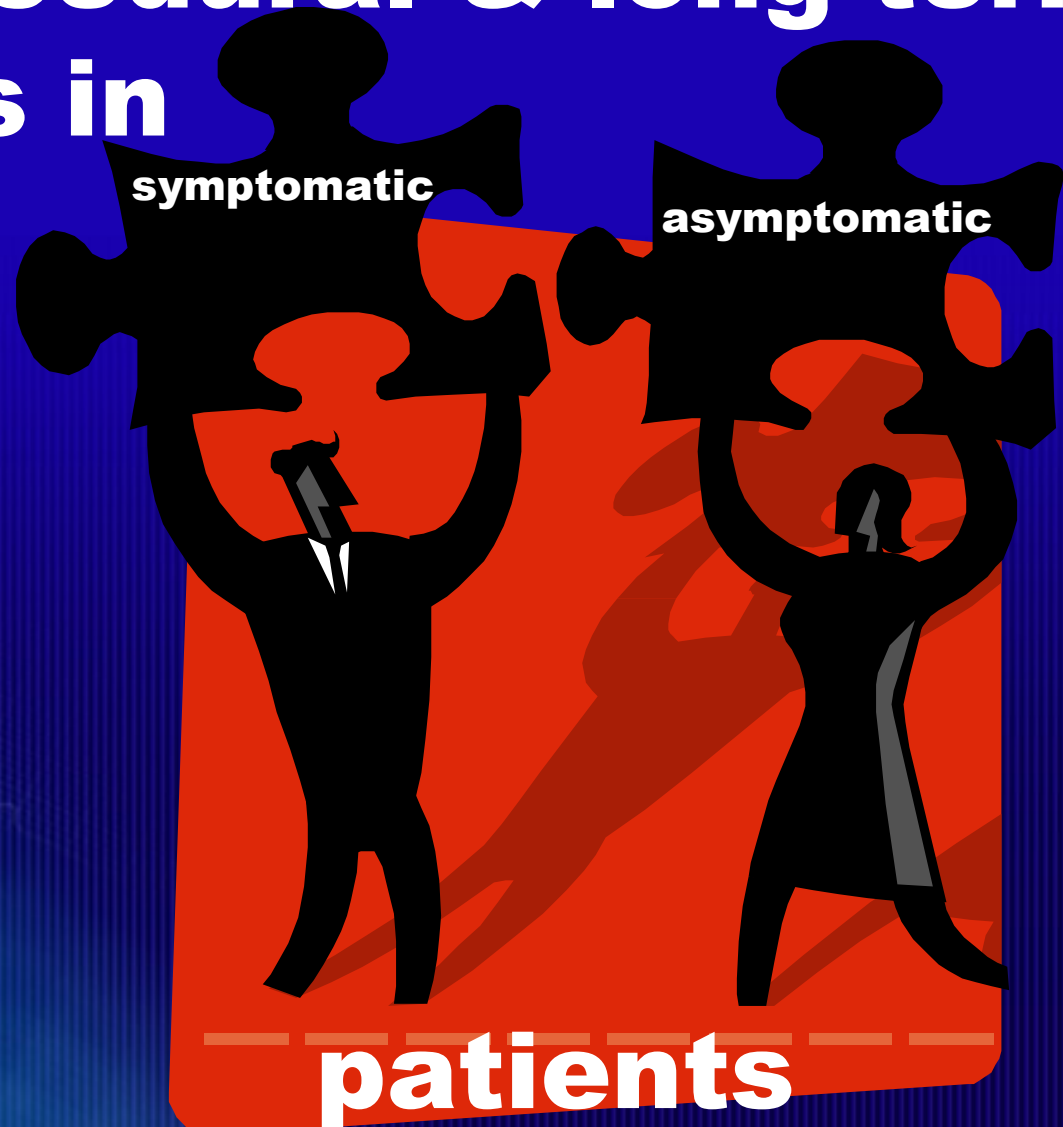


Review of clinical carotid stent procedural & long-term outcomes in





Conflict of Interest Statement

Within the past 12 months, I or my spouse have had a financial interest/arrangement or affiliation with the organization(s) listed below.

No conflicts regarding this presentation

Mark Wholey, MD

The asymptomatic patient

**I have
Nothing
To
disclose**



Carotid Stent Crusade



1995-...

Overwhelming Resistance in the Early Stages



Is this justified?

post-gazette.com

Health, Science & Environment

Pittsburgh, Pa.
Thursday, Oct. 19, 2006

Oct 18, 8:22 PM EDT

Study: Neck Stents Present Stroke Risk

By MIKE STOBBE
AP Medical Writer

An experimental treatment used to clear clogged neck arteries carries a higher-than-expected risk of stroke and death, according to a study that was stopped early for safety reasons.

The study compared the use of stents - small tubes that prop open blood vessels - with a common surgical



Carotid Stenting

Ready for Prime Time?

NOT YET!



When?

Not until – we solve the problem:

1. Asymptomatic patients

1. Octogenarian patients



AHA published guidelines

Surgical risk $< 3\%$

Life expectancy > 5 yrs.

CAS or CEA may be desirable option



Carotid Stenting

In the Capture trial in the asymptomatic population with exclusion of octogenarians – 3% stroke rate.

The 3% threshold was also achieved in Crest, Caress, & Cabernet.

CAS with DPD

200 pts

98% tech success (avg f/u 22 mo)

70% Asymptomatic

Diabetic 36%

Hyperlipidemia 90%

HTN 96%

≥ 80 yrs > 34%



Asymptomatic pts. (141) \leq 30 days

Stroke 1 - 0.7%

Death 0

MI 1

TIA 2

SDMI = 1.4%

Tech success 98%

Asymptomatic patients > 30 days

Follow up (123 pts.) 87% average f/u 22 mos.

Ipsilateral stroke 1.6% (2)

MI 5.7% (7)

TIA ipsilateral 3.3% (4)

Stent restenosis 3.3% (4)

non neuro death 12% (14)



Octogenarians – PVI CAS with DPD

200 most recent patients

28.5% 80 yr. and over

12% death (non neurologic)

2% stroke

2% restenosis

Follow up 6 mos. – 2 yrs.

Average follow up – 22 mos.



Caress Trial

**Lead in
Registry**

CEA

CAS

Stroke / death %

3%

3.6%

2.1%



German Registry; over 2,000 pts.

Asymptomatic subset (N=939)

Major stroke 1.6%

Minor stroke 1.1%

All stroke - 2.7%

**It can be done – but to do so
will require experienced
operators & careful attention
at the aortic arch.**



(The Achilles heel for carotid stenting.)



This may require:

- 1. Improvement in stent design**
- 2. More efficient filters, including proximal flow control**
- 3. Aortic arch access**
- 4. Plaque analysis prior to stenting**



SAPPHIRE and ARCHER

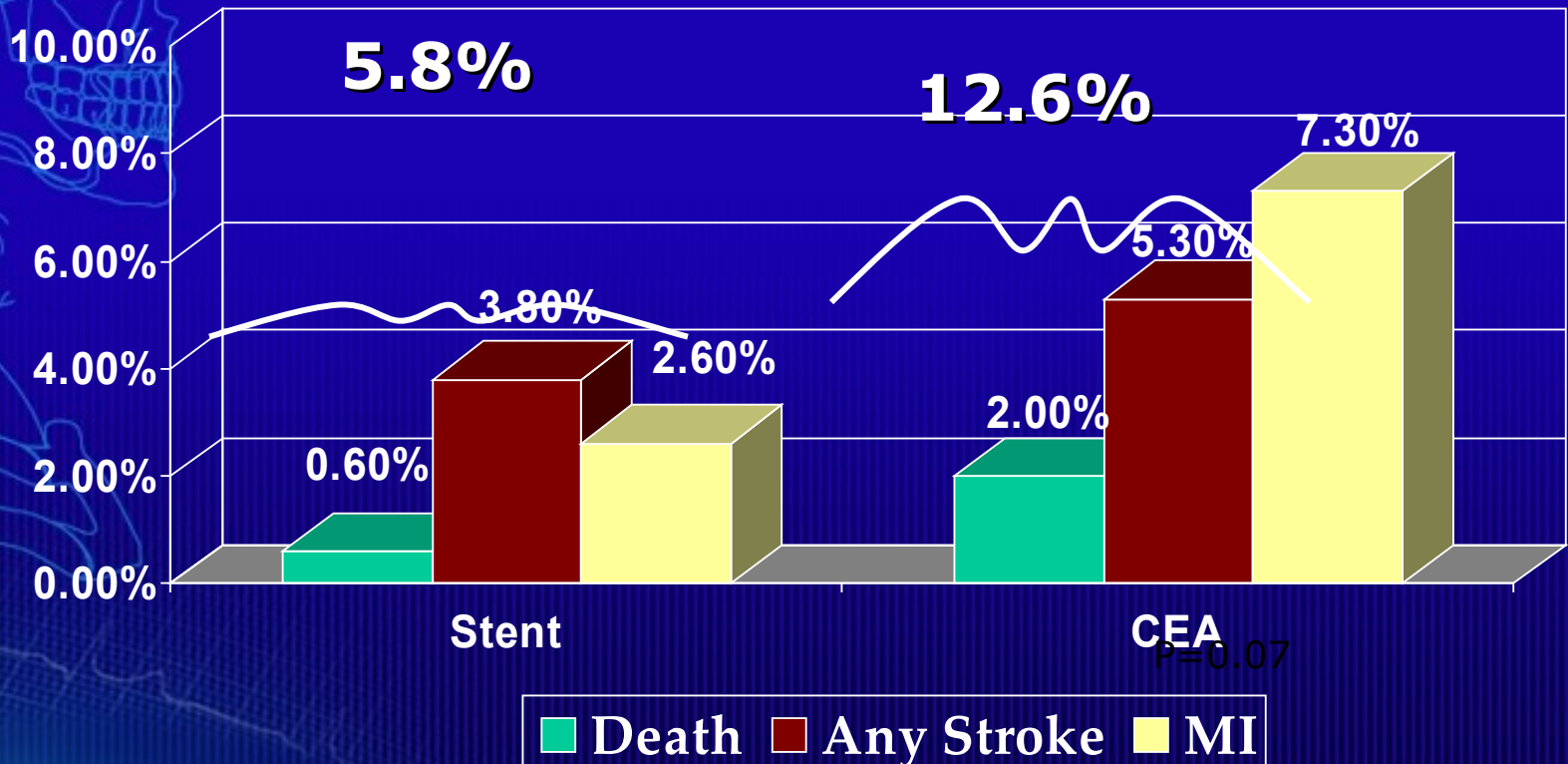
2 0 0 4 Landmark Trials



Which patients are really *high risk*?

