Hemorrhagic Stroke Treatment Update

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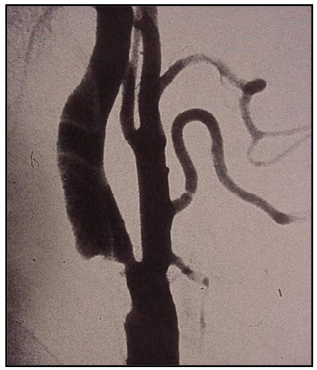
Cerebrovascular Disease: Pathogenesis

Ischemic Stroke (83%)

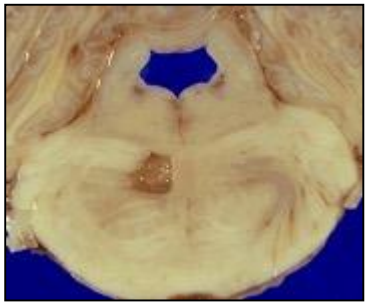
Atherothrombotic Cerebrovascular Disease (20%)



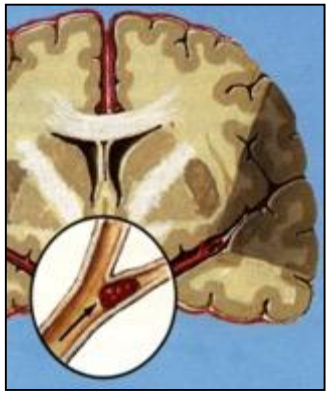
Cryptogenic (30%)

?

Lacunar (25%)
Small vessel disease



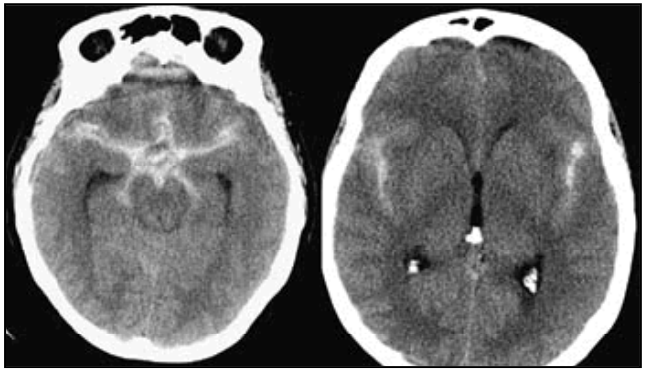
Embolism (20%)



Hemorrhagic Stroke (17%)

Intracerebral Hemorrhage (59%)

Subarachnoid Hemorrhage (41%)



Albers GW, et al: Chest 114:683S-98S, 1998.
Rosamond WD, et al: Stroke 30:736-43, 1999.

INTRACEREBRAL HEMORRHAGE (ICH)

An Evolving Paradigm

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A Significant Problem

- Mortality rate – 35% - 52%
  - 30 day mortality > 90% with an ICH > 60 ml.
- Morbidity rate – 80% - 90%
  - Speech, motor, or cognitive impairment.
- 5% of patients undergo surgery (~100,000 bleeds per year, only 5,000 get surgery).
- $13 billion annually for patient care, recovery, and rehab

Trials

- STITCH and STITCH 2 trials randomized patients to medical management or surgical evacuation
  - 1033 randomized patients
  - Surgery did not result in any significant difference in obtaining a favorable primary outcome at 6 months (26% in the surgical group, 24% in the medical group)
  - No effect on mortality (36% in the surgical arm and 37% in the medical-treatment group).
  - No differences in outcome were seen with the prognosis-based modified Rankin score.

Trials

- **High crossover rate in the initial conservative management group: 26% percent**
  - For clinical deterioration, increased intracranial pressure (ICP), rebleeding, or lack of improvement on conservative treatment.
- **In the surgical group, 6% of patients did not receive a surgical intervention**.
- Lack of surgical standardization.
- Subgroup analysis showed a trend toward more favorable outcome after clot evacuation if the hematoma resided 1 cm or less underneath the cortical surface or if an open craniotomy was performed.

Trials

- MISTIE trial corrected these issues and showed further trend towards surgical improvement.
- Statistically significant cost savings with surgical resection of hematoma.
- MISTIE II – Preliminary significant benefit to surgical intervention.
  - Likely completed within next year.
  - Still no standardized surgical technique.

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The Safety and Feasibility of Image-Guided BrainPath-Mediated Transsulcul Hematoma Evacuation: A Multicenter Study

BACKGROUND: Subcortical injury resulting from conventional surgical management of intracranial hemorrhage may counteract the potential benefits of hematoma evacuation.
OBJECTIVE: To evaluate the safety and potential benefits of a novel, minimally invasive approach for clot evacuation in a multicenter study.
METHODS: The integrated approach incorporates 5 competencies: (1) image interpretation and trajectory planning, (2) dynamic navigation, (3) atraumatic access system (BrainPath, NICO Corp, Indianapolis, Indiana), (4) extracorporeal optics, and (5) automated atraumatic resection. Twelve neurosurgeons from 11 centers were trained to use this approach through a continuing medical education–accredited course. Demographical, clinical, and radiological data of patients treated over 2 years were analyzed retrospectively.
RESULTS: Thirty-nine consecutive patients were identified. The median Glasgow Coma Scale (GCS) score at presentation was 10 (range, 5-15). The thalamus/basal ganglion regions were involved in 46% of the cases. The median hematoma volume and depth were 36 mL (interquartile range [IQR], 27-65 mL) and 1.4 cm (IQR, 0.3-2.9 cm), respectively. The median time from ictus to surgery was 24.5 hours (IQR, 16-66 hours). The degree of hematoma evacuation was $\geq$90%, 75% to 89%, and 50% to 74% in 72%, 23%, and 5.0% of the patients, respectively. The median GCS score at discharge was 14 (range, 8-15). The improvement in GCS score was statistically significant ($P < .001$). Modified Rankin Scale data were available for 35 patients. Fifty-two percent of those patients had a modified Rankin Scale score of $\leq$2. There were no mortalities.
CONCLUSION: The approach was safely performed in all patients with a relatively high rate of clot evacuation and functional independence.

KEY WORDS: Intracerebral hemorrhage, Minimally invasive clot evacuation, Stroke, Surgery, Transsulcul

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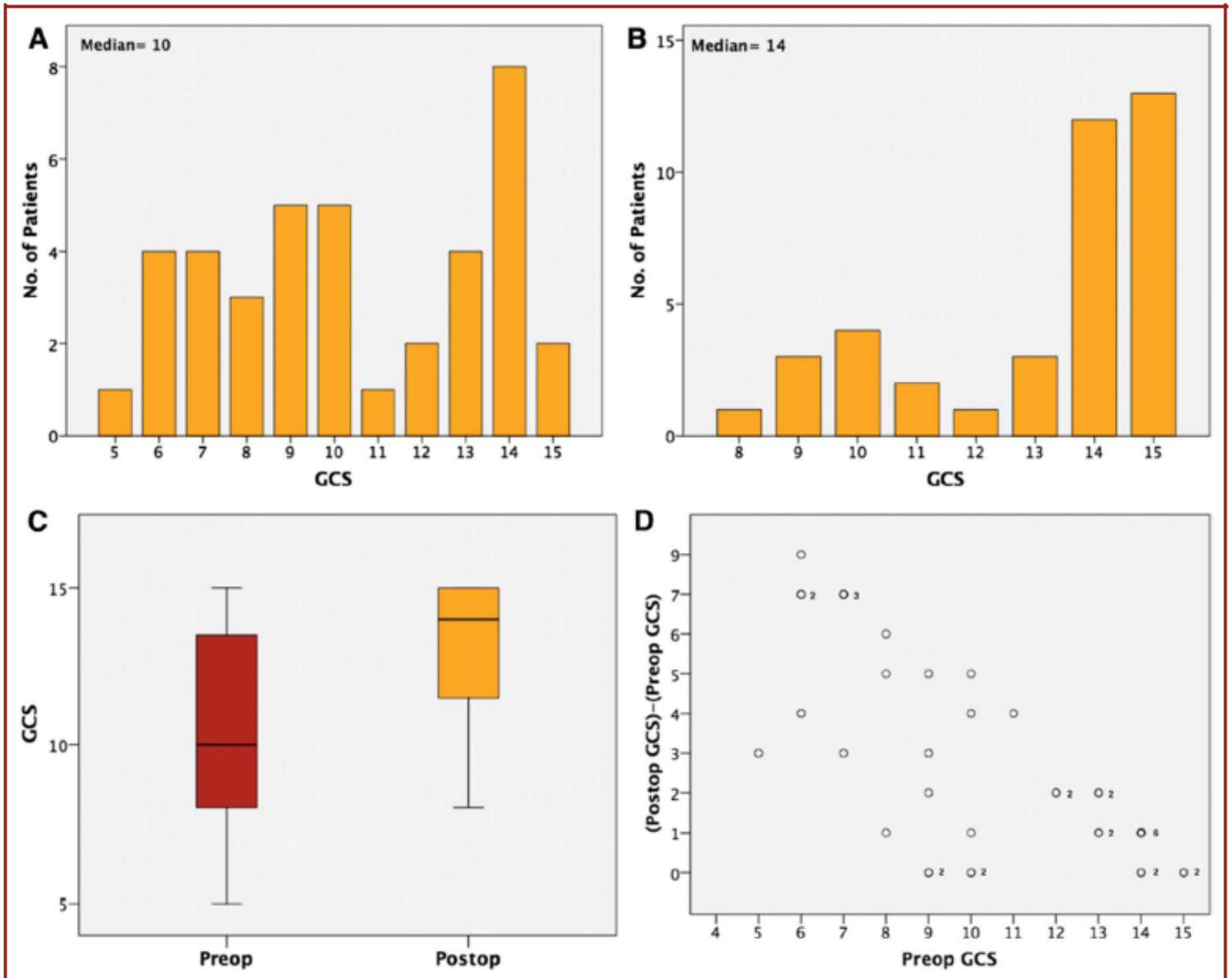
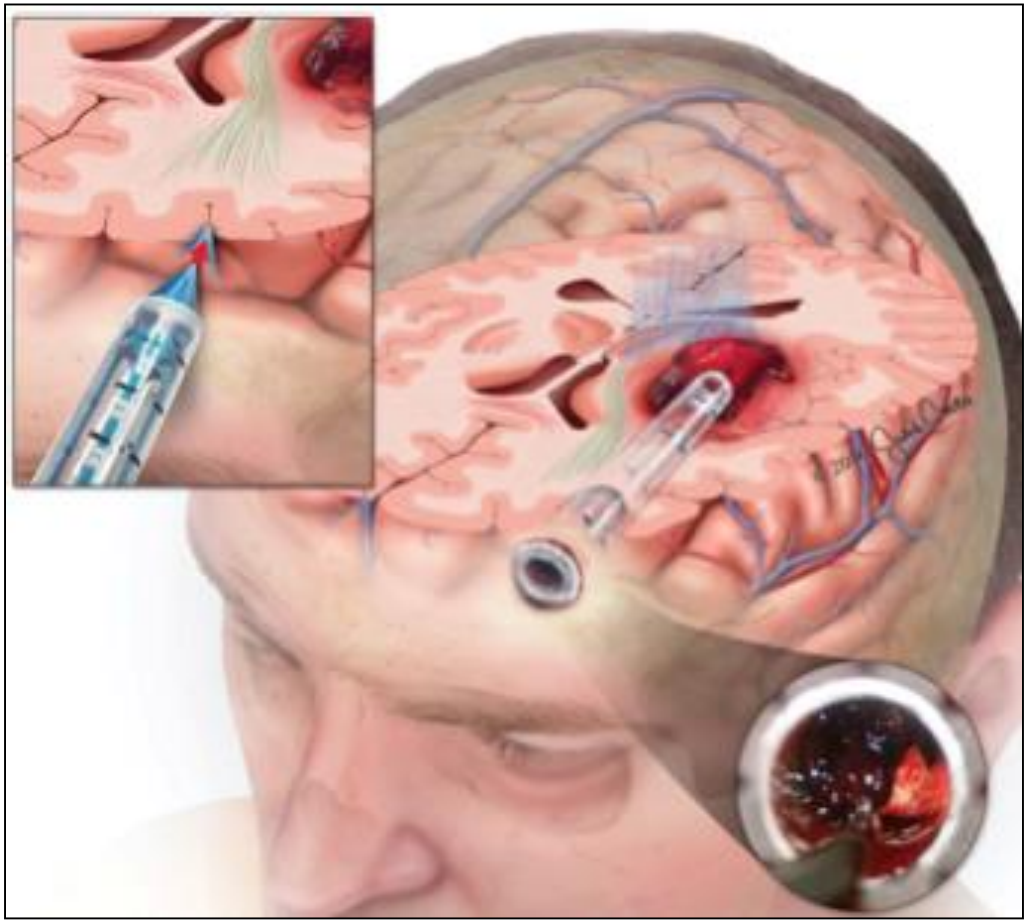


FIGURE 5. *Patients' preoperative and postoperative Glasgow Coma Scale (GCS) scores.* **A**, *the median preoperative GCS score was 10.* **B**, *the median postoperative GCS score was 14.* **C**, *the improvement in GCS score was statistically significant.* **D**, *the scatterplot displays the extent of GCS improvement in relation to the preoperative GCS score.*

The NICO Port

NICO
CORPORATION



ENRICH Trial

- Early miNimally invasive Removal of ICH
  - Randomized controlled trial of up to 300 patients.
  - Comparison early surgical hematoma evacuation (surgery within 24 hours) to standard medical care.
  - Using standard equipment and approaches.
  - Parafascicular surgery - entry point parallel to long cortical tracts rather than conventional perpendicular approach (less traumatic?)
- Primary endpoint is modified Rankin Score at 180 days.

