risk factor associated with death
 - HOWEVER, 30% nonconvulsive status.
 - Ideally....

Acute Management

7. Euthermia: goal 35.5 to 37.5; fever worsens outcome
8. Euglycemia: hyperglycemia associated with worse outcome; old goal 80-110
 - hypoglycemia also worsens outcome
9. DVT: after 24hrs AND cessation of bleeding
10. Peptic ulcer prophylaxis

Imaging

1. Noncontrast CT head
(standard)- STAT

When do I repeat imaging?

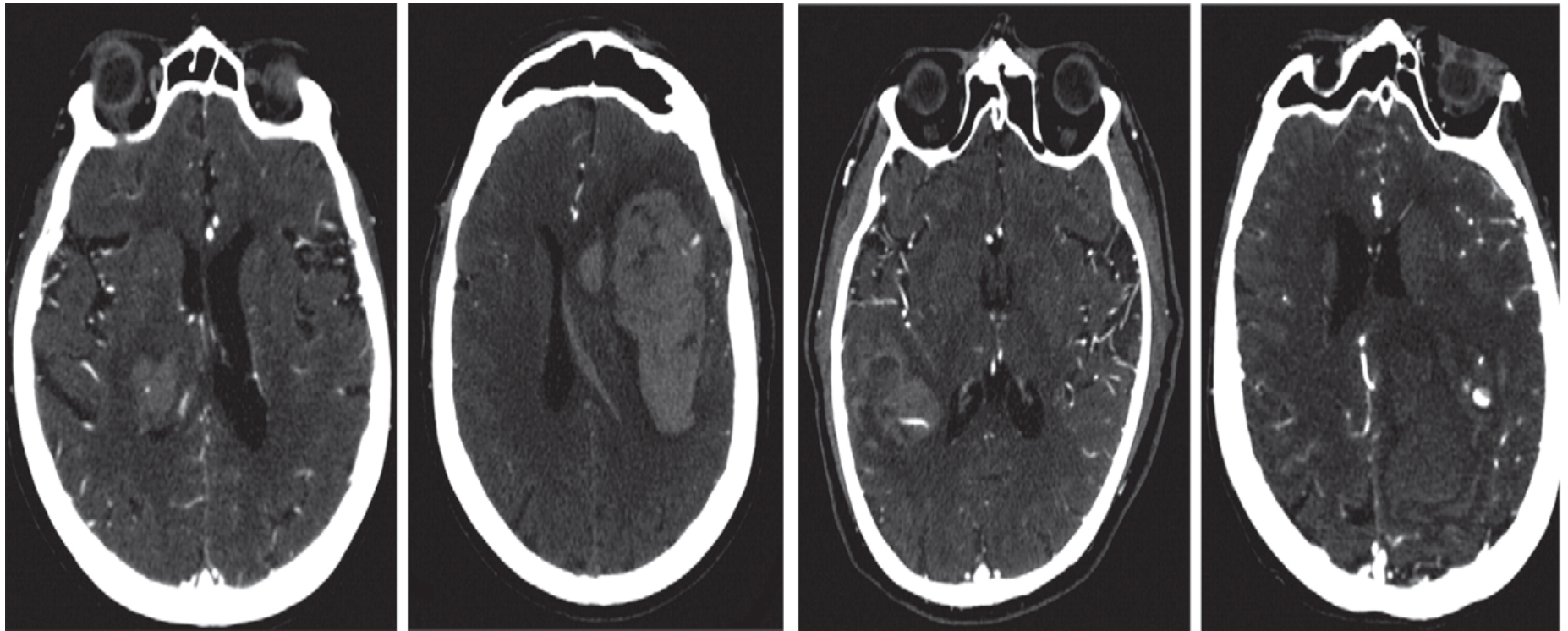
1. You need a second stability scan
 - CT#2 at 4-6 hrs
 - CT#2 at 24hrs

2. You should worry if..
 - Neurologic deterioration
 - Rebound coagulopathy

Hematoma Expansion

1. 40% of true expansion (> 33% size increase) occur within the first 3 hours
2. 70% have some degree of expansion develops within the first 24hrs
3. Predictors: spot sign, large volume, heterogeneity, warfarin, biomarkers (IL6, TNF, Cr, fibrinogen) , hyperglycemia, hx CVA, AMS, liver disease

Spot Sign on CTA or CT with contrast indicates hematoma expansion



Work UP

1. CTA – “young” and no HTN hx, vascular malformations
2. MRI with gad – cavernous malformations, tumors, amyloid (DASH – diagnostic utility of MRI in Intracerebral Hemorrhage)
3. Cerebral angiogram: aneurysm, AVM but NOT cav mal
4. MRV or CTV

Blood Pressure Control

SBP goal 100-140: Do it quickly!!! Nicardipine gtt

INTERACT: early SBP <140 vs SBP < 180; 26% less expansion in <140 group

ATACH: early nicardipine gtt is safe in ICH (3 SBP ranges; 33%, 15%, 22% HE rates)

Phase 2 for both underway looking at clinical outcome

Anticoagulants and ICH

- OAC users account for 12-14% of ICH patients
 - ↑ HTN, Age, Amyloid, INR>3.5
- Management: Emergently reverse coagulopathy!

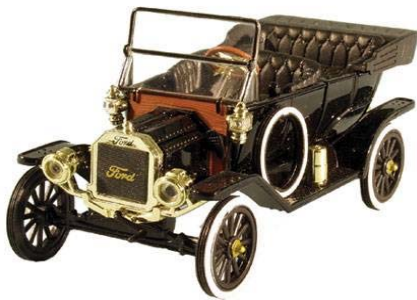
VITAMIN K SQ

FFP

FACTOR VIIa

VITAMIN K IV

PCC (Bebulin/Profilnine)



- Restarting Anticoagulants?
 - Case-by-case basis. 7-14 dys for mechanical valves

Reversing Medications

1. Heparin or lovenox: protamine (50mg max)
2. Plavix or Aspirin: platelets x1 unit
3. Coumadin: stat INR after infusions
 - **unactivated Prothrombin Complex**
(Bebulin): wt (kg) x 25 x 1 unit/kg
 - Factor VII – dangerous rebound
 - FFP/vitamin K
4. Platelet < 100,000: transfused x1 unit

Ncalrwc-A, Rwcvalida* MRN 110020000333 Room/Bed VIRAMIRA-01* Age 20 yrs Sex F DOB 4/1/1991 Allergies Pcn Class, Latex, Sulfs* Isolation Code None Prior Attending N/A LOS 272days Inactive

- ← →
- Patient Reports
- Chart Review
- Synopsis
- Results Review
- Problem List
- Rounding Report
- History
- Notes
- Demographics
- Allergies
- Order Entry
- Orders Modify**
- Intake/Output
- Reports Window
- Work/Activity Status
- Case Request
- Direct Admission
- ED Consult/Admission
- Transfer
- Discharge
- Rounding
- Consult
- Proc WITH Sedation
- Proc w/OUT Sedation
- FYI

Orders Modify (Contact Date: 2/23/2011)

Rounding Reorder PTA Meds

- Rounding
- BestPractice**
- Rounding Report
- MAR Report
- Problem List
- Discharge Info
- Discharge Prep
- Orders
- Order Sets**
- Progress Notes

