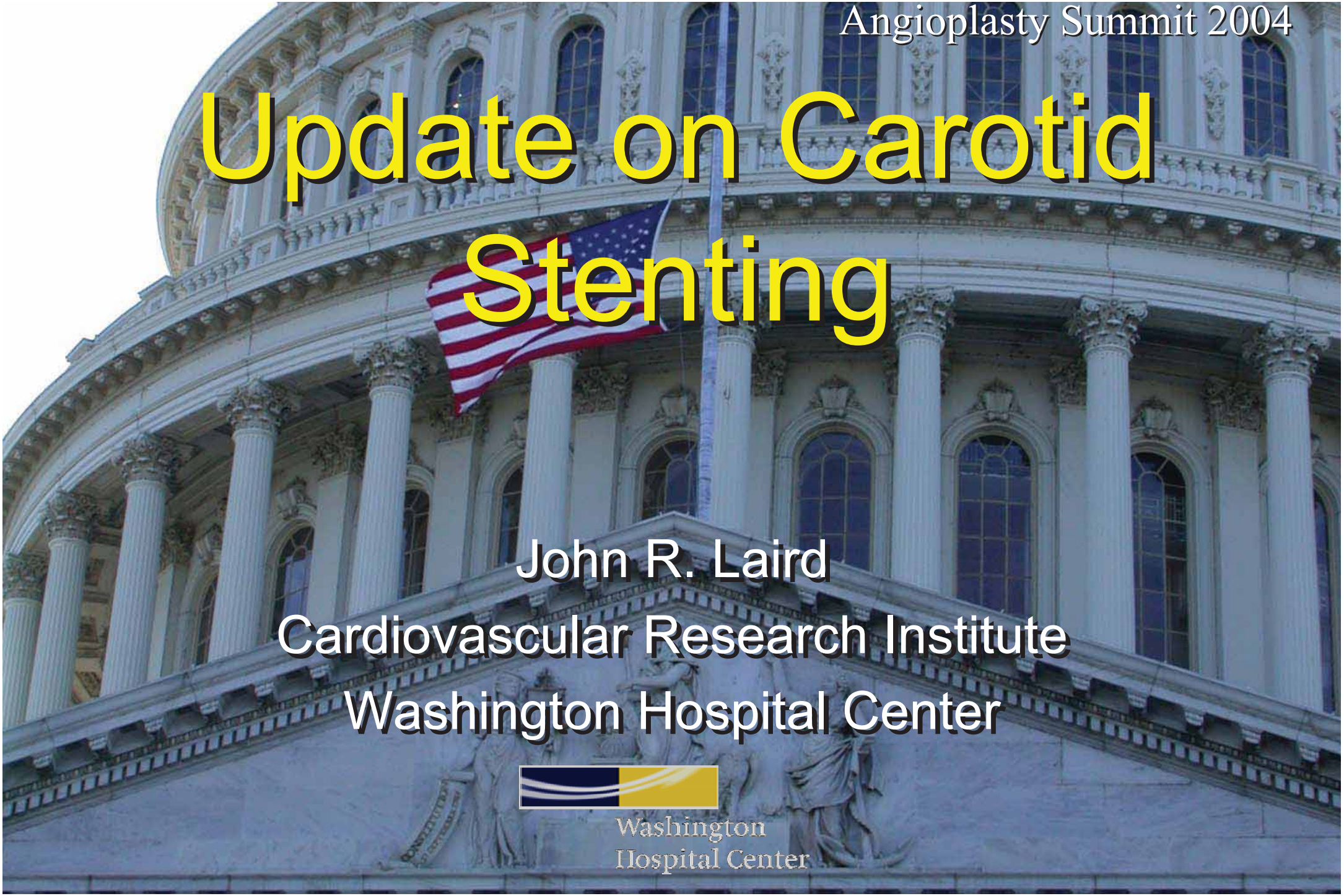
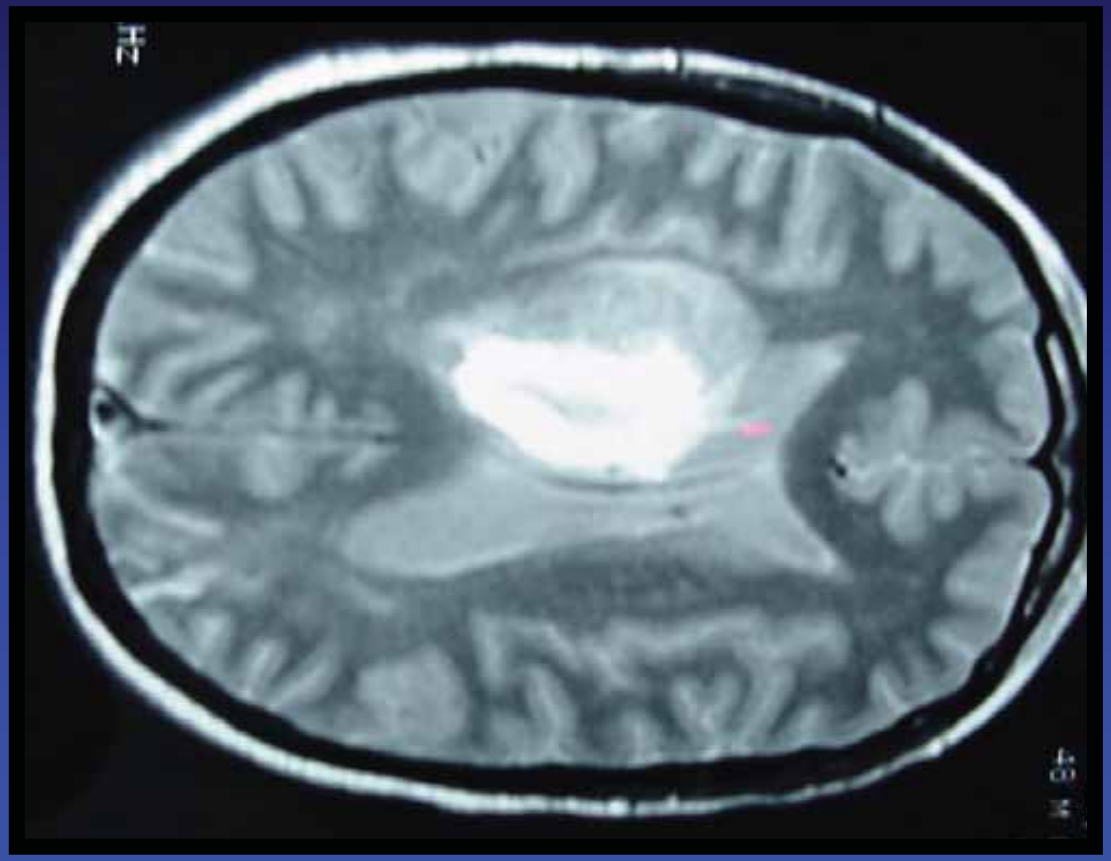
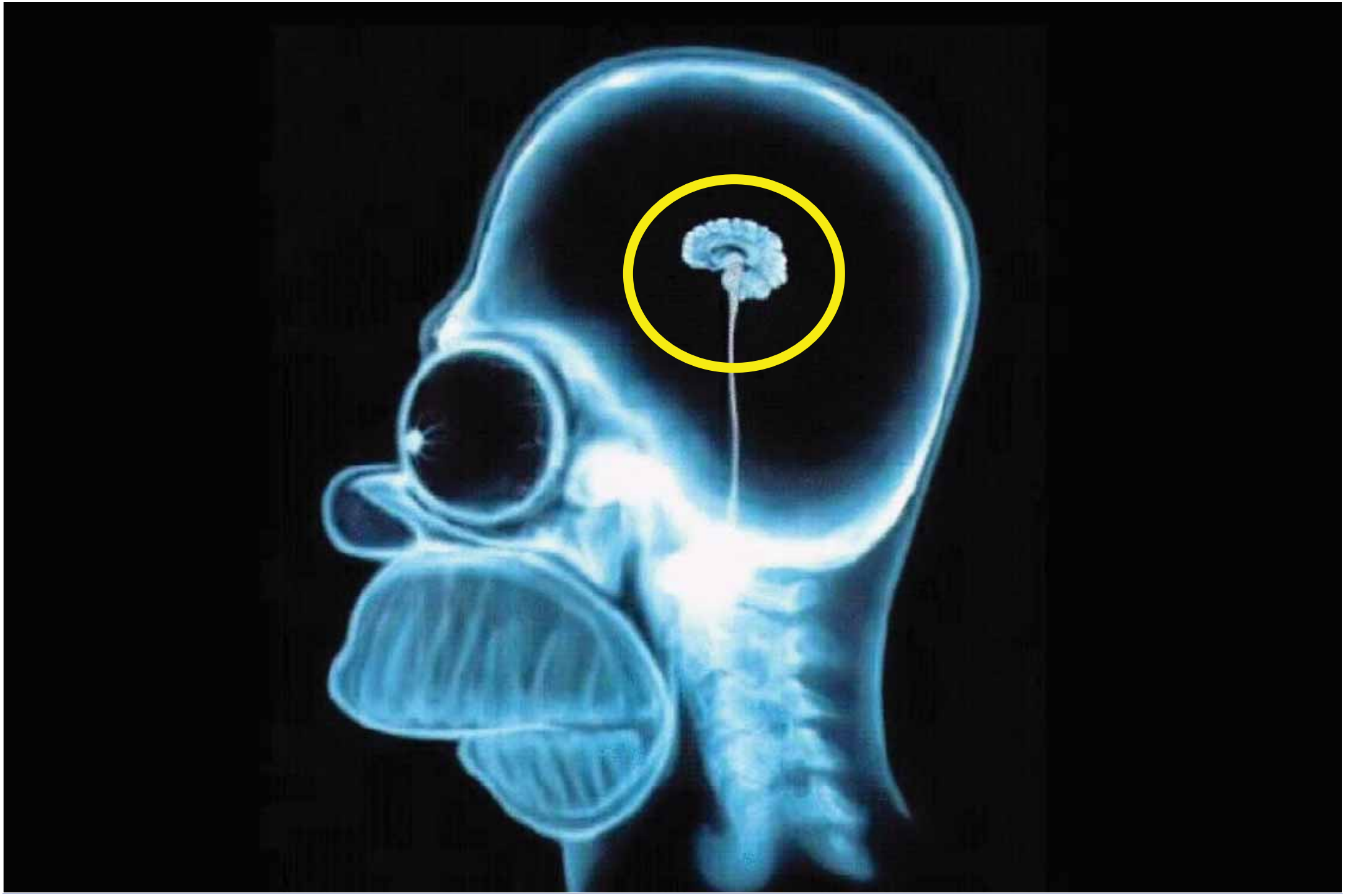