Criteria

Inclusion Criteria:

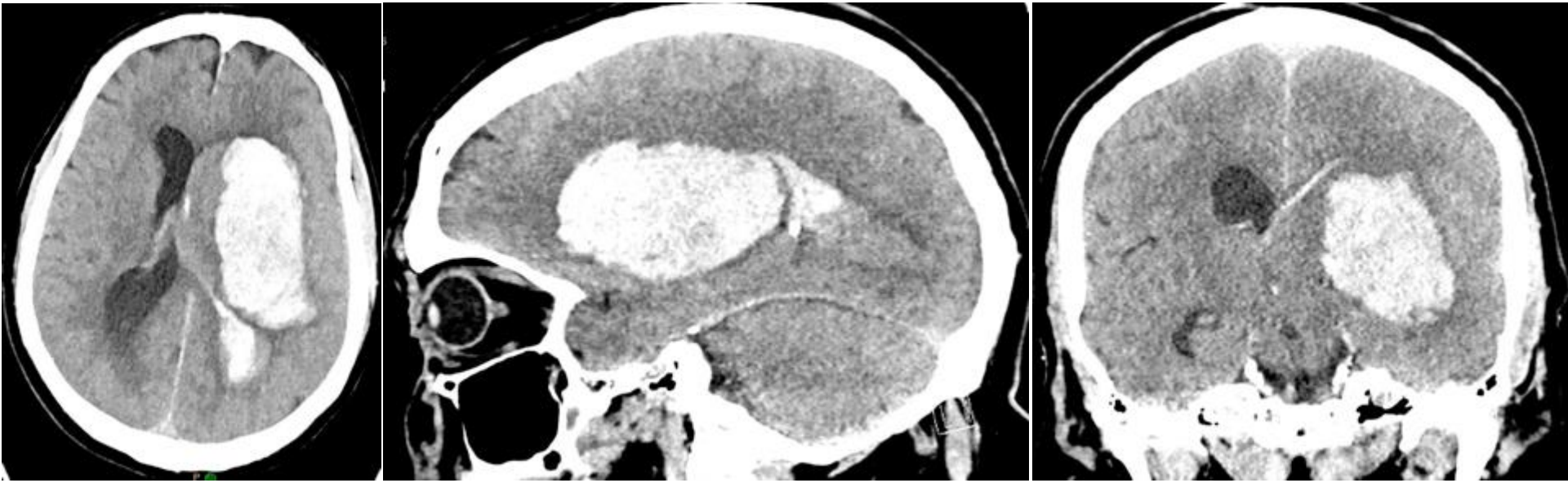
- Age 18-80 years
- Pre-randomization head CT demonstrating an acute, spontaneous, primary ICH
- Manual ICH volume between 30 - 80 mL
- Study intervention can reasonably be initiated within 24 hours after the onset of stroke symptoms. If the actual time of onset is unclear, then the onset will be considered the time that the subject was last known to be well
- Glasgow Coma Score (GCS) 5 - 14
- Historical Modified Rankin Score 0 or 1

Exclusion Criteria:

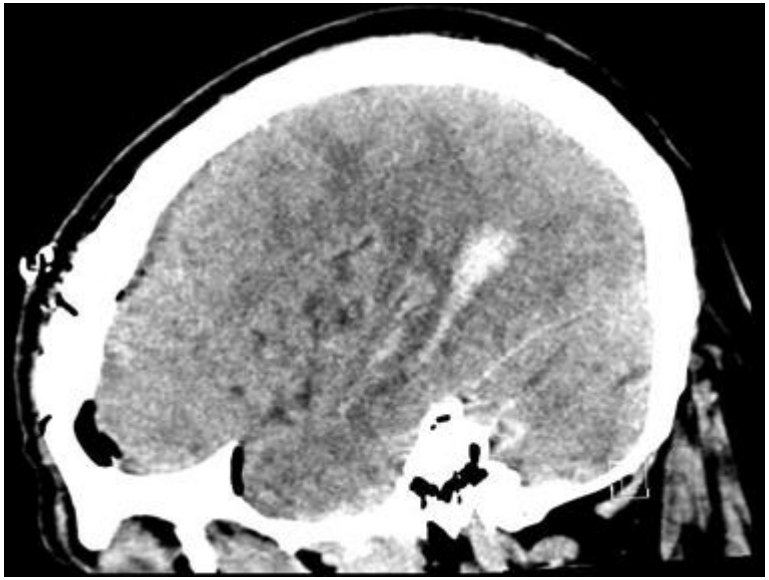
- Ruptured aneurysm, arteriovenous malformation (AVM), vascular anomaly, Moyamoya disease, venous sinus thrombosis, mass or tumor, hemorrhagic conversion of an ischemic infarct, recurrence of a recent (<1 year) ICH, as diagnosed with radiographic imaging
- NIHSS < 5
- Bilateral fixed dilated pupils
- Extensor motor posturing
- Intraventricular extension of the hemorrhage is visually estimated to involve >50% of either of the lateral ventricles
- Primary Thalamic ICH
- Infratentorial intraparenchymal hemorrhage including midbrain, pontine, or cerebellar
- Use of anticoagulants that cannot be rapidly reversed
- Evidence of active bleeding involving a retroperitoneal, gastrointestinal, genitourinary, or respiratory tract site
- Uncorrected coagulopathy or known clotting disorder
- Platelet count < 75,000, International Normalized Ratio (INR) > 1.4 after correction
- Patients requiring long-term anti-coagulation that needs to be initiated < 5 days from index ICH
- End stage renal disease
- Patients with a mechanical heart valve
- End-stage liver disease
- History of drug or alcohol use or dependence that, in the opinion of the site investigator, would interfere with adherence to study requirements
- Positive urine or serum pregnancy test in female subjects without documented history of surgical sterilization or is post-menopausal
- Known life-expectancy of less than 6 months
- No reasonable expectation of recovery, Do-Not-Resuscitate (DNR), or comfort measures only prior to randomization
- Participation in a concurrent interventional medical investigation or clinical trial.
- Inability or unwillingness of subject or legal guardian/representative to give written informed consent
- Homelessness or inability to meet follow up requirements

Big bleed

- 59-year-old male with history of HTN, alcohol dependence transferred from OSH concern for hemorrhage



- Patient currently in rehab
- Follows commands on left


The Naturopath

- 58-year-old male with “no past medical history” presented with left-sided hemiplegia
- CT demonstrated large right frontal intraparenchymal hemorrhage in the motor strip with brain edema and herniation
- Bleed extended deep into brain

- Out of the ICU
- At 6 week follow-up patient WALKED into my clinic
- Performing all activities of daily living independently

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Aneurysm Clinical Presentation, Natural History and Therapeutic Options

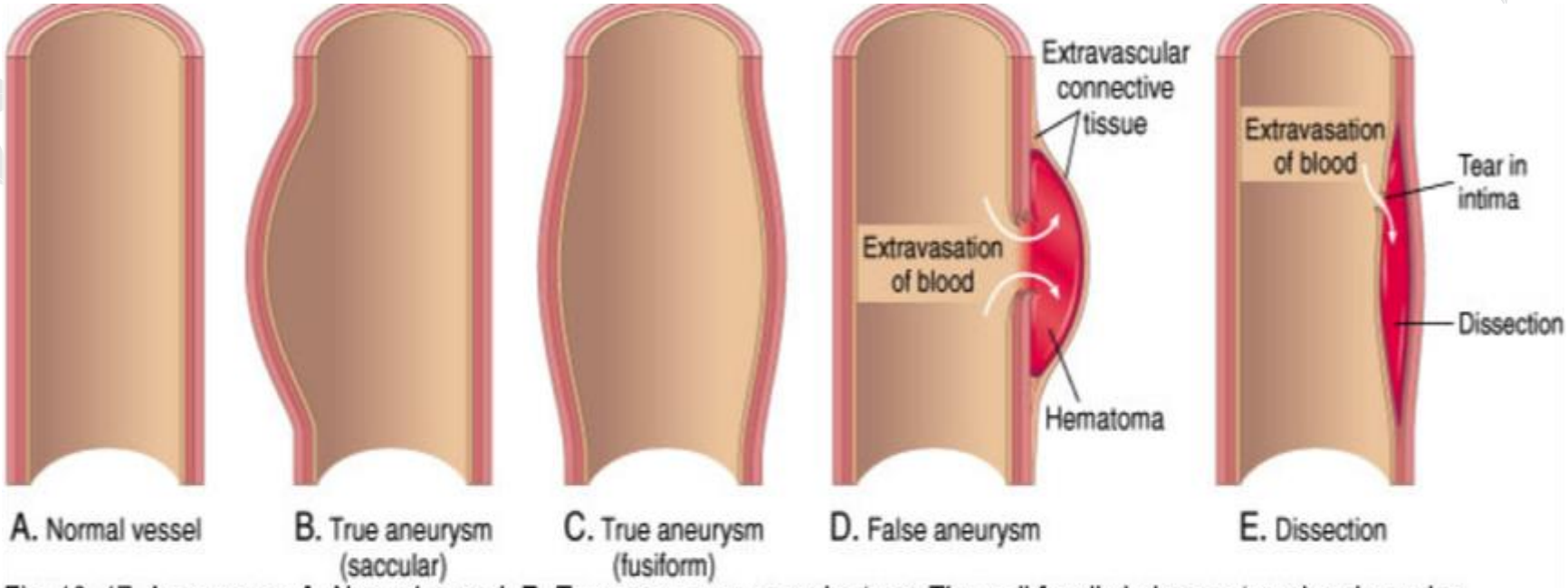
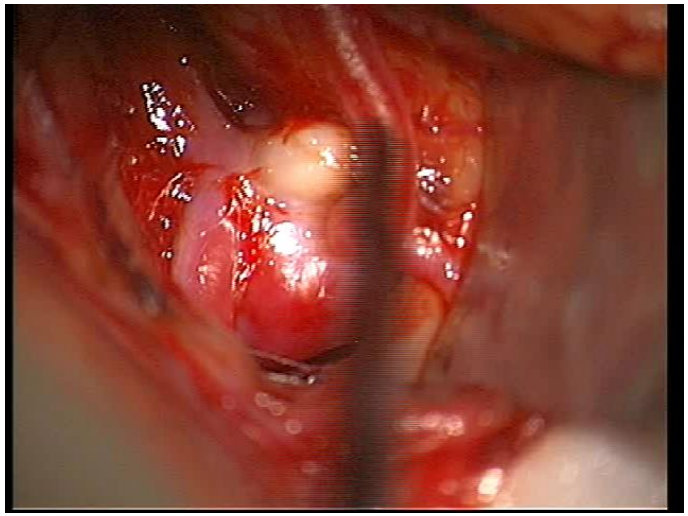


Fig. 10–17. Aneurysms. **A**. Normal vessel. **B**, True aneurysm, saccular type. The wall focally bulges outward and may be attenuated but is otherwise intact. **C,** True aneurysm, fusiform type. There is circumferential dilation of the vessel, without rupture. **D**, False aneurysm. The wall is ruptured, and there is a collection of blood (hematoma) that is bounded externally by adherent extravascular tissues. **E,** Dissection. Blood has entered (*dissected*) the wall of the vessel and separated the layers. Although this is shown as occurring through a tear in the lumen, dissections can also occur by rupture of the vessels of the vaso vasorum within the media.

- Pathological study by Ishikawa et al.[7] in 1997 – Atherosclerotic carotid artery composed of a thin layer of adventita covering a focal defect in the intima and media layers of the vessel.
- Lack usual collagenous and muscular layer.

