

Carotid Stenting: Unanswered Questions and Future Directions

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TOSHIBA
STROKE
RESEARCH
CENTER



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Potential Conflicts

Consultant & research support:
Boston Scientific, Cordis, Medtronic,
Guidant

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Boston Scientific EPI, Cordis, J&J,
Micrus, Endotex, Access Closure Inc

Outline

- I. Current Results...Ongoing Trials
- II. Will proximal embolic protection find a niche?
 - I. Manpower
 - II. Training
- V. When will patients get full access?

New Results

- Endarterectomy versus Stenting in Patients with Symptomatic Severe Carotid Stenosis
- EVA-3S Trial
- New England Journal of Medicine
- October 19, 2006

- **Off The Chart !!!!**

EVA-3S Trial: Design

- Prospective, Multicentered, Randomized
- **Sponsored by French Ministry** of Health
- Inclusion:
 - **Symptomatic** Carotid Stenosis > 60%
 - Patients equal candidate for either option
- Primary endpoint:
 - Any stroke or death within 30 days- **(Not MI)**
- **Stopped prematurely** by safety monitoring committee after 527 patients were enrolled

EVA-3S Trial: Results

- 30 Day rate of any stroke or death
 - Endarterectomy = 3.9%
 - Carotid Stent = 9.6%
 - Relative Risk of 2.5 (95% CI 1.2 to 5.1)
- 30 Day rate of disabling stroke or death
 - Endarterectomy = 1.5%
 - Carotid Stent = 3.4%
 - Relative Risk of 2.2 (95% CI 0.7 to 7.2)^{***}
 - Not statistically significant

EVA-3S Trial: Results

- 6 month rate of any stroke or death
 - Endarterectomy = 6.1%
 - Carotid Stent = 11.7% ($p = 0.02$)
- Conclusion:
 - For symptomatic patients (>60%) with acceptable surgical risk, rates of death and stroke were lower with CEA than with stenting

EVA-3S Trial: Limitations

- Distal protection was only “[strongly] recommended” after February 2003 (50% trial duration)
 - 30 day stroke or death
 - Without DEP = 25% (5 of 20)
 - With DEP = 7.9% (18 of 227)
- If 7.9% rather than 9.6% is used:
 - Relative Risk = 2.0 ($p = 0.07$)

EVA-3S Trial: Limitations

- Rates of MI were not assessed
 - (Reduced rate of MI was one source of benefit identified in the SAPPHIRE Trial)
- Only 30 day and 6 month follow up
 - (Despite trial ongoing since 2000)

EVA-3S Trial: Limitations

- Experience bias
 - Vascular surgeons:
 - Required 25 CEAs in the year prior to study entry
 - Endovascular physicians:
 - Required 12 carotid stents or 35 “supra-aortic stents” with at least 5 carotid stents
 - Or, Allowed to receive training and credentialing “under supervision” as they enrolled patients in the trial
 - Allowed to use new stents after only **two cases**

EVA-3S Trial: Limitations

- Enrollment Bias...?
 - Total CEA case volumes were not discussed
 - Estimated $\ll 10\%$ of all patients randomized
 - Thirty hospitals
 - Assuming only 1 vascular surgeon per hospital with the enrollment criteria minimum 25 cases/yr
 - 4.75 years of enrollment = 3562.5 patients
 - 5 pts taken to **OR (bailout)....2 strokes**

CAPTURE 2500

Age & Symptoms

- DSMI overall **Sx** 12.2 **Asx** 5.3 (.0001)
- DS (F Worse) **Sx F** <80 vs **Sx M** <80 (.03)

CREATE High Risk Registry

EV3 Stent + Spider Filter

30 Day Results

- ***30 day death, stroke and MI*** **6.2%**
- ***Major Stroke*** **3.5%**
- ***Hemorrhage*** **1.3%**

- ***Risk Factors***

Symptomatic carotid stenosis

Renal failure

Duration of filter deployment

SPACE Trial

RPCT (Sx) N=1200

Death, Stroke and MI - 30 day

CAS 6.8%

CEA 6.3%

p = 0.09

CEA better in older patients

CAS Risk Factors

- 1) *Symptomatic lesion***
- 2) *Sx > age 80***
- 3) *Renal Failure***
- 4) *Multiple stents***
- 5) *Duration Filter deployment***
- 6) *Pre dilitation***
- 7) *Corkscrew/calcified arteries***

CAS

Non Predictors of Risk

- 1. Sex**
- 2. Calcification**
- 3. Residual stenosis**
- 4. Filter**
- 5. Contralateral occlusion**
- 6. Smoking**
- 7. Diabetes**
- 8. Statins**

Complementary Techniques

- Most evidence shows Stents are not inferior in efficacy and safety to CEA.
 - ARChER, CaRESS, SAPPHIRE
- We know which pts are not suited for CEA...from EXPERIENCE !
- We are learning which pts are not suited for CAS...from trials and from experience

NASCET Exclusion Criteria

Poor Candidates for CEA

- Age > 79
- Previous ipsilateral endarterectomy
- Intracranial stenosis > carotid lesion
- Lung, liver, or renal failure
- Unstable angina
- MI < 6 months
- Uncontrolled hypertension or diabetes
- Contralateral CEA < 4months
- Progressive neurologic dysfunction
- Major surgery < 30 days

Low Risk Sx Patients

- **NASCET** Surgical risks (30 day peri-op M&M)
- Symptomatic with $\geq 70\%$ stenosis
 - 5.8% total
 - 3.7% minor stroke,
 - 1.5% major stroke
 - 0.6% death
- How about “moderate risk” ??
 - Symptomatic $\geq 70\%$ and Contralateral Occlusion
 - 14.3% total

Long Term Durability

- Major events at 3 years
 - Stent 25.5% vs. CEA 30.3% (p=0.231)
- Death at 3 years
 - Stent 20.0% vs. CEA 24.2% (p=0.280)
- Ipsilateral stroke at 3 years (All stroke 30 days)
 - Stent 7.1% vs. CEA 6.7% (p=0.945)
- Need for same vessel revascularization
 - Stent 3.0% vs. CEA 7.1% (p=0.084)

Long Term Durability

- Need for revascularization
 - 2.2% at 1 year
-

Doppler Ultrasound Follow Up

	1mo	1yr	2yr	3yr
n =	504	437	166	86
<50% Stenosis	80%	65%	70%	70%
>70 % Stenosis	1%	5%	2%	2%

What will CREST teach us that we don't already know?

- Differences from EVA-3S
 - Distal Embolic Protection in most patients
 - Vetting of all surgeons & interventionalists
 - MI rates are monitored
 - Dual antiplatelet therapy in all patients
 - Long term follow up
 - More rigorous interventionalist credentialing
- CREST is now more important than ever
 - Challenges to Recruitment are present

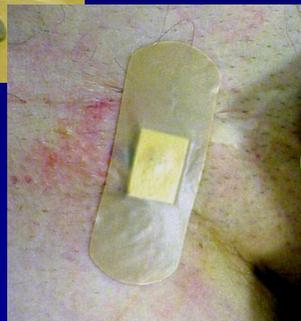
Conclusions

- CAS and CEA are complementary
- High-risk CEA patients should be treated by CAS: proven efficacy with less risk
- Asymptomatic patients deserve treatment...we don't know which is best yet
- Low-risk patients should be enrolled in further trials! CREST, ACT 1...

**Clinical
Equipoise**

=

**Endovascular
Superiority**



Will proximal embolic protection find a niche?



