Cervical Carotid And Vertebral Artery Stenting

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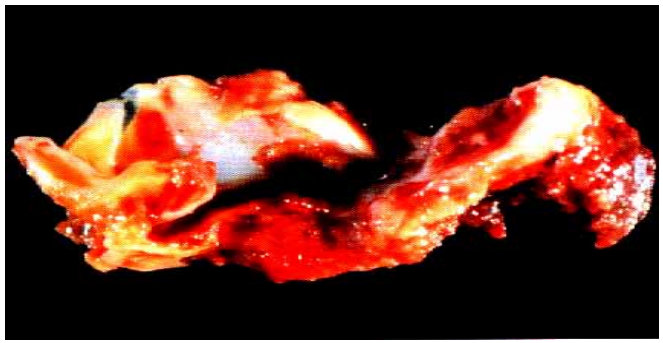
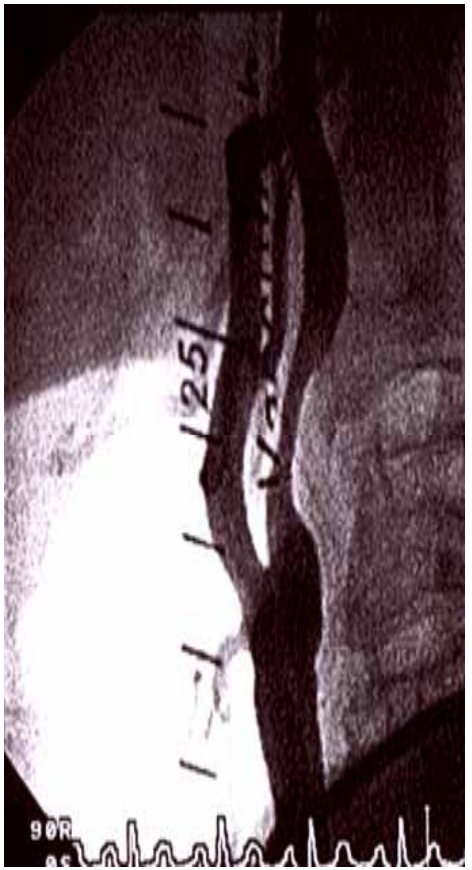
Carotid artery stenosis

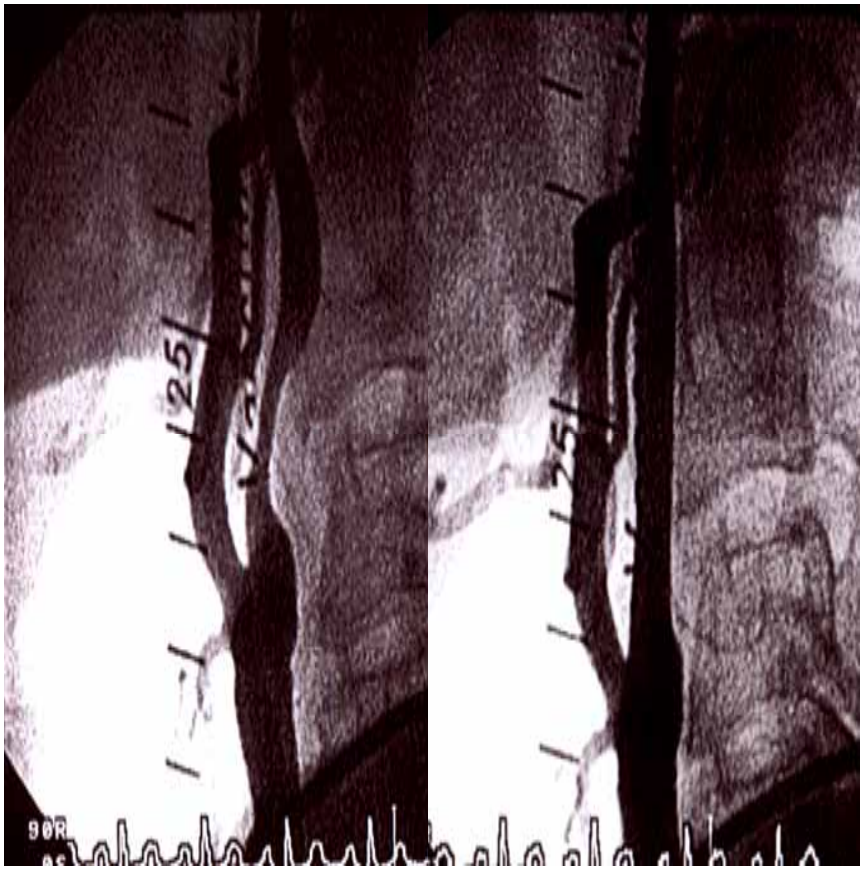
- Atherosclerotic lumen narrowing
- Plaque rupture and artery-to-artery embolism
- Accounts for 20-30% of ischemic cerebral strokes
- Annual stroke rate in symptomatic severe stenosis is 15-30%
- Endarterectomy (CE) was superior to medical control (in low surgical risk patients only), with many limitations





Carotid artery stenting (CS)