The "Dual Specialist"

- Modern day treatment of intracranial aneurysms requires a multidisciplinary approach
  - Nowadays, two or more of those disciplines can be combined in one practitioner
    - Neurosurgeon as
      - Microsurgeon
      - Endovascular therapist
      - Neurointensivist
      - Stroke Neurologist



Goal of Treatment:

Complete exclusion of aneurysm from normal circulation

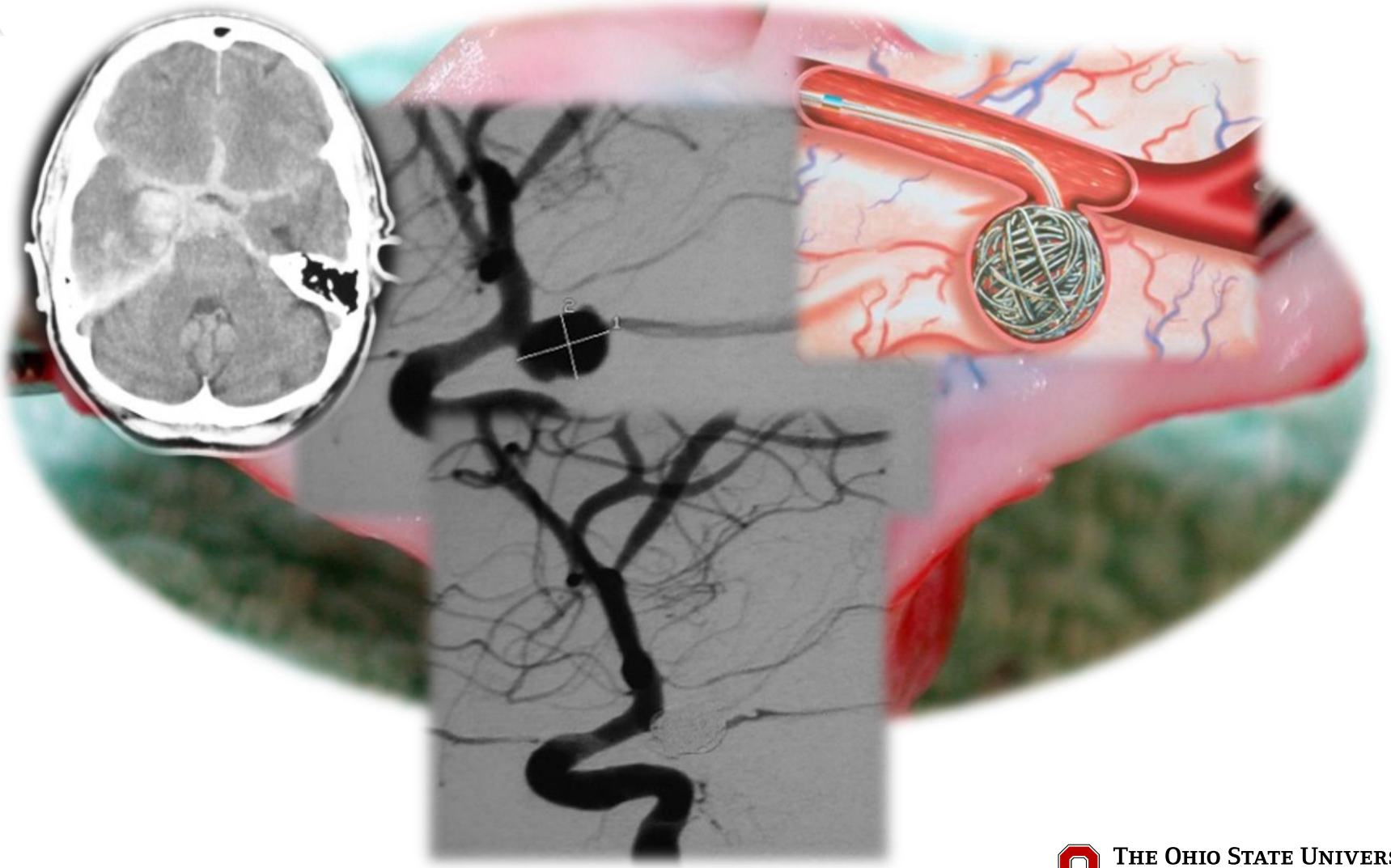
Clip & Coil, NOT Clip vs. Coil

- Focus must be on optimal method for excluding a given aneurysm from the cerebral circulation
  - Minimizing risks
  - Maximizing durability
- Practitioner must recognize biases, and deal with them--always putting the patient first
  - The "Dual Specialist" is uniquely positioned to do this

Just because a lesion CAN be coiled, does not mean it SHOULD be coiled

And the same goes for clipping…

Endovascular Coiling



ISAT

Lancet 2002
Lancet 2005

- 2143 SAH patients randomized – 80% not randomized.
  - "clinical *equipoise* or uncertainty"
    - 1070 clip
    - 1073 coil
- F/U at 1 year
  - Clip: 30.6% mRS 3-6
  - Coil: 23.7% mRS 3-6
  - ***22.6% RR reduction & 7% AR reduction associated with coiling***
  - ***Benefit maintained out to 7 years***

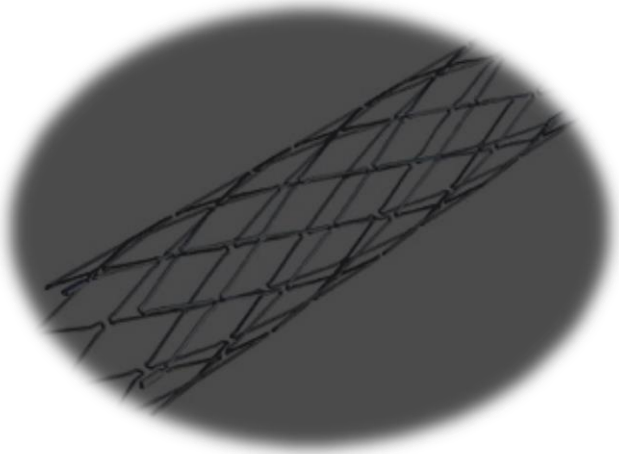
ISAT Follow-up
Stroke 2007

- EVT: 0.6% (7) re-bleed; 17.4% (191) re-treat
- Clip: 0.3% (3) re-bleed; 3.8% (39) re-treat
  - @mean of 20.6 months

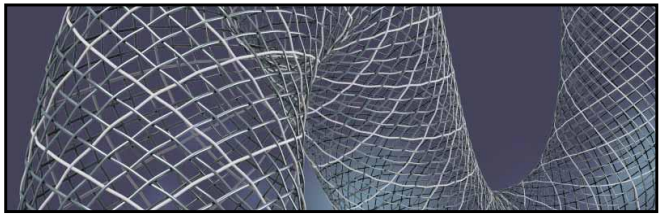
- Late re-treatment: Younger age, larger lumen, incomplete occlusion
  - Requirement for continued follow-up
  - Recurrence is a real problem with EVT

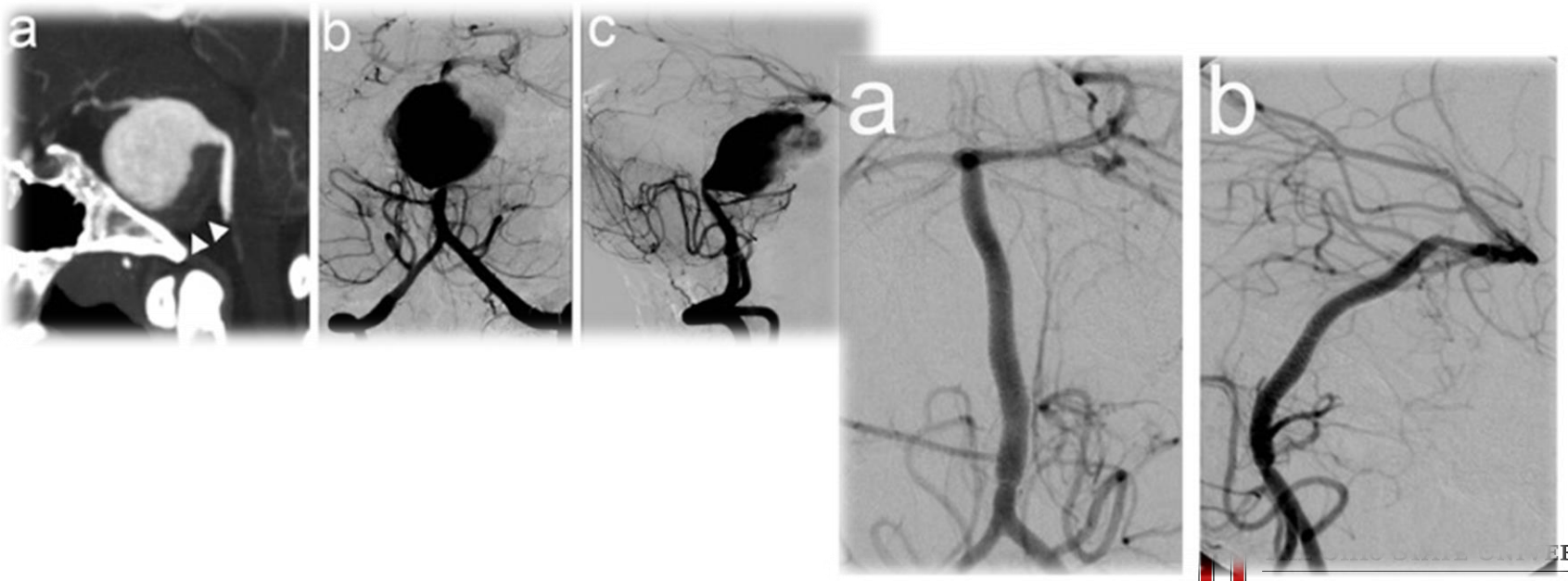
What do we do?

- 1. Develop better patient selection criteria
- 2. Develop better surgical salvage techniques
- 3. Develop better endovascular technology & techniques
  - Mechanically enhanced coils
  - Bioactive coils
  - Liquid embolics
  - Balloon remodeling
  - ***Stenting***
  - ***Flow Diverters***



New stent technology:
Flow Diversion: “Pipeline”





Pipeline Embolization Device

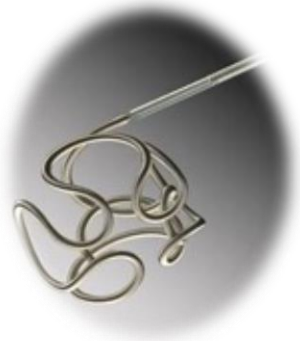
- Pipeline® device is made of a flexible braided cylindrical mesh
  - Platinum/ cobalt-chromium alloy
  - Self-expanding
- Pipeline received FDA approval in April of 2011 after completing a clinical trial called PUFs (Pipeline for Uncoilable or Failed Aneurysms)
  - Approved for large and giant aneurysms of the cavernous/paraclinoid region
- Pipeline device has been used to treat patients in Europe since 2009

Generalities

- Clipping
  - Durable
  - Time-honored
  - Versatile

  - Invasive
  - Technically challenging
  - Risky

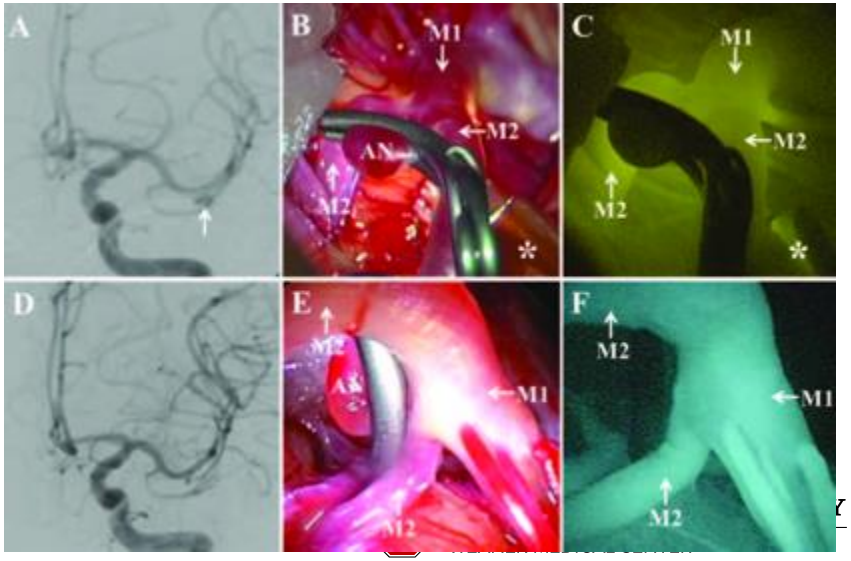
- Coiling
  - Less invasive
  - Treatment multiplicity
  - Quicker/easier?



  - ? Durability
  - Less versatile
  - Mass effect
  - Risky

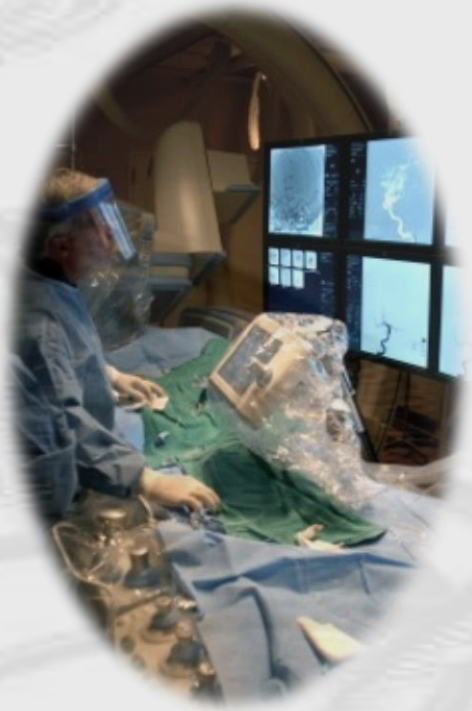
Microsurgical Advances

- Endovascular techniques advancing
  - Next generation coils and catheters; remodeling, liquid embolics
  - Next generation Stents
- **Microsurgical techniques also advancing**
  - **Skull base exposures**
  - **Brain protection**
  - **Next generation clips**
  - **3D angiography, IOA, ICG**
  - **Bypass techniques**



Conclusion: Aneurysms ***Ideal*** for Coiling

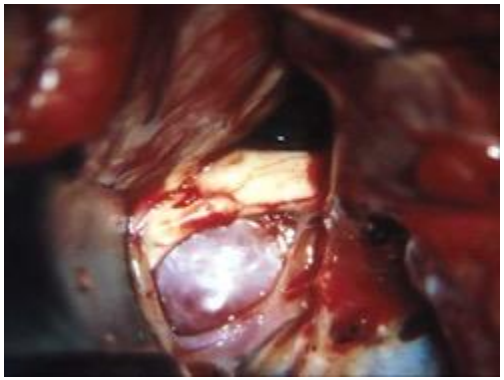
- Elderly patient
- Poor grade patient
- Concurrent vasospasm
- Difficult location
- Calcification
- Multiple aneurysms
- Previous surgery
- Forecast requirement for remote surgery
- ***Microsurgeon availability***



Aneurysms ***STILL*** Ideal for Clipping?