Angioplasty Summit 2004
Update on Carotid Stenting
John R. Laird
Cardiovascular Research Institute
Washington Hospital Center
Washington
Hospital Center



"Don't hurt my brain, it's my second favorite organ"

--Woody Allen



Guidelines…

CEA: Acceptable morbidity and mortality *

Symptomatic → **< 6%**

Asymptomatic → **< 3%**

Ad Hoc Committee, AHA

Carotid Stenting
The Early Years

- Use of equipment designed for other vascular beds
- Balloon expandable stents
- High profile systems
  - 9 Fr guides or 7Fr or 8Fr sheaths
  - 0.035 inch balloon catheters
- No embolic protection systems

UAB/LHH Total Experience

9/8/94 – 1/16/02

	Patients (N=999)	Vessels (n=1106)
Death	13 (1.3%)	13 (1.2%)
Minor Stroke	41 (4.1%)	41 (3.7%)*
Major Stroke	8 (0.8%)	8 (0.7%)
All Strokes & Deaths	62 (6.2%)	62 (5.6%)

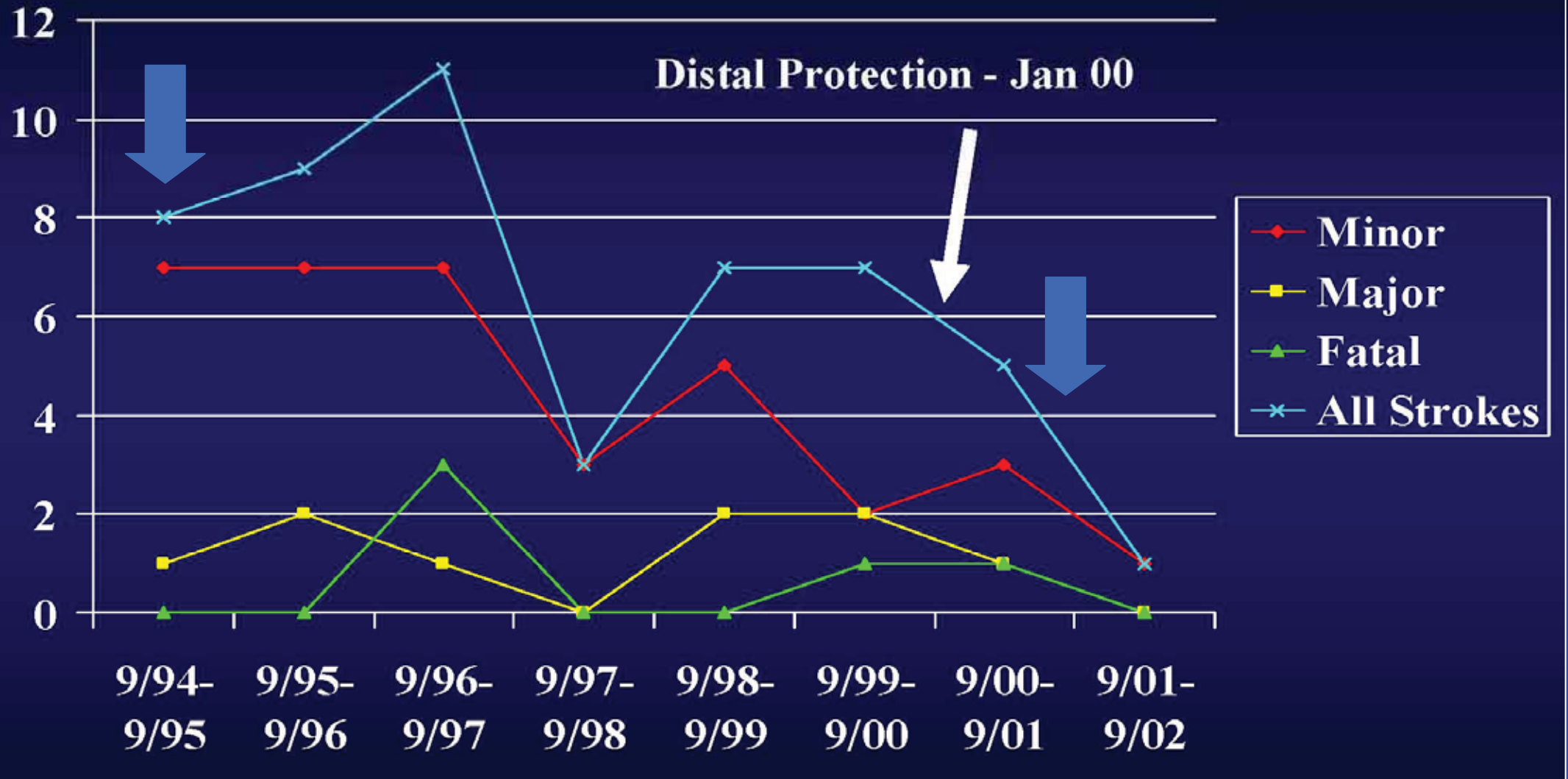
**** Includes: 2 patients with retinal embolus and 2 patients with hyperperfusion syndrome***

Lenox Hill Experience
11/20/97 – 1/16/02

	Patients (N=679)	Vessels (n=730)
Death	3 (0.4%)	3 (0.4%)
Minor Stroke	20 (2.9%)*	20 (2.7%)
Major Stroke	4 (0.6%)	4 (0.5%)
All Strokes & Deaths	27 (4.0%)	27 (3.7%)