- Low GSM score
- Perilesional Kinks
- Distal Tortuosity
- No landing zone
- Complete occl
- Luminal thrombi

- Ok arch
- Ok CCA

Distal Embolic Protection Devices

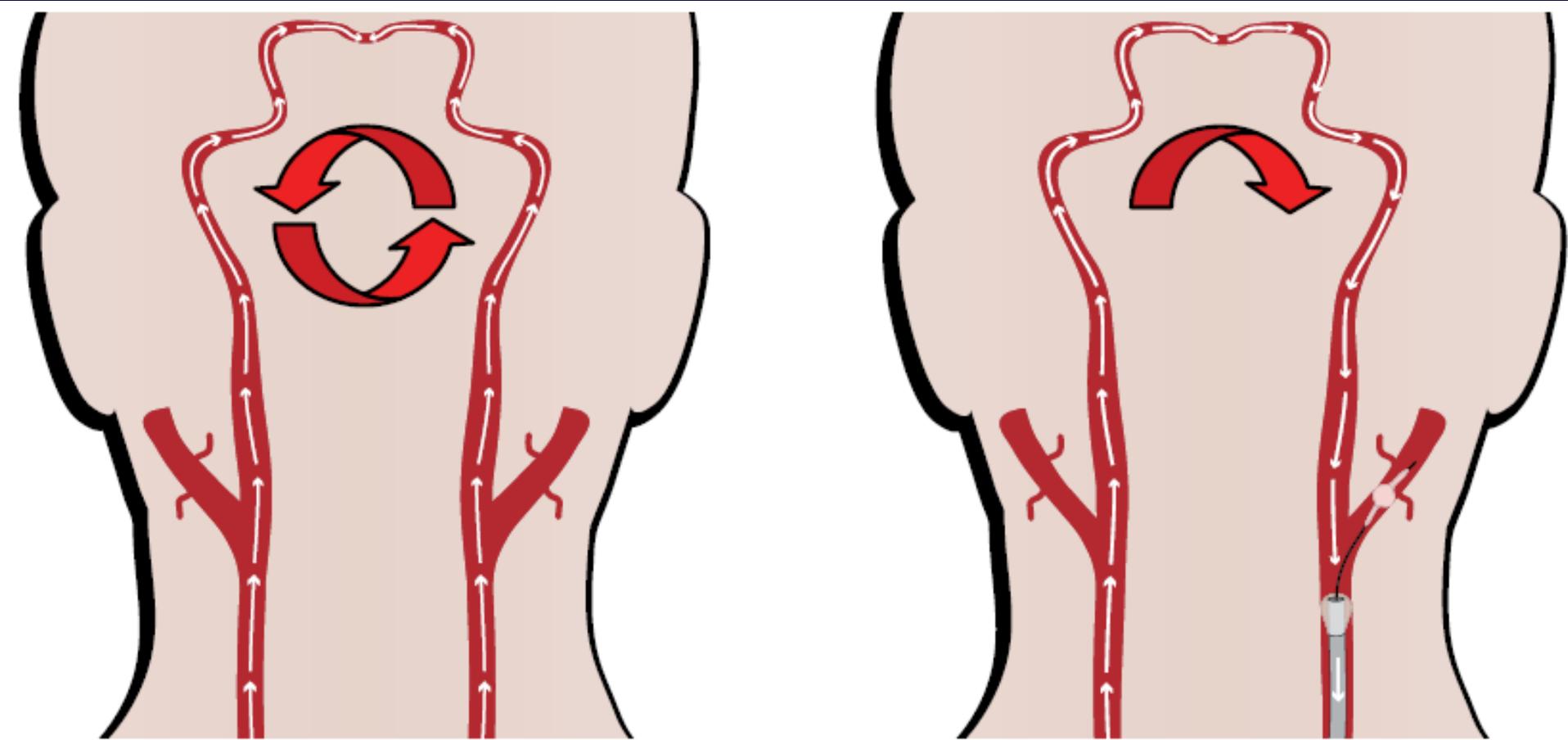


In all FDA studies on CAS with embolic protection, visible debris was collected in over 50 % of cases

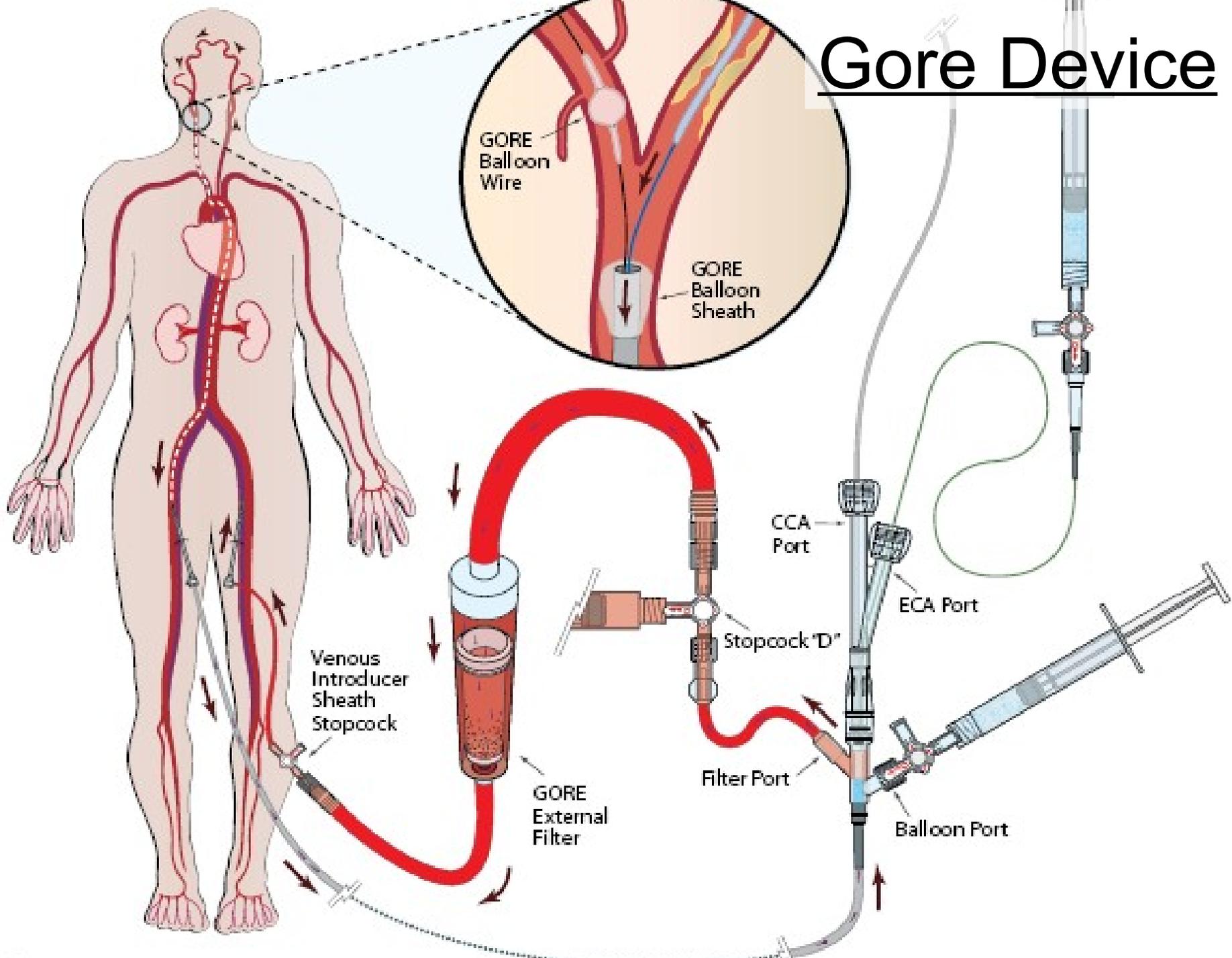
CAS With and Without Protection

	<u>Without DEP</u>	<u>With DEP</u>
• Minor stroke	3.7% (94/2537)	0.5% (5/896)
• Major stroke	1.1% (28/2537)	0.3% (3/896)
• Death	0.3% (8/2537)	0.8% (8/896)
• Any stroke or death	5.5% (40/2537)	1.7% (16/896)