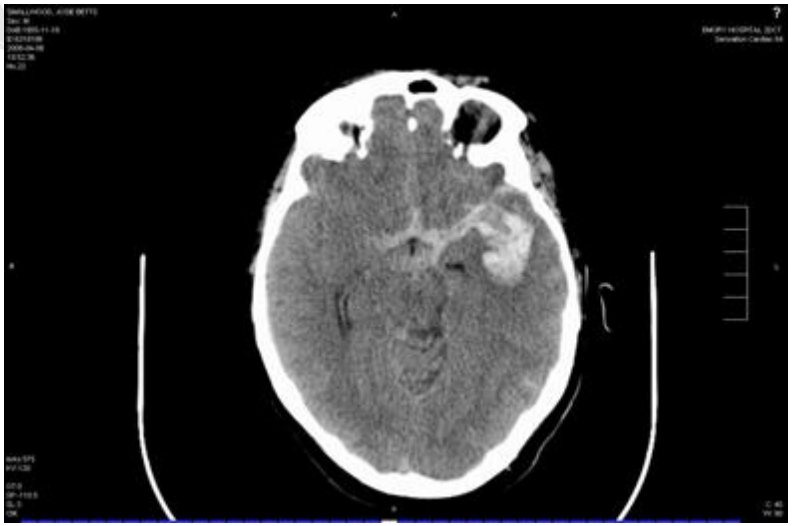
Group 1

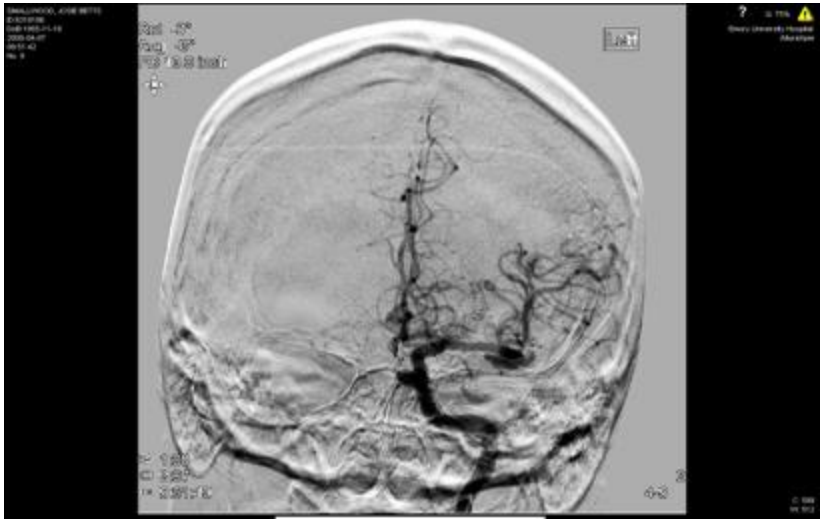
- ***Specific locations (MCA, ACA)***
- ***Multiplicity not amenable to coils***
- ***Complex or wide-neck*****
- ***Very small or blister aneurysms*****
- Giant aneurysms
- Partially thrombosed lesions
- Fusiform aneurysms
- Associated ICH
- Associated mass effects
- Failed endovascular therapy

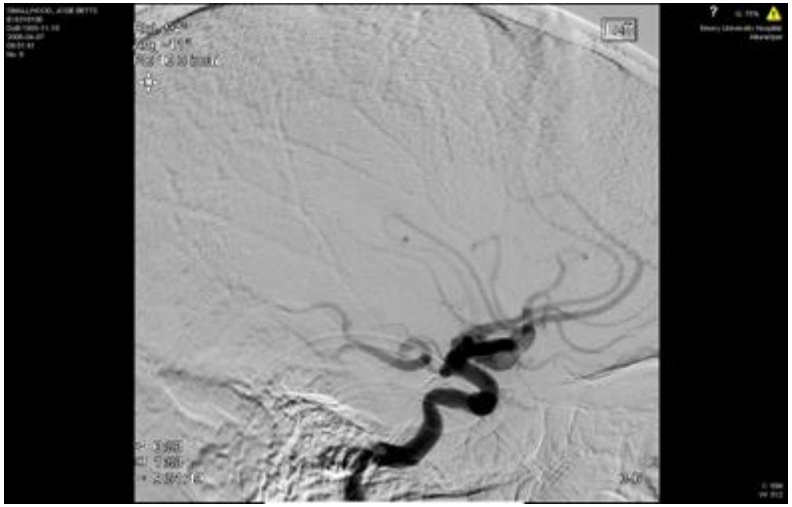


Case 1

Location: MCA

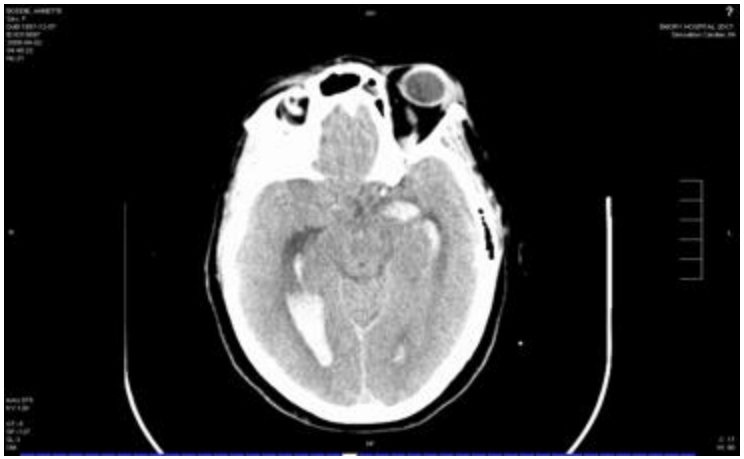


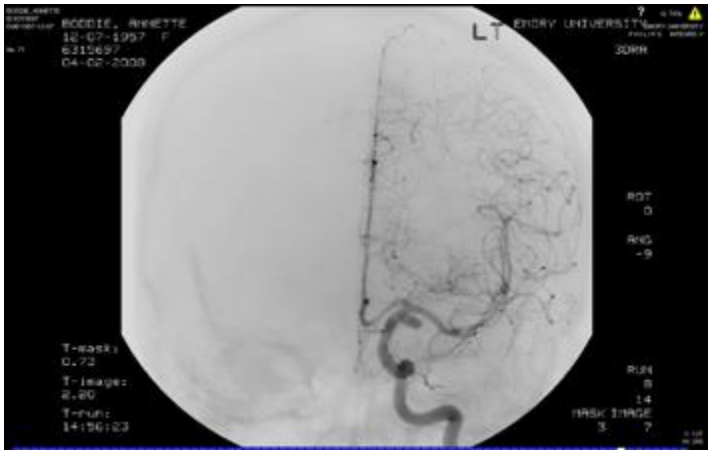




Case 2

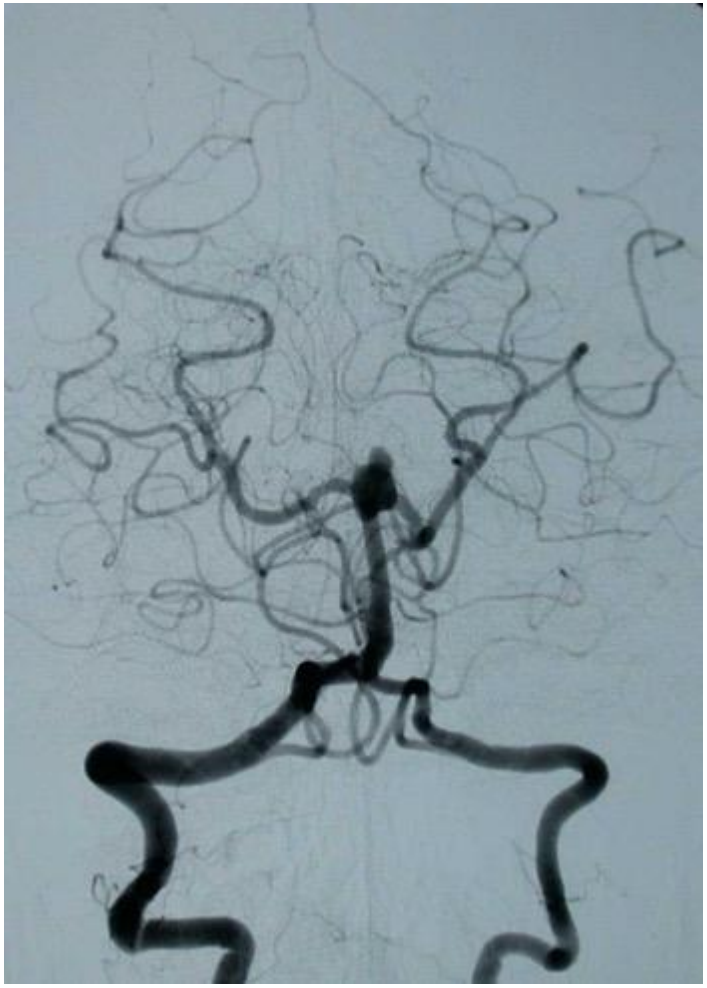
Multiplicity*



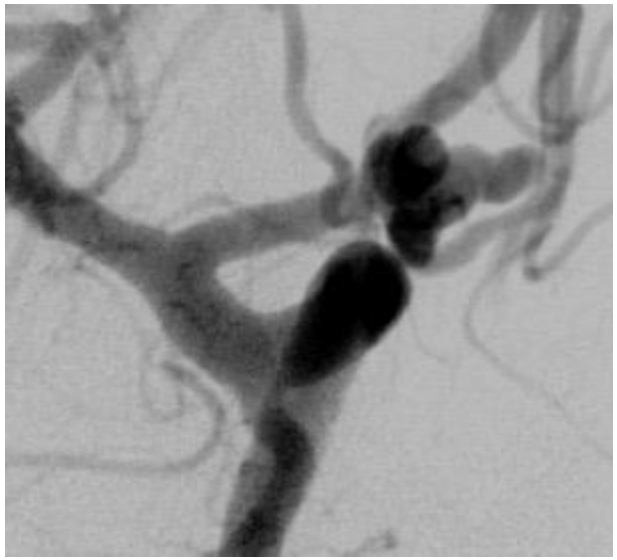


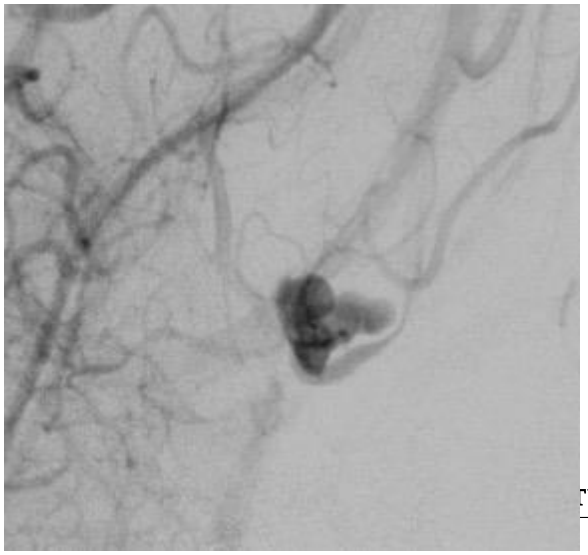
Case 4

Complex Morphology? Evolving Indication



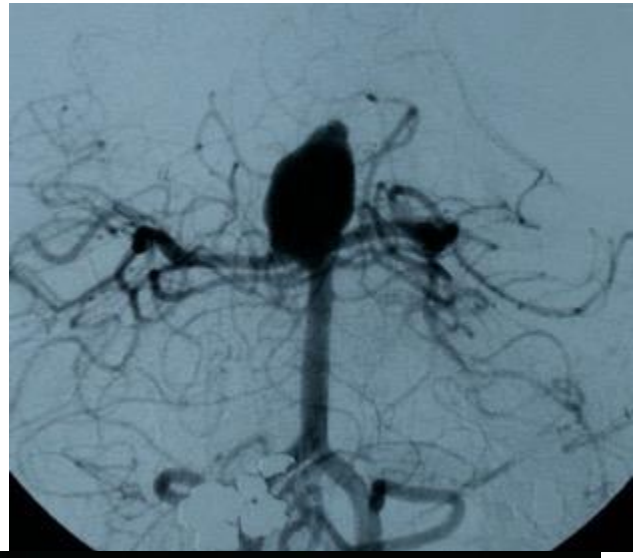
CH: 53 WF. IPH at 2 and 20 days post-stent (fatal)

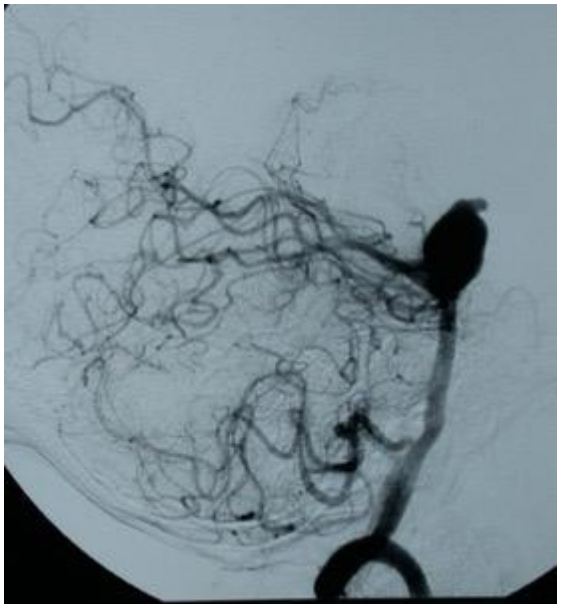




Wide Neck?