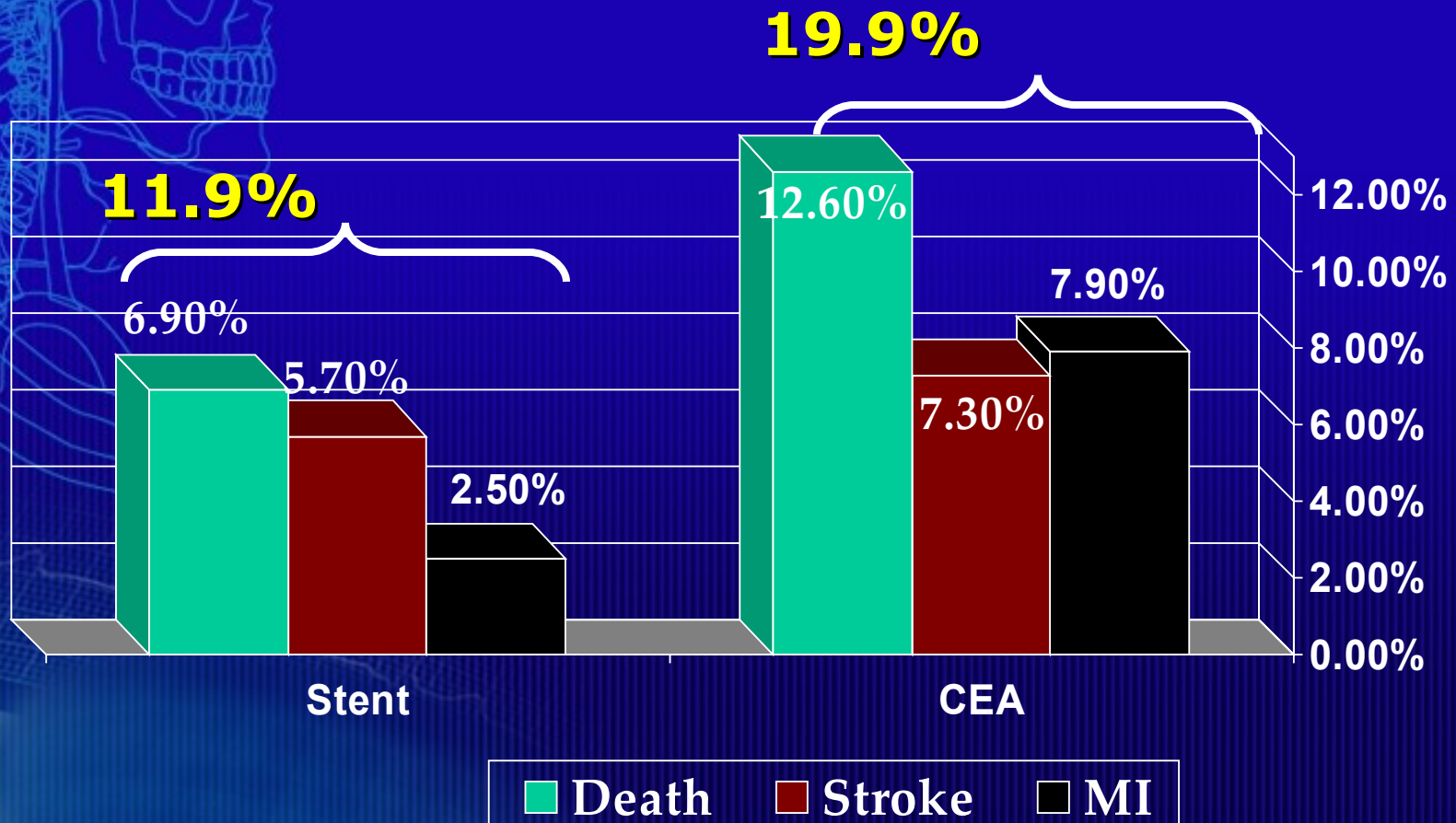
- * Surgically inaccessible**
- * Hostile neck; radiation rx.**
- ? Contralateral occlusion**
- ? Prior CEA - restenosis**
- ? CABG & C.S.**
- * Tandem lesions**
- * Ostial arch vessels (stenosis)**
- ? Medical comorbidity**

SAPPHIRE Randomized Patients 30-Day Events



Stent=156 patients, CEA=151 patients

1-Year SAPPHIRE Data Individual Endpoints



Stent=156 patients, CEA=151 patients



Diabetic Subgroup – Randomized ITT Patients

Major Adverse Events to 1 Year

<u>Events</u>	<u>Stent (42 pts)</u>	<u>CEA (44 pts)</u>	<u>p Value</u>
MAE	7 (16.7%)	14 (31.8%)	0.13
Myocardial Infarct	1 (2.4%)	8 (18.2%)	0.03
Major Bleeding	2 (4.8%)	9 (20.5%)	0.05
MAE w/o non-neurologic death	2 (4.8%)	11 (25.0)	0.01