Order Sets

rapid

- Intracranial Hemorrhage HBS (Mergeable) (User)
- Suggestions**
 - Altered Level of Consciousness
 - Atrial Fibrillation
 - Electrolyte Abnormalities
 - Fever (User)
 - GI Bleed (Mergeable)
 - Rounding Orders (Long)
 - Rounding Orders (Short)
 - Syncope
- Favorites**
 - Amiodarone (User)
 - Atrial Fibrillation
 - Cardiac Heparin ED and Hospital With
 - Comfort Care (User)
 - CVATIA Initial Evaluation HBS/ED
 - DELIRIUM HBS IP NCAL (User)
 - Electrolyte Abnormalities
 - Fever (User)
 - Hyperkalemia
 - INFLUENZA IMMUNIZATION HBS IP NCAL
 - Insulin Sliding Scale / Supplemental In
 - Interfacility Transport Orders
 - Intracranial Hemorrhage HBS (Mergeable)
 - Ischemic Stroke HBS (Mergeable) (User)
 - Ischemic Stroke Post TPA Inpatient HBS

You can set your favorites by right-clicking on an order set.

Record Select

Search: rapid

%	Protocol Name	Protocol ID
■	RAPID SEQUENCE INTUBATION ED NCAL	414320
■	ARRHYTHMIA ED NCAL(aka RAPID HEARTRATE)	414292
■	NEUROSURGICAL RAPID REVERSAL OF COAGULOP...	415866

3 records total, all records loaded.

Progress Notes --- Please use the appropriate note type.
Create Note | Go to Notes | Refresh

No notes filed since 11/21/11 0528.

- Mechanical Ventilation ICU with Protocol Hyperlink (User)
- With Hyperlinked Protocol (User)
- apid Reversal Of Coagulopathy
- omplemental Adult Orders (User)
- Orders Adult
- e Orders
- IMMUNIZATION ORDERSET HBS IP NCAL
- SURGICAL STEROID (User)
- ement with Protocol Hyperlink ICU
- DT with Protocol Hyperlink ED/ICU/HBS
- on HBS IP NCAL (User)
- Stroke HBS
- (User)
- It (User)
- n-Analgesia (ICU)
-
- artnote, .obcspnote, .obobsnote etc.

Neurosurgical Rapid Reversal of Coagulopathy

Physicians treating life-threatening CNS bleeding in the setting of coagulopathy should quickly consult with the nearest KP comprehensive neuroscience center (Kaiser Redwood City 650-299-3800 or Kaiser Sacramento 916-973-5288, on-call neurosurgery) for additional guidance regarding management.

Vitamin K

Vitamin K

- Phytonadione (MEPHYTON) 10 MG ORAL
10 mg, Oral, DAILY (INPT RN CHECK 1ST DOSE) for 3 doses
- Phytonadione (AQUA-MEPHYTON) 10 MG IV ONE TIME
10 mg, Intravenous, ONE TIME, * Slow infusion over 15 minutes
- Phytonadione (AQUA-MEPHYTON) 10 MG IV DAILY X 3
10 mg, Intravenous, DAILY (INPT RN CHECK 1ST DOSE) for 3 doses, * Slow infusion over 15 minutes

Protamine

Protamine

Usual dose: 1 mg IV for every 100 units of heparin remaining in patient; if 30 minutes have elapsed since the injection of heparin one-half the dose may be sufficient; maximum 50 mg given over 10 minutes

- Protamine IV
Intravenous, ONE TIME, 1 dose

Advisory

Antihemophilic agents (Recombinant Factor VII and Prothrombin Complex Concentrate) are recommended for use in life endangering hemorrhages such as intra-cranial hemorrhage. These products may NOT be in stock at all facilities. Please verify availability with the Inpatient Pharmacy prior to ordering.

Recombinant Factor VIIa (NovoSeven)

Recombinant Factor VIIa

REMINDER: Place orders for post infusion labs.

- Coagulation Factor VIIa Recomb (NOVOSEVEN RT) 40 MCG/KG IV
40 mcg/kg/dose, Intravenous, ONE TIME
- Coagulation Factor VIIa Recomb (NOVOSEVEN RT) 80 MCG/KG IV
80 mcg/kg/dose, Intravenous, ONE TIME

STAT INR Post Factor VII

- STAT INR Post Factor VII
PER COMMENT, MULTIPLE OCCURRENCES - STAT for 4 occurrences, Obtain STAT INR after Factor VII (NovoSeven). Notify physician if INR is greater than 1.3 and blood products are not ordered.

Prothrombin Complex Concentrate (Factor IX Complex / Profilnine SD)

Prothrombin Complex Concentrate

This clinical calculator is for dosing PCC to reverse warfarin coagulopathy in the clinical setting of a Neurosurgical Emergency ONLY The final dosage should be further adjusted based on clinical factors such as cardiac status. REMINDER: Place orders for post infusion labs.

[Dose Calculator \(click to view\)](#)

- Factor IX Complex (PROFILNINE SD) IV
Intravenous, Following reconstitution, do NOT refrigerate and use within 3 Hours. Rate not to exceed 10 mL/minute for Profilnine SD.

STAT INR Post Prothrombin Complex Concentrate (Factor IX / Profilnine SD)

- STAT INR Post Prothrombin Complex Concentrate (Factor IX / Profilnine SD)
PER COMMENT, MULTIPLE OCCURRENCES - STAT for 4 occurrences, Obtain STAT INR after Prothrombin Complex Concentrate (Factor IX / Bebulin). Notify physician if INR is greater than 1.3 and blood products are not ordered.

TRANSFUSION

Transfuse Fresh Frozen Plasma

This clinical calculator is for dosing FFP to reverse warfarin coagulopathy in the clinical setting of a Neurosurgical Emergency ONLY The final dosage should be further adjusted based on clinical factors such as cardiac status. If Pre-Transfusion medication is ordered, please select the nursing notification order.

[FFP Calculator](#)

- Transfuse Fresh Frozen Plasma

Perihematomal Edema Management

1. Hypertonic saline: neurosurgical supplement order set. Raise Na 140-150 range. Or higher...
 - serum Na q6 hrs (hold > 165)
 - Central pontine myelinolysis!!!
2. Mannitol 0.5g/kg q 6 hours
 - serum osmolality q6 hrs (hold >320)

1. Does my patient need a neuroICU?

2. Does my patient need an ICP monitor or ventriculostomy?

ICH AND GCS < 8

ICP is high until proven otherwise!!!! So treat as such:

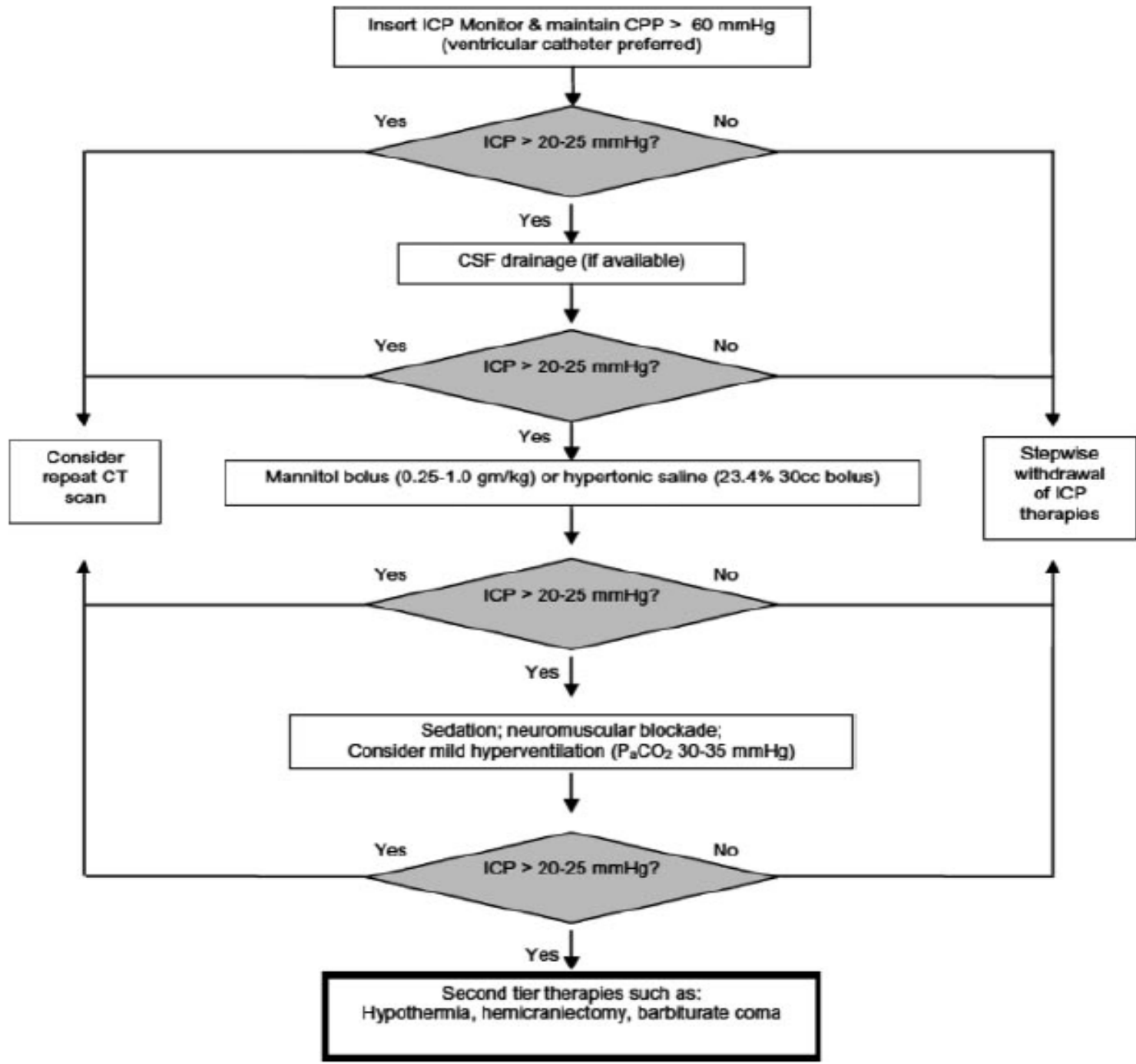
1. Consider *transfer* to NeuroICU
2. EVD or ICP monitor: (AHA 2010)
 - a) GCS < 8 and/or
 - b) hydrocephalus (+/-) IVH
3. Hyperventilate: paCO₂ 30-35
4. Load with anti-epileptic
5. Use combination mannitol/hypertonic saline

Additional Management of Refractory HIGH ICP

1. Sedation with continuous infusions: prevent agitation and ventilator dyssynchrony
2. Hypothermia: may need to paralyze
3. Pentobarbital coma: bolus 15mg/kg, titrate to burst suppression

Even if your patient is not a surgical candidate, there are many medical treatments that may be necessary if GCS < 8

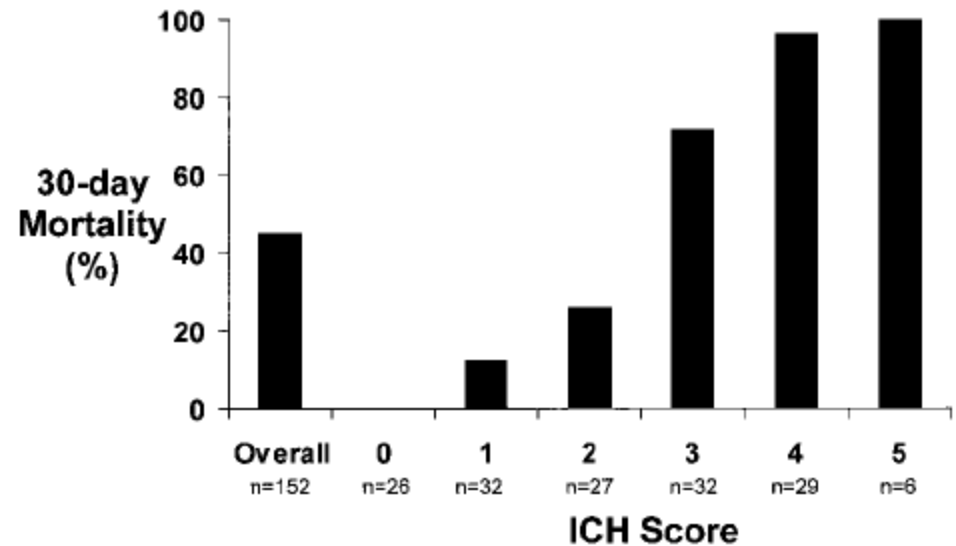




Outcome determinants (*medical management alone*): ICH Score

TABLE 3. Determination of the ICH Score

Component	ICH Score Points
GCS score	
3–4	2
5–12	1
13–15	0
ICH volume, cm ³	
≥30	1
<30	0
IVH	
Yes	1
No	0
Infratentorial origin of ICH	
Yes	1
No	0
Age, y	
≥80	1
<80	0
Total ICH Score	0–6



(*Stroke*. 2001;32:891-897.)

Surgical vs Medical management

VS

Minimally Invasive Management

Candidate.....

Who is a surgical candidate?

STICH Trial Lancet 2005

1033 ICH patients (all locations)

Early craniotomy (<96hr) vs medical management

NO overall benefit (26% vs 24% favorable outcome;
p=0.41

Subgroup analysis: trend toward benefit IF
supratentorial ICH < 1cm from surface (STICH II)

AHA Guidelines 2010

1. **Cerebellar ICH (>3cm)** with
 - a. neurological decline *or*
 - b. brainstem compression *and/or*
 - c. hydrocephalus

should undergo urgent surgery !

2. **Cerebellar ICH**, initial treatment with EVD/CSF drainage alone is not recommended! (new)

AHA Guidelines 2010

2. **Lobar ICH** > 30ml and within 1cm of the surface should be considered for craniotomy

3. Usefulness of surgery is uncertain. NO evidence for ultra-early evacuation of hematoma on mortality and ultra-early surgery has potential risk for recurrent bleeding.

What about subcortical or basal ganglia ICH?