Case 6

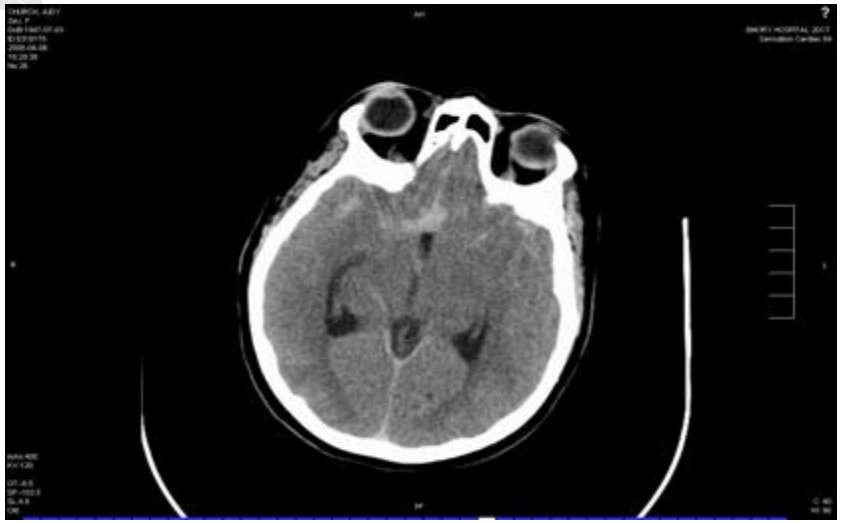


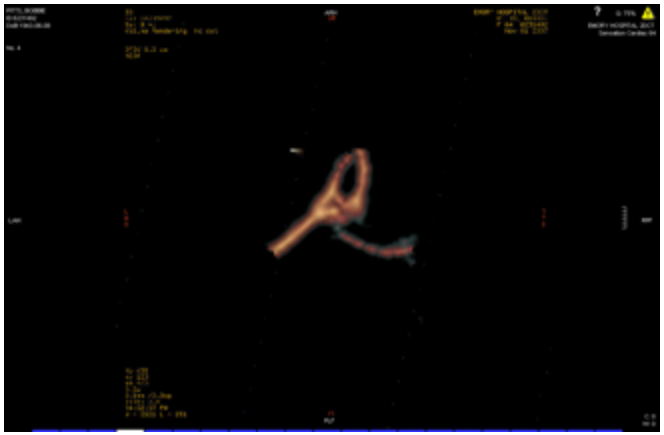


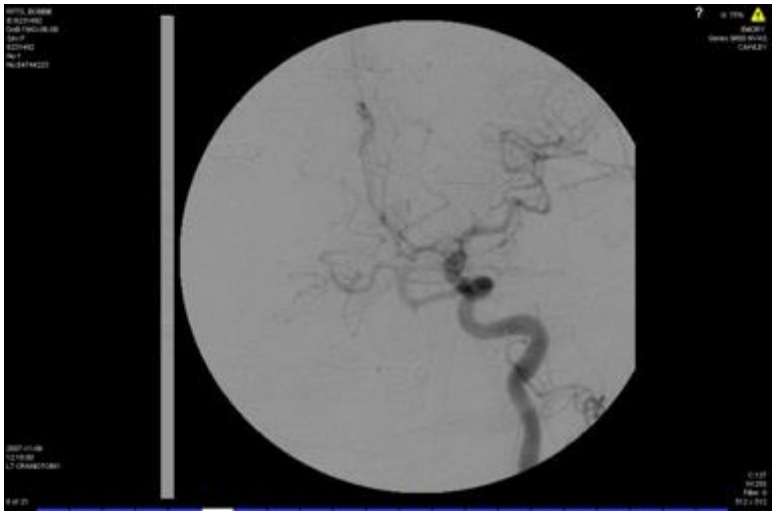
Evolving indication

Case 7

Small Aneurysm/Coil Attempt
Evolving Indication – Nano trial at OSU

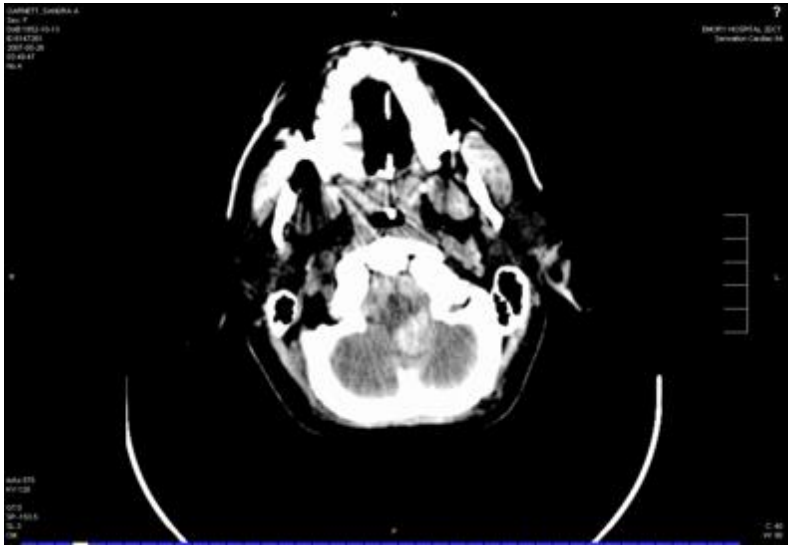


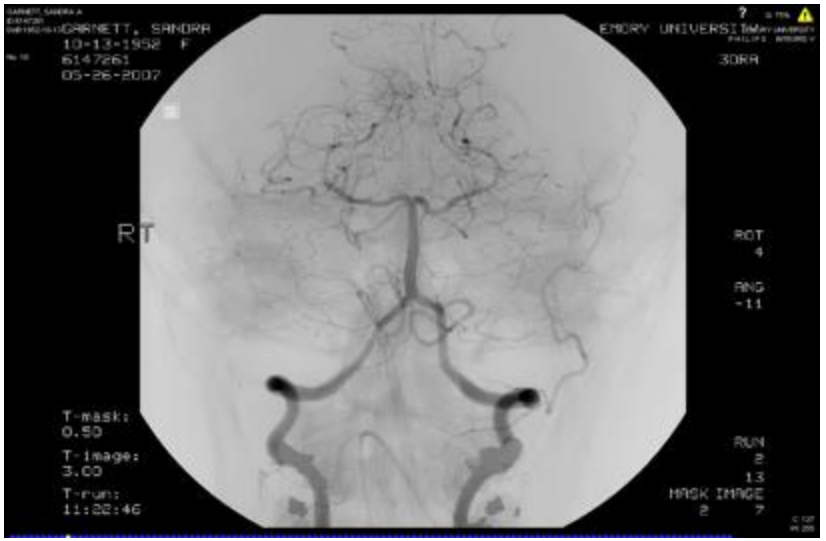


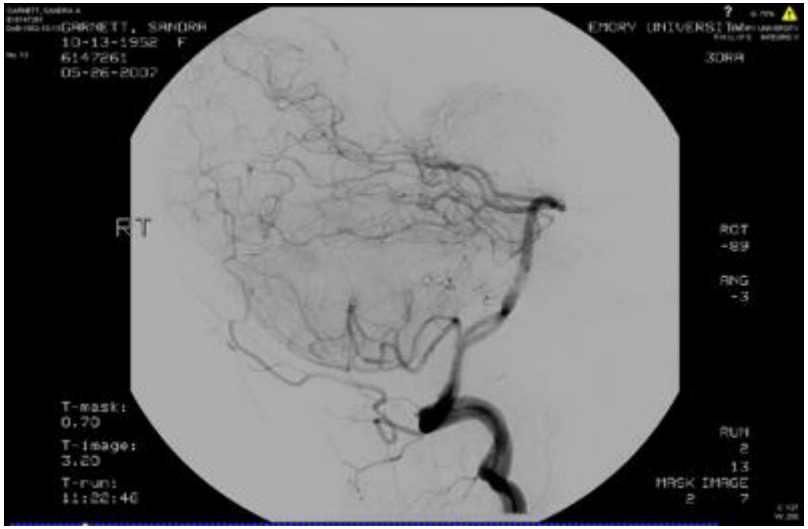


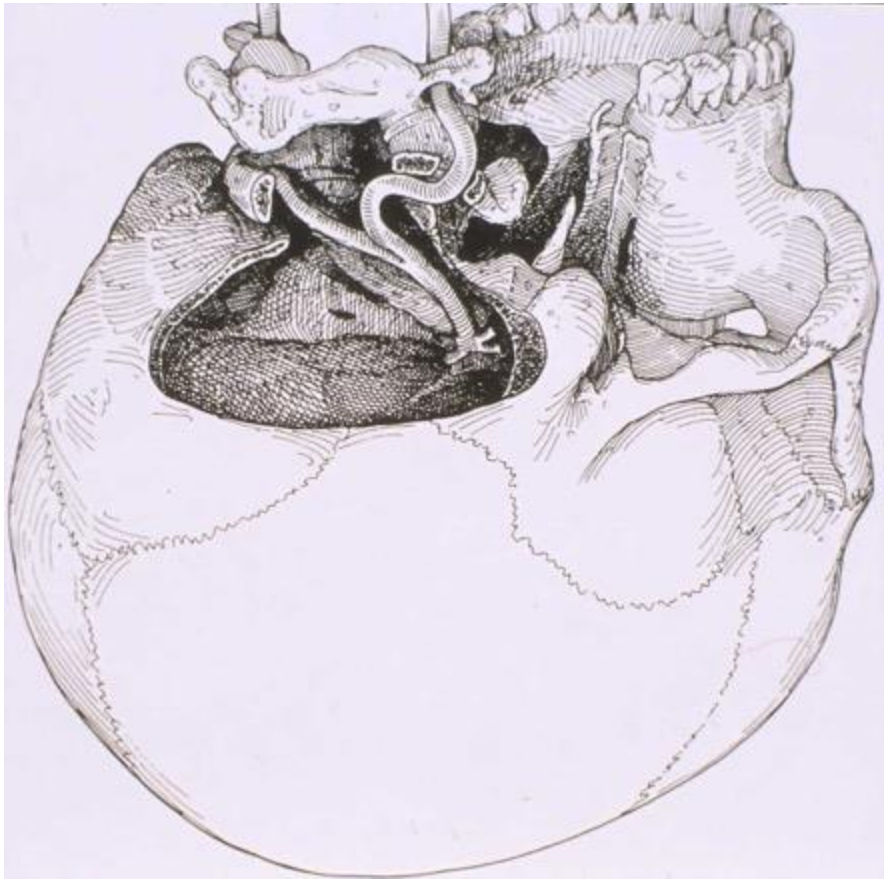
Case 8

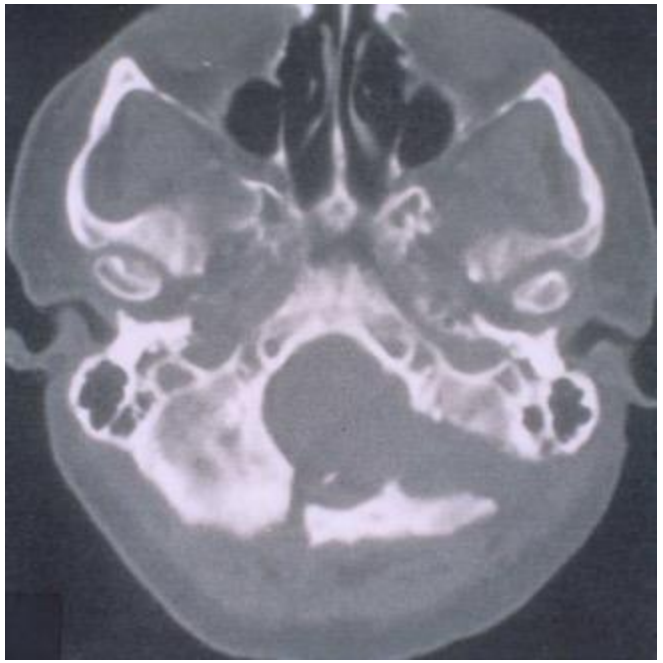
Very Small Aneurysm





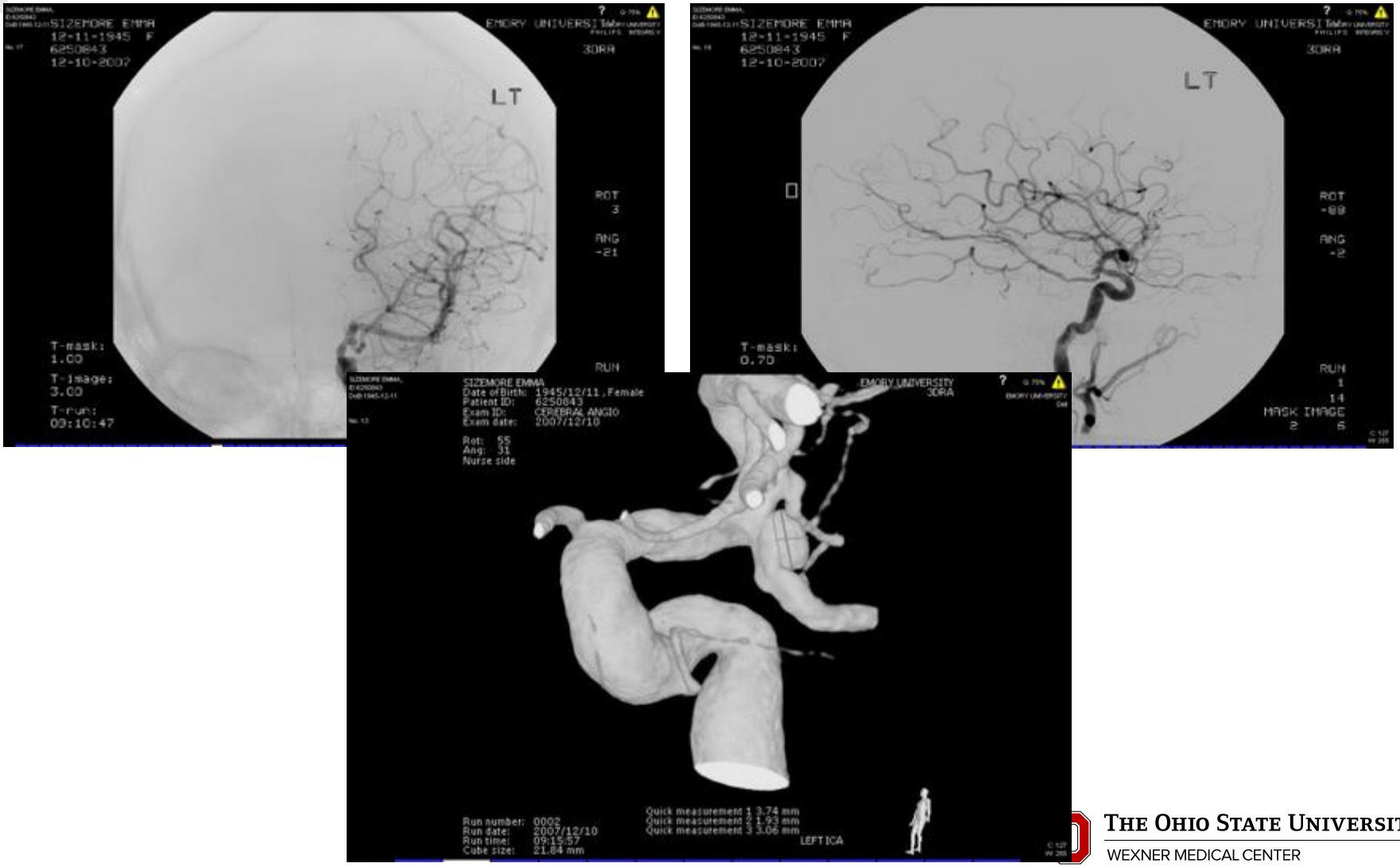




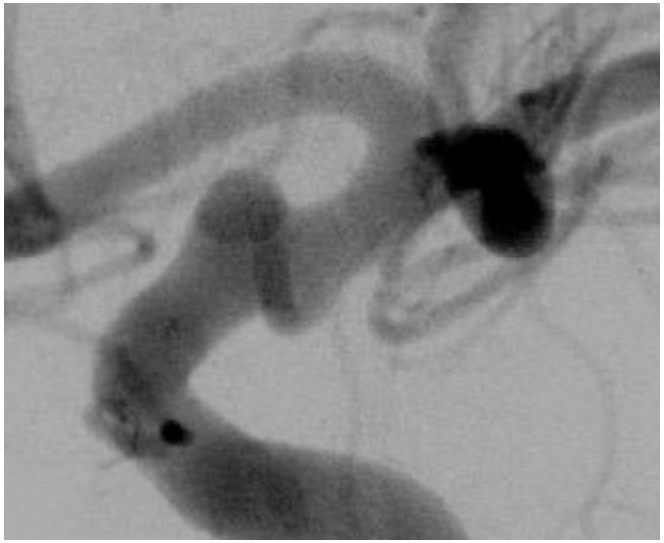


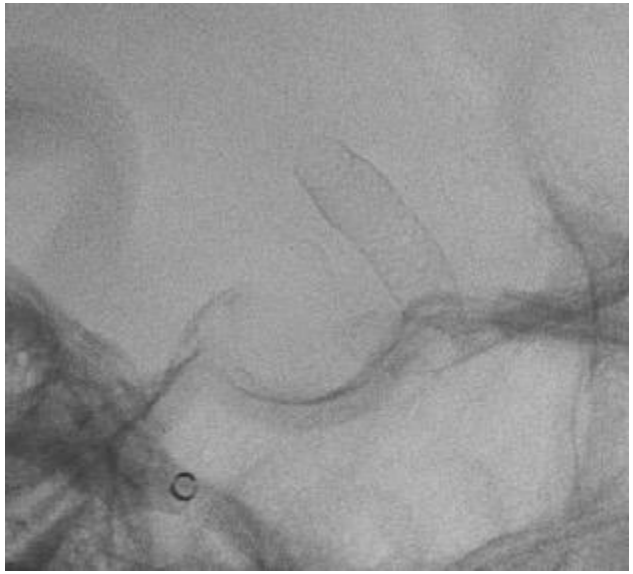
Case 9

Blister Aneurysm



BN: 51 AF SAH; re-hemorrhage x2





6 Days

18 Days

Recovered “well”; back in New Zealand (no further follow-up yet)

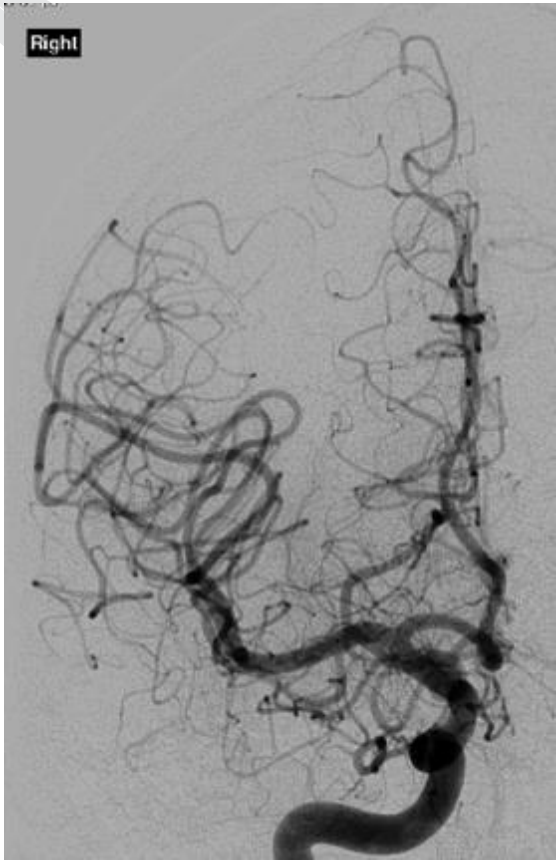
Clip wrapping

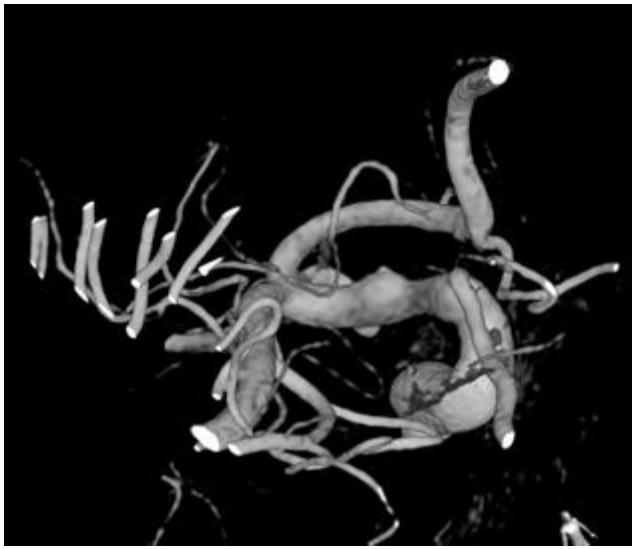
- Various materials have been used to wrap including: gauze, muslin, muscle, fascia, and Gore-Tex.
- Wrap placed around aneurysm segment of ICA.