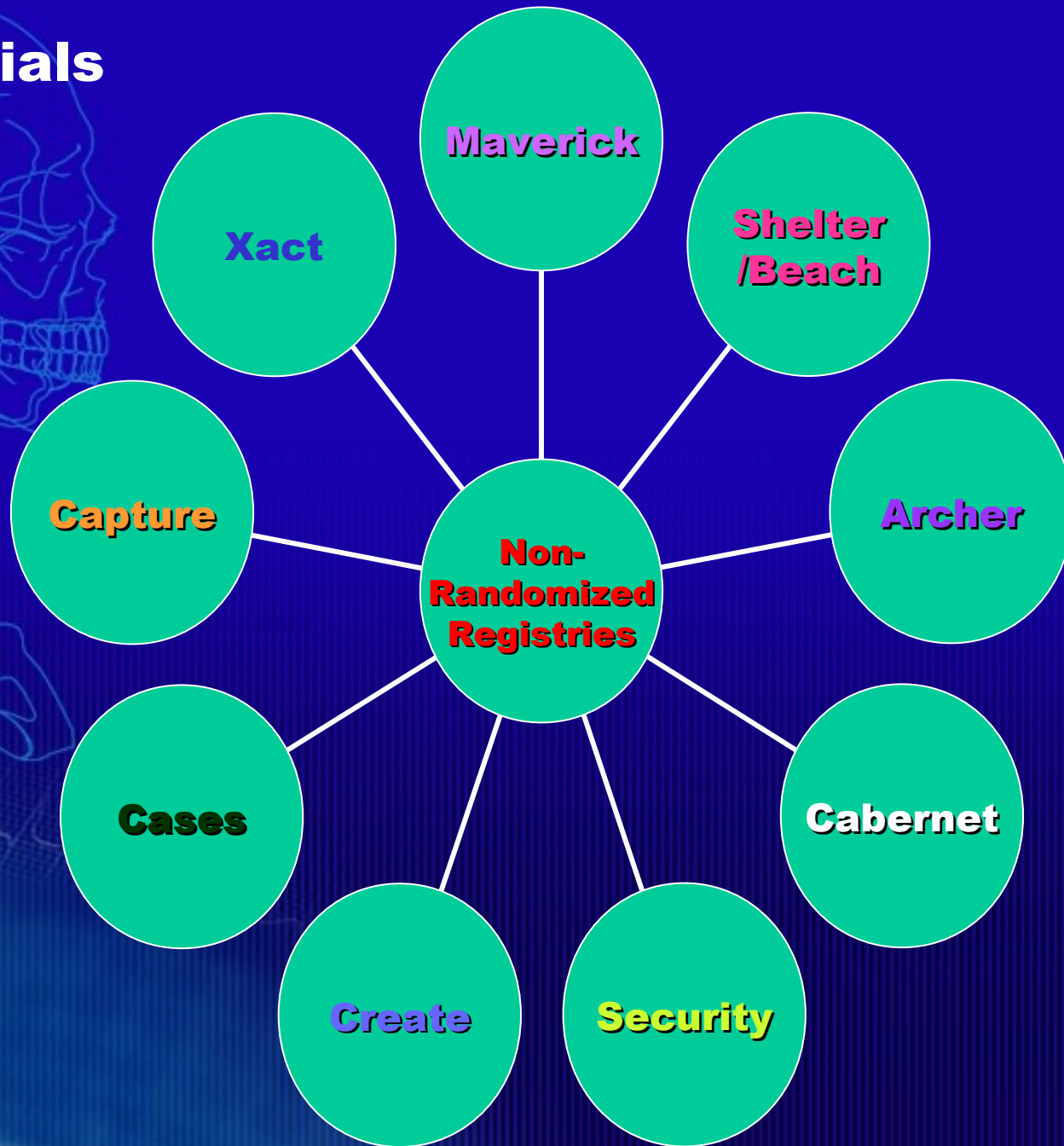
Archer Results

Pathology

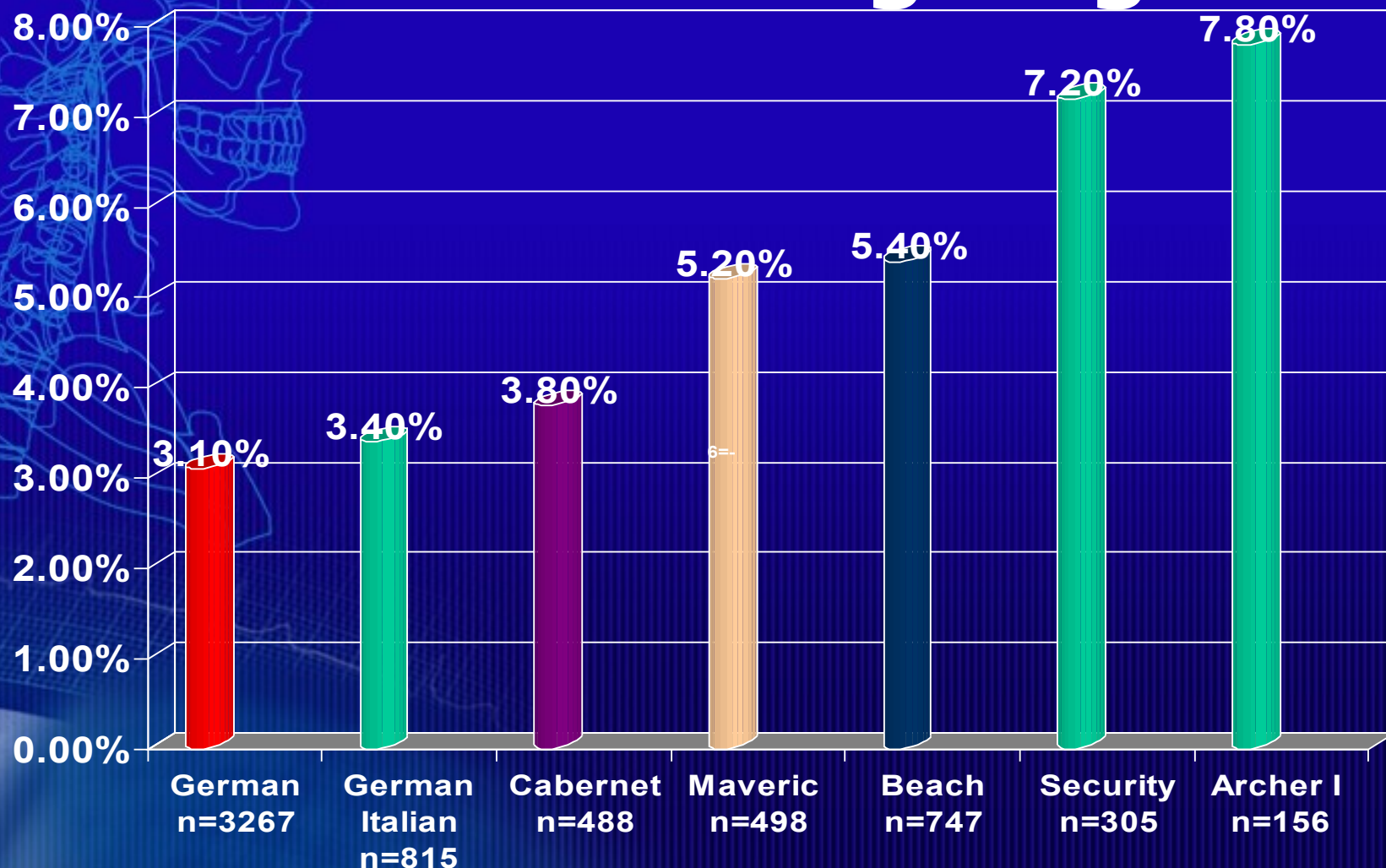
Stroke, Death ,MI.

Restenotic CEA Pts	0.7%	1.4%
Contra. Occlusions	4.5%	7.6%
2 Comorbidities	4.8%	6.4%
ESRD (14 pts)	28.6%	
same		

The Trials



30-Day Comp Endpoint in Carotid Stenting Registries





Carotid trials are showing downward trend in adverse events:

- **Why?**
 - operator experience
 - device improvement
 - distal embolic protection



Major Stroke - 1 year US Trials

Symptomatic + Asymptomatic

–Sapphire	.0%
–Caber net	1.4%
–Archer	1.4%
–Maveric	2.0%
–Lennox Hill	.3%
–PVI	1.1%

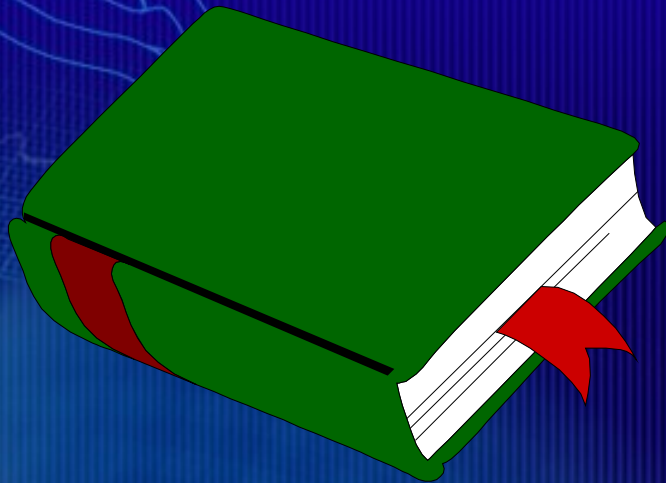


Minor Stroke - 1 Year US Trials

Symptomatic + Asymptomatic

–Maveric	2.0%
–Cabernet	2.0%
–PVI	2.5%
–Archer	2.4%
–Sapphire	3.6%

**The answer for the high risk is in
and
that chapter could be closed**

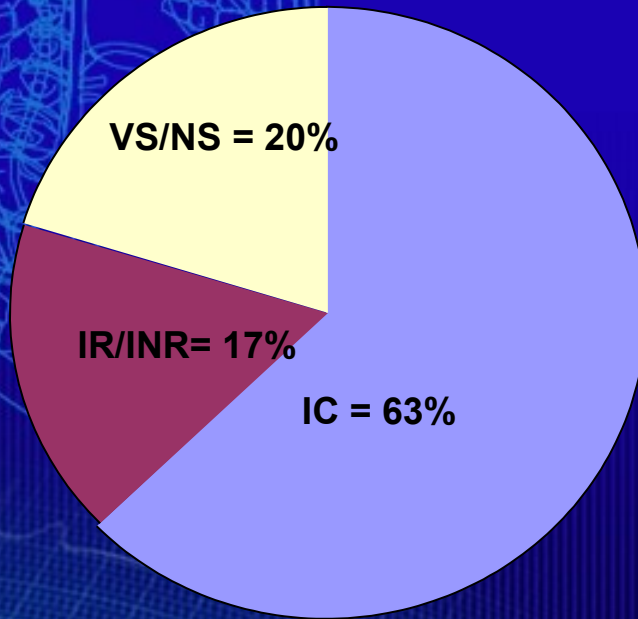




CAPTURE

Post Approval Study

CAPTURE: Physician Specialty Mix



IC: Interventional Cardiologist
IR: Interventional Radiologist
INR: Interventional NeuroRadiologist
VS: Vascular Surgeon
NS: Neurosurgeon

CAPTURE: Primary Safety Events ≤ 30 days Compared to ARChER

^a Non-hierarchical ^b Hierarchical	CAPTURE N = 1603	ARChER N = 581
Death ^a Stroke-related	1.6% 1.1%	2.1% 0.5%
Stroke ^a Major Minor	4.1% 1.8% 2.3%	5.5% 2.4% 3.1%
MI ^a	0.9%	2.4%
S/D/MI ^b	5.1%	8.3%
S/D ^b	4.6%	6.9%

CAPTURE: Primary Safety Events by Physician Experience Level

CAPTURE (N=1603) ^a Non-hierarchical ^b Hierarchical	High N=166	Medium N=1177	Low N=260
Death ^a	0.0%	1.6%	2.3%
Stroke ^a	5.4%	3.7%	4.6%
Major	1.2%	1.7%	2.7%
Minor	4.2%	2.0%	1.9%
MI ^a	0.6%	0.8%	1.2%
S/D/MI ^b	6.0%	4.8%	5.8%
S/D ^b	5.4%	4.3%	5.0%

No statistical difference found between physician experience levels.

CAPTURE: Primary Safety Events ≤ 30 Days by Asymptomatic Status Compared to ARChER

	Asymptomatic		Difference
	CAPTURE N = 1447	ARChER N= 443	[95% CI]
Death	1.2% (n=18)	2.0%	- 0.79% [-2.22%, 0.64%]
Stroke-related	0.7% (n=10)	0.2%	- 0.47% [-0.15%, 1.08%]
Stroke	3.1%	3.8%	-0.73% [-2.73%, 1.27%]
Major	1.5%	0.7%	0.77% [-0.21%, 1.76%]
Minor	1.7%	3.2%	-1.50% [-3.26%, 0.26%]
MI *	0.8%	2.5%	-1.72% [-3.24%, - 0.21%]
S/D/MI *	4.1%	6.8%	-2.63% [-5.18%, - 0.07%]
S/D	3.7%	5.6%	-1.75% [-4.07%, 0.56%]

CAPTURE: Primary Safety Events \leq 30 Days by Symptomatic Status Compared to ARCHeR

	Symptomatic		Difference [95% CI]
	CAPTURE N = 156	ARChER N = 138	
Death	4.5% (n=7)	2.2%	2.31% [-1.75%, 6.73%]
Stroke-related	4.5% (n=7)	1.5%	3.04% [-0.77%, 6.85%]
Stroke	12.8%	10.9%	1.95% [-5.43%, 9.33%]
Major	5.1%	4.3%	0.78% [-4.07%, 5.63%]
Minor	7.7%	6.5%	1.17% [-4.70%, 7.04%]
MI	1.9%	2.2%	-0.25% [-1.75%, 6.37%]
S/D/MI	14.1%	13.0%	1.06% [-6.78%, 8.90%]
S/D	12.8%	11.6%	1.23% [-6.26%, 8.71%]