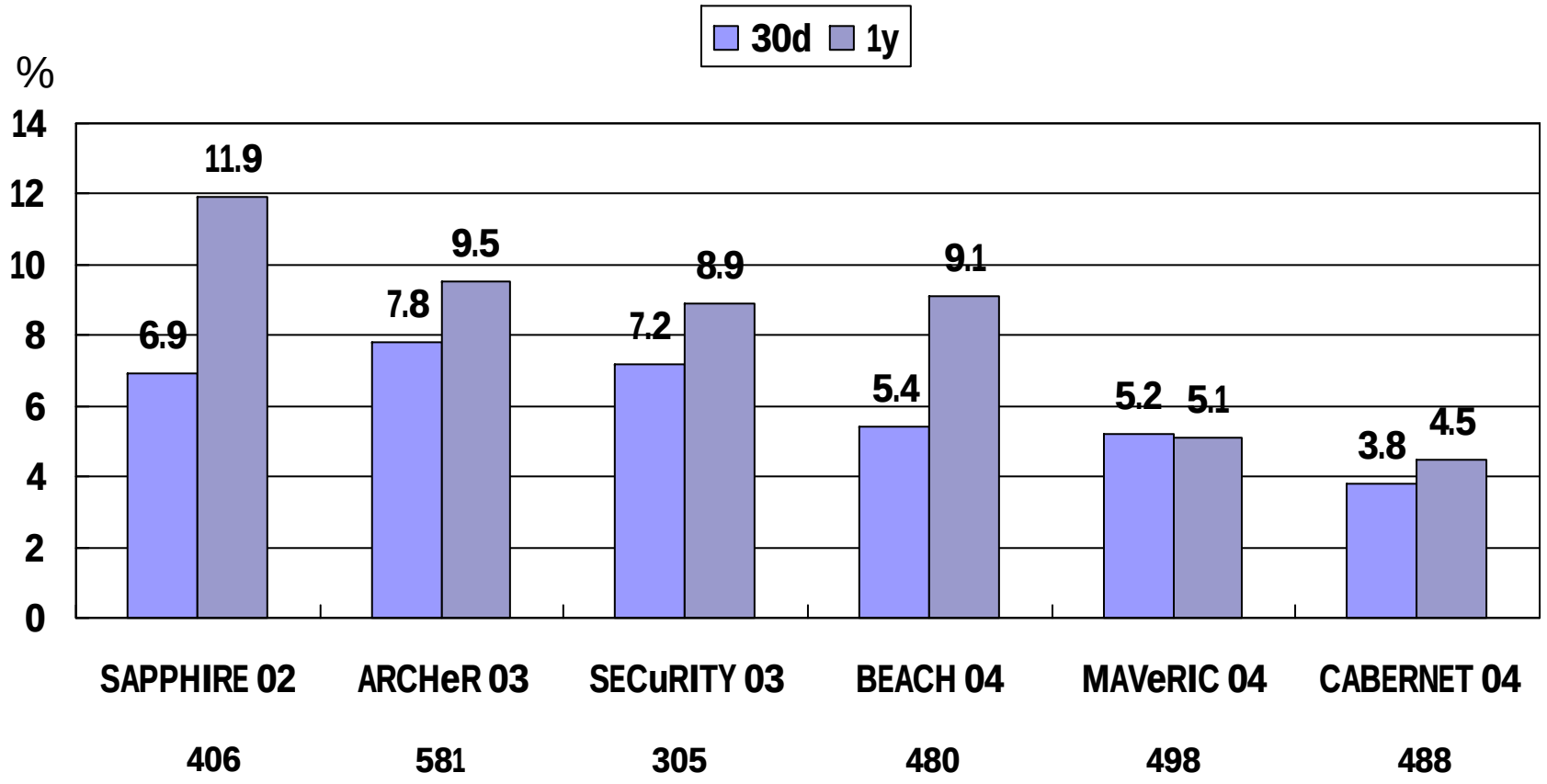
- Minimally invasive
- Improves hemodynamics and stabilizes plaque
- NTUH program started in 4/98
- Proven equivalent, if not superior, to CE in high surgical risk patients
- FDA approval in 8/04