- Slits placed if needed to allow perforating vessels through wrap.
- Clip applied to wrap material to avoid trauma to aneurysm wall.
- If successful, will always result in some degree of parent vessel stenosis to presumably reapproximate tissue layers.
  - High recurrence risk (>70%) if no stenosis observed.
- Necessary optic nerve retraction can lead to mechanical injury.

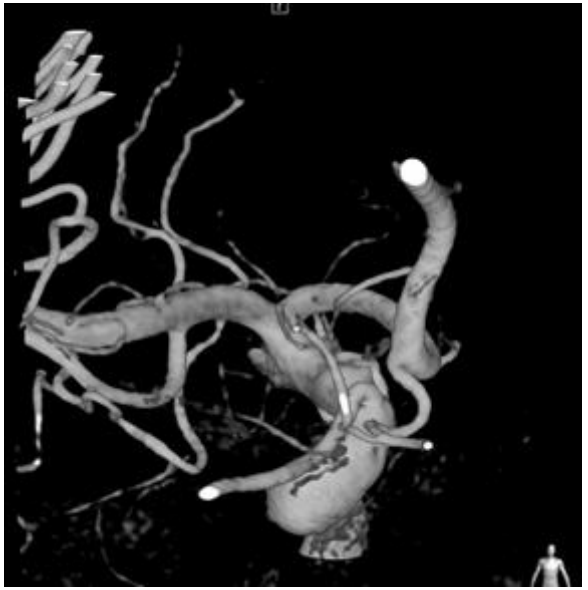
Clip Wrapping

CT showing SAH

Angiogram demonstrates right ICA “blister” aneurysm



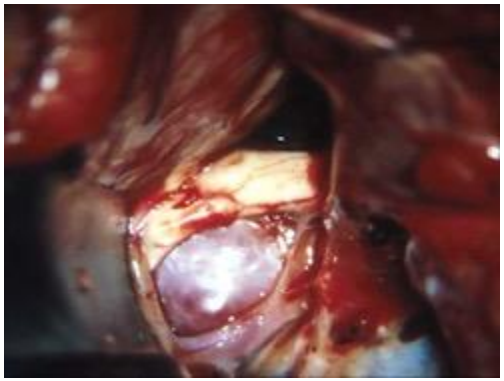




Aneurysms ***STILL*** Ideal for Clipping?

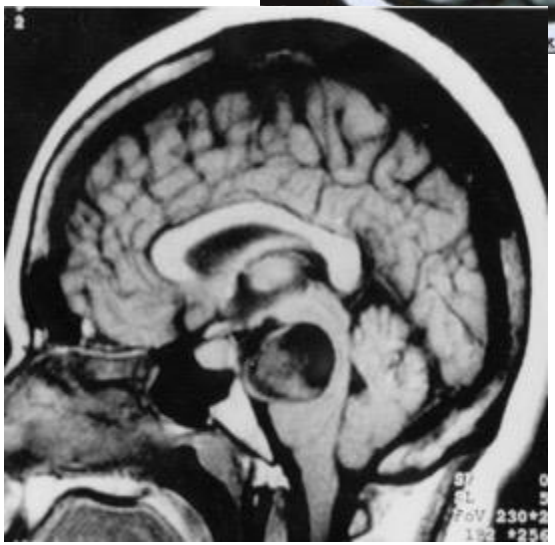
Group 2

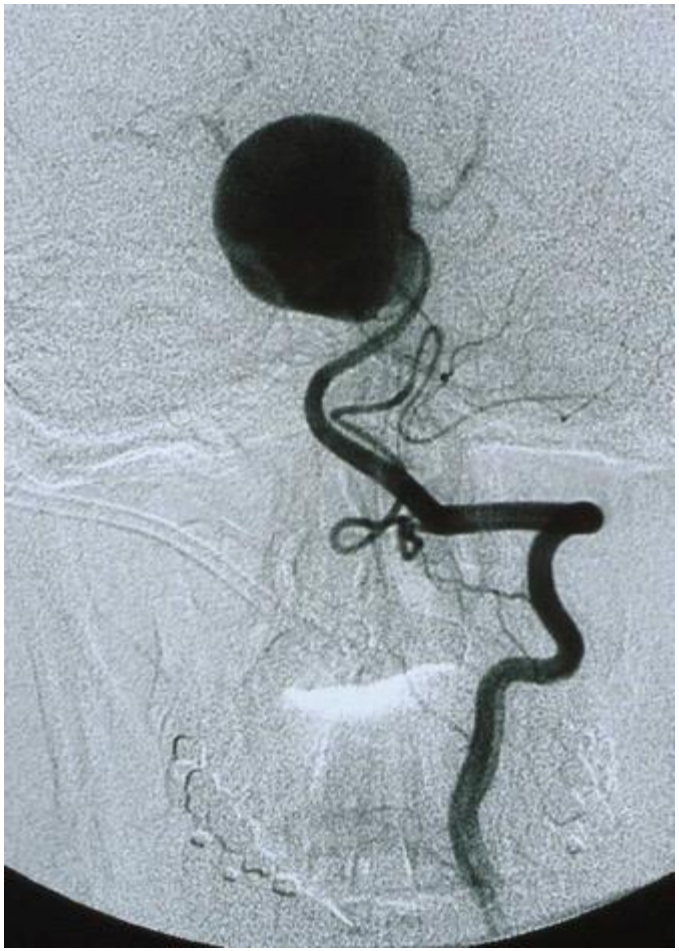
- Specific locations (MCA, ACA)
- Multiplicity not amenable to coils
- Complex or wide-neck
- Very small or blister aneurysms
- ***Giant aneurysms*****
- ***Partially thrombosed lesions*****
- ***Fusiform aneurysms*****
- Associated ICH
- Associated mass effects
- Failed endovascular therapy