MISTIE trial includes both lobar and basal ganglia ICH

Neurointensivists 😊

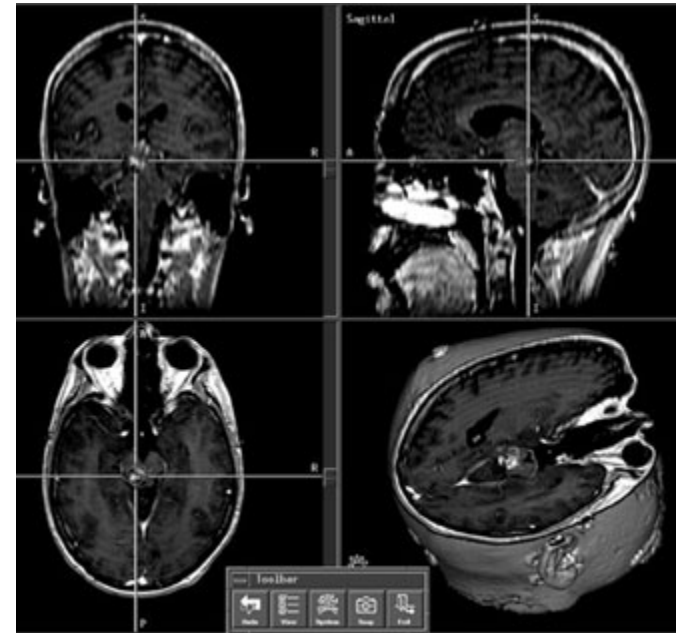
Minimally Invasive (Stereotactic) Surgery + tPA for ICH Extraction (MISTIE)

Inclusion Criteria

- Age 18-75
- GCS \leq 13 or NIHSS \geq 6
- Spontaneous supratentorial ICH \geq 20cc
- Stable clot at second CT scan done six hours later
- First dose given within 54 hrs of the initial diagnostic CT scan
- SBP < 200 mmHg or MAP < 130 mmHg over 6 hours
- Historical Rankin score of 0 or 1

Exclusion Criteria

- Infratentorial ICH
- Vascular malformation or brain tumor
- Irreversibly impaired brainstem function
- Unlikely to complete follow-up procedures
- Co-morbidity unlikely to survive at 180 days



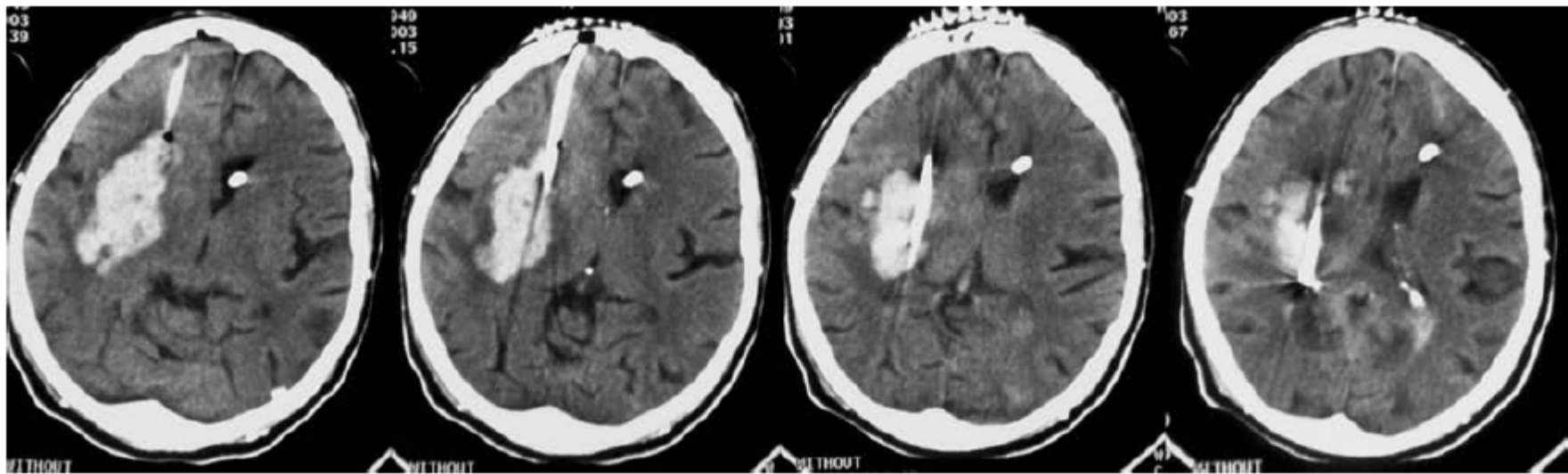
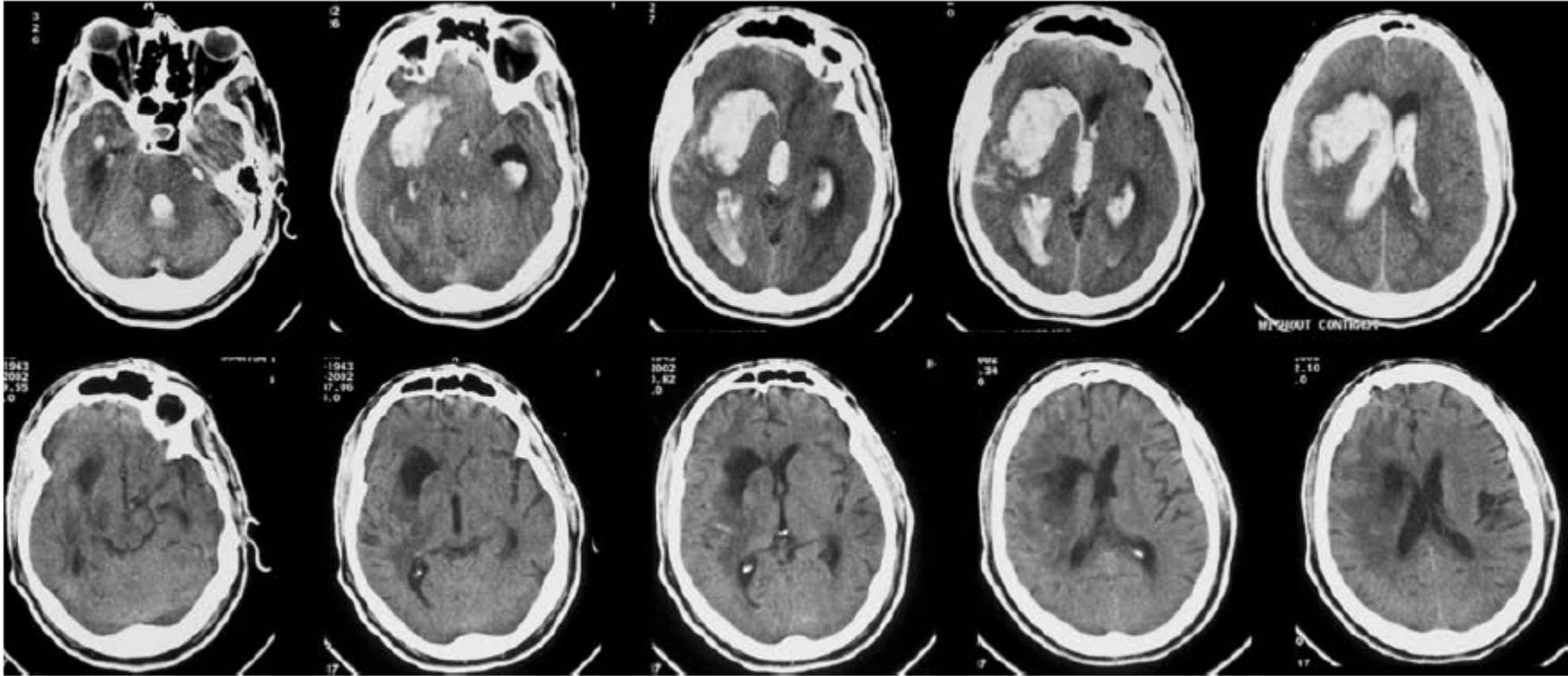


Fig. 1. Head CT scan showing intraclot catheter placement in a patient with a right basal ganglia ICH (patient 5). Note the spatial relationship between the catheter and the long axis of the blood clot.