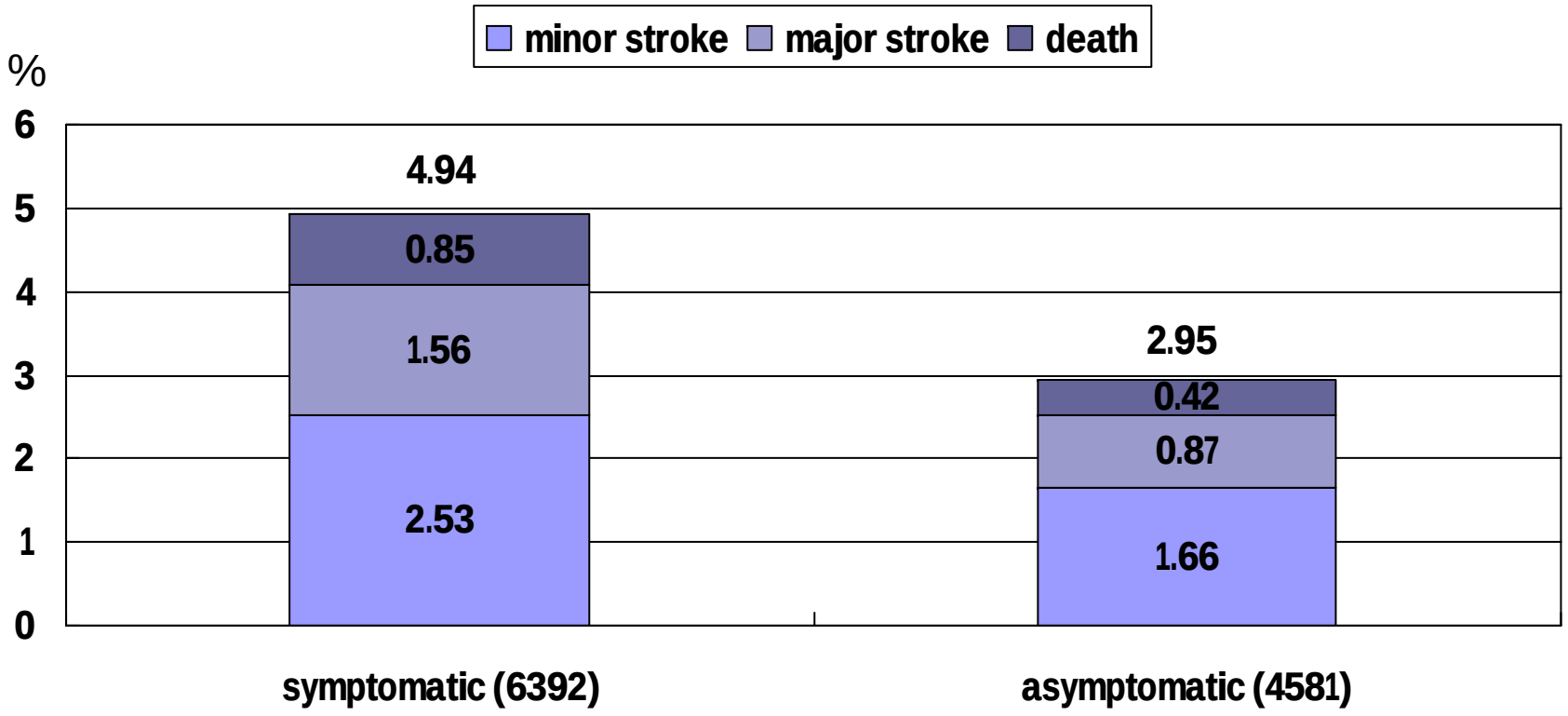
CS trials and registries with n>200

	Place	Risk	Symptom	Type	Status
ARCHeR	US	high	all	registry	complete
BEACH	US	high	all	registry	complete
CABERNET	US	high	all	registry	complete
CAPTURE	US	high	all	post-market registry	complete
CARESS	US	normal	all	parallel registries	complete
CAVATAS	EU	all	symptomatic	RCT vs. CE	complete
CREST	US	normal	all	RCT vs.CE	enrolling
EV3S	EU	normal	symptomatic	RCT vs. CE	enrolling
ICSS/CAVATAS II	EU	all	symptomatic	RCT vs.CE	enrolling
Maverick	US	high	all	registry	complete
ProCAS	EU	all	All	registry	enrolling
SECURITY	US	high	All	registry	complete
SAPPHIRE	US	high	all	RCT vs. CE	complete
SPACE	EU	all	symptomatic	RCT vs. CE	enrolling