Carotid Stenting with Flow Reversal

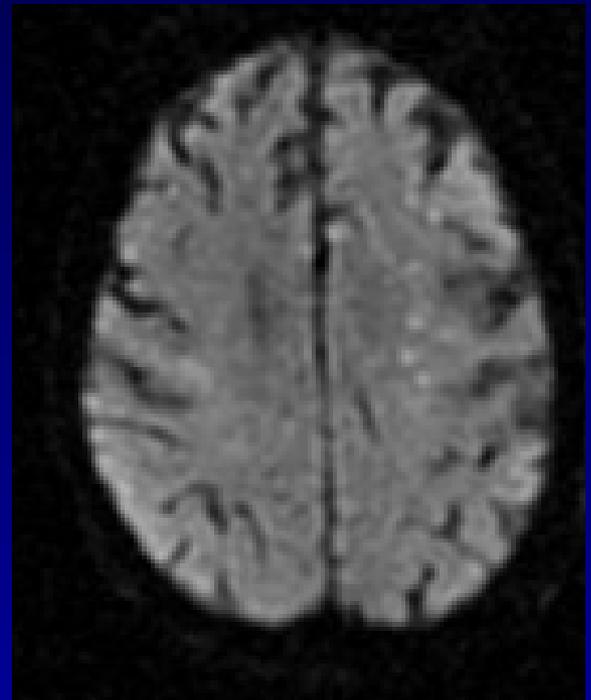
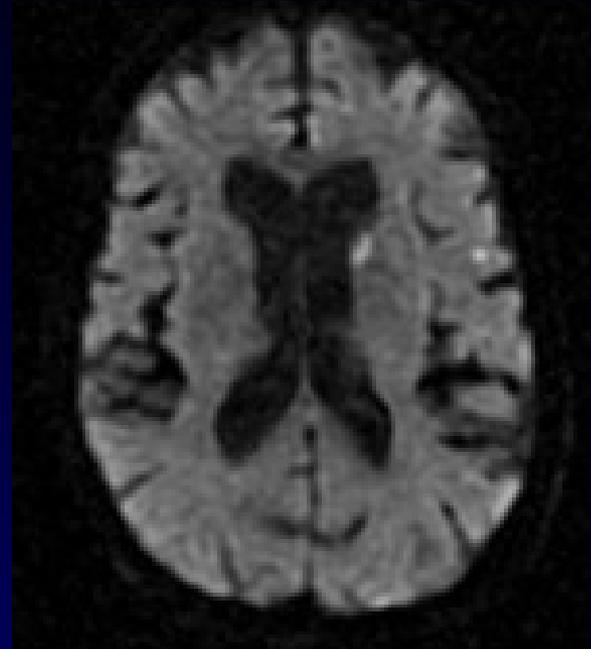


Gore Device



Illustrative Case

- 82 year old woman
 - Three episodes of dysarthria, paucity of speech
 - One episode with right upper extremity weakness
- Neurological exam normal – NIHSS 0





61% Symptomatic
Stenosis

Flow Reversal

- Ischemic time - 6 minutes
- Patient became less arousable and developed expressive aphasia
- Rapidly normalized with return of antegrade flow

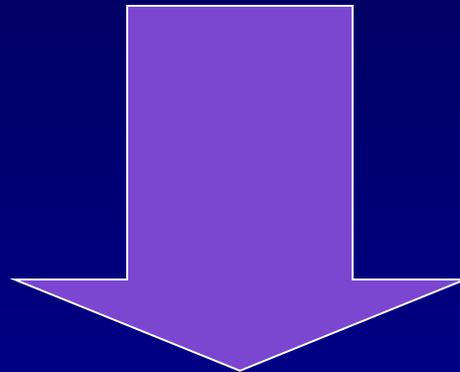


Carotid Stent Evolution

10 year history

Initial results discouraging ...High M&M

- Technology evolution
- Embolic protection
- Better patient selection
- Large clinical experience



Evolution of Trial Results

How much will CAS cost?

- Costs are already within the range of other preventative strategies
 - Highly effective, Small NNT
 - Shorter ICU stay and hospitalization
- The materials cost will improve with more market competition
- **Carotid stenting may become one of the most cost effective stroke prevention strategies**

When will patients' get full access?

- Low Risk Trials are underway...
- **EVERYONE** is watching

There is no stopping CAS...more data and technology evolution will make CAS mainstream

Best Guess.... 2010 ?

What Effect Will Subspecialty “Standards” and Lobbying Have on Cardiologists and Carotid Stenting ?



OPPORTUNITY



You'll always
miss 100%
of the shots
you don't take.

Who Will Treat Acute Stroke?

- 750,000 CVAs per year and growing
- ~ 250 neurointerventionalists
- ~ 60 endovascular neurosurgeons
- ~ 5 endovascular neurologists
- 8,000 interventional cardiologists

How Do We Get There ?

- Training
- Collaborating

Collaboration

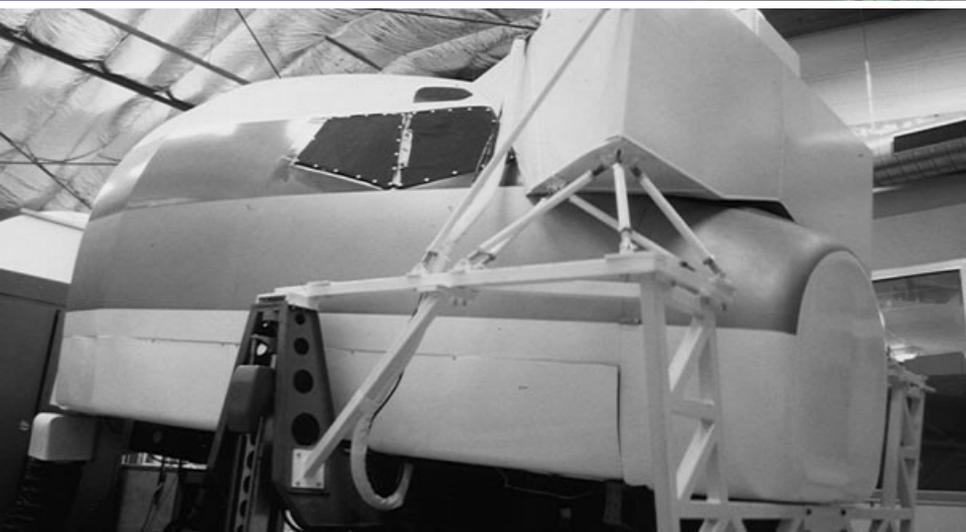
Subspecialty Strengths

- Neurology
- Radiology
- Vascular surg
- Vascular med
- Cardiology
- End organ cognitive
- Imaging/cath skills
- Own CEA market
- Cognitive/imaging
- Cath/angioplasty skills
- Clinicians
- Industry partners
- Clinical research