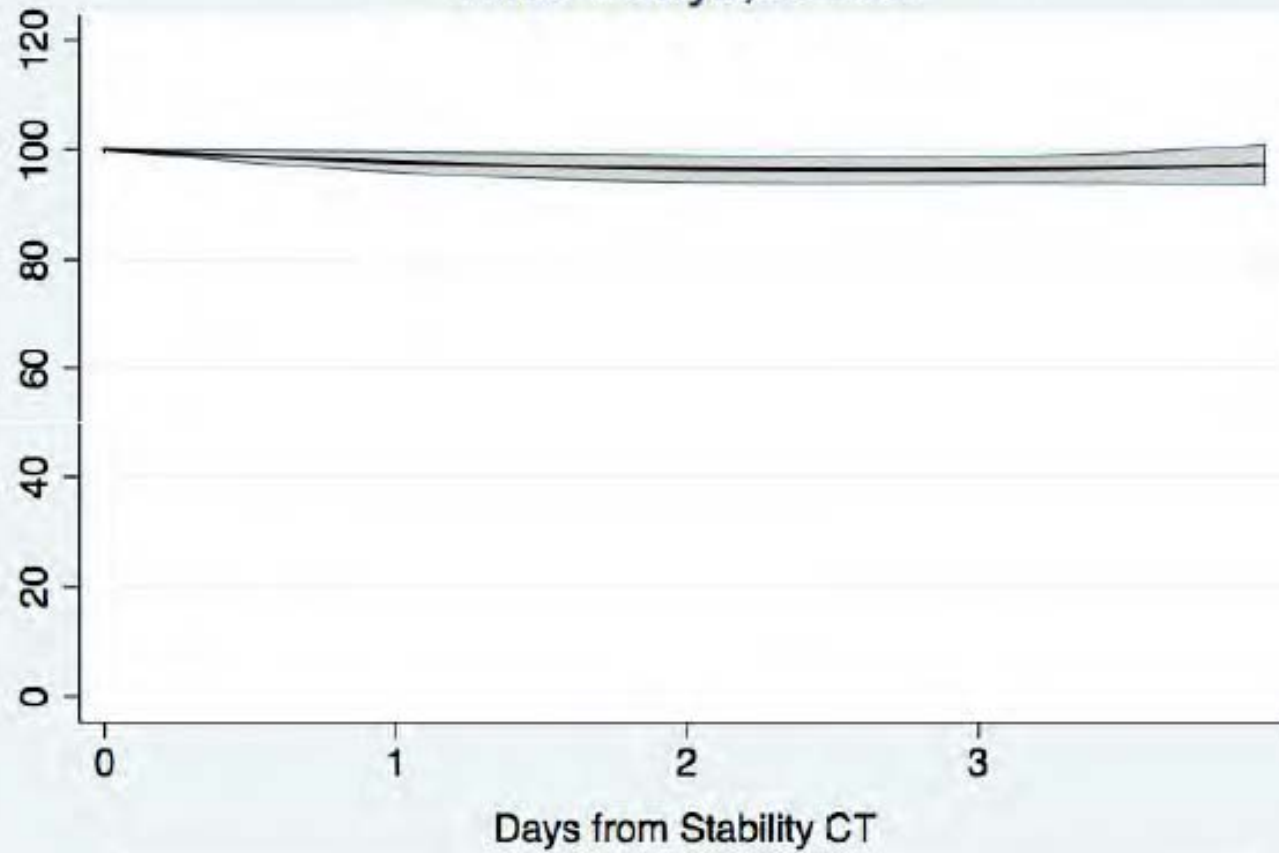


Subject Presentation (Severity)

Presenting Parameter		Medical N=39	Surgical N=54	Total N=93
ER Presentation SBP		186.3 (33.9)	186.4 (33.0)	186.3 (33.2)
ER Presentation DBP		101.7 (21.1)	106.8 (27.7)	104.7 (25.1)
ER Presentation MAP		129.9 (23.4)	133.2 (27.4)	131.8 (25.7)
ER Presentation GCS Total		12.6 (2.1)	11.1 (3.8)	11.6 (3.4)
Diagnostic ICH Volume		34.7 (16.2)	43.1 (22.9)	39.6 (20.7)
Diagnostic IVH Volume		1.2 (2.4)	4.5 (9.0)	3.2 (7.3)
Clot Location				
	Lobar	38.5%	33.3%	35.5%
	Deep	61.5%	66.7%	64.5%