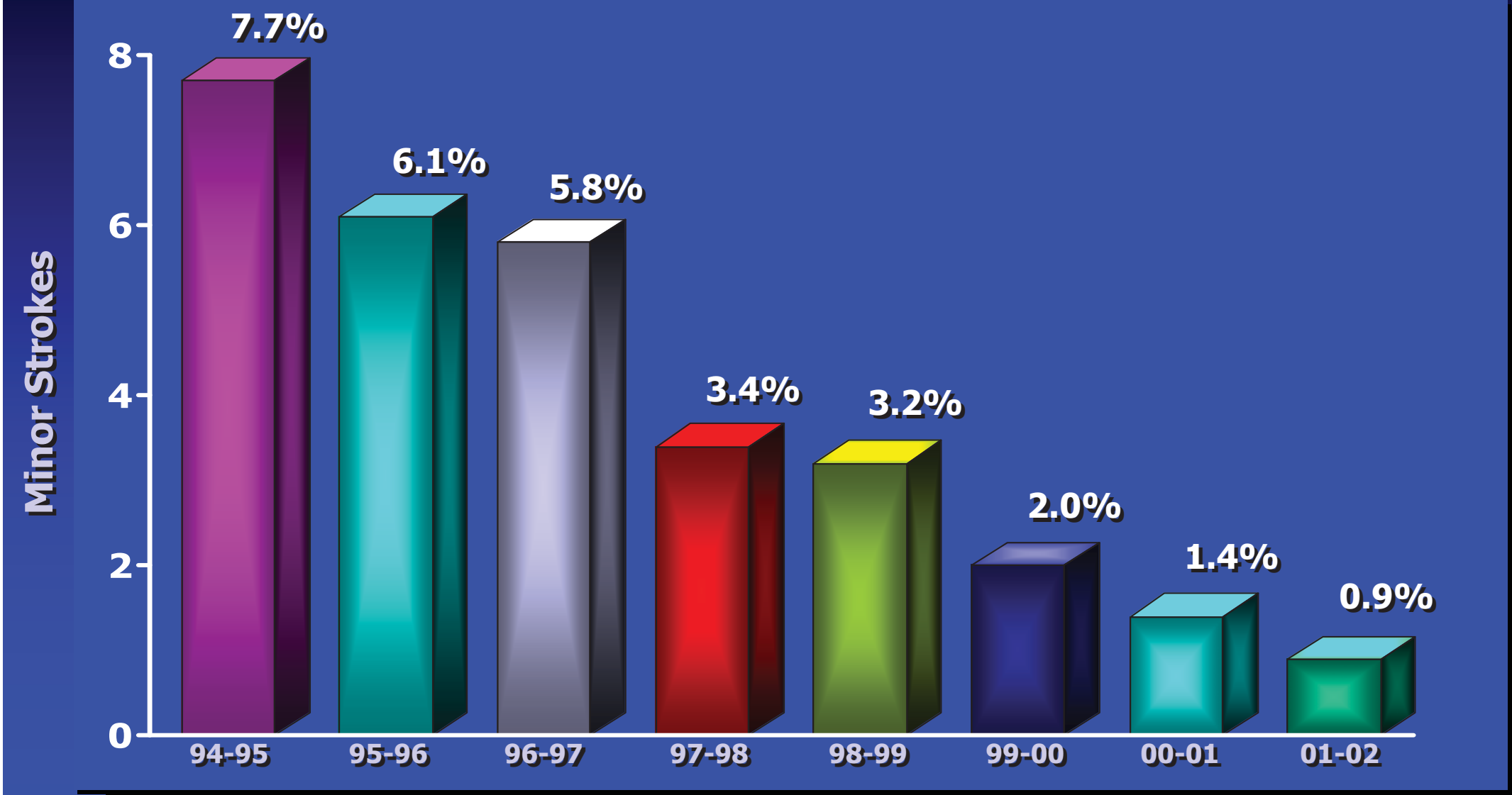
**** Includes: 2 patients with retinal embolus and 2 patients with hyperperfusion syndrome***