Simulator Training Model

Commercial Pilot

- Mandatory yearly training
- 60 hours ***simulated*** instrument training
- 60 hours ***actual*** instrument training



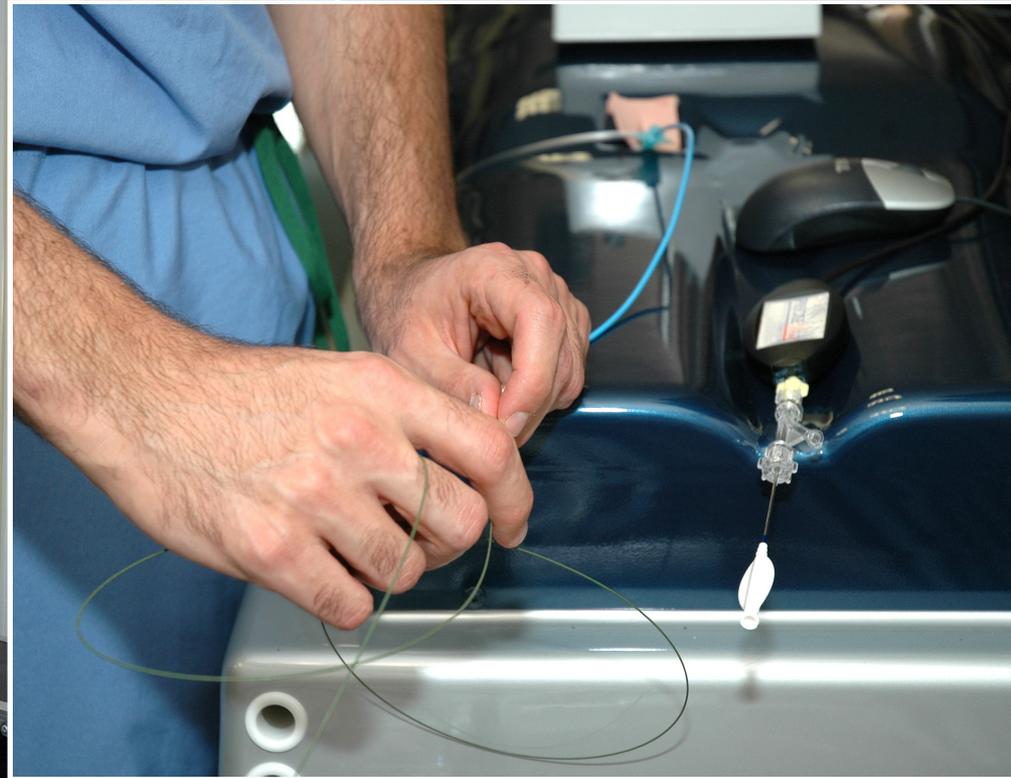
“Virtual Reality Training Improves Operating Room Performance”

- Seymour, Gallagher, et al.
- Annals of Surgery 2002.
- Randomized, Double-Blinded Study
- 16 surgical residents
- Assessment during laparoscopic cholecystectomy by surgeon-investigator blinded to the resident’s training status.

Learn Angiography with No Patient Risk



Scan In Tomorrow's Case and Practice Before You Treat



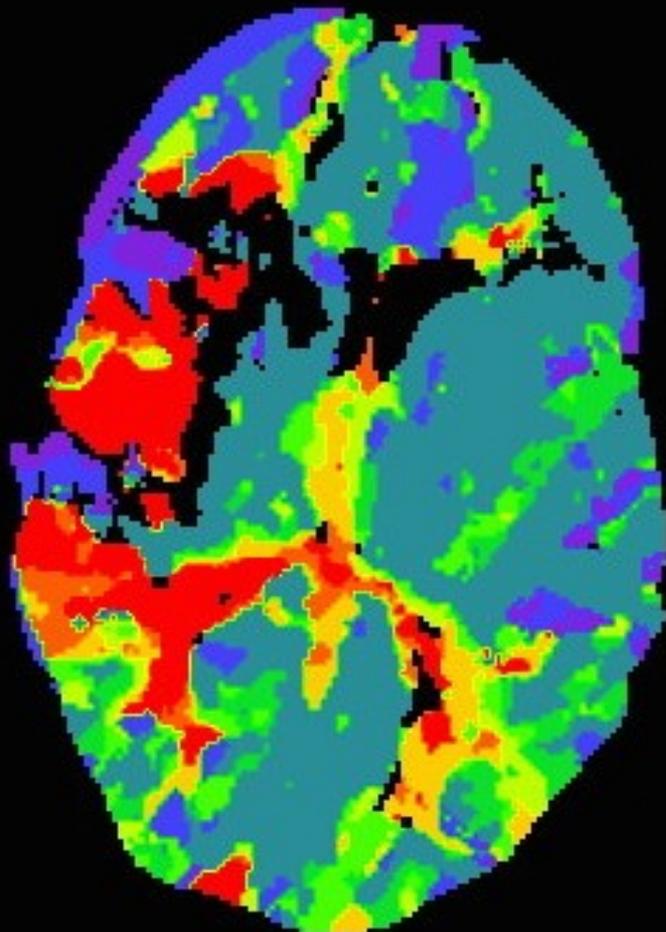
The Future...

- 27 year old female
- Cesarean delivery 8 weeks prior
- Ground level fall and head impact
- No LOC, No seizure
- Acute onset right neck and head pain
- Left upper extremity weakness
- Slurred speech

Illustrative Case

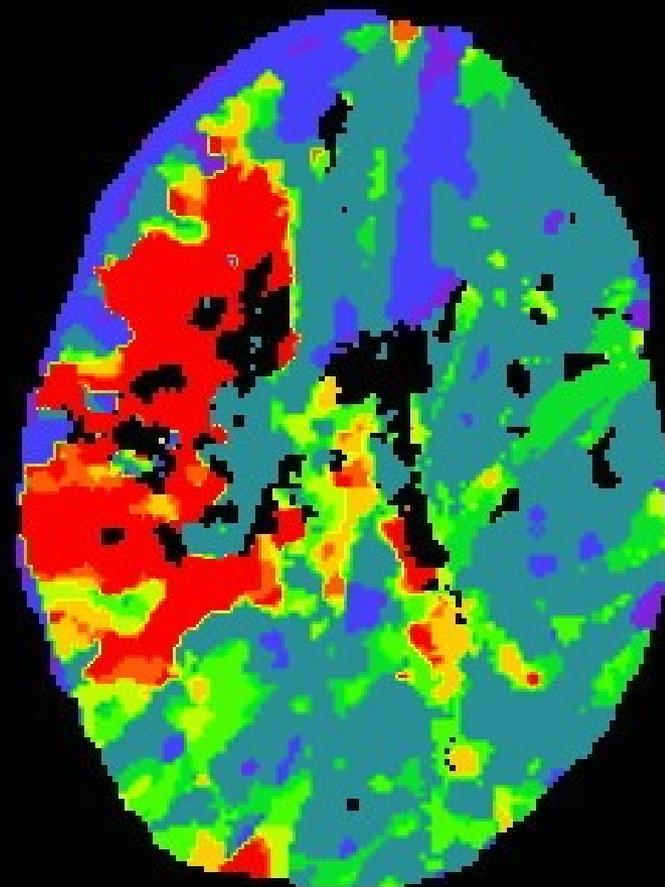
- Meds: Oral contraceptives
- In ED: NIHSS = 11
- Left facial weakness, dysarthria, left upper extremity weakness, left sided anesthesia
- Head CT: no acute trauma
- Head CT perfusion...