Medical Group Estimated Clot Reduction First 4 days, n= 39

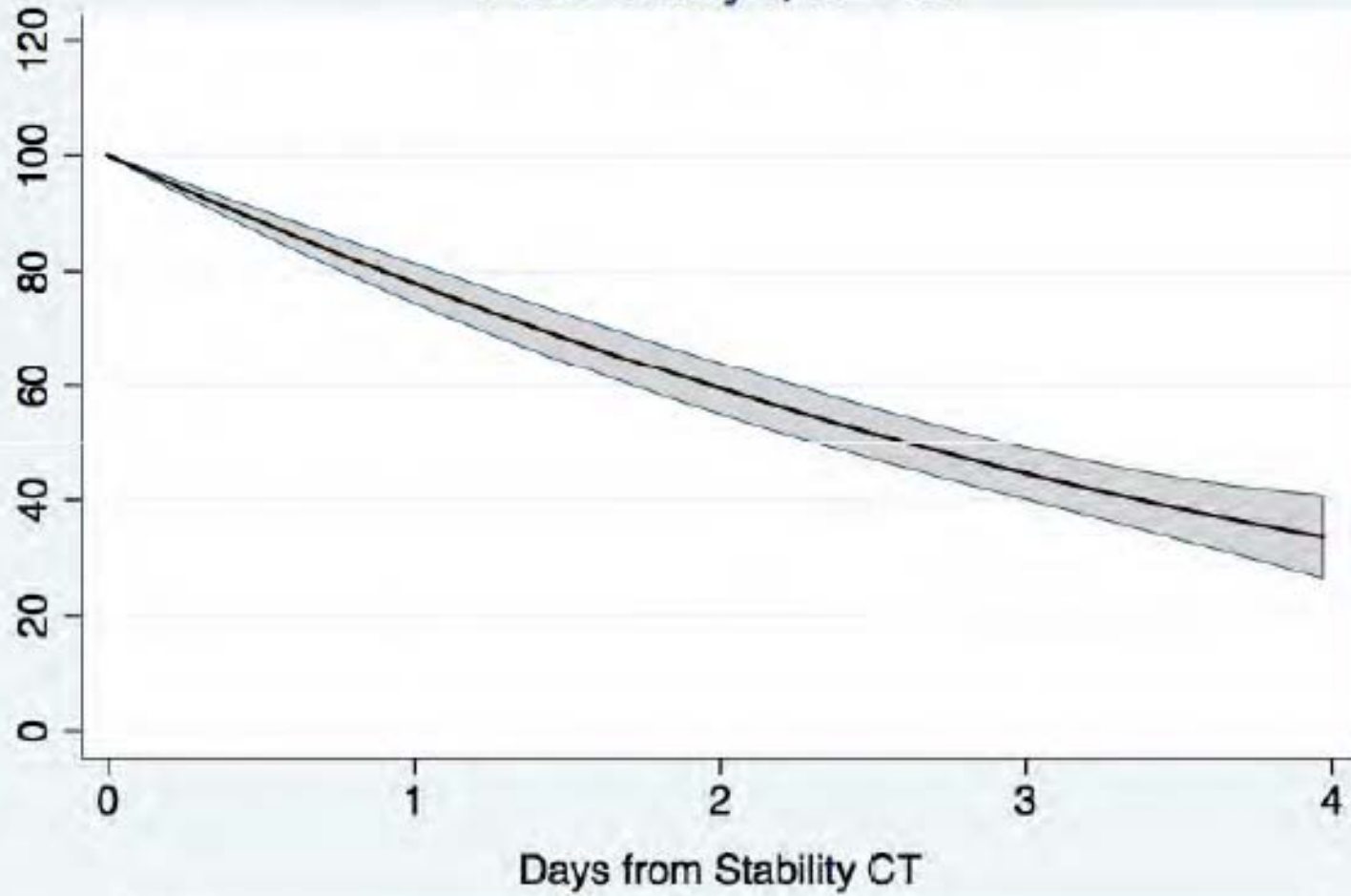
ICH Volume as % of Stability CT, Analysis of 4 Days



95% CI % of Stability Clot Remaining

All tPA-Dosed Group Estimated Clot Reduction First 4 days, n= 46

ICH Volume as % of Stability CT, Analysis of 4 Days



95% CI % of Stability Clot Remaining

MISTIE Summary

- MIS + rt-PA is safe
- MIS + rt-PA is effective at removing clot
 - 28 ml in 3 days
- Surgical Performance of MIS + rt-PA can be standardized

MISTIE II – Surgical Implications

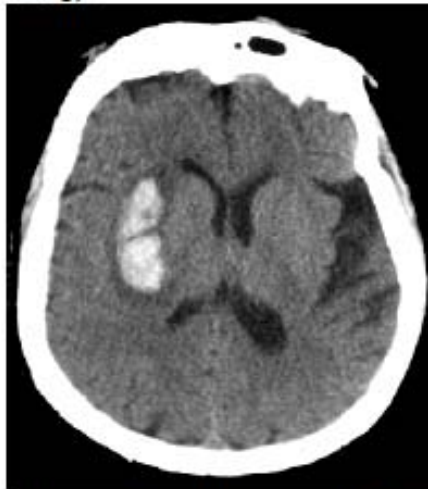
- MIS reduced average clot size by 28 ml
- Accuracy of MIS surgery is critical to clot size reduction
- The trial data may establish a “surgical goal” for MIS:
....to reduce clot to 15 ml or less by 3-4 days.
- MIS is a surgical technique that could be
 - widely available
 - practical to deliver to ICH patients.

MISTIE II – Clinical Trial Implications

- Most likely MIS + rt-PA produces increased independence for ICH patients
- The most probable mechanism is reduction of clot burden

Minimally Invasive Surgery plus rt-PA for ICH Evacuation (MISTIE) Phase II Results: Safety, Efficacy and Surgical Performance

- **Objectives & Purpose:** The purpose of this trial is to determine the safety of using a combination of minimally invasive surgery plus clot lysis (using rt-PA) to remove ICH. The MISTIE trial uses image-based surgery (MRI or CT) to provide catheter access to ICH. This study tested if the intervention facilitates more rapid and complete recovery of function and decreased mortality compared to conventional medical management without subjecting the patient to craniotomy. The specific objective of this trial is to test safety and assess ability to remove blood clot from brain tissue.
- **Methods:** The MISTIE study is a double-blind, multi-center, multi-national, randomized trial, using a minimally invasive surgical technique plus rt-PA compared to standard medical management. One-time clot aspiration followed by instillation of up to 9 doses of rt-PA (either 0.3 mg or 1.0 mg).



- **Results:**
 - 93 subjects were randomized to either minimally invasive surgery (MIS) plus t-PA (n=54) or medical therapy (n=39)
 - Age 60.8 yrs, 66% male,
 - 35% were lobar, 65% basal ganglia.
 - Presentation clot size: ICH = 40mL ± 21; IVH = 3 mL ± 7
 - ED presentation GCS 11.6
 - NIH Stroke Scale 22 ± 9
 - The safety and surgical profile were within pre-specified thresholds
 - Mortality levels for the medical arm: Days 7 and 30 were 0%, 7.7% respectively Surgical arm: Days 7 and 30 were 1.8% and 14.8%. Symptomatic in the medical and surgical arms were 2.6% and 3.7%.
 - One report of brain infection.
 - Clot removal rates were 19%/day for subjects receiving 0.3 mg, and 21%/day for 1.0 mg.
 - Removal rates for the treatment groups were significantly higher than in medical subjects (5%/ day).
 - Strong correlation between accuracy of catheter placement and resulting residual clot volume at end-of-treatment was demonstrated (Spearman rho= -0.651).
- **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.

ICES: Surgical Arm of MISTIE

Neurosurgeons

ICES TRIAL

Intraoperative CT guided Endoscopic Surgery
for intracerebral hemorrhage



Paul Vespa, MD

Neil Martin, MD

Dan Hanley, MD

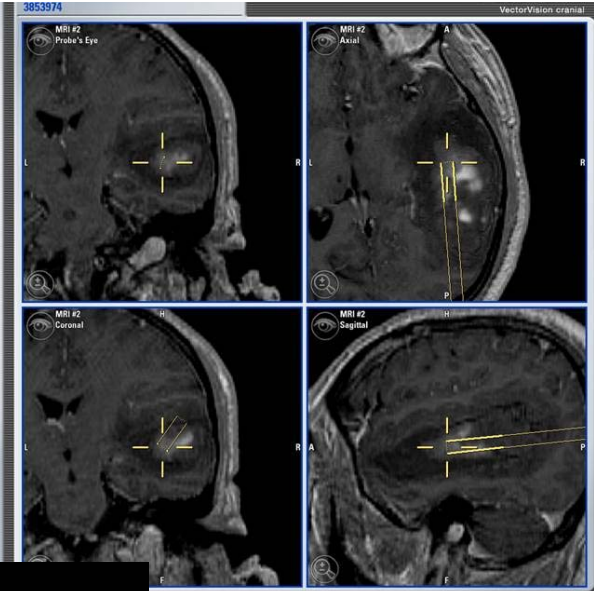
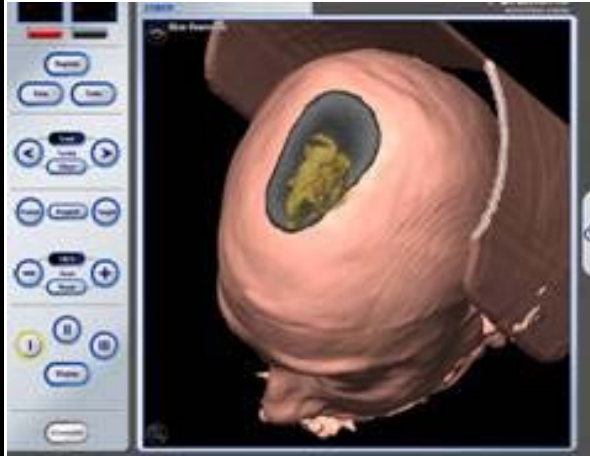
ICES Overview