CAPTURE: Primary Safety Events ≤ 30 Days by $<80, \geq 80$ Age For Symptomatic Patients

^a Non-Hierarchical ^b Hierarchical	< 80 y/o N = 108	≥ 80 y/o N = 48	Difference [95% CI]
Death ^a	1.9% (n=2)	10.4% (n=5)	8.56% [-0.44%, 17.57%]
Stroke-related	1.9% (n=2)	10.4% (n=5)	8.56% [-0.44%, 17.57%]
Stroke ^a	11.1% (n=12)	16.7% (n=8)	5.56% [-6.54%, 17.65%]
Major	3.7% (n=4)	8.3% (n=4)	4.63% [-3.96%, 13.22%]
Minor	7.4% (n=8)	8.3% (n=4)	0.93% [-8.32%, 10.17%]
MI ^a	2.8% (n=3)	0.0% (n=0)	-2.78% [-5.88%, 0.32%]
S/D/MI ^b	13.0% (n=14)	16.7% (n=8)	3.70% [-8.60%, 16.00%]
S/D ^b	11.1% (n=12)	16.7% (n=8)	5.56% [-6.54%, 17.65%]



Preliminary Data Analysis

**CAPTURE 3000: Carotid RX Acculink®/
RX Accunet™ Post- Approval Trial to
Uncover Unanticipated or Rare Events**

**EXACT 900: Emboshield® and Xact™ Post
Approval Carotid Stent Trial**


TCT October 2006



CAPTURE 3000 vs EXACT 900: Patient Demographics- All Patients

Characteristic	CAPTURE N=3000	EXACT^ N=900
Mean Age	72.8	72.4
Age ≥ 80	23.8%	24.1%
% Symptomatic	13.7%	8.2%
% Male	61.0%	61.9%
Diabetes Mellitus	34.9%	33.6%
Hypertension	88.8%	89.5%
Hypercholesterolemia	78.5%	74.2%
CHF	16.1%	17.7%
Anatomic	10.3%	7.6%
Current Smoker	20.9%	17.0%
PVD	35.5%	39.2% ³⁸

[^] Preliminary Results



CAPTURE 3000 vs EXACT 900: Patient Demographics- Symptomatic Patients

Characteristic	CAPTURE N=410	EXACT^ N=74
Mean Age	73.2	68.4
Age ≥ 80	28.0%	16.2%
% Male	63.9%	60.8%
Diabetes Mellitus	35.9%	27.0%
Hypertension	89.7%	87.7%
Hypercholesterolemia	73.3%	70.0%
CHF	16.8%	10.8%
Anatomic	11.5%	10.8%
Current Smoker	22.5%	29.2%
PVD	23.2%	29.7%

^ Preliminary Results

CAPTURE 3000 vs. EXACT 900: 30 day Outcomes – All Patients

Event	CAPTURE N=3000	EXACT^ N=900	DIFFERENCE 95% CI~
Death, Stroke and MI*	6.4%	5.3%	-1.07% [-2.78%, 0.64%]
All Stroke and Death*	5.7%	5.1%	-0.62% [-2.28%, 1.04%]
Major Stroke and Death*	2.8%	2.1%	-0.69% [-1.80%, 0.42%]
Death	1.7%	1.0%	-0.70% [-1.50%, 0.10%]
All Stroke	4.9%	4.4%	-0.42% [-1.97%, 1.13%]
Major Stroke	1.9%	1.4%	-0.49% [-1.41%, 0.43%]
Minor Stroke	3.0%	3.0%	0.00% [-1.27%, 1.27%]
MI	1.0%	0.2%	-0.74% [-1.21%, -0.28%]

* Hierarchical – Includes only the most serious event for each patient and includes only each patient's first occurrence of each event

^ Preliminary Results

CAPTURE 3000 vs. EXACT 900: 30 day Outcomes- Asymptomatics

Event	CAPTURE N=2590	EXACT^ N=826	DIFFERENCE 95% CI~
Death, Stroke and MI*	5.5%	4.6%	-0.88% [-2.56%, 0.79%]
All Stroke and Death*	5.0%	4.4%	-0.62% [-2.25%, 1.00%]
Major Stroke and Death*	2.3%	1.8%	-0.50% [-1.58%, 0.58%]
Death	1.3%	0.8%	-0.43% [-1.19%, 0.33%]
All Stroke	4.2%	3.8%	-0.42% [-1.92%, 1.09%]
Major Stroke	1.5%	1.2%	-0.30% [-1.18%, 0.59%]
Minor Stroke	2.7%	2.5%	-0.20% [-1.44%, 1.05%]
MI	0.8%	0.2%	-0.57% [-1.05%, -0.09%]


* Hierarchical – Includes only the most serious event for each patient and includes only each patient's first occurrence of each event

^ Preliminary Data Analysis

~ Provided for Comparative Purposes Only

CAPTURE 3000 vs. EXACT 900:

30 day Outcomes- Symptomatic Patients

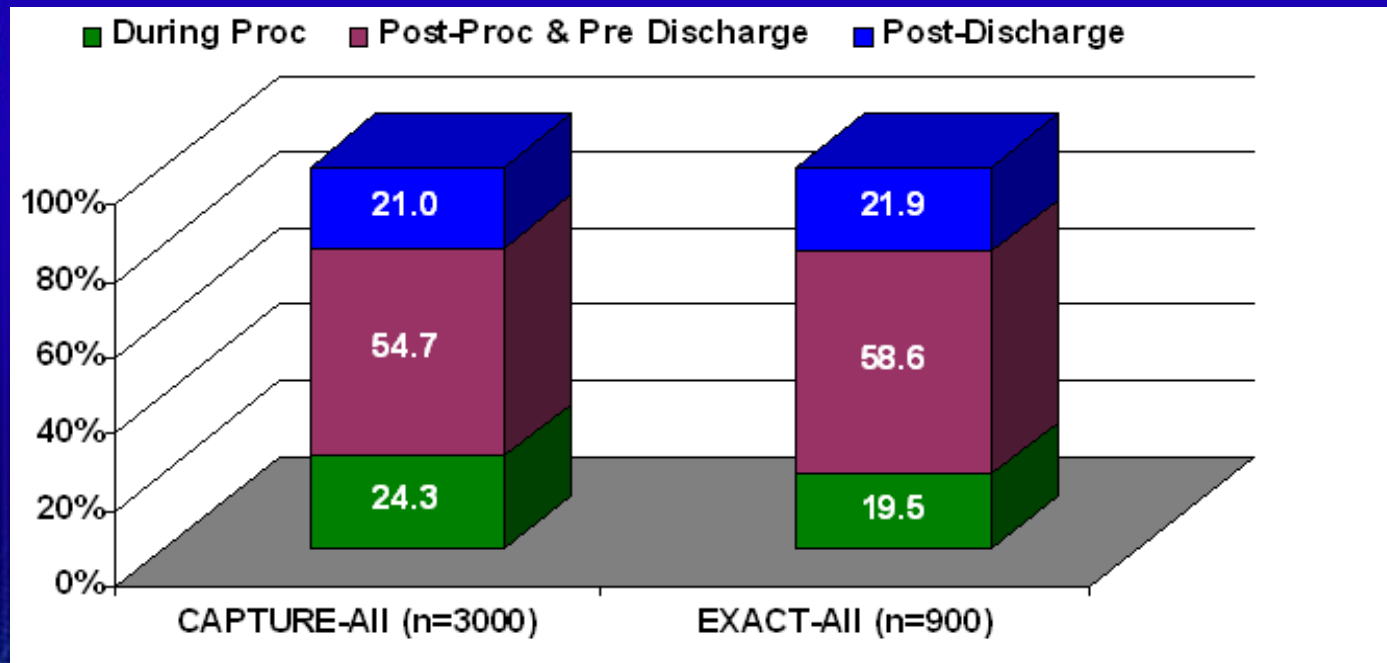


Event	CAPTURE N=410	EXACT^ N=74
Death, Stroke and MI*	12.2%	13.5%
All Stroke and Death*	10.5%	13.5%
Major Stroke and Death*	5.9%	5.4%
Death	4.4%	2.7%
All Stroke	9.3%	12.2%
Major Stroke	4.6%	4.1%
Minor Stroke	4.6%	8.1%
MI	2.0%	0.0%

* Hierarchical – Includes only the most serious event for each patient and includes only each patient's first occurrence of each event

^ Preliminary Results

CAPTURE 3000 vs. EXACT 900: Timing of Stroke



The majority of strokes occur post-procedure and before discharge

Preliminary Results



CAPTURE 3000 vs. EXACT 900:

Conclusions

- Data analysis provides insights into questions about outcomes with closed and open cell designs
- Similar:
 - Rigorously collected prospective, multicenter data
 - Rigorous neurologic follow up and independent adjudication
 - Methodologies and demographics across studies
 - 30 day stroke or stroke/death rate for entire cohorts and for symptomatic subgroups
 - Rates of late stroke (post discharge) for entire cohorts between both studies
- Data suggests that open or closed stent design does not influence outcome