Original CT Perfusion



Time to Peak

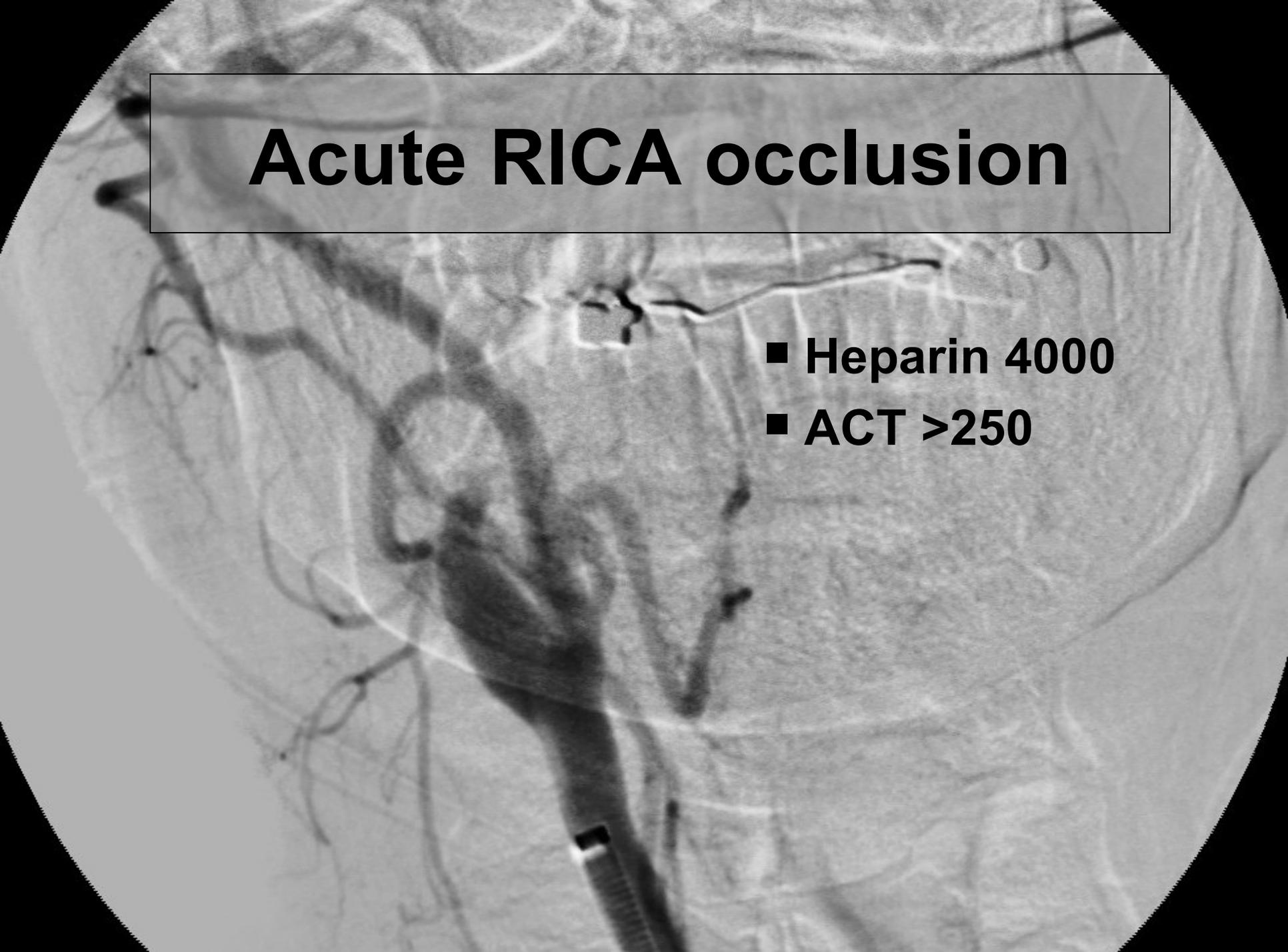
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Emergent Angiogram