- Prospective randomized controlled trial of endoscopic surgery to remove primary intracerebral hemorrhage using frameless stereotatic guidance
- MISTIE and ICES joined forces in 2009 to formulate a common approach and medical control arm

Main Aspects of study

- Age: 18-80
- ICH Volume > 20 cc
- Surgery within 48 hours of onset
- Structured endoscopic surgical protocol
- Serial imaging and examination
- Outcome assessments: 30, 60, 90, 180, 275, 365 days
- Safety is primary endpoint

Surgical Procedure



Centers

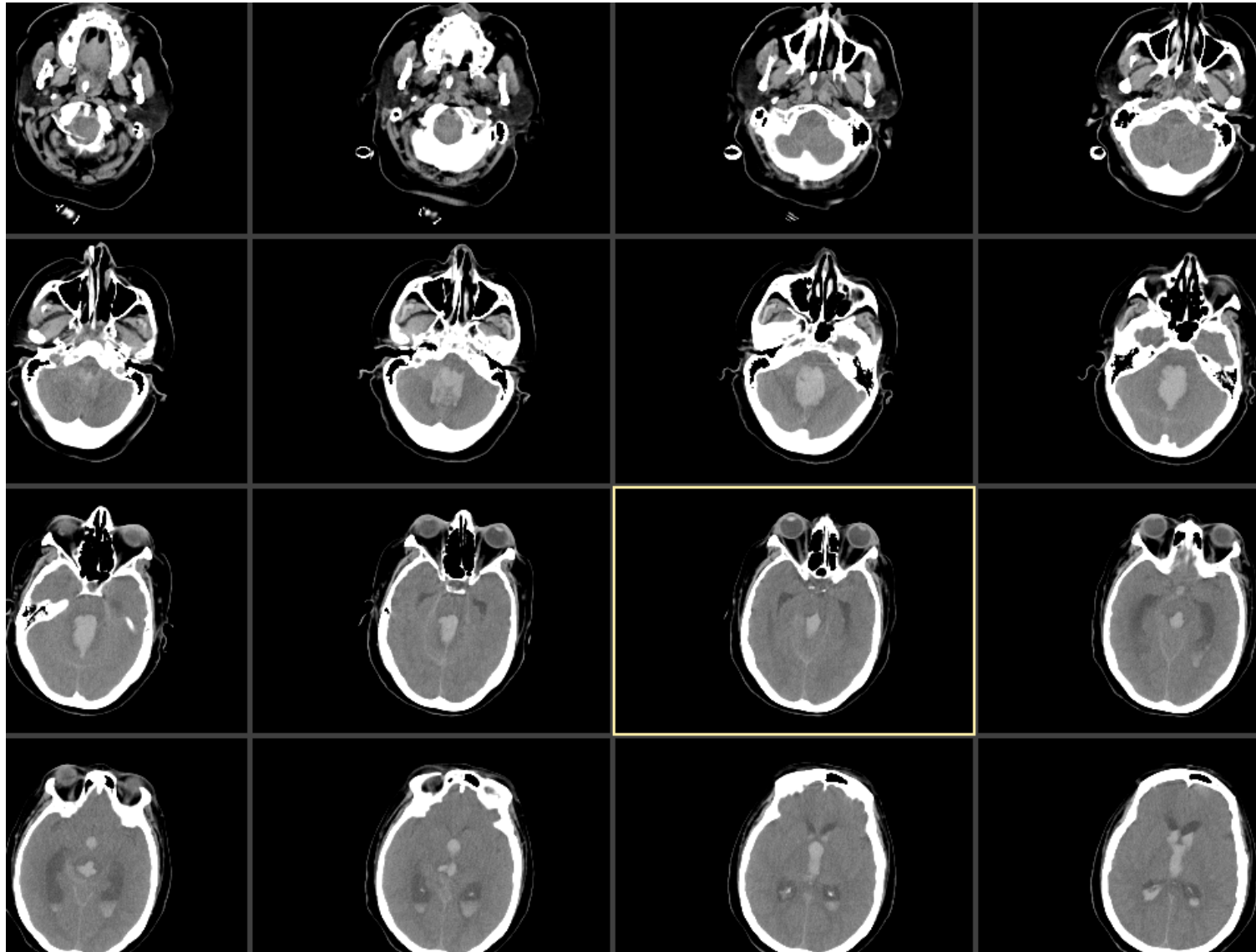
- UCLA – Vespa, Martin
- Univ Pittsburgh - Lo
- Case Western Reserve University – Selman, Hoffer
- UCSD - Carter
- MGH - Ogilvy
- Columbia - Connolly
- Jefferson - Rosenwasser

Death

Table 8. Mortality by treatment group

	Medical Randomized	Surgical Randomized	Run-Ins	Total
	N	N	N	N
Death Within 0-7 Days	0	0	0	0
Death Within 0-30 Days	0	1	1	2
Death Within 30-180 Days	2	1	0	3
Death Within 180-365 Days	0	0	0	0
Total	2	2	1	5