Improving Results of Carotid Stenting



New, Roubin JACC Suppl. 41;79a, 2003

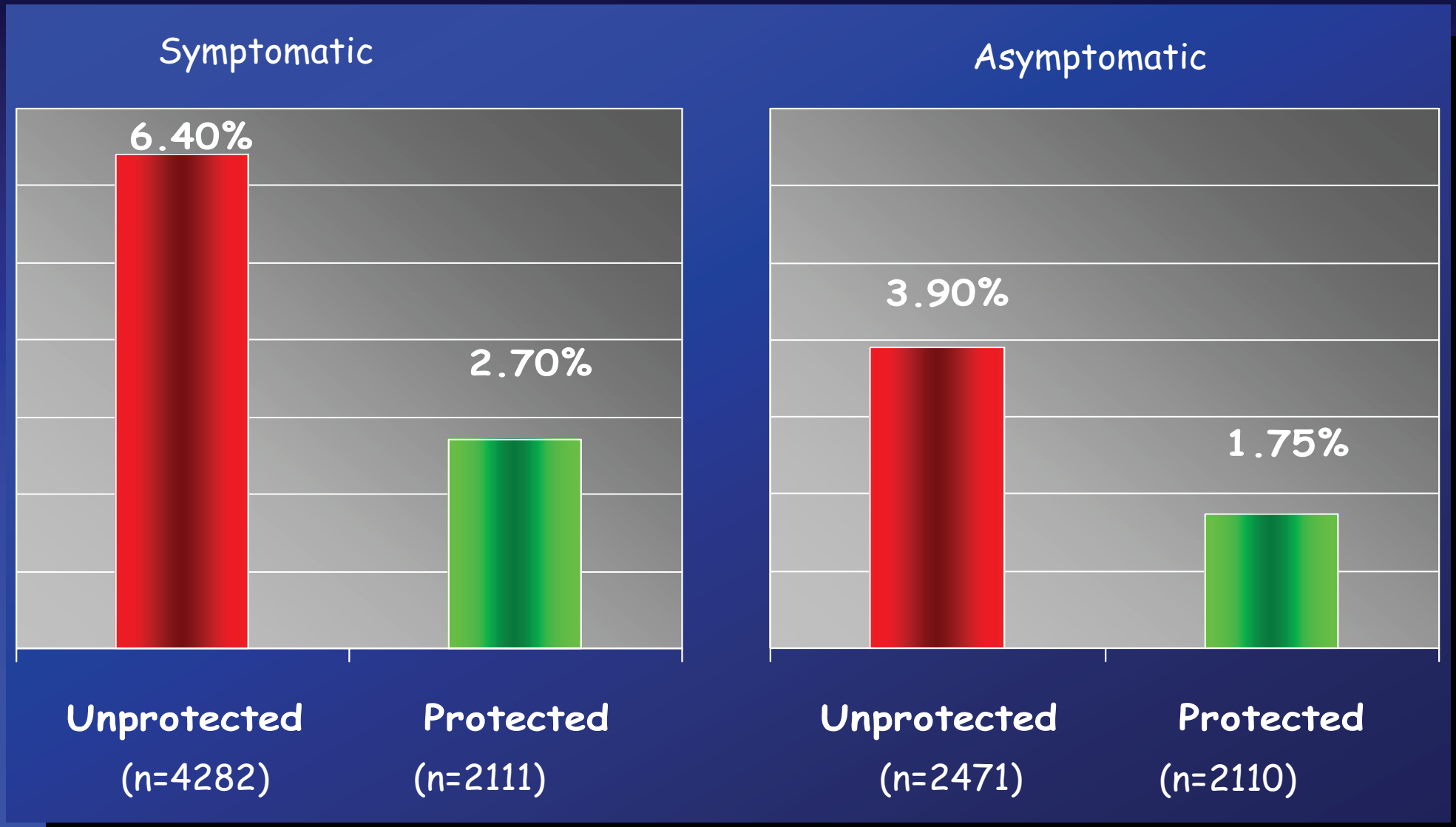
Temporal Trend - Minor Strokes



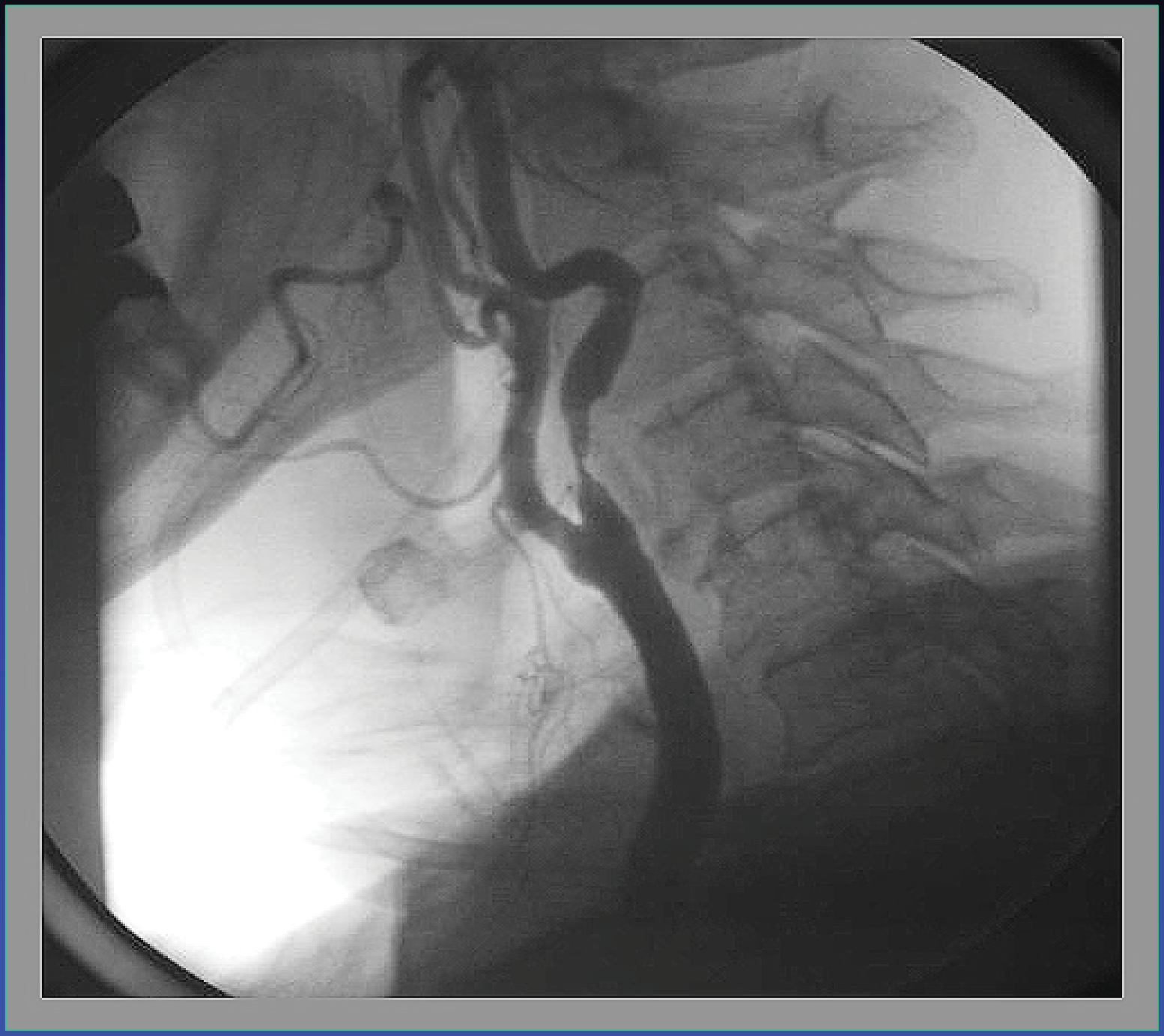
Carotid Stenting
Improved Results

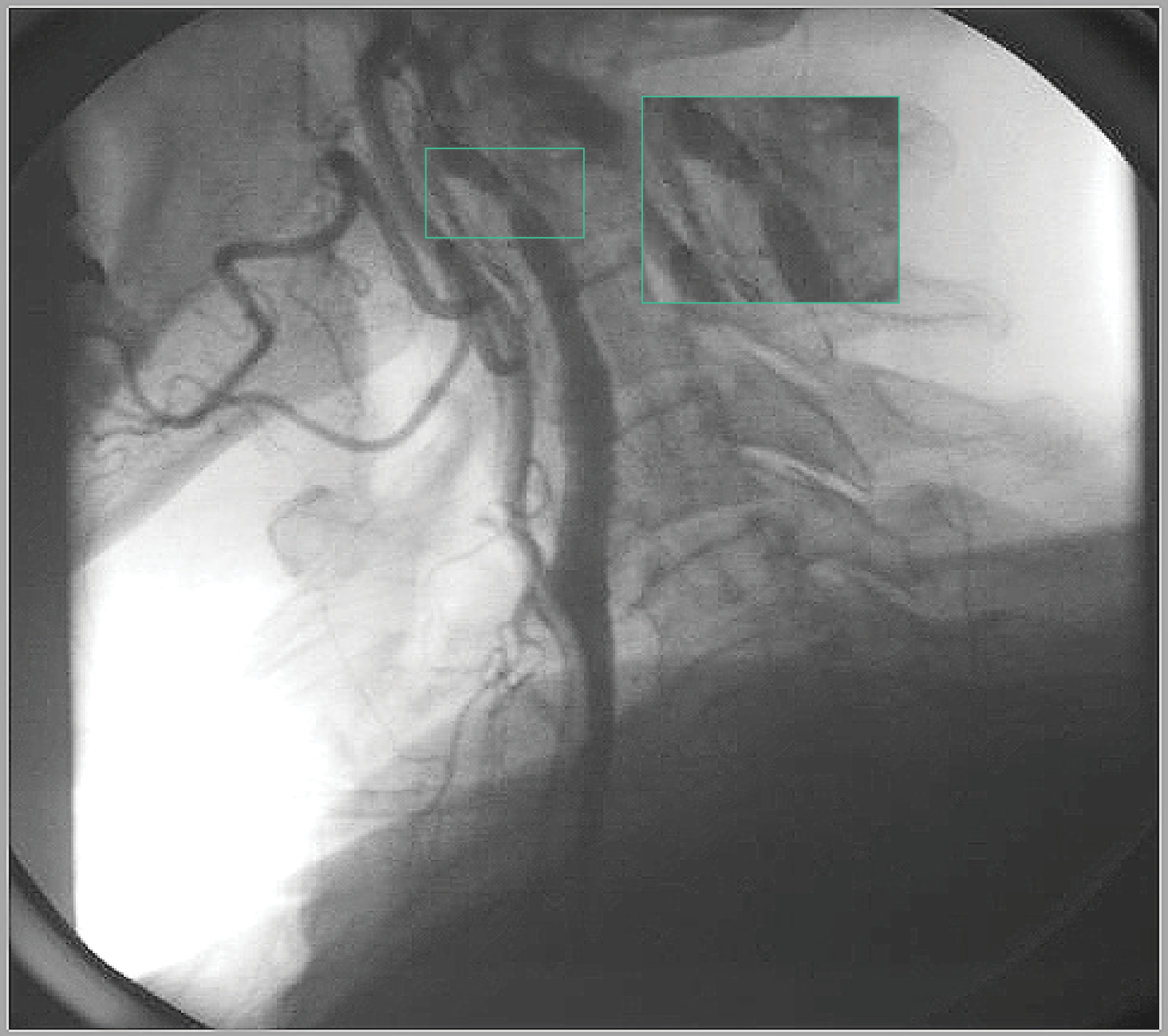
- Better patient selection
- Standardized techniques
- Dedicated carotid stent platforms
- Lower profile systems
  - 6 Fr sheath
  - 0.014 balloons
  - Self-expanding stents (Wallstent, Nitinol stents)
- Emboli protection systems
- Better adjunct pharmacology