DSM in high risk registries

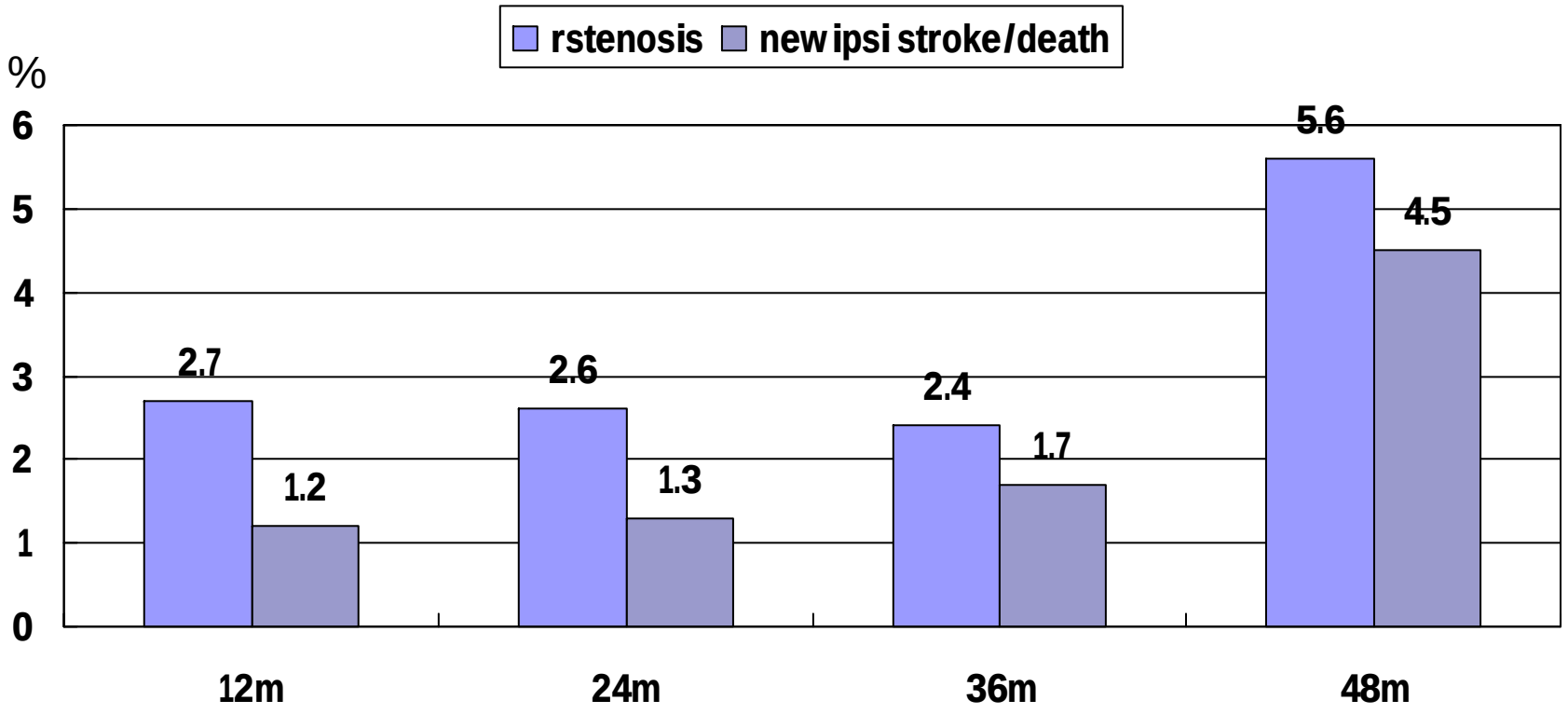


Global experience on 30d events



Wholey et al. CCI 2003

Global experience on long term results

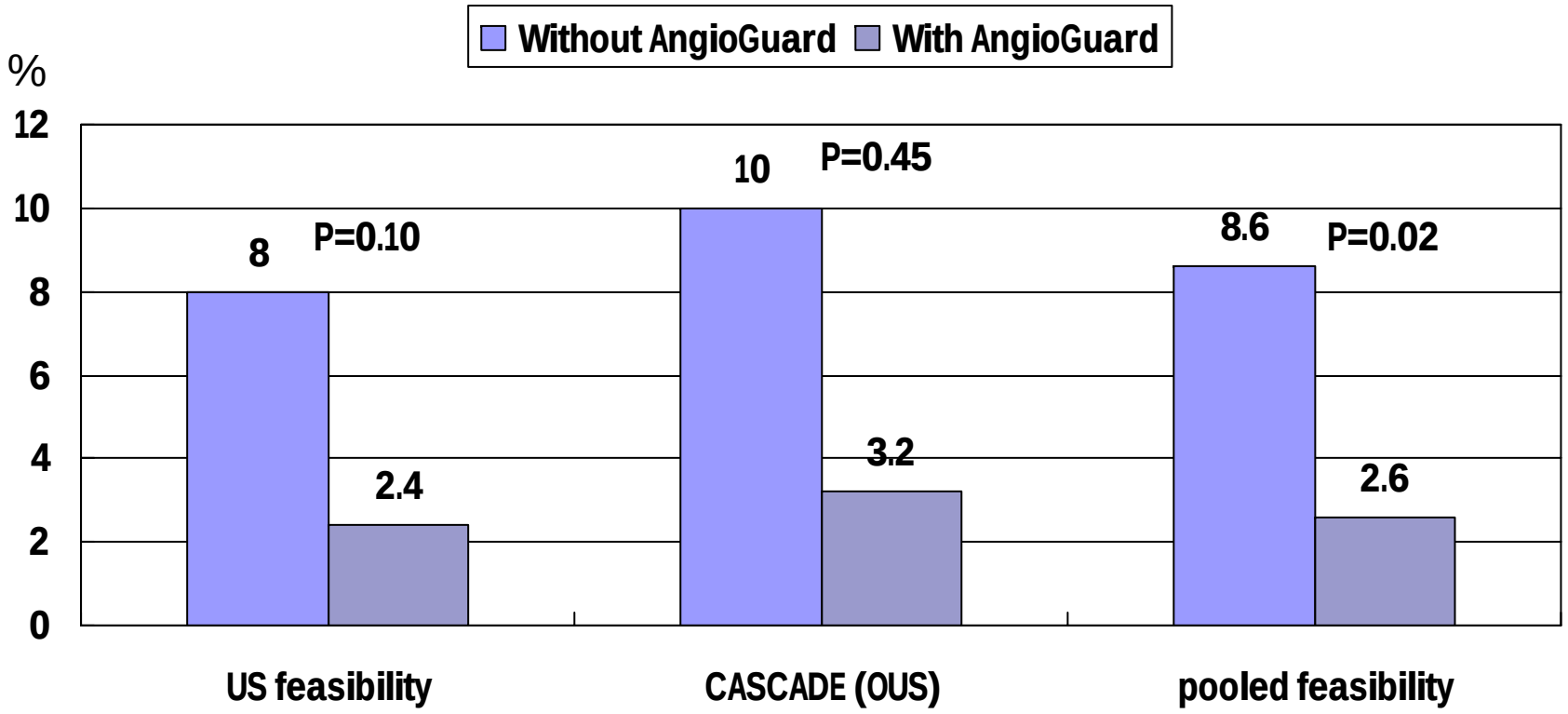


Wholey et al. CCI 2003

NTUH CS experience

530 lesions in 451 patients	N (%)
Technical success	517 (97.5)
Right/left ICA	272/258 (51/49)
Symptomatic	322 (61)
NASCET exclusion	281 (53)
30d stroke/death	20 (3.8)
1y stroke/death	38 (7.2)
1y restenosis	17 (3.3)

Is EPD necessary in CS?