Screens and near misses



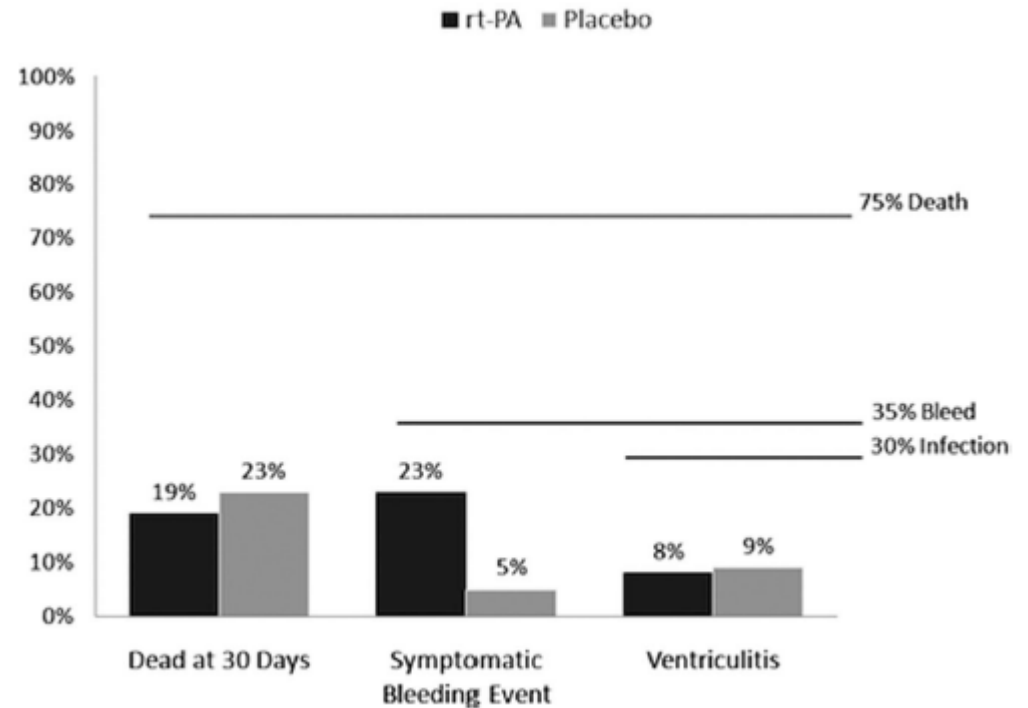
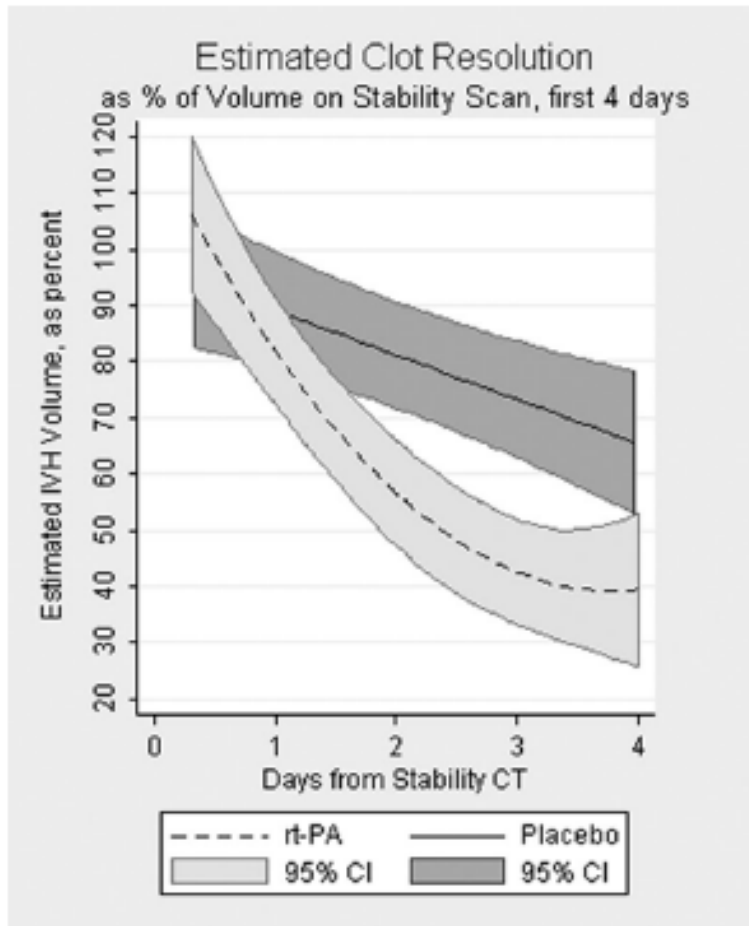
Study Status

- DSMB for MISTIE-ICES has approved ongoing recruitment
- Feasibility of multiple surgeons at various sites being able to perform complex surgery
- Safety appears to be reasonable
- Completed 24 subjects
- Very low Mortality
- New results will be presented at ISC 2013 Hawaii
– be there, Aloha!

Summary of Studies

Authors & Year	Indication	Timing	Pt Characteristics	Technique	Evacuation Rate	Rebleeding Rate	Long-Term Outcome†
Nishihara et al., 2000	putaminal ICH vol >40 ml	median time to op: 3 hrs (range 1.5–11 hrs)	9 pts w/ putaminal ICH	10-cm-long rigid transparent sheath made of acrylic plastic attached to SS handle w/ round-tipped metal stylet	86%–100%	NA	NA‡
Nakano et al., 2003	hematomas w/ vol >20 ml & <40 ml; putaminal ICH of small-intermediate size, hematoma situated deep in the brain (e.g., thalamic hemorrhage), intraventricular hematoma	NA	7 pts; 4 w/ putaminal ICH, 2 w/ thalamic ICH, & 1 w/ subcortical hemorrhage; avg age 55 yrs	NA	NA	NA	NA§
Suyama et al., 2004	NA	0–14 days	48 pts; 32 w/ putaminal ICH, 9 w/ thalamic ICH, & 7 w/ lobar ICH	transparent sheath, hematoma cavity irrigated w/ artificial CSF	putaminal ICH 82%; thalamic ICH 76%; lobar ICH 82%	2.0%	NA
Nishihara et al., 2005	putaminal, thalamic, & subcortical ICH w/ vol >20 & cerebellar ICH w/ vol >15 ml w/ deterioration of consciousness	ultra-early op (w/in 3 hrs) for hemorrhages w/ vol >30 ml or hemorrhages causing impending herniation	82 pts w/ ICH or IVH; 44 w/ putaminal ICH, 12 w/ thalamic ICH, 8 w/ subcortical ICH, 8 w/ cerebellar ICH, 10 w/ IVH	transparent sheath; hemostasis by electric coagulation at suction end; transparent cap attached to flexible endoscope provides clear visualization of op field during hematoma evacuation, which can prevent injury of ventricular walls	96% (range 86%–100%)	no postop rebleeding	NA
Chen et al., 2005	putaminal ICH vol >20 ml, GCS 5–12 w/ focal neuro deficit	1–5 hrs (median 2 hrs)	7 pts w/ hypertensive putaminal ICH; age range: 45–69 yrs	an 11-cm-long SS tube was adapted to serve as endoscopic sheath; op route along long axis of hematoma, requiring frontal approach	90%–97% (median 93%); ICH vol 20–180 ml (median 78 ml) preop, 2–16 ml (median 6 ml) postop	no postop rebleeding	6 pts were fully independent, including 4 who had no residual disability & 2 who had mod disability; 1 pt remained in a persistent vegetative state at clinical FU after 6 mos
Nagasaka et al., 2010	putaminal ICH vol >31 ml, cerebellar ICH w/ diam >3 cm, or thalamic ICH w/ vol >20 ml & acute hydrocephalus	median time to op: 4 hrs	23 pts; 15 w/ putaminal ICH, 6 w/ cerebellar ICH, 2 w/ thalamic ICH; mean age 61.4 yrs (range 36–85 yrs); mean preop GCS score: 7.2 (range 4–13)	a combination irrigation-coagulation suction cannula or multifunctional suction cannula was used	99%	0%	long-term outcome not mentioned, but the rate of good outcome (good recovery & mod disability) at discharge was 17.3%

CLEAR IVH q8 hr intrathecal TPA



Other Interesting Ideas

1. DFO in ICH:Dose Finding and Safety study of deferoxamine in patients with brain hemorrhage- iron lowering agent
2. SHRINC: Safety of Pioglitazone for Hematoma resolution in Intracerebral Hemorrhage- clot absorbing agent

Thank You!