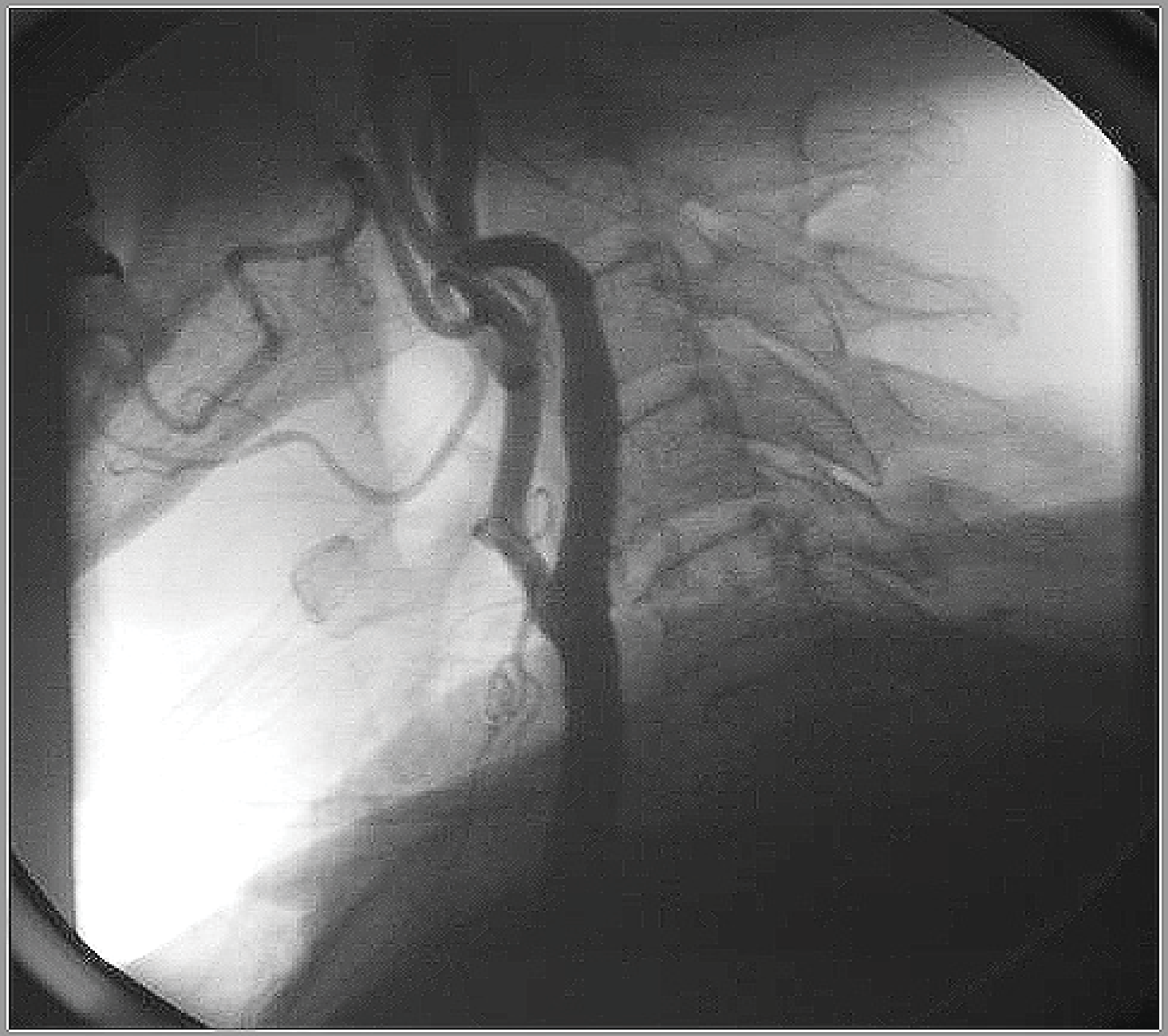
Global Carotid Registry

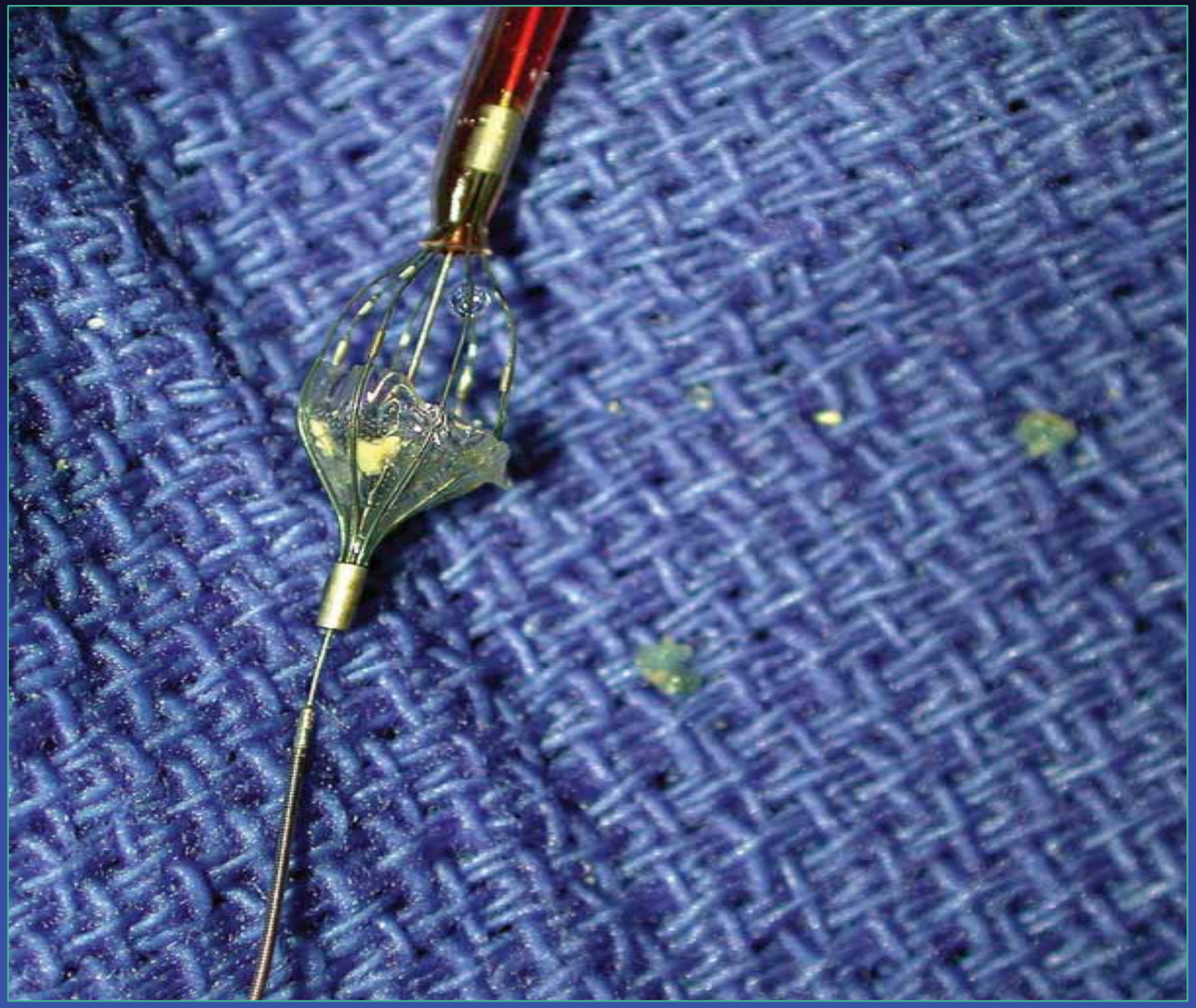


Wholey, Catheter Cardiovasc Interv 2003; 601: 259-266

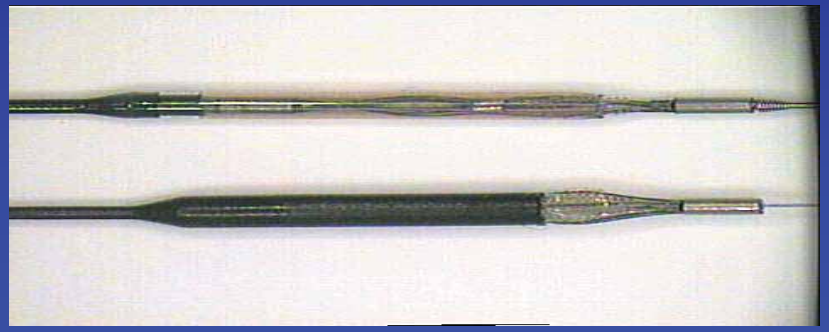


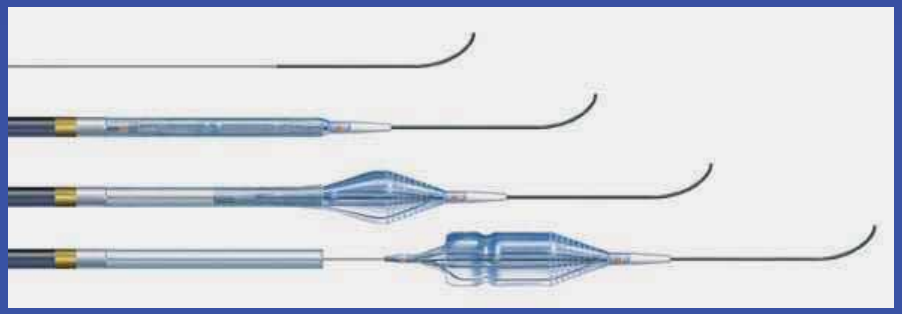






Review of Carotid Stent/Embolic Protection Platforms





Carotid Stent Clinical Trials

- **Registries**
  - SHELTER (BSC/Percusurg)
  - ARCHER (Guidant)
  - MAVERICK (Medtronic)
  - CARESS (ISES)
  - BEACH (BSC,EPI)
  - SECURITY (Abbot, Mednova)
  - CABERNET (BSC, Endotex
- **Randomized**
  - CREST (NIH)
  - SAPPHIRE (Cordis)