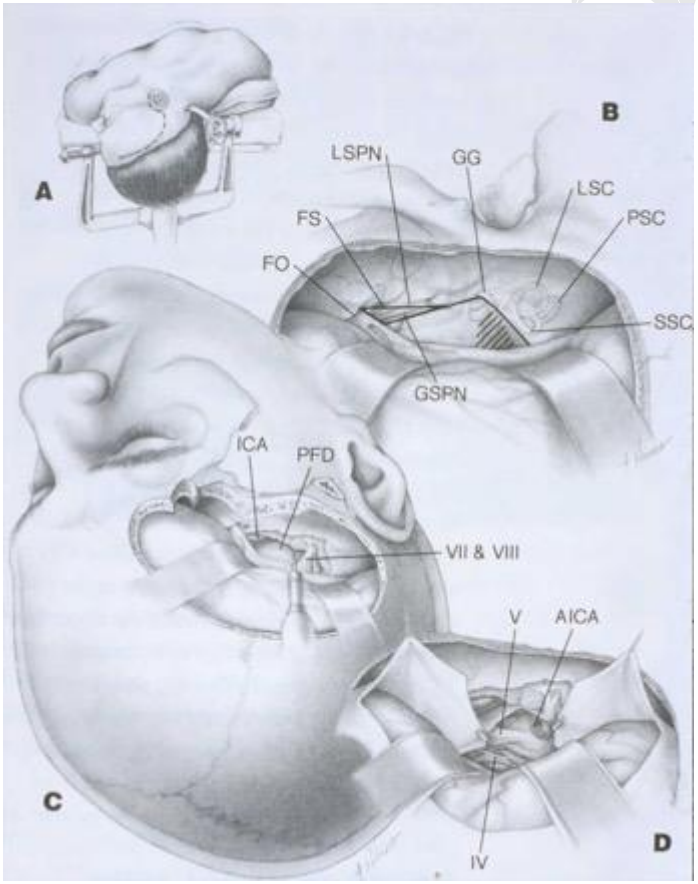


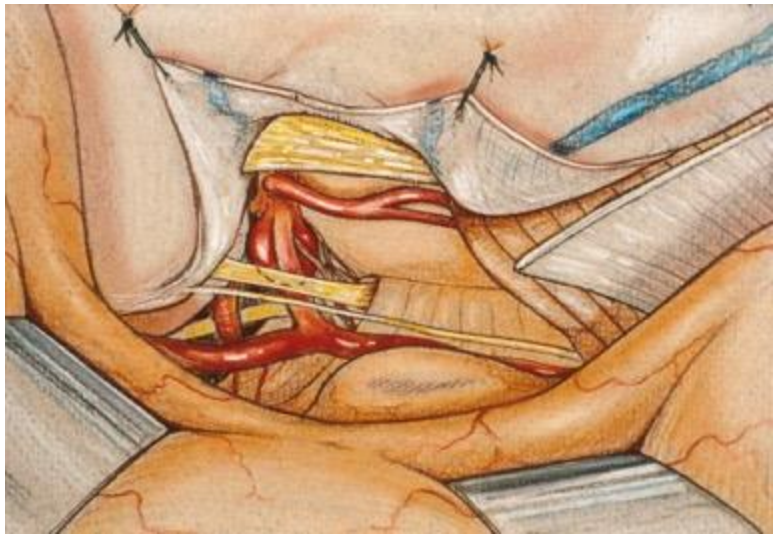
Case 10

Giant Aneurysm – Evolving Indication

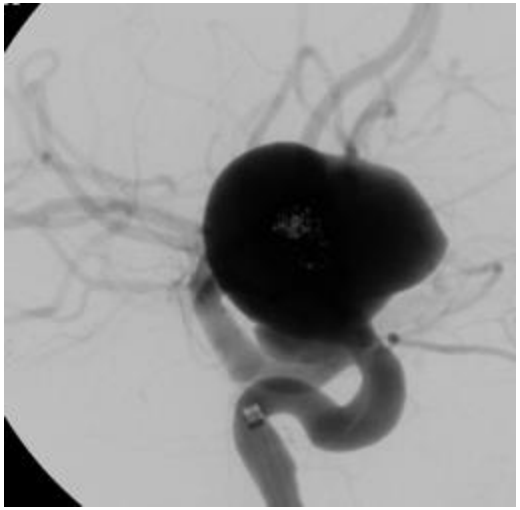


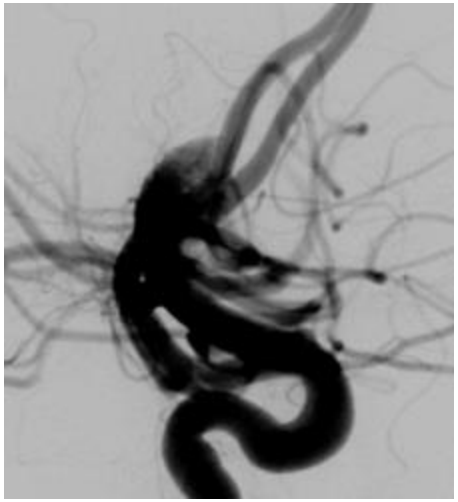


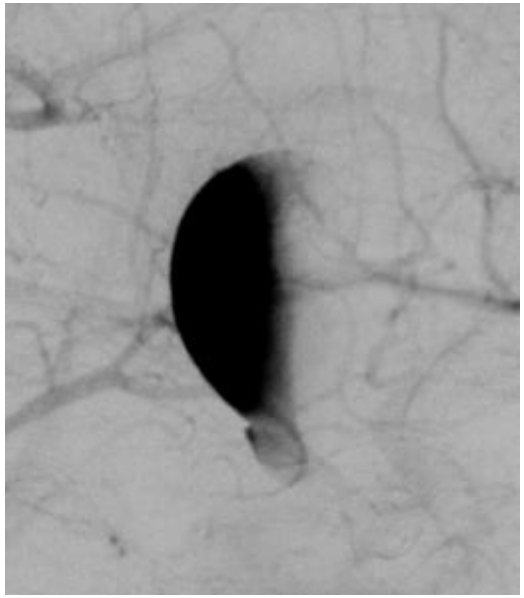

A
B
LSPN
GG
LSC
PSC
FS
FO
SSC
GSPN
ICA
PFD
VII & VIII
V
AICA
C
D
IV

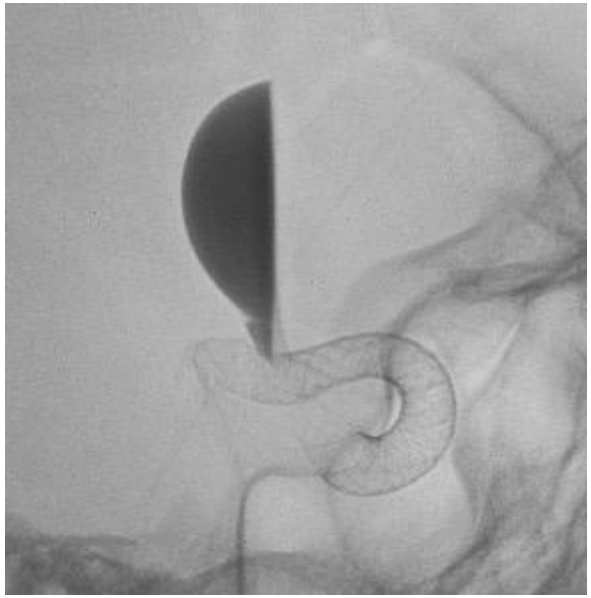


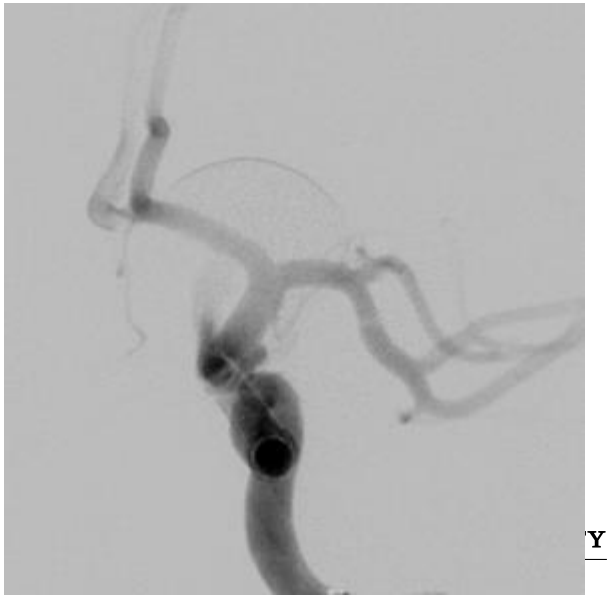
Giant OA Aneurysm





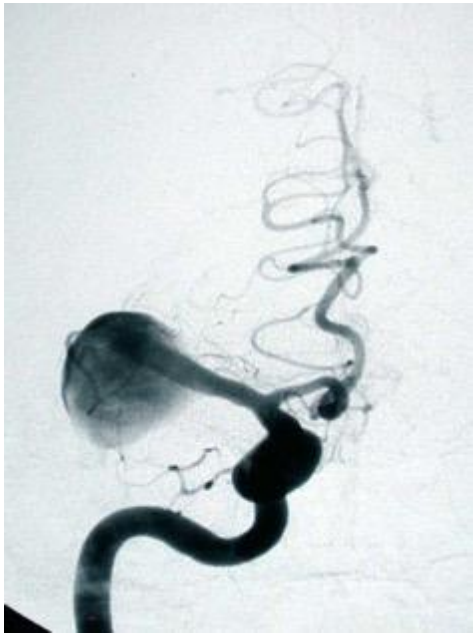


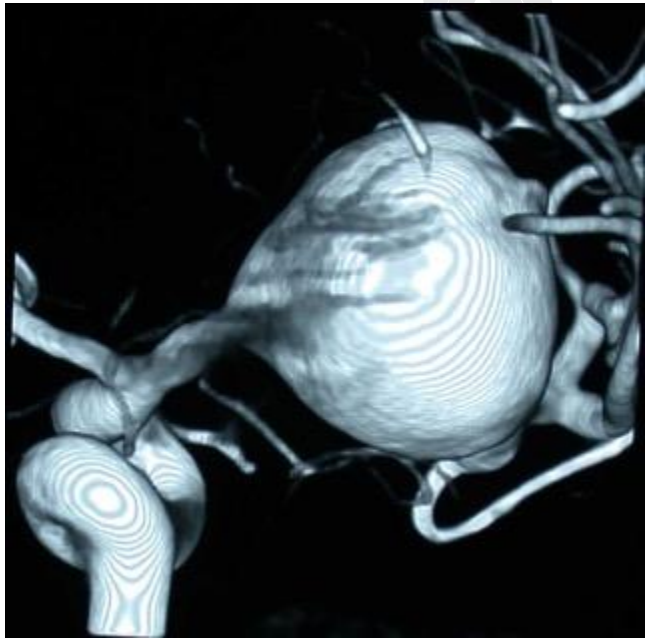


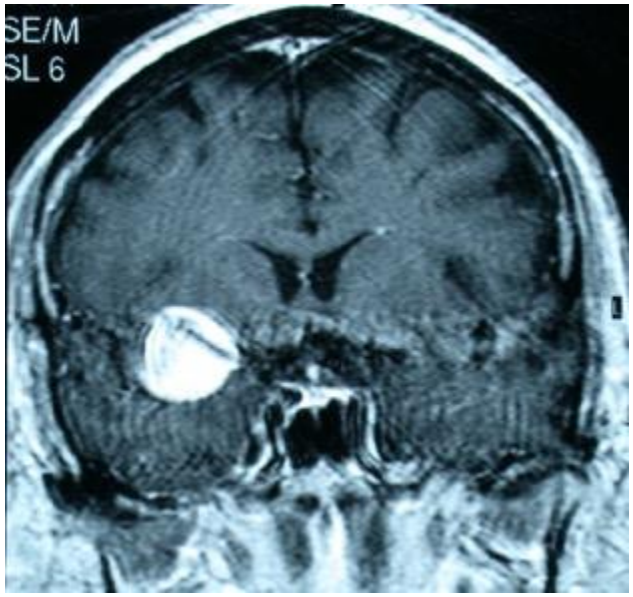


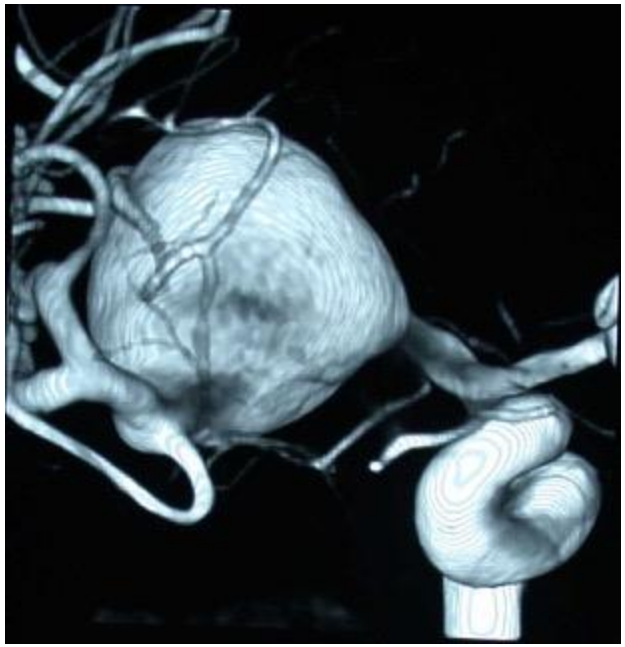
Case 11

Giant Fusiform Aneurysm of MCA Bifurcation



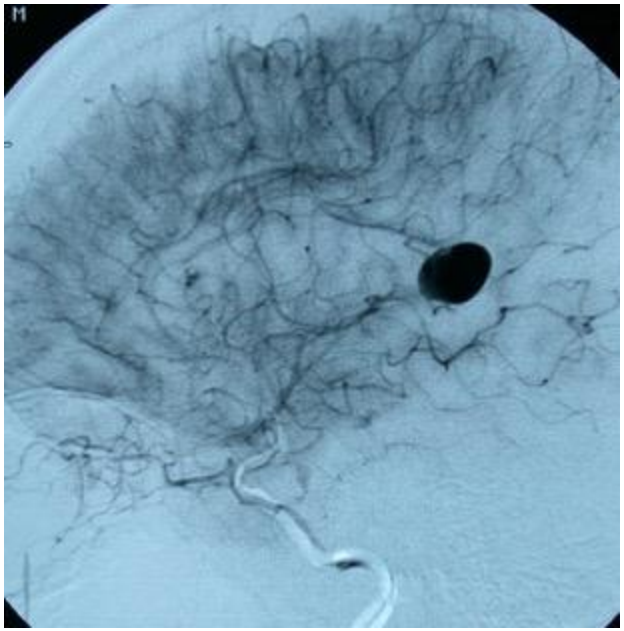


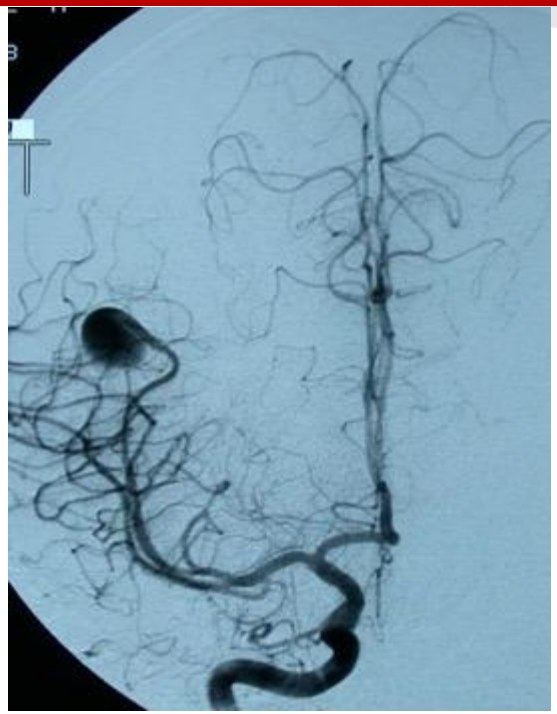


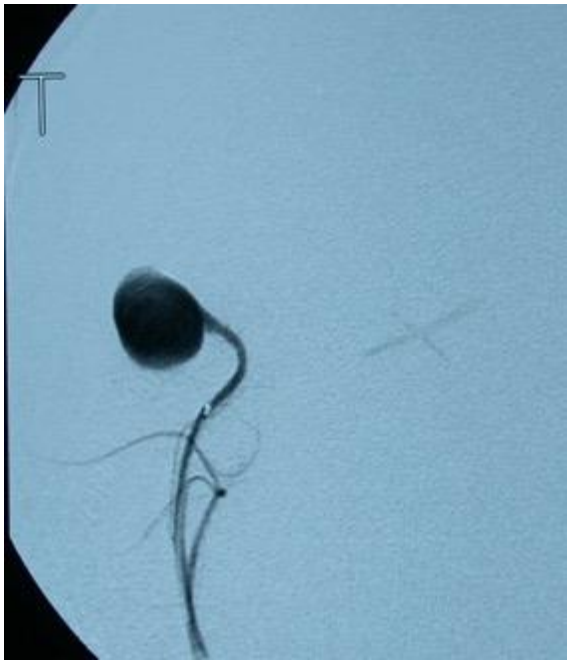


Case 12

Distal Fusiform Aneurysm







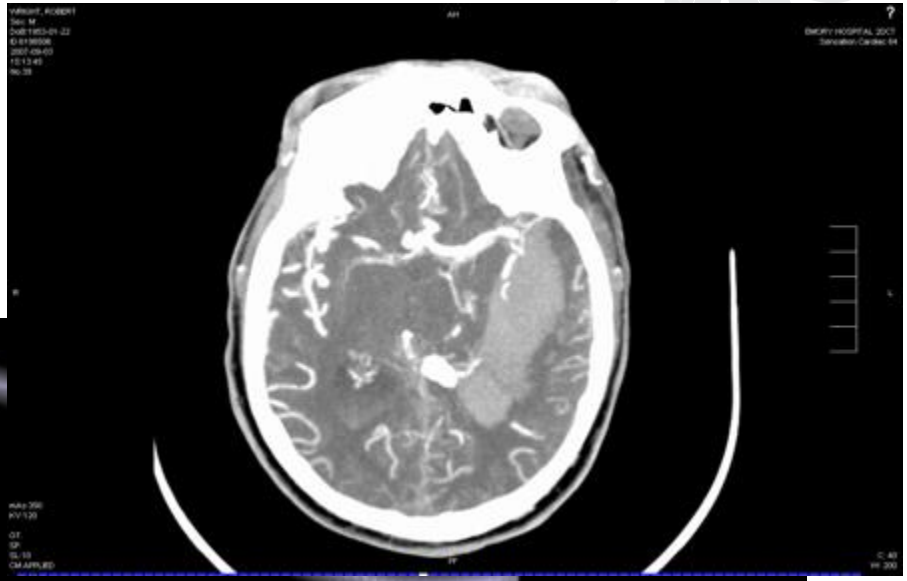
Combined Approach with NICO

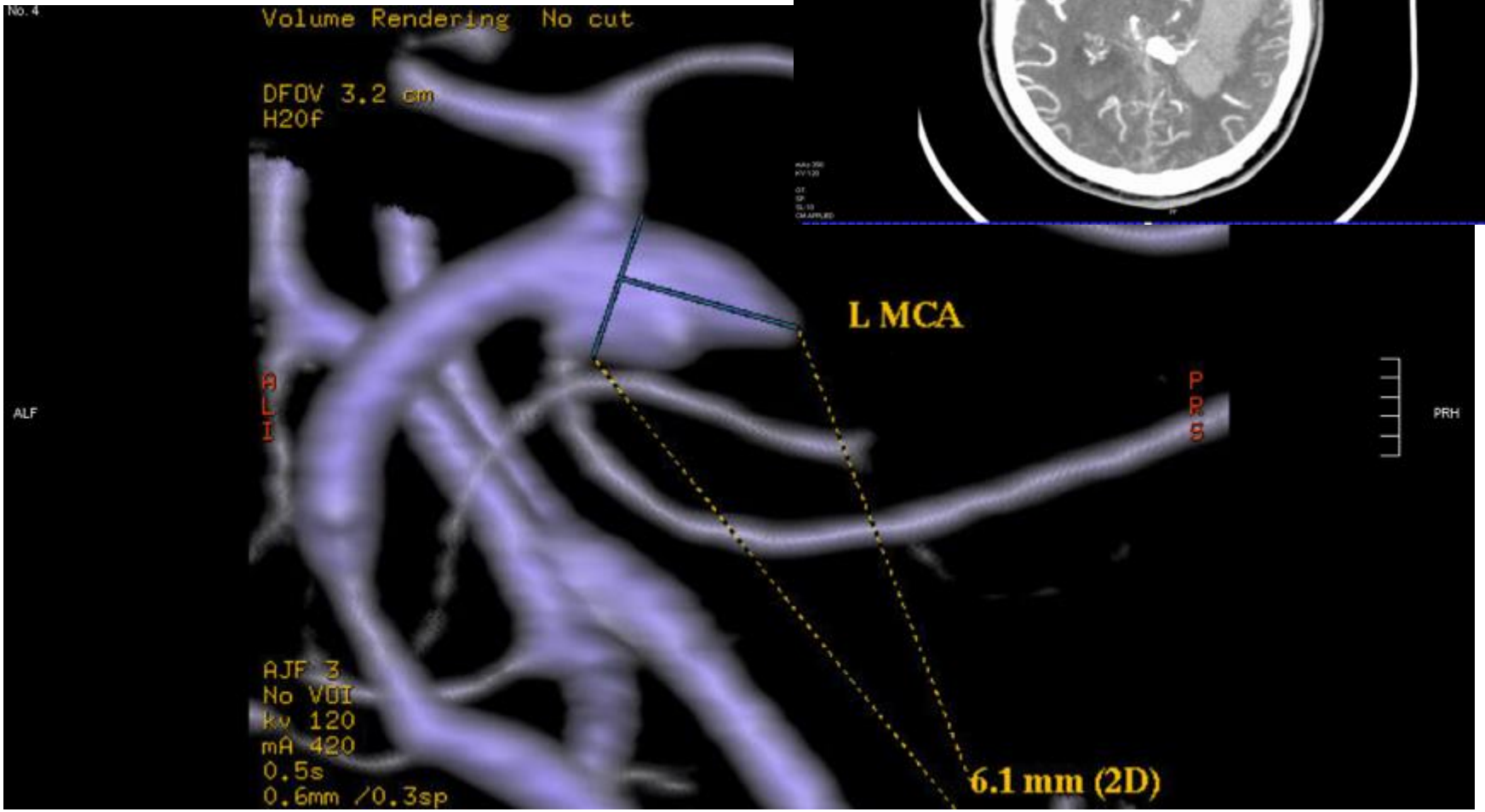
Aneurysms ***STILL*** Ideal for Clipping?
Group 3

- Specific locations (MCA, ACA)
- Multiplicity not amenable to coils