Compilation of Key CAS Trials

Symptomatic Subgroups

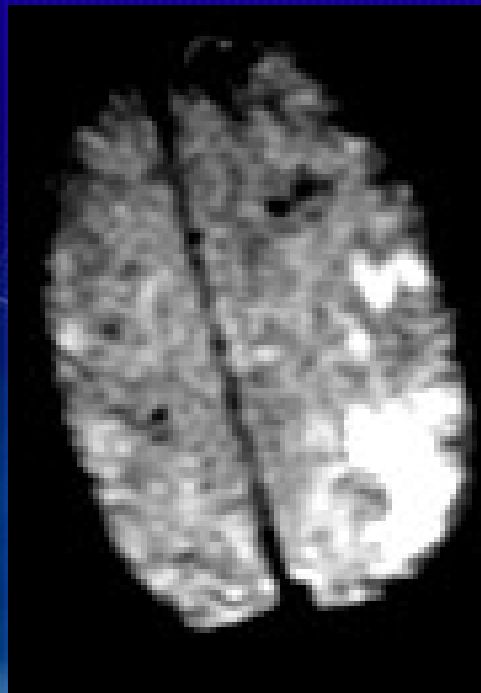
	ARCHeR n=138	BEACH n=113	CAPTURE n=410	EXACT n=74	CASES n=274	CREST Lead-in n=343
30d Death, Stroke, MI	13.0%	8.8%	12.2%	13.5%	6.2%	6.8%
30d All Stroke, Death	11.6%	--	10.5%	13.5%	--	6.5%
30d Major Stroke, Death	--	2.7%	5.9%	5.4%	--	--
Long-term Death, Stroke, MI	6.9% (2.5y) (includes major ipsilateral strokes)	12.9% (1y)	--	--	--	--

Without ability to do Octogenarians



Are Lesion Characteristics

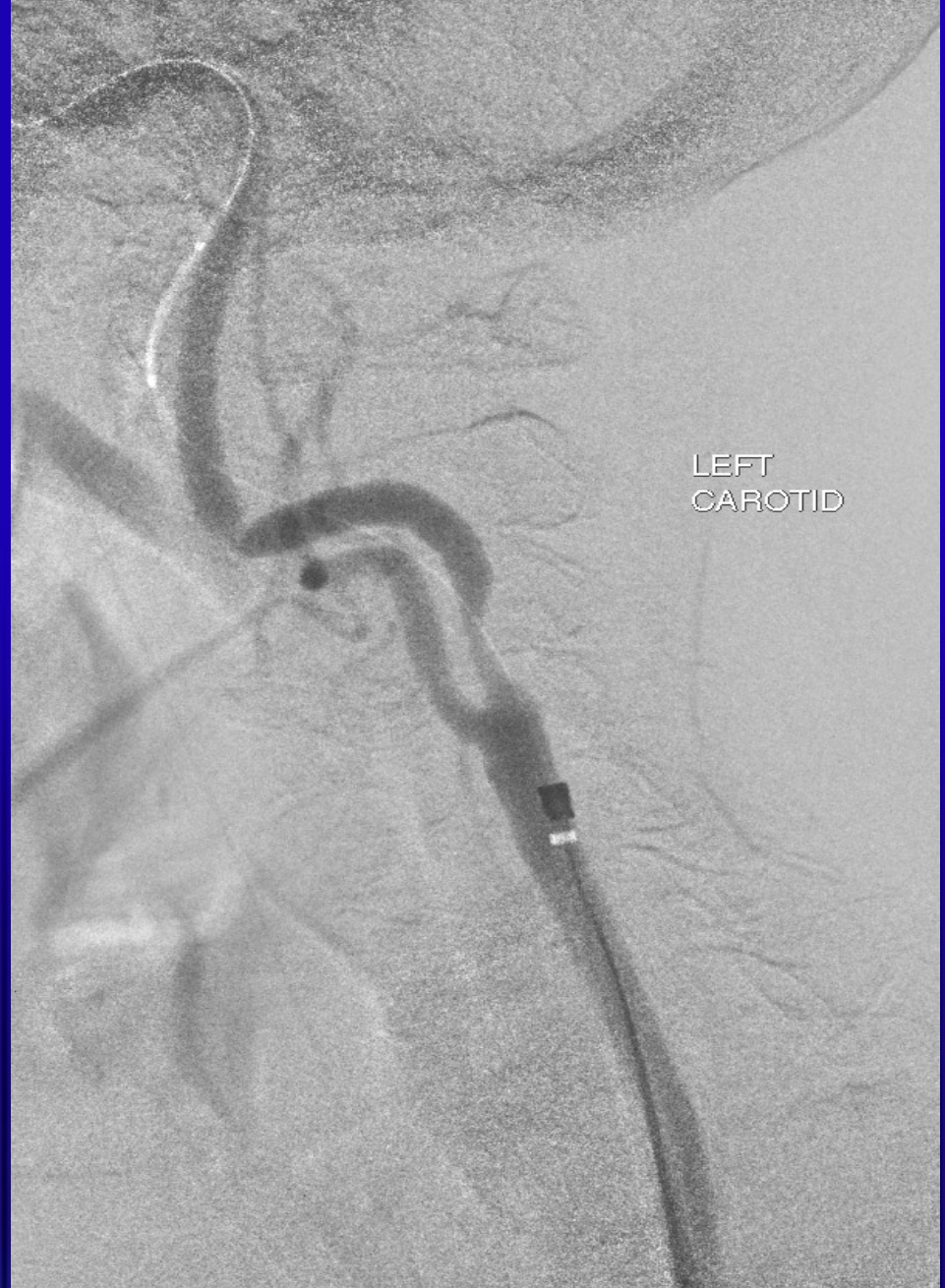
Stroke Predictors??





TYPE A Lesion

TYPE 4 ARCH



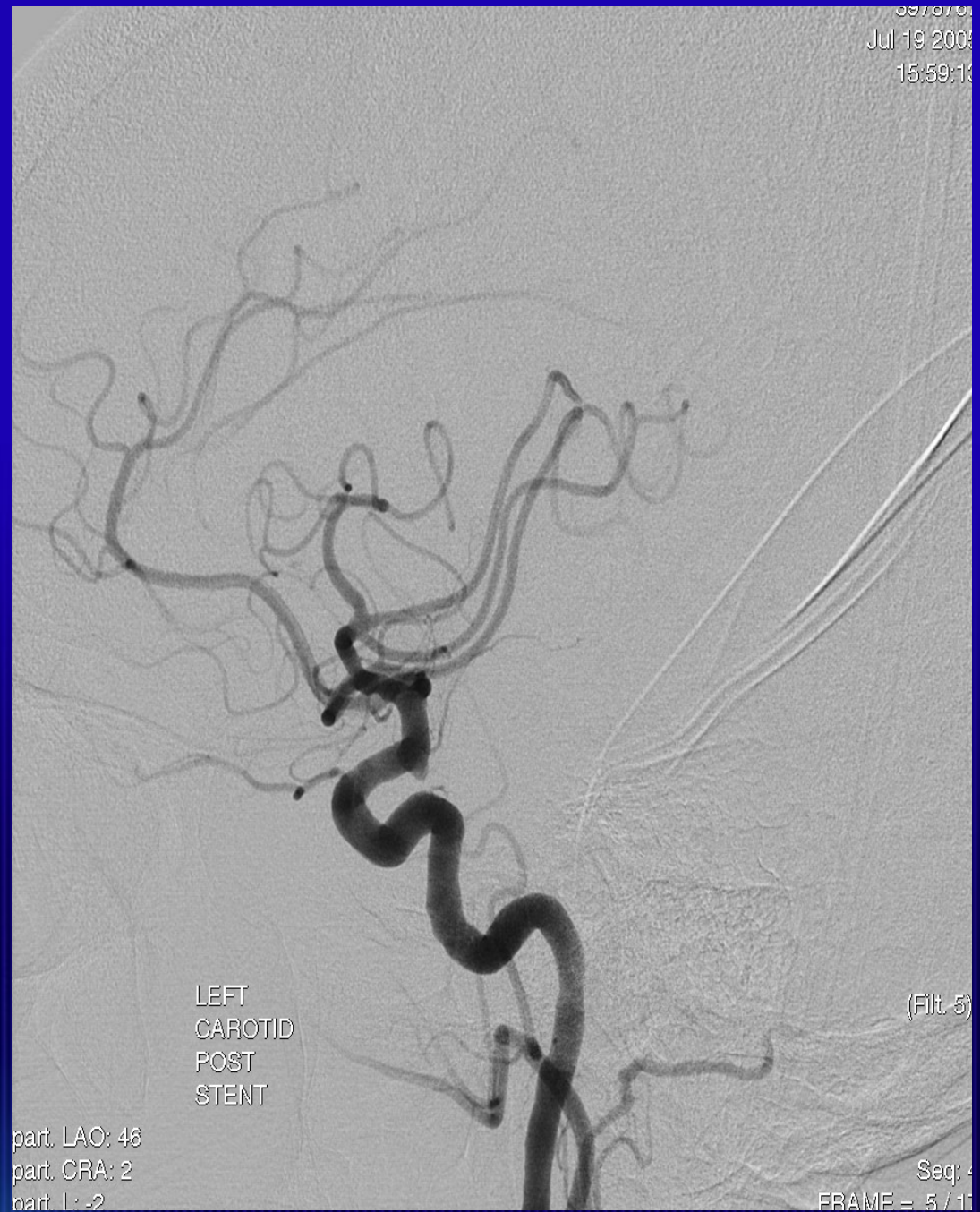
Procedure completed

FILTER REMOVED





Normal Angiogram



Normal Angio .