Unfavorable CEA Subsets

Anatomic High Risk

- High (C2) carotid bifurcation
- Prior neck irradiation or radical neck dissection
- Restenosis following prior CEA
- Contralateral Occlusion
- Ostial common carotid lesion
- Spine immobility

Unfavorable CEA Subsets

Medical High Risk

- Severe CAD – Not revascularized or awaiting CABG
- Class III or IV CHF
- Severe COPD
- Age > 80

SAPPHIRE

> 50% Stenosis Sx

> 80% Stenosis Asx

One or More Comorbidity Criteria

Physician Team: Neurologist, Surgeon, Interventionalist

CONSENSUS

SURGICAL REFUSAL

STENT REGISTRY 409

RANDOMIZED 307

Stenting=156 **CEA=151**

INTERVENTIONAL REFUSAL

SURGICAL REGISTRY 7

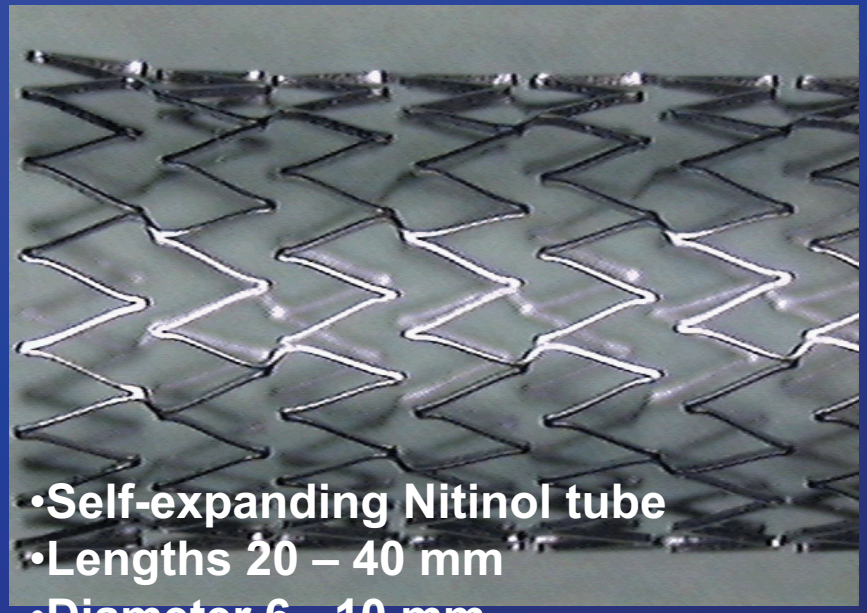
SAPPHIRE Trial
Primary Endpoints

- Death, any Stroke, and MI at 30-days post-procedure
- 30 day MAE plus Death and Ipsilateral Stroke between 31-days and 12-months post-procedure

SAPPHIRE
Carotid Stent Platform

Cordus Endovascular

- Precise stent
- Angioguard



•Self-expanding Nitinol tube
•Lengths 20 – 40 mm
•Diameter 6 - 10 mm

•Pore size
•≤ 100 microns

CAROTID STENTING

SAPPHIRE

CULUMATIVE 30 DAY RESULTS

Events	Stent (156 pts) [95% CI]	CEA (151 pts) [95% CI]	p Value
Death:	0.6% [-0.6%,1.9%]	2.0%[-0.2%,4.2%]	0.36
Stroke:	3.8% [0.8%,6.9%]	5.3% [1.7%,8.9%]	0.59
Major Ipsilateral:	0.0%	1.3%	0.24
Major Non-Ipsilateral:	0.6%	0.7%	>0.99
Minor Ipsilateral:	3.2%	3.3%	>0.99
Minor Non-Ipsilateral:	0.6%	0.0%	>0.99
MI (Q or NQ)	2.6% [0.1%,5.0%]	7.3% [3.1%,11.4%]	0.07
Q-Wave MI	0.0%	1.3%	0.24
Non-Q Wave MI	2.6%	6.0%	0.16
Death/Stroke:	4.5% [1.2%,7.7%]	6.6% [2.7%,10.6%]	0.46
Death/Stroke/MI	**5.8%[2.1%,9.4%]**	**12.6%[7.3%,17.9%]**	**0.047**

CAROTID STENTING

SAPPHIRE

SAPPHIRE ASYMPTOMATIC 30 DAY RESULTS

Events	Stent (104 pts) [95% CI]	CEA (98 pts) [95% CI]	p Value
Death:	1.0% [-0.9%,2.8%]	1.0% [-1.0%,3.0%]	>0.99
Stroke:	4.8% [0.7%,8.9%]	5.1% [0.7%,9.5%]	>0.99
Major Ipsilateral:	0.0%	2.0%	0.23
Major Non-Ipsilateral:	1.0%	0.0%	>0.99
Minor Ipsilateral:	3.8%	3.1%	>0.99
Minor Non-Ipsilateral:	1.0%	0.0%	>0.99
MI (Q or NQ):	2.9% [-0.3%,6.1%]	7.1% [2.0%,12.2%]	0.20
Q-Wave MI	0.0%	2.0%	0.23
Non-Q Wave MI	2.9%	5.1%	0.49
Death/Stroke:	5.8% [1.3%,10.3%]	6.1% [1.4%,10.9%]	>0.99
Death/Stroke/MI:	6.7% [1.9%,11.5%]	11.2% [5.0%,17.5%]	0.33

CAROTID STENTING

SAPPHIRE

SAPPHIRE SYMPTOMATIC 30 DAY RESULTS

Event	Stent (48 pts) [95% CI]	CEA (39 pts) [95% CI]	p Value
Death:	0.0% [- , -]	5.1% [-1.8%,12.1%]	0.20
Stroke:	2.1% [-2.0%,6.1%]	7.7% [-0.7%,16.1%]	0.32
Major Ipsilateral:	0.0%	0.0%	---
Major Non-Ipsilateral:	0.0%	2.6%	0.45
Minor Ipsilateral:	2.1%	5.1%	0.58
Minor Non-Ipsilateral:	0.0%	0.0%	---
MI (Q or NQ):	2.1% [-2.0%,6.1%]	5.1% [-1.8%,12.1%]	0.58
Q-Wave MI	0.0%	0.0%	---
Non-Q Wave MI	2.1%	5.1%	0.58
Death/Stroke:	2.1% [-2.0%,6.1%]	10.3% [0.7%,19.8%]	0.17
Death/Stroke/MI:	4.2% [-1.5%,9.8%]	15.4% [4.1%,26.7]	0.13

1 Year Data
Randomized Patients (Per Protocol)

Events	Stent (159 pts)	CEA (151 pts)	p Value
Death:	**11 (6.9%)**	**19 (12.6%)**	**0.12**
Stroke:	**9 (5.7%)**	**11 (7.3%)**	**0.65**
Major Ipsilateral:	**0 (0.0%)**	**5 (3.3%)**	**0.03***
Major Non-Ipsilateral:	1 (0.6%)	1 (0.7%)	>0.99
Minor Ipsilateral:	6 (3.8%)	3 (2.0%)	0.50
Minor Non-Ipsilateral:	3 (1.9%)	3 (2.0%)	>0.99
MI (Q or NQ)	**4 (2.5%)**	**12 (7.9%)**	**0.04***
Q-Wave MI	0 (0.0%)	2 (1.3%)	0.24
Non-Q Wave MI	4 (2.5%)	10 (6.6%)	0.10