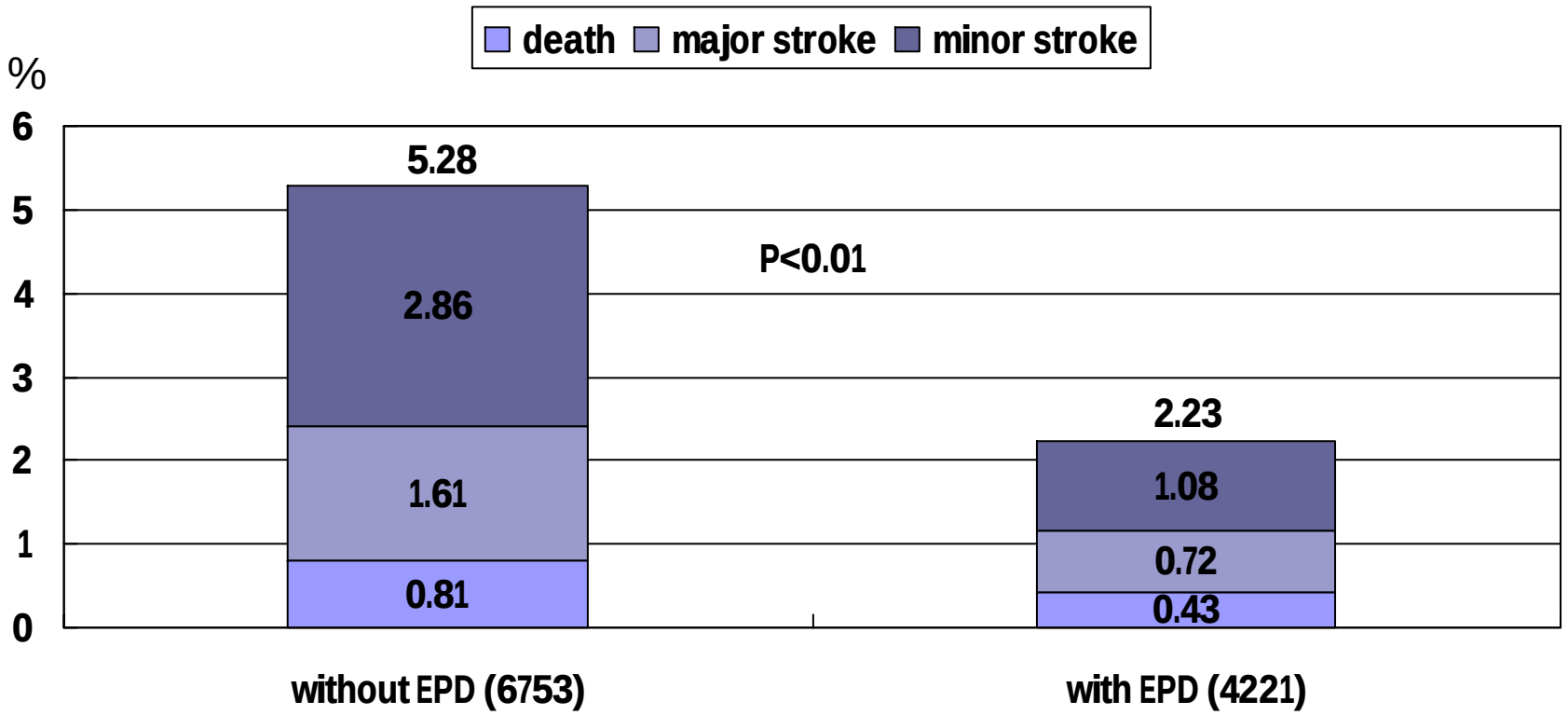
Meta-analysis on EPD effect

- 30d results of stenting series published in 1996-2003

	without EPD	with EPD
n	2537	896
Minor stroke (%)	3.7	0.5
Major stroke (%)	1.1	0.3
Death (%)	0.7	0.9
Any stroke/death	5.5	1.8

Kastrup et al. Stroke 2003

Global experience of EPD on 30d events



Wholey MH, et al. CCI 2003

NTUH experience on EPD

	Unprotected (n=175)	Protected (n=355)
Age (y)	72±8	74±8
Symptomatic (%)	65	61
CCA diameter (mm)	7.5±1.2	7.6±0.9
ICA diameter (mm)	5.4±0.8	5.5±0.7
Lesion length (mm)	21±9	20±9
DS (%)	86±10	89±10
Tech. success (%)	97.1	97.7
Proc. stroke/death (%)	5.1	3.2
ipsi. stroke (%)	4	1.8

SAPPHIRE RCT 30d results

	CS (n=159)	CE (n=151)	P
Death	1 (0.6)	3(2.0)	0.29
Stroke	5 (3.1)	5 (3.3)	0.94
major ipsi	0	2 (1.3)	0.15
major non-ipsi	1 (0.6)	1 (0.7)	0.97
minor ipsi	4 (2.5)	1 (0.7)	0.20
minor non-ipsi	1(0.6)	1 (0.7)	0.97
MI	3 (1.9)	10 (6.6)	0.04
Q	0	2 (1.3)	0.15
Non-Q	3 (1.9)	8 (5.3)	0.11
DSM	7 (4.4)	15 (9.9)	0.06
Major vascular complication	2 (1.3)	1 (0.7)	0.60

Yadav et al. NEJM 2004

SAPPHIRE RCT 1y results

	CS (n=159)	CE (n=151)	P
Death	11 (7.0)	19 (12.9)	0.08
Stroke	9 (5.8)	11 (7.7)	0.52
major ipsi	0	5 (3.5)	0.02
major non-ipsi	1 (0.6)	1 (0.7)	0.97
minor ipsi	6 (3.8)	3 (2.2)	0.37
minor non-ipsi	3 (2.0)	3 (2.1)	0.89
MI	4 (2.5)	12 (8.1)	0.03
Cranial nerve palsy	0	8 (5.3)	0.003
TVR	1 (0.7)	6 (4.6)	0.04
30d DS + 1y ipsi S + 1y neuro D	8 (5.1)	11 (7.5)	0.40
30d DSM + 1y ipsi S+ 1y neuro D	19 (12)	30 (20.1)	0.05

Yadav et al. NEJM 2004

CAPTURE vs. ARCHeR (real-world vs. elite)

30d events	CAPTURE (n=2500)	ARCHeR (n=581)
Death/stroke/MI	5.7	8.3
Death	1.6	2.1
Stroke-related death	0.8	0.5
All stroke	4.2	5.5
Major stroke	1.7	1.5
Minor stroke	2.6	4.0
MI	0.9	2.4
All stroke and death	5.1	6.9
Major stroke and death	2.5	2.9