- Complex or wide-neck
- Very small or blister aneurysms
- Giant aneurysms
- Partially thrombosed lesions
- Fusiform aneurysms
- ***Associated ICH***
- ***Associated mass effects***
- ***Failed endovascular therapy***
  - ***(3.7%)***

Case 15

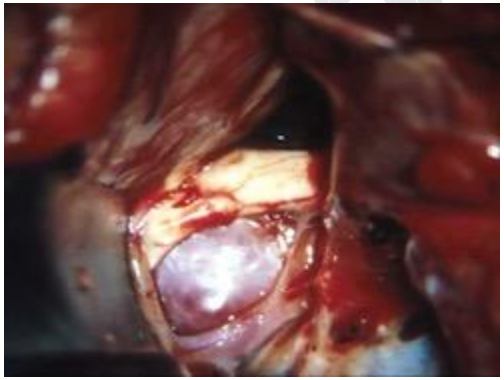
ICH

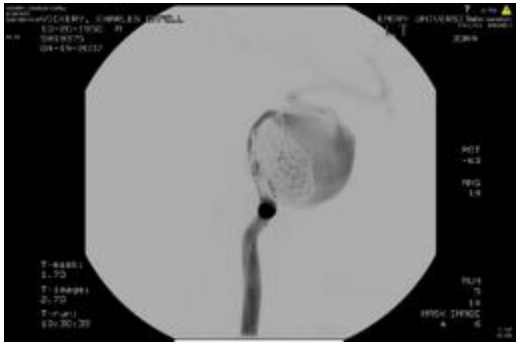



No. 4
Volume Rendering No cut
DFOV 3.2 cm
H20f
L MCA
ALF
PRH
AJF 3
No VOI
kv 120
mA 420
0.5s
0.6mm /0.3sp
6.1 mm (2D)

Mass Effect

- Cranial Nerve Palsy due to mass effect
  - Oculomotor Palsy & PComm Aneurysm
  - Visual Field & OA Aneurysm
  - Giant Cavernous Sinus Aneurysm
- Brainstem Compression
  - Large posterior circulation aneurysm





Aneurysms ***STILL*** Ideal for Clipping 2017-?

- Specific locations (MCA, ACA)
- Multiplicity not amenable to coils
- ***Complex or wide-neck*****
- ***Very small or blister aneurysms****
- ***Giant aneurysms*****
- ***Partially thrombosed lesions*****
- ***Fusiform aneurysms*****
- Associated ICH
- Associated mass effects
- Failed endovascular therapy