Cranial Nerve Injury

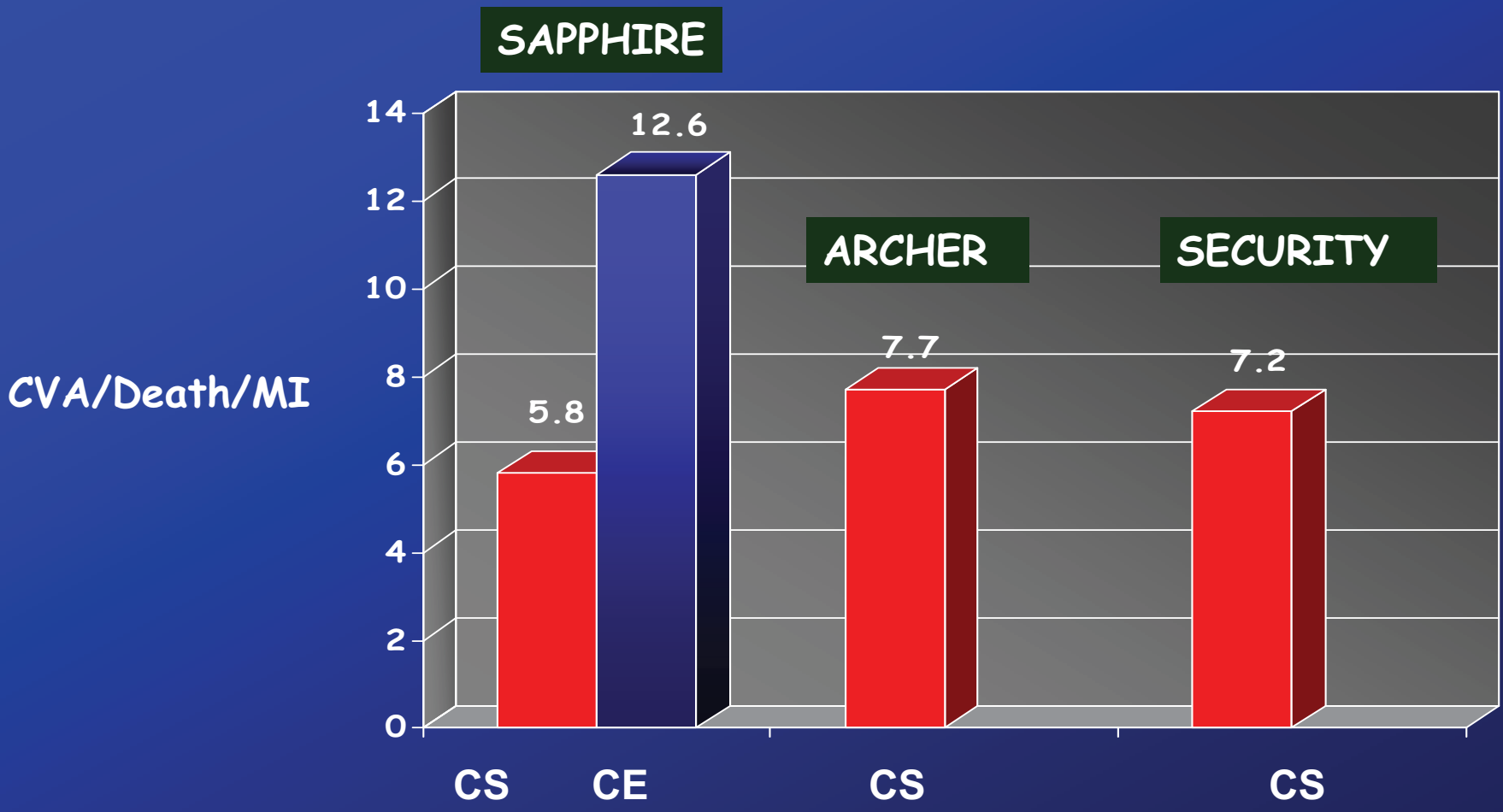
- CEA = 4.6% (7/151)
- Stent = 0.0% (0/159)

- P value = 0.006

Target Lesion Revascularization

- Randomized
  - Stent Arm:
    - Clinically Driven TLR: 0.6% (1/159)
  - CEA Arm:
    - Clinically Driven TLR: 4.0% (6/151)
- Stent Registry Arm:
    - Clinically Driven TLR: 0.7% (3/406)

SAPPHIRE, ARCHER, SECURITY: 30 DAY OUTCOMES



CS =Carotid stent
CE =Carotid endartectomy

Carotid Stenting with Distal Protection
WHC Experience

- 146 patients treated from August 2001 to early December 2003
- All patients treated as part of high risk Carotid stent IDE trials (ARCHER, MAVERICK, BEACH, SHELTER, CARESS, COBRA, etc.)
- 30 Day event rate:
  - Stroke: 2% (one major, two minor)
  - Death: 2%*

*2 post CABG, 1 CHF, pneumonia

Carotid Revascularizaton with Endarterectomy or Stenting Systems CARESS

Sponsor

Steering Committee: Rodney White, Edward B. Dietrich, Thomas J. Fogarty, Louis N. Hopkins, Gary S. Roubin, Mark H. Wholey, Christopher K. Zarins

Study Design

- Non-randomized, prospective, cohort comparison
  - Asymptomatic and symptomatic subjects
  - Documentation of ineligible subjects
- Assess the utility of both technologies (CEA and CSS) in current practice
- 3000 patients total
  - Feasibility Study: 300 CEA, 150 CSS
  - Pivotal Study: 850 CEA, 1700 CSS

Results

- 14 clinical sites enrolled 439 patients of which 397 were treated (254 with CEA, 143 with CSS)
- 42 patients withdrew prior to treatment
- 90% had >75% stenosis
- 68% were asymptomatic
- More frequent history of prior CEA in CSS group (30% vs 11%, $p<0.0001$)

Results

	CSS	CEA
30-Day stroke/death	2.1%	2.4%
30-Day stroke/death/MI	2.1%	3.0%

Carotid Revascularization Endarterectomy versus Stenting Trial (CREST)

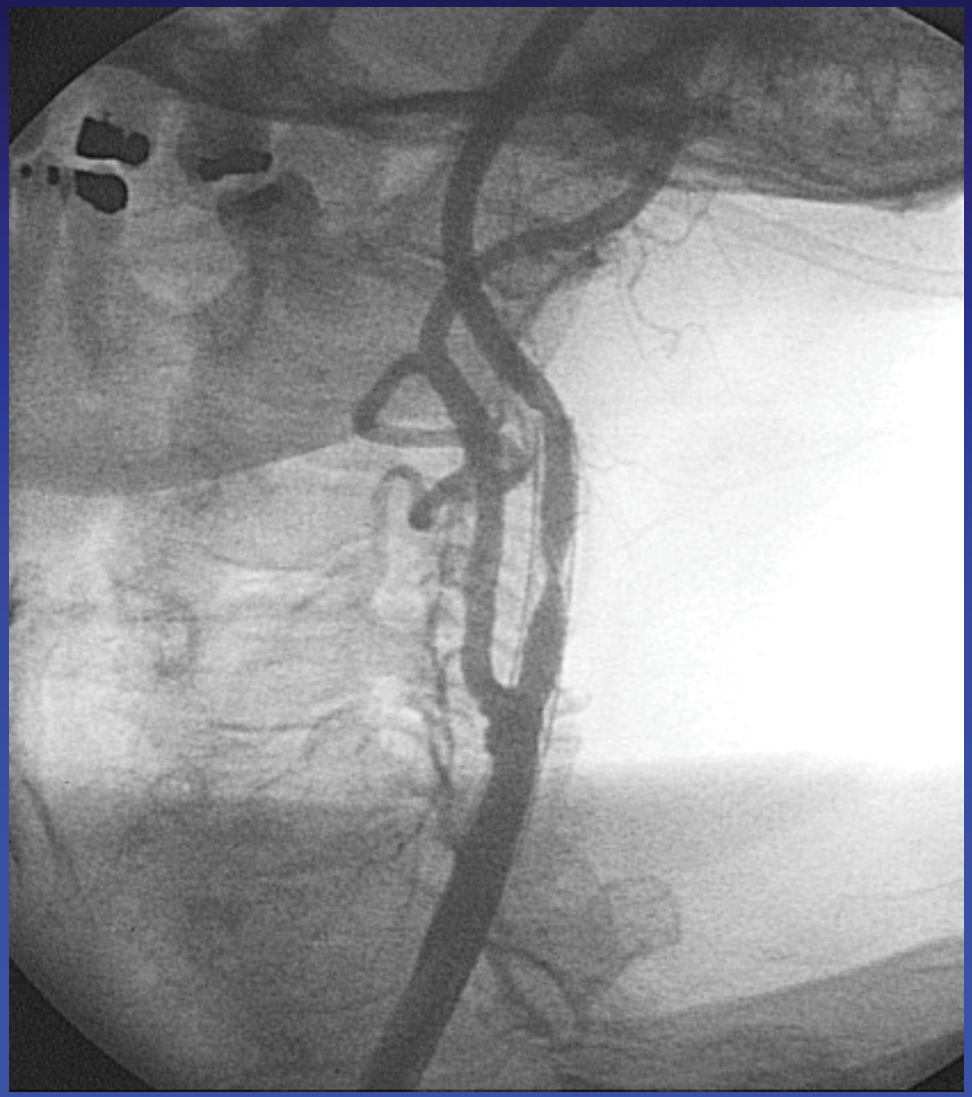
- NIH-NINDS funded, randomized trial
- 2500 patients with symptomatic carotid stenosis randomized to CEA or carotid stenting with protection
- TIA or non-disabling stroke within 180 days
- Ipsilateral carotid stenosis $\geq$ 50%