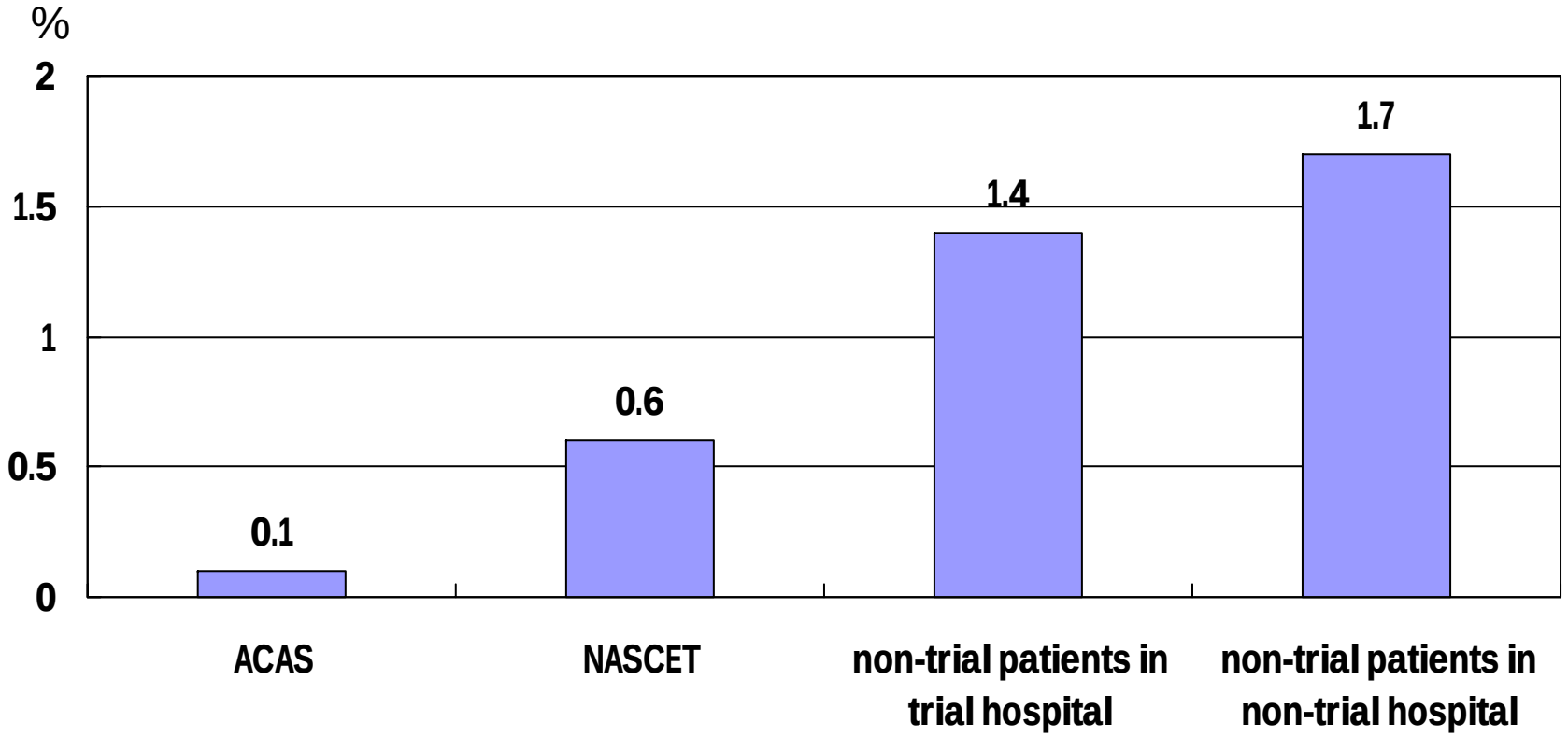
Gray et al. ACC 2006

CAPTURE operator experience

	High (n=226)	Medium (n=1770)	Low (n=504)
Death/stroke/MI	6.2	5.8	5.4
Death	0.0	1.7	2.0
All stroke	5.8	4.2	3.8
Major stroke	1.3	1.8	1.6
Minor stroke	4.4	2.5	2.2
MI	0.4	0.9	1.2
Stroke/death	5.8	5.1	4.6
Major stroke/death	1.3	2.7	2.4