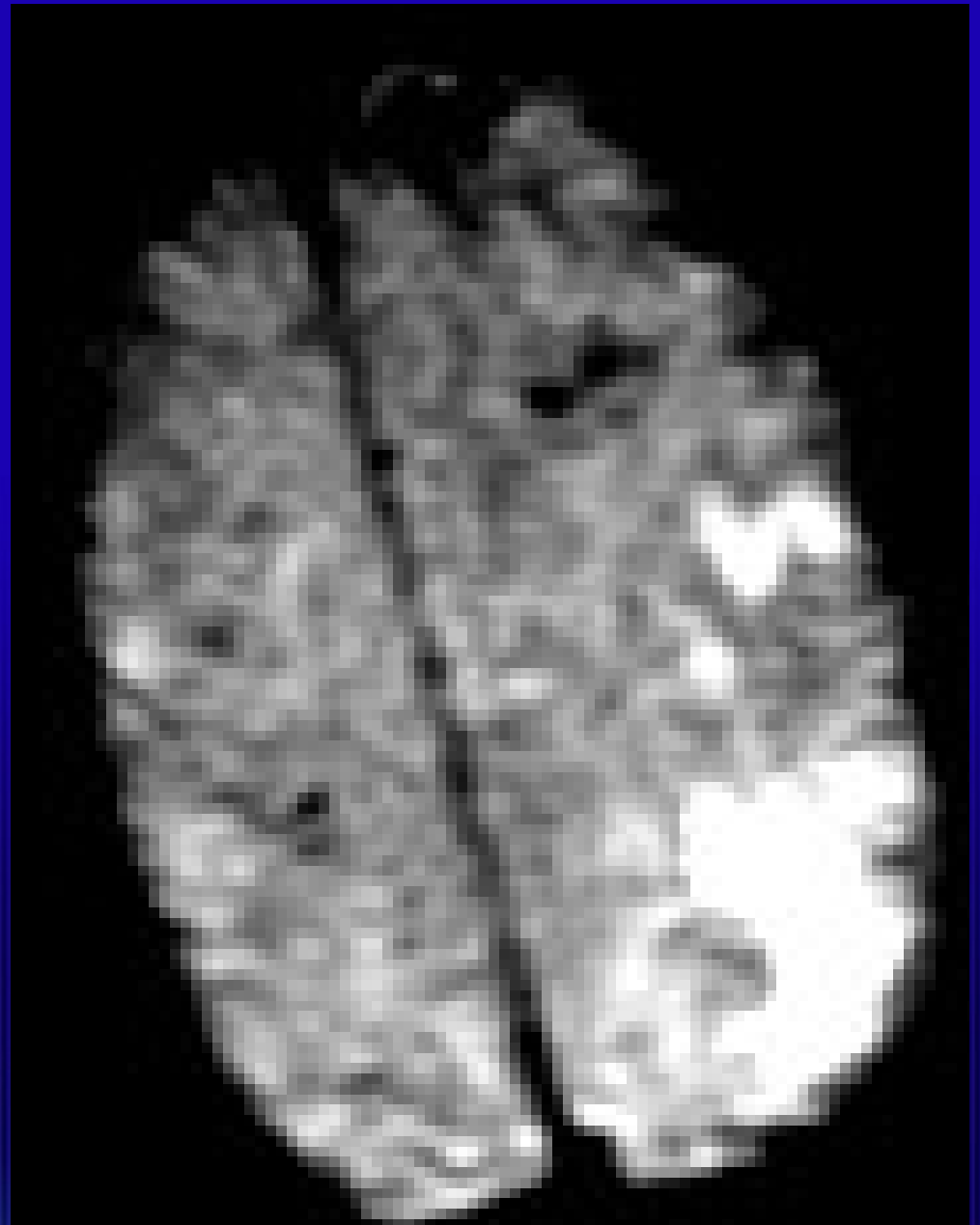


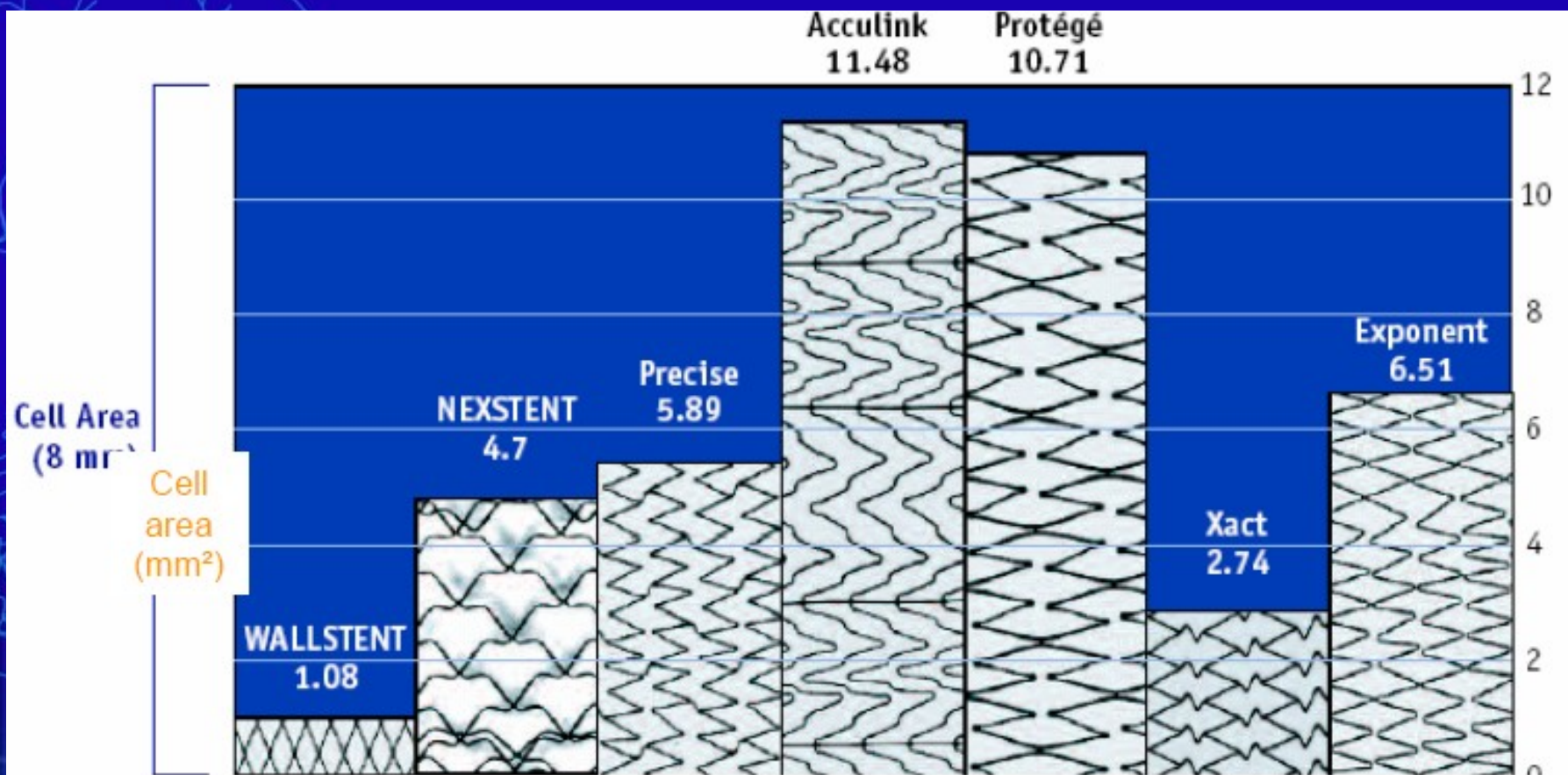
CT NORMAL



Shower Emboli

Diffusion weighted

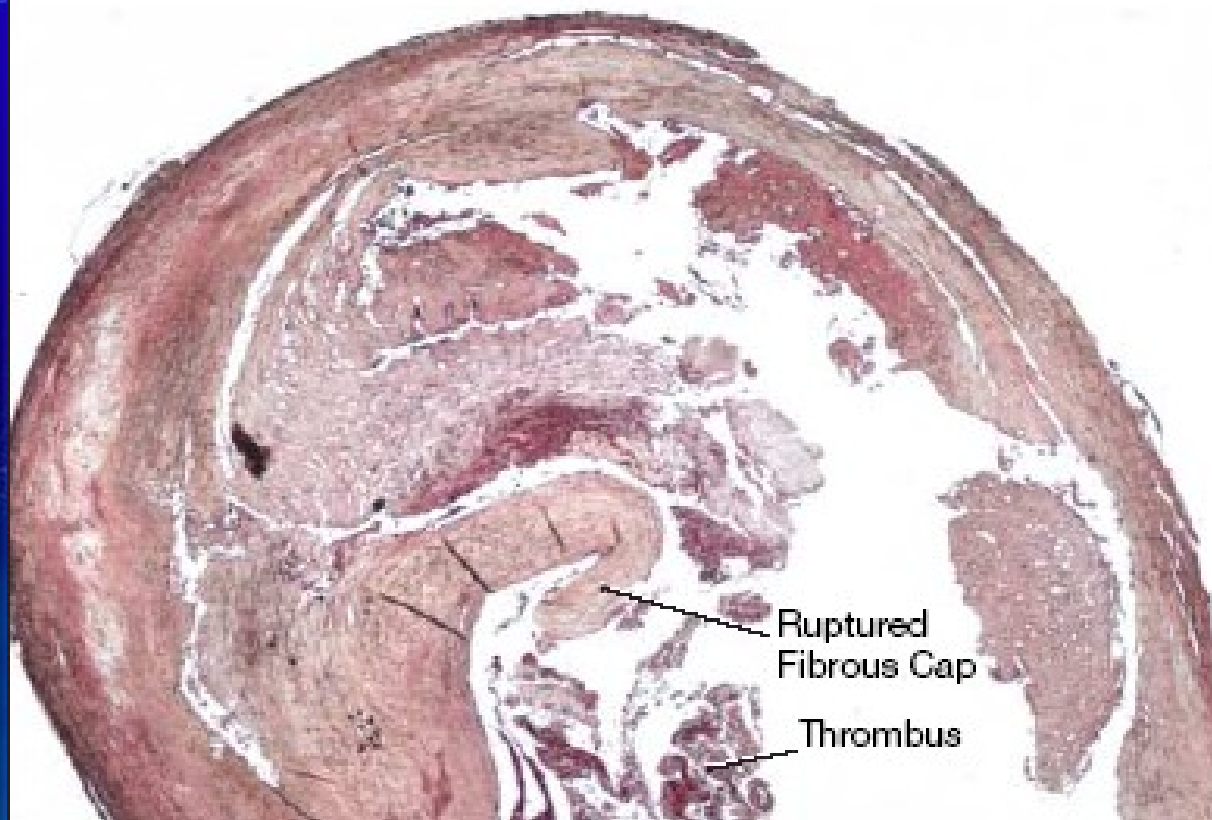




Surface of cells in mm²

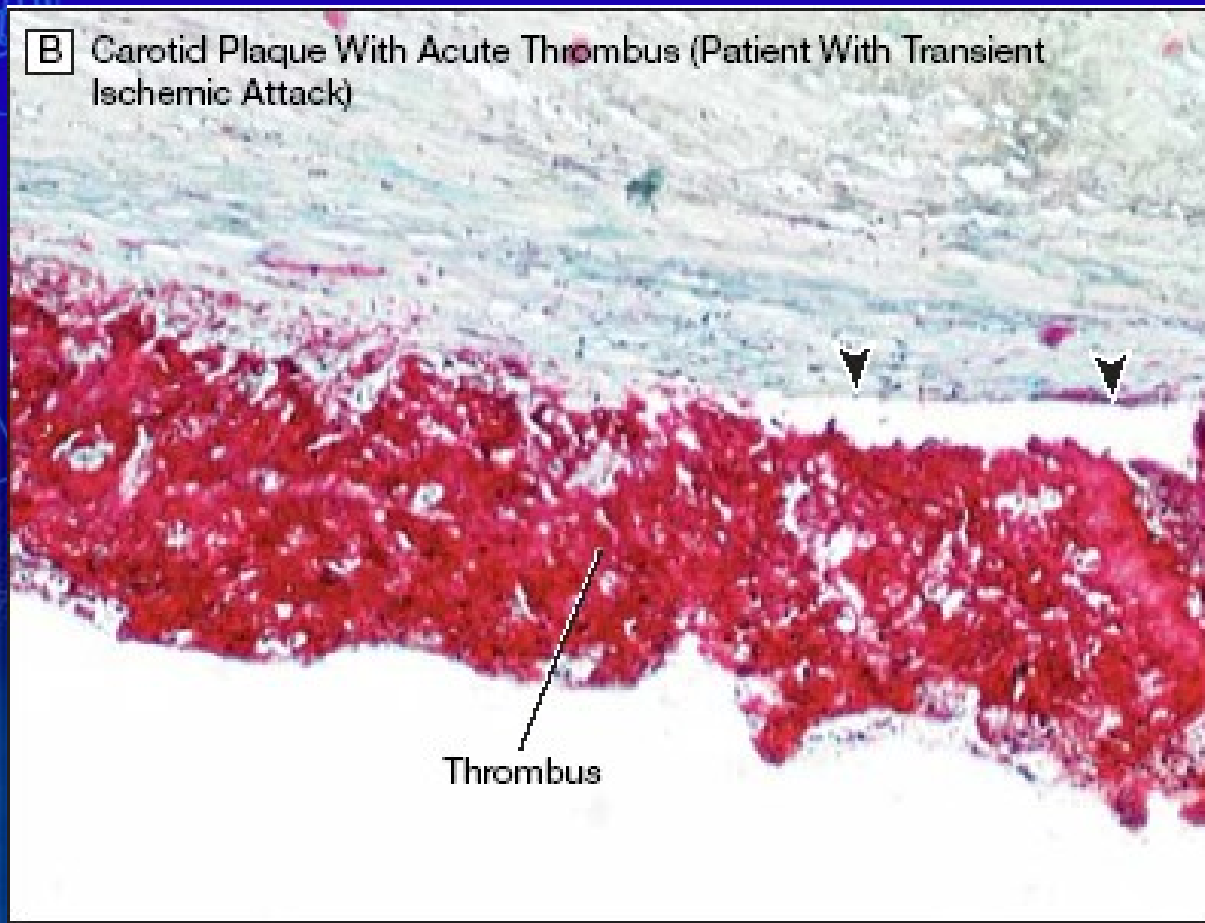
The Really Ugly

A Ruptured Carotid Plaque (Patient With Ipsilateral Major Stroke)



The Bad

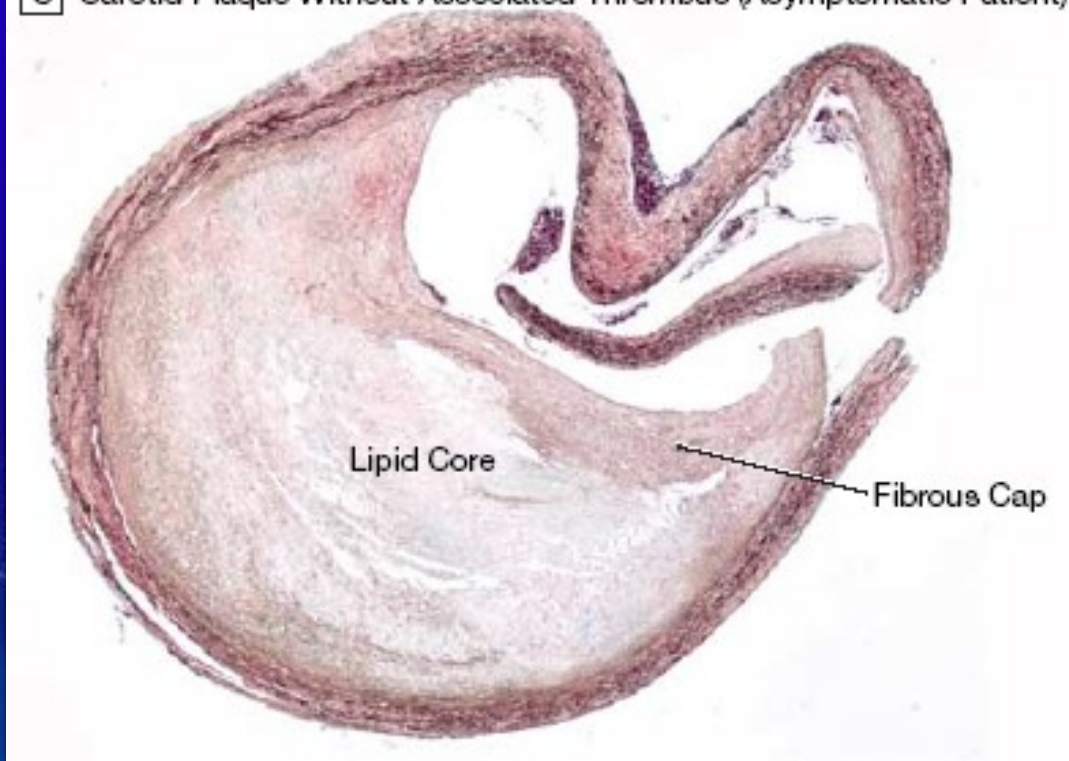
B Carotid Plaque With Acute Thrombus (Patient With Transient Ischemic Attack)