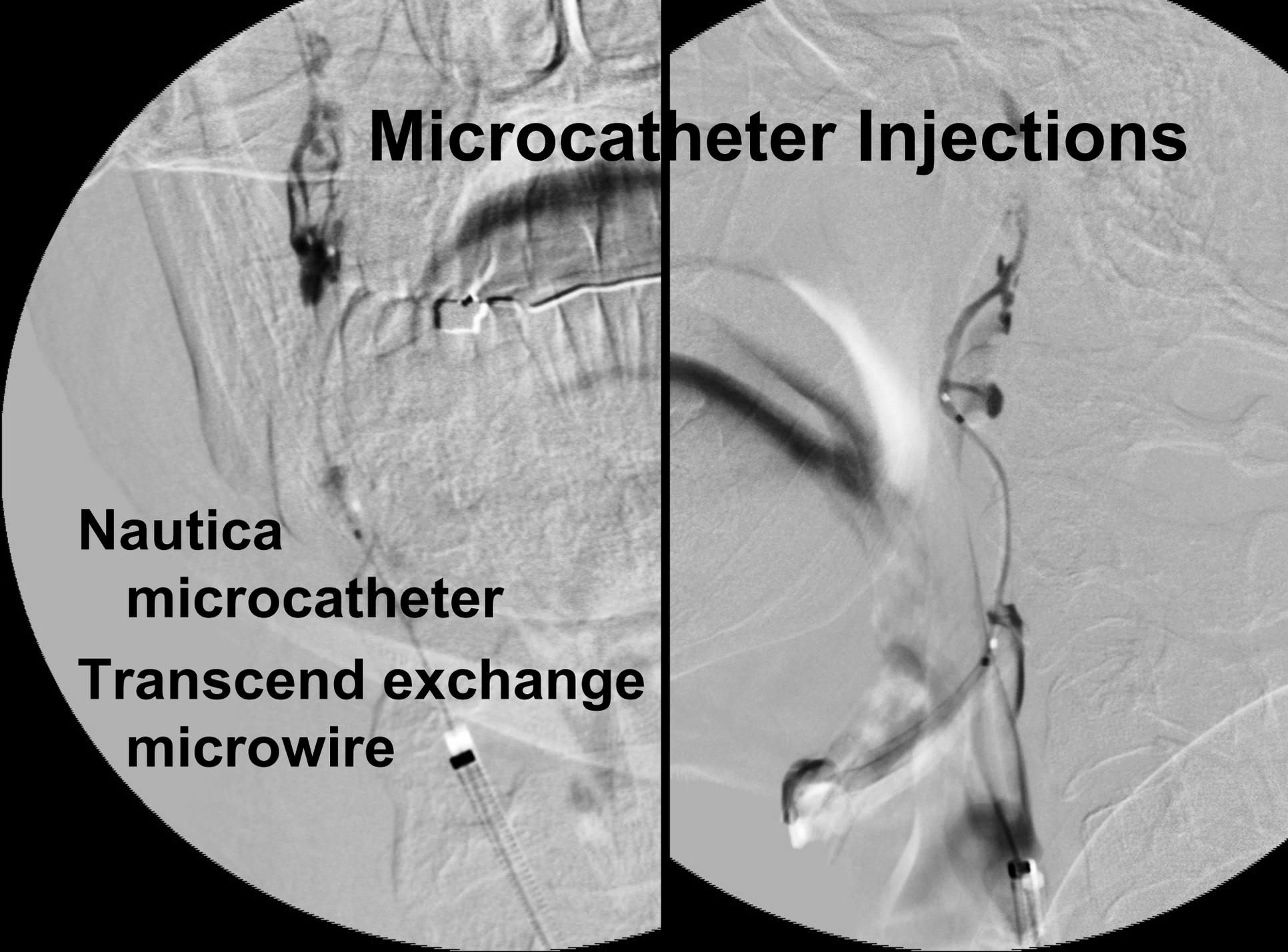


A catheter angiogram of the right coronary artery (RCA) showing an acute occlusion. The image displays the coronary artery tree with a clear blockage in the mid-segment of the RCA. The occlusion is characterized by a complete cessation of contrast flow, with a visible filling defect. The proximal and distal segments of the artery are opacified with contrast. A catheter is visible at the bottom of the frame, connected to the RCA. The background shows the intricate network of the coronary artery system.

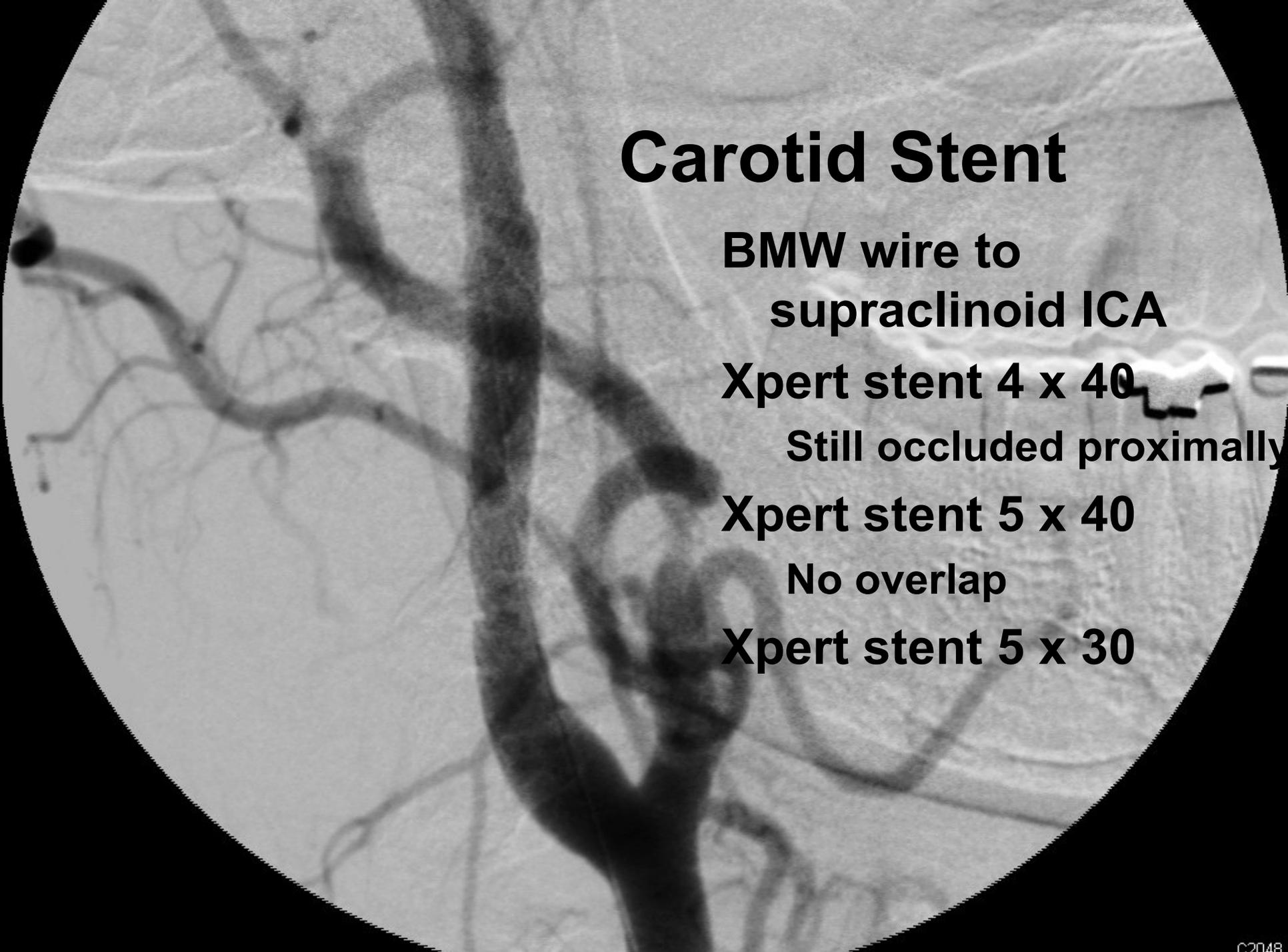
Acute RCA occlusion

- Heparin 4000
- ACT >250

Microcatheter Injections



**Nautica
microcatheter
Transcend exchange
microwire**

A grayscale angiogram of the carotid arteries. A BMW wire is visible extending to the supraclinoid ICA. Three Xpert stents are placed in a non-overlapping fashion: a 4 x 40 mm stent, a 5 x 40 mm stent, and a 5 x 30 mm stent. The text on the right side of the image provides details about the stent placement.