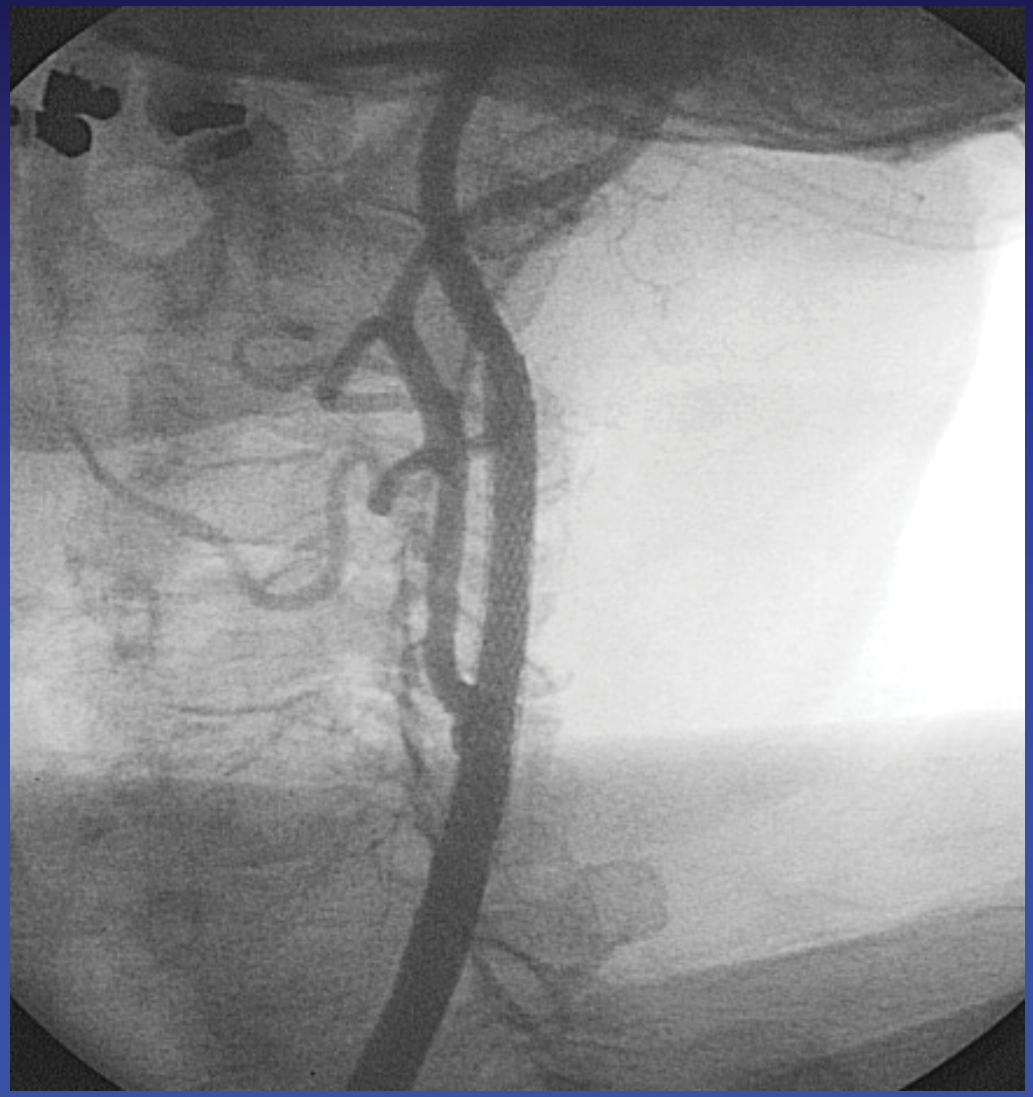
Is Carotid Stenting Durable?

Stent Restenosis

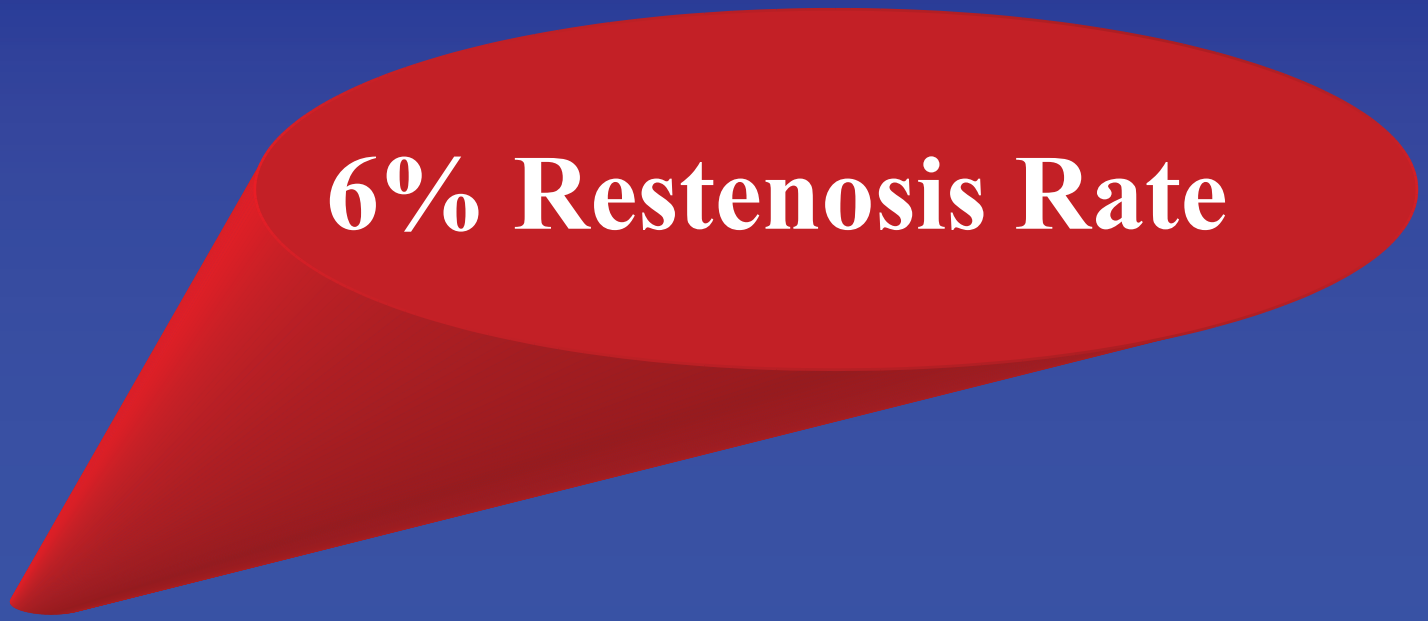
Can it Prevent Stroke?

Restenosis after Carotid Stenting





Long Term Follow-Up



Restenosis after Carotid Stenting

- 122 carotid stent procedures in 118 patients from September 1996 – March 2003
- Indications for procedure:
  - Restenosis after CEA: 66%
  - High risk for surgery: 29%
  - Previous radiation: 5%
- Mean follow-up: 18.8 months (1 -74)
- Life table analysis and Kaplan-Meier curves predict restenosis rate (>80%) of 6.4% at 60 months
- Instent restenosis not associated with any neurologic symptoms

J Vasc Surg 2003;38:1162-9

Long-Term Outcomes

Event	Patients (n=520), N (%)
Major ipsilateral nonfatal strokes	2 (0.4)
Minor ipsilateral nonfatal strokes	1 (0.2)
Major contralateral or vertebrobasilar nonfatal strokes	5 (1.0)
Minor contralateral or vertebrobasilar nonfatal strokes	4 (0.8)
Fatal strokes	4 (0.8)
All fatal and nonfatal strokes	31 (3.2)

Carotid Stenting
Ready for Prime Time

- Strong Evidence that carotid stenting is safe and effective
- Equivalent or superior to CEA for the high risk patient
- Carotid stenting appears to be a durable procedure
  - Single digit restenosis
  - Paucity of late neurologic events

FDA Panel Approval April 2004