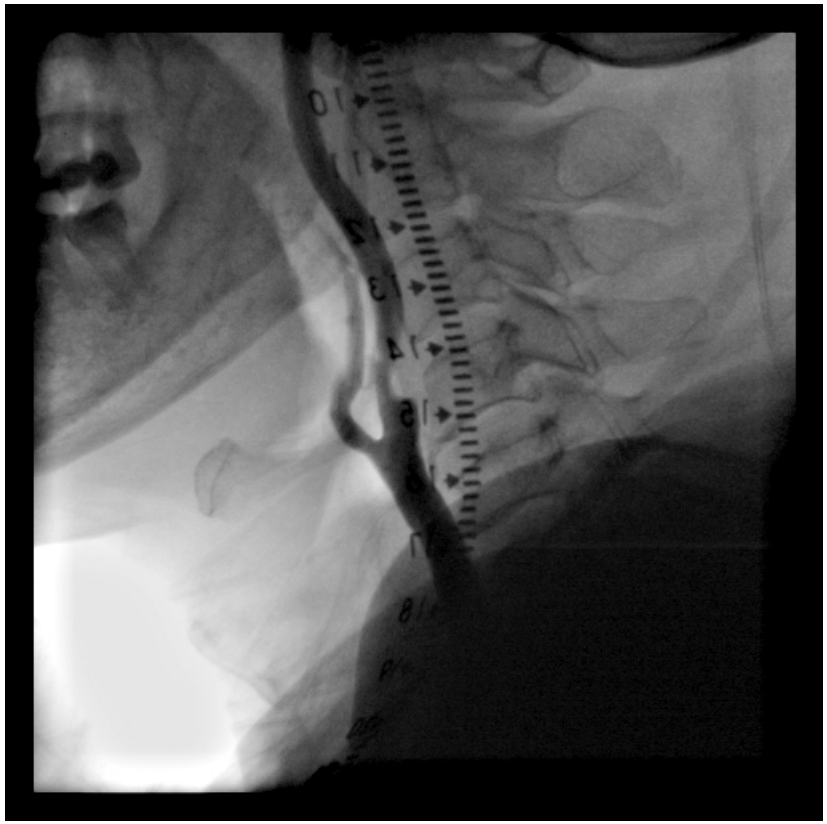
Gray et al. ACC 2006

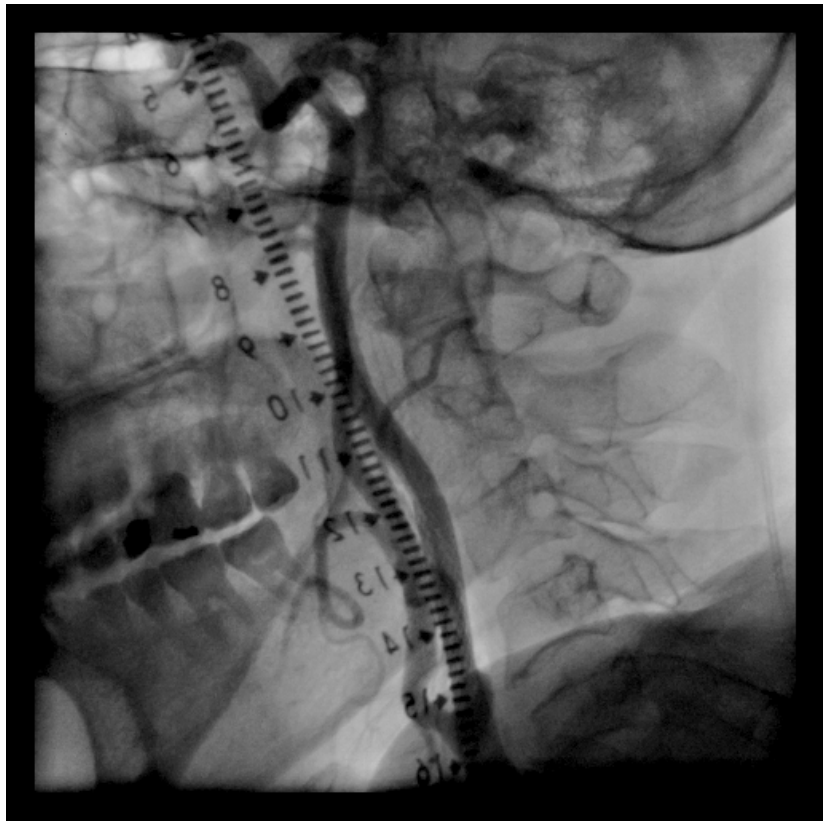
30d CE mortality: the harsh real-world



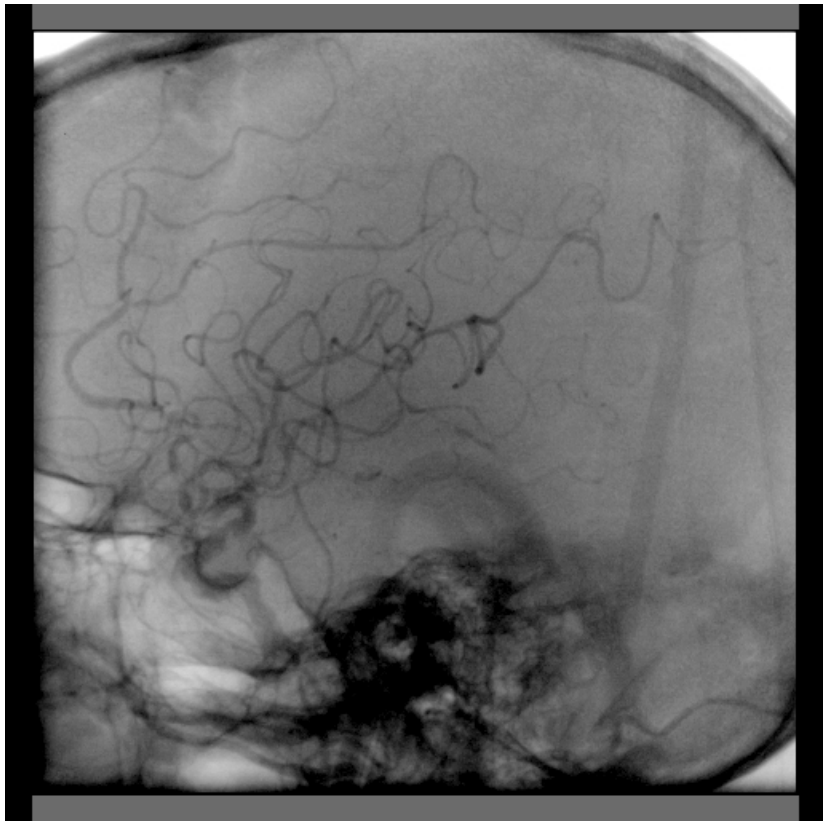
Wennberg et al. JAMA 1998

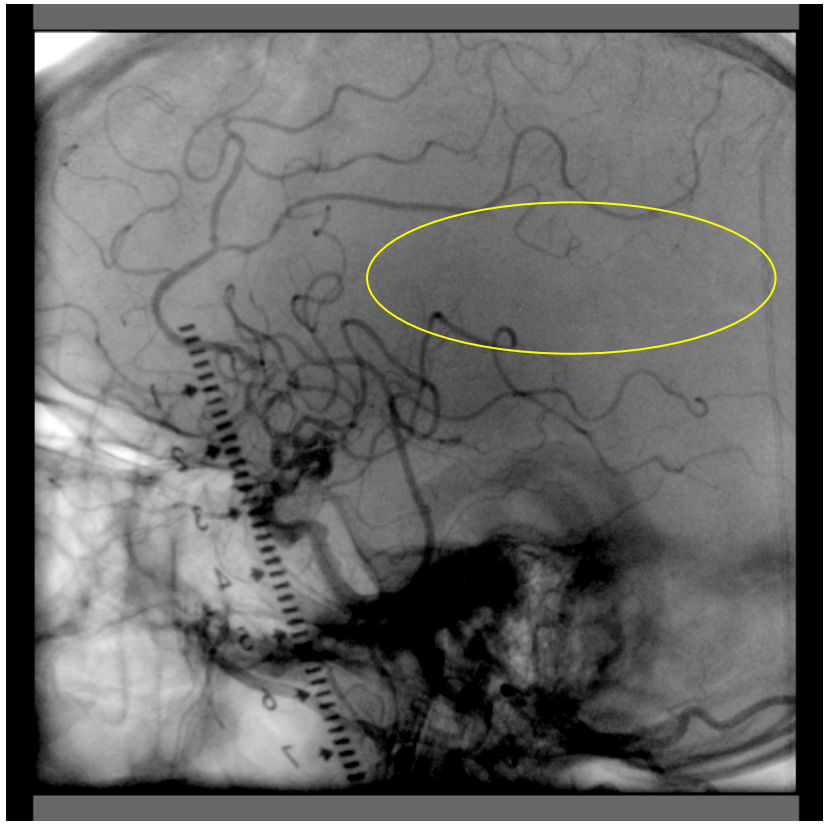