Carotid Stent

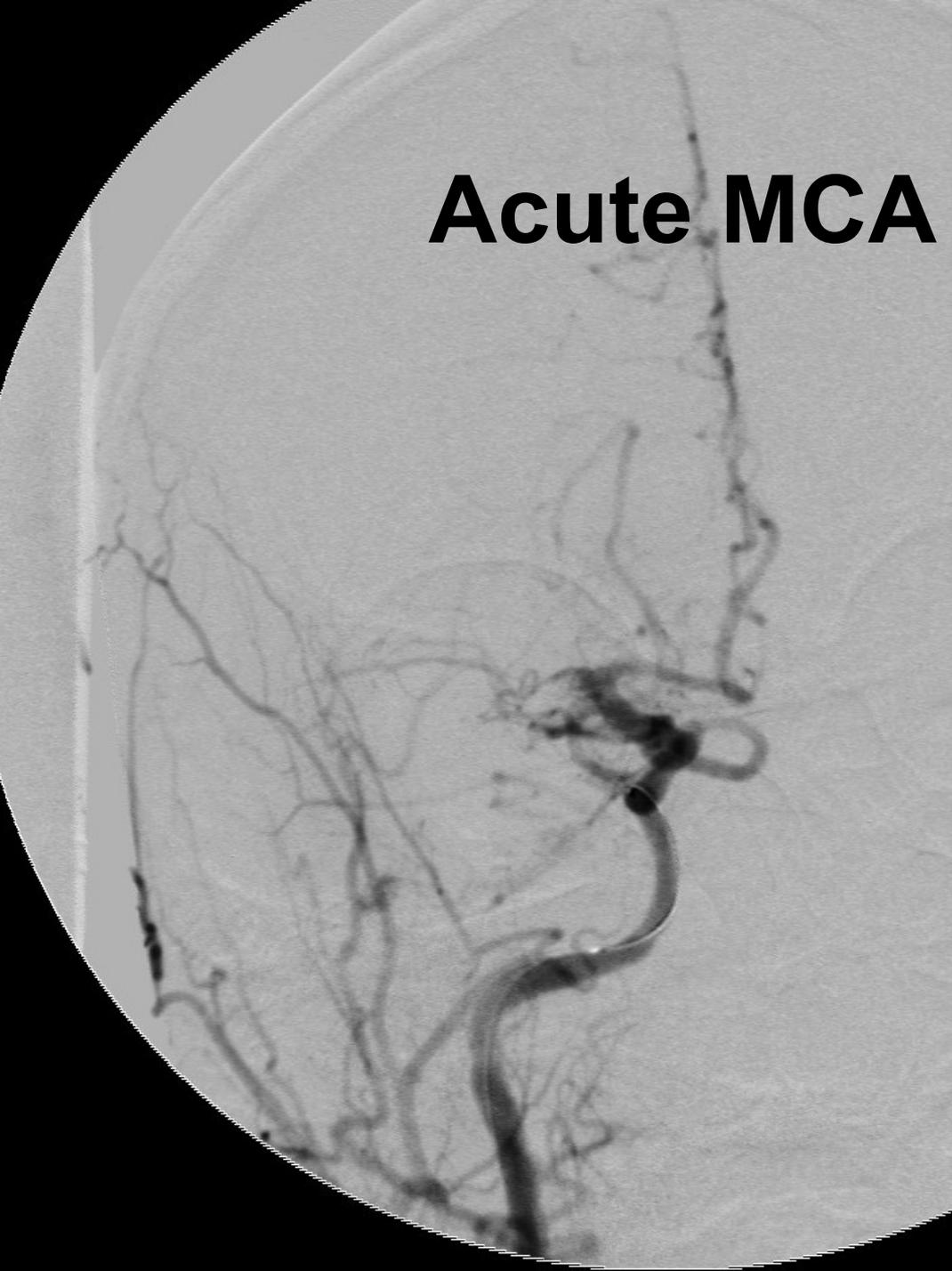
**BMW wire to
supraclinoid ICA**

Xpert stent 4 x 40
Still occluded proximally

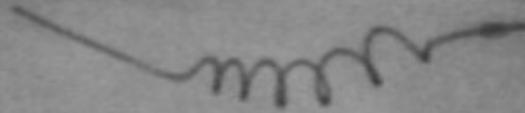
Xpert stent 5 x 40
No overlap

Xpert stent 5 x 30

Acute MCA Occlusion



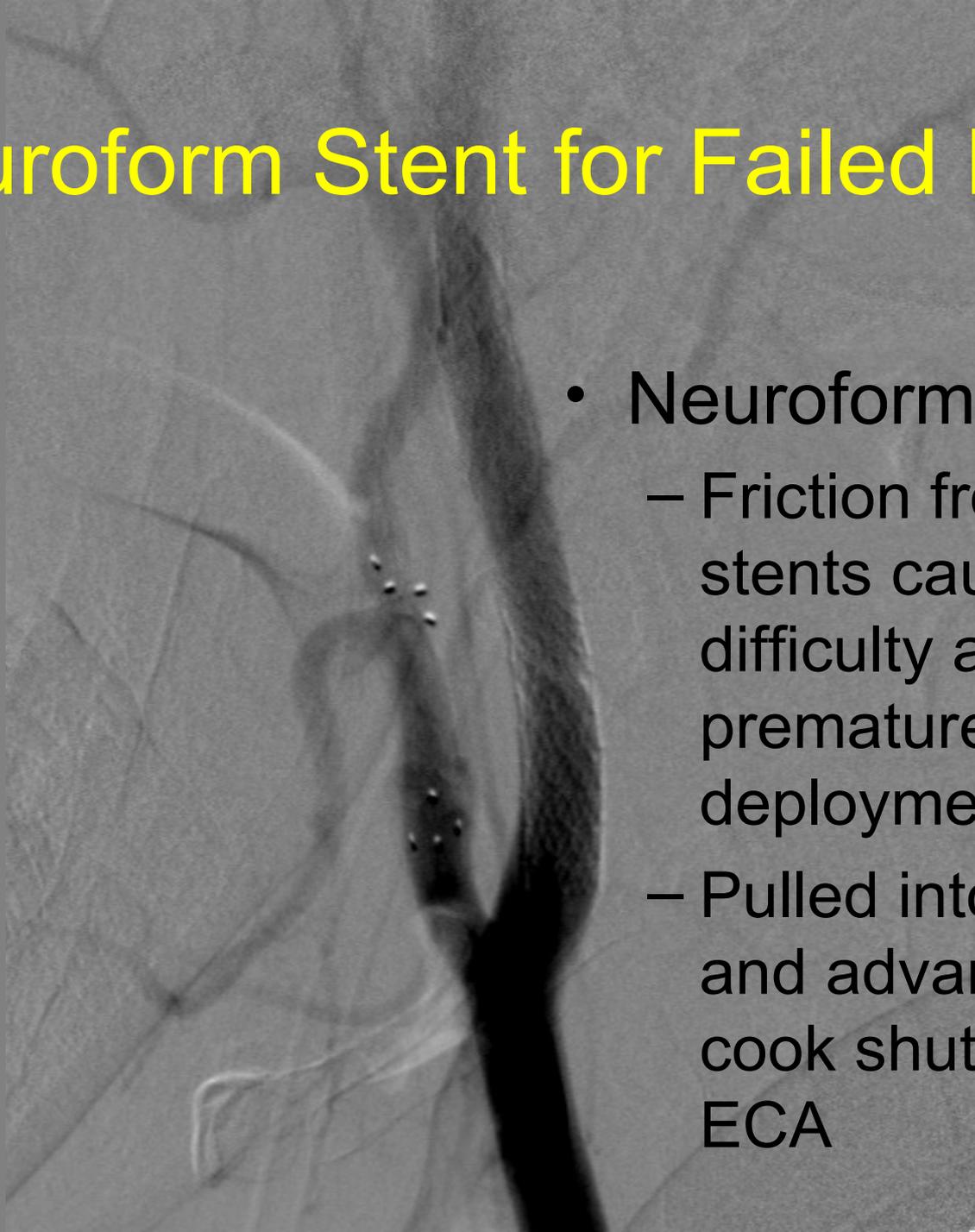
Merci Clot Retrieval



... Integrilin

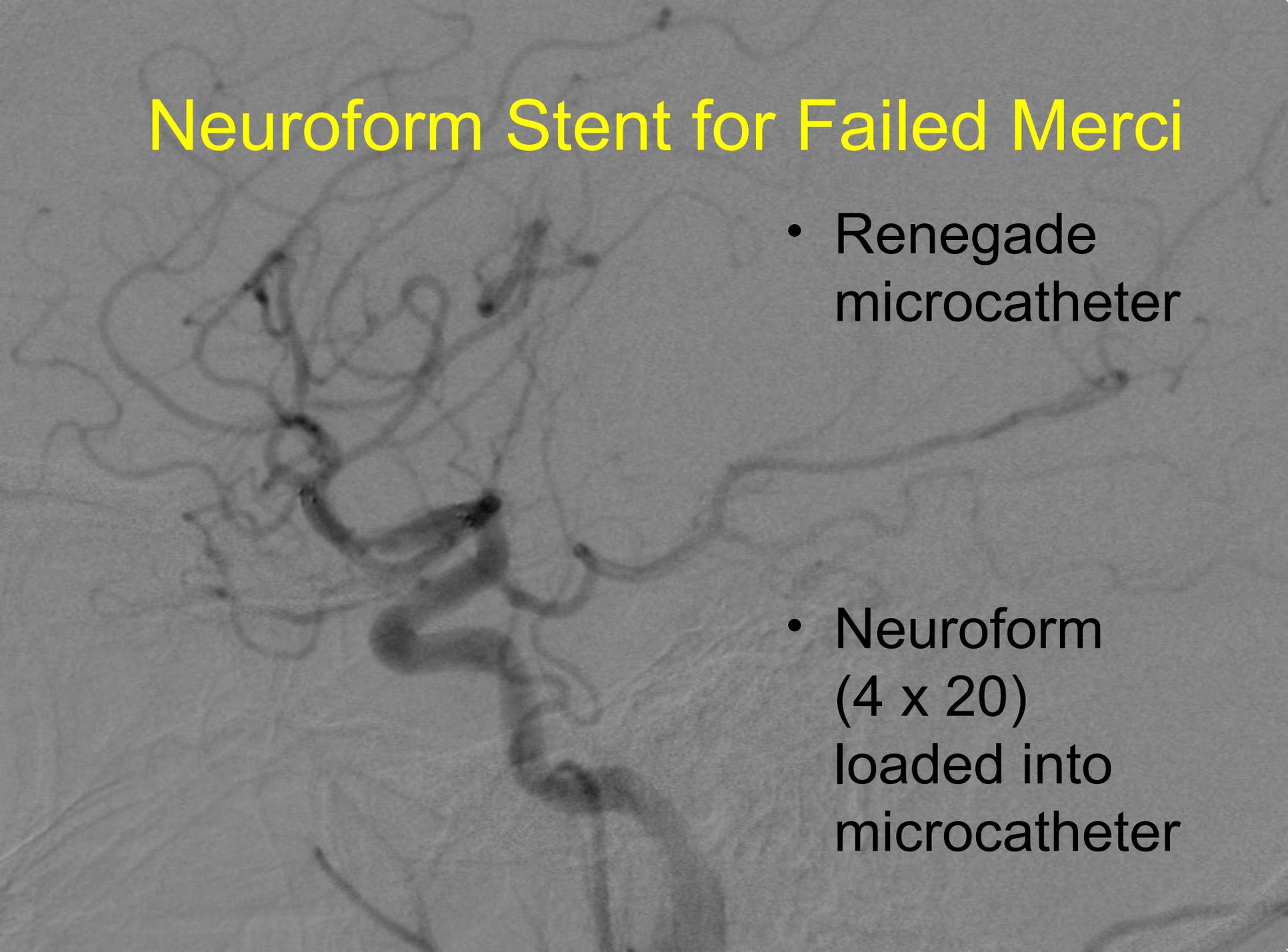
Neuroform Stent for Failed Merci