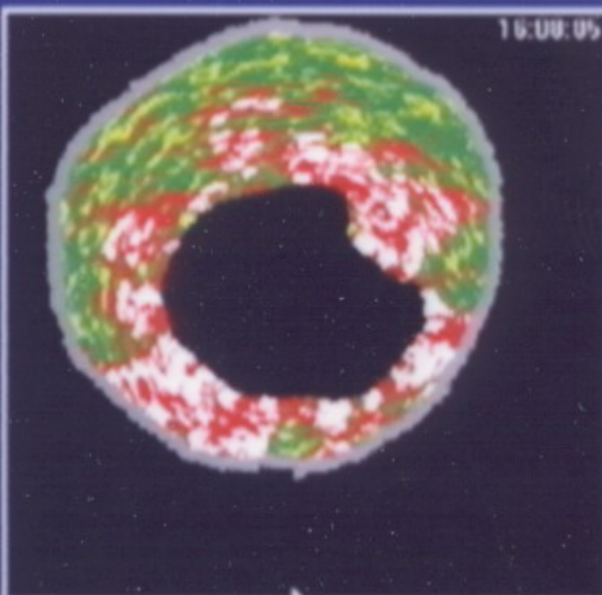
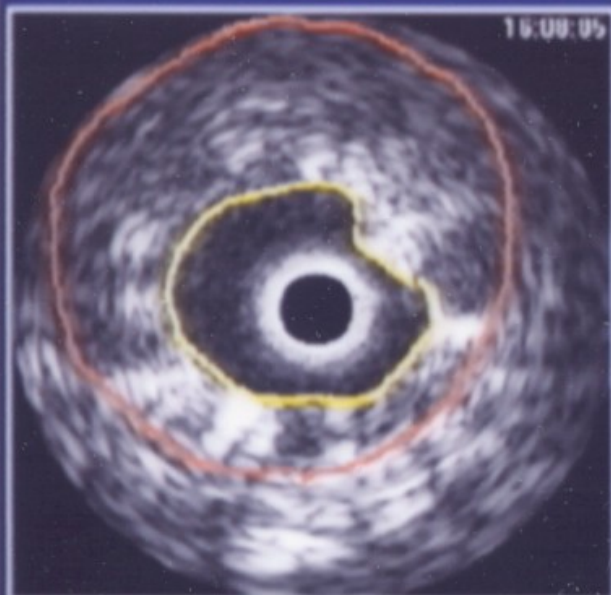
Thrombus

The Good

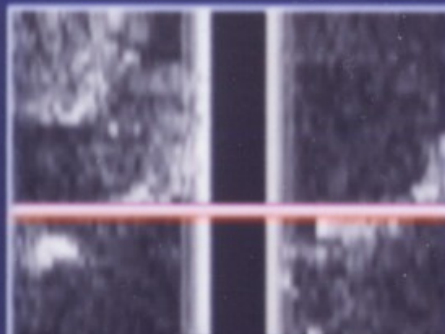
[C] Carotid Plaque Without Associated Thrombus (Asymptomatic Patient)







VL B, Segment: 1



Lumen Area	11.9 mm ²	
EEL Area	46.6 mm ²	
Plaque Area	34.7 mm ²	
% Plaque Burden	74 %	
Fibrous Area	10.7 mm ²	37 %
Fibro-Fatty Area	3.0 mm ²	10 %
Dense Calcium Area	5.9 mm ²	20 %
Necrotic Core Area	9.5 mm ²	33 %

More ...



Distal Frame	—	20
Current Frame	—	20
Proximal Frame	—	20

< Back

Step #4: Frame Results

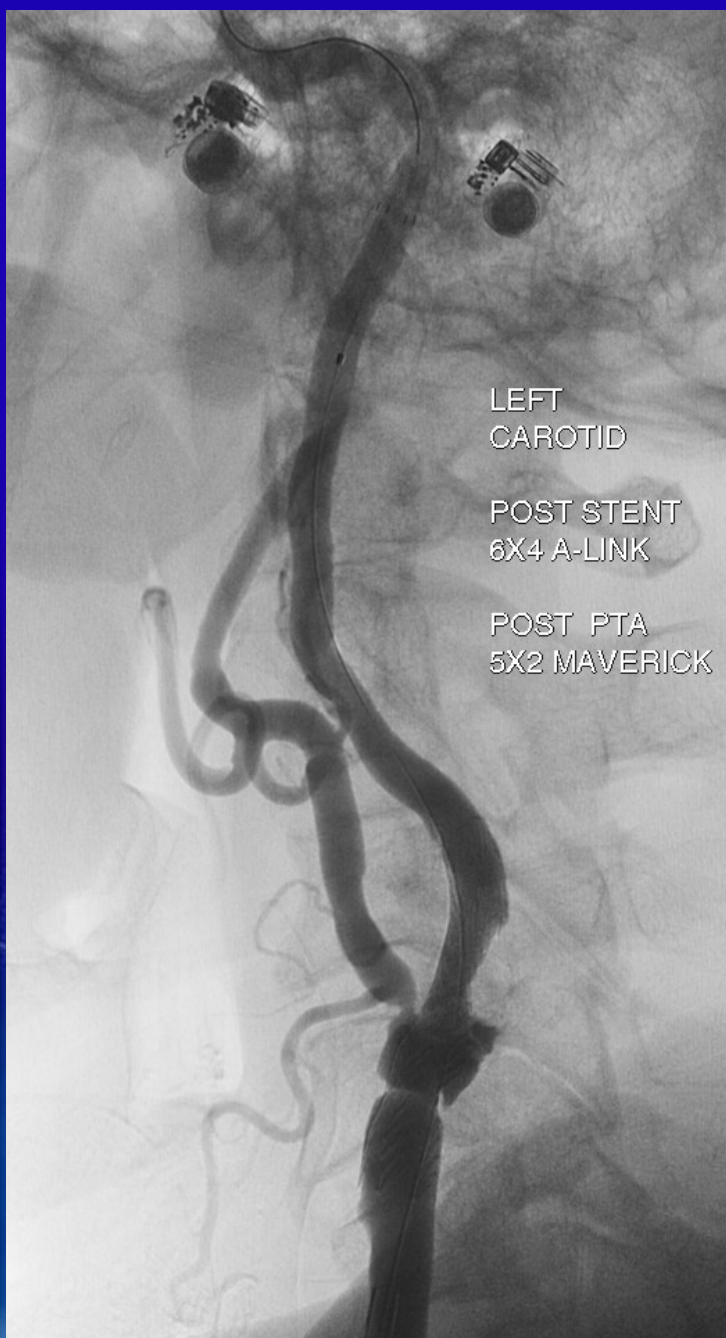
HOME

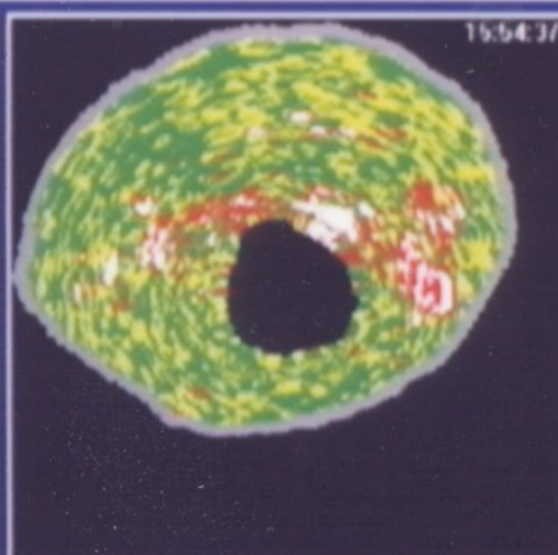
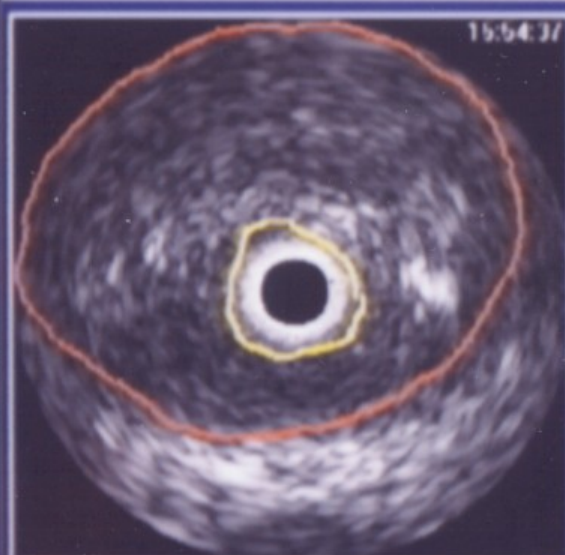
PLAYLOOP

REW / FWD

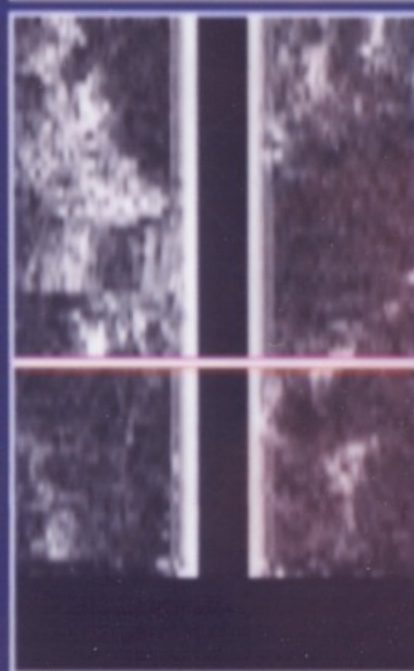
BORDERS ON/OFF

GO TO SEGMENT





VL A, Segment: 1



Lumen Area	4.5 mm ²	
EEL Area	52.5 mm ²	
Plaque Area	47.9 mm ²	
% Plaque Burden	91 %	
Fibrous Area	22.3 mm ²	53 %
Fibro-Fatty Area	13.3 mm ²	32 %
Dense Calcium Area	2.0 mm ²	5 %
Necrotic Core Area	4.4 mm ²	10 %



Distal Frame	—	37
Current Frame	—	37
Proximal Frame	—	37

< Back

Step #4: Frame Results

HOME

PLAY LOOP

REW / FWD

BORDERS ON/OFF

GO TO SEGMENT

Reverse
Angle



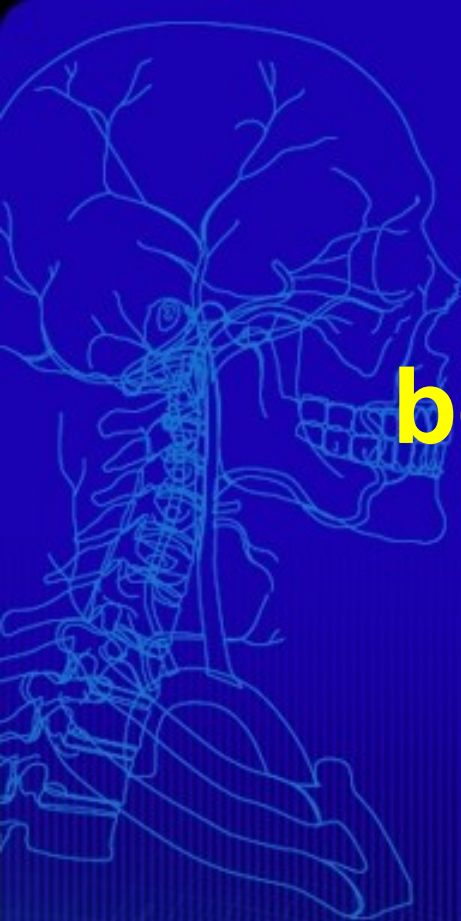
JR4 Needed





This Will NOT Fly!!

- **Asymptomatic 4%**
- **But Symptomatic 7.7%**
- **& Symp. Octogenarians 16%**
- **& Asymp. Octogenarians 13%**



**Should over 80
be an exclusion for all
symptomatic &
asymptomatic
carotid stenting?**

PVI - Octogenarians

Octogenarians n=154 Procedural Events 0 – 30 days

Asymptomatic

Symptomatic

N = 112

N = 42

Death	2.7%	(2)	2.4%	(1)
All Maj Strokes	2.6%	(3)	2.4%	(1)
IPSI Maj Strokes	2.6%	(3)	2.4%	(1)
All Minor Strokes	2.7%	(2)	2.4%	(1)
IPSI Minor Strokes	2.7%	(2)	0%	0
MI	0.9%	(1)	0%	0

Other events that have taken a long time...



Siege of Leningrad
two years

Moses and 40
years in the
desert



**Chicago White Sox 87 years
For World Series**