- Neuroform 3.5 x 20
 - Friction from 3 ICA stents caused difficulty and premature deployment
 - Pulled into CCA and advanced with cook shuttle into ECA

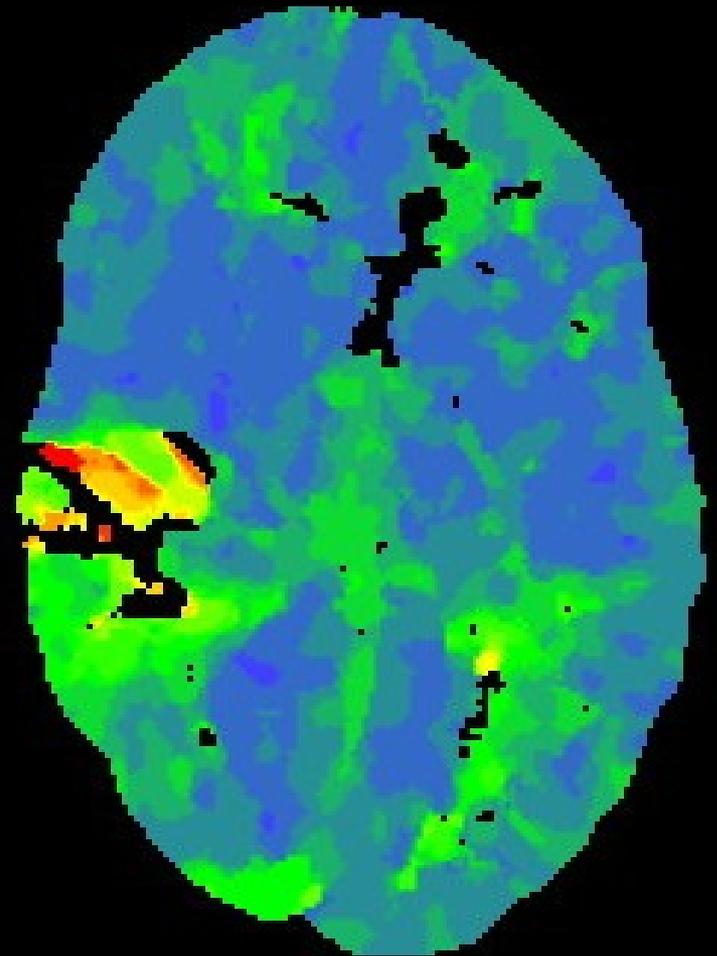
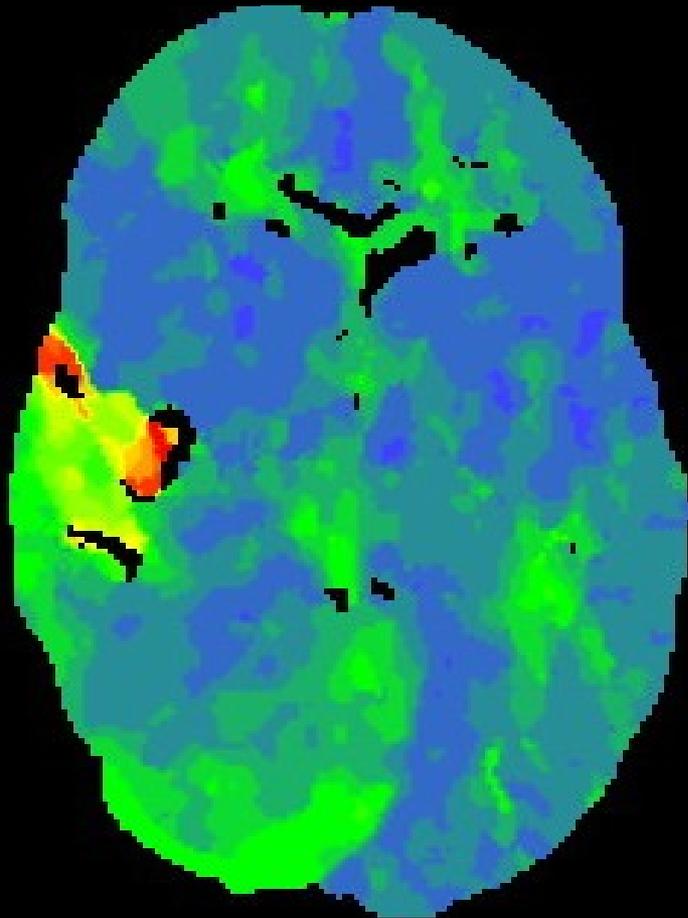


Neuroform Stent for Failed Merci

- Renegade microcatheter
- Neuroform (4 x 20) loaded into microcatheter



Follow Up CT perfusion



Post Procedure MRI