Routine RICA CS, but aphasia on table



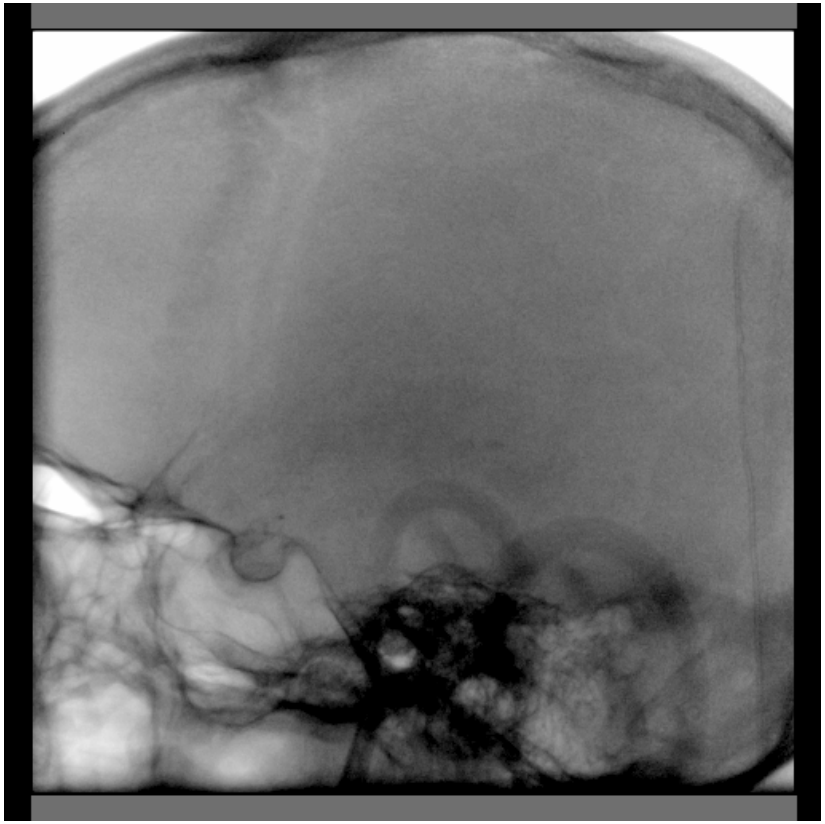


A closer look

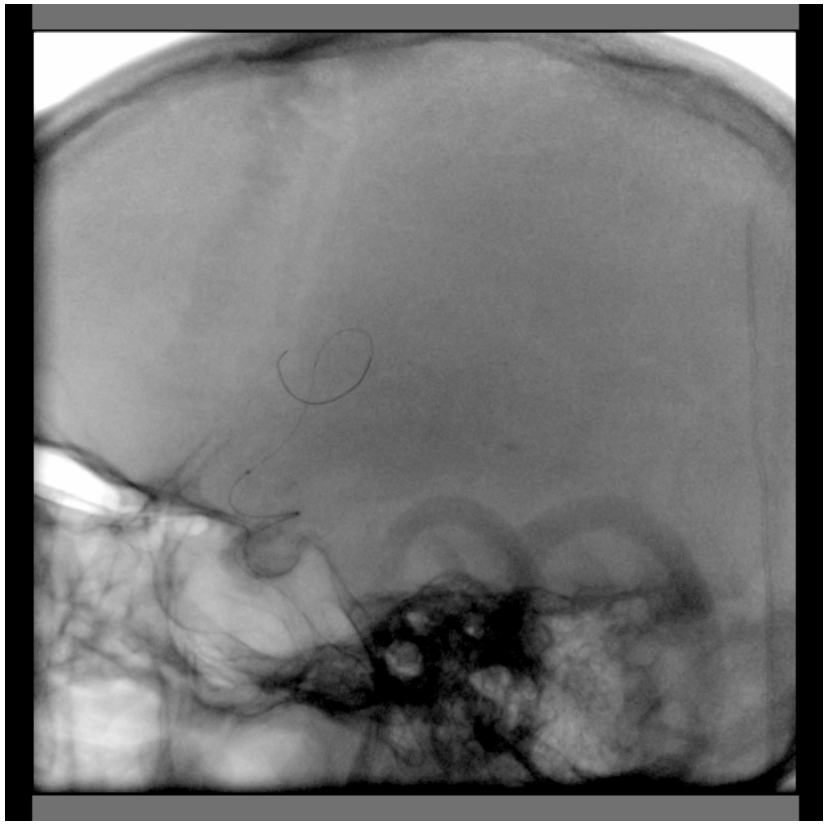


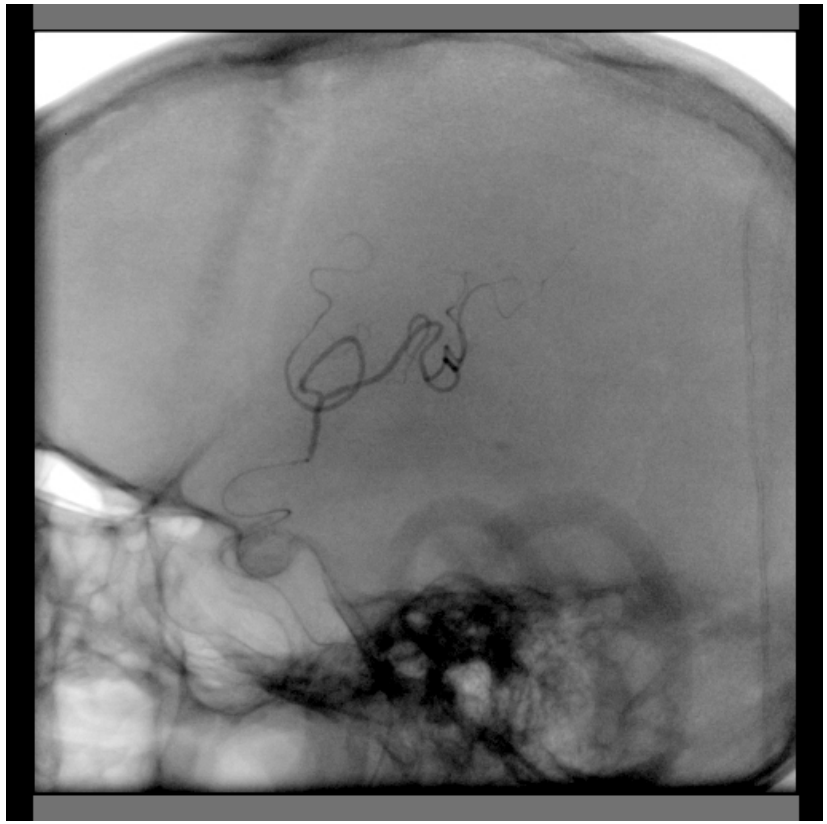


rt-PA 20mg via microcatheter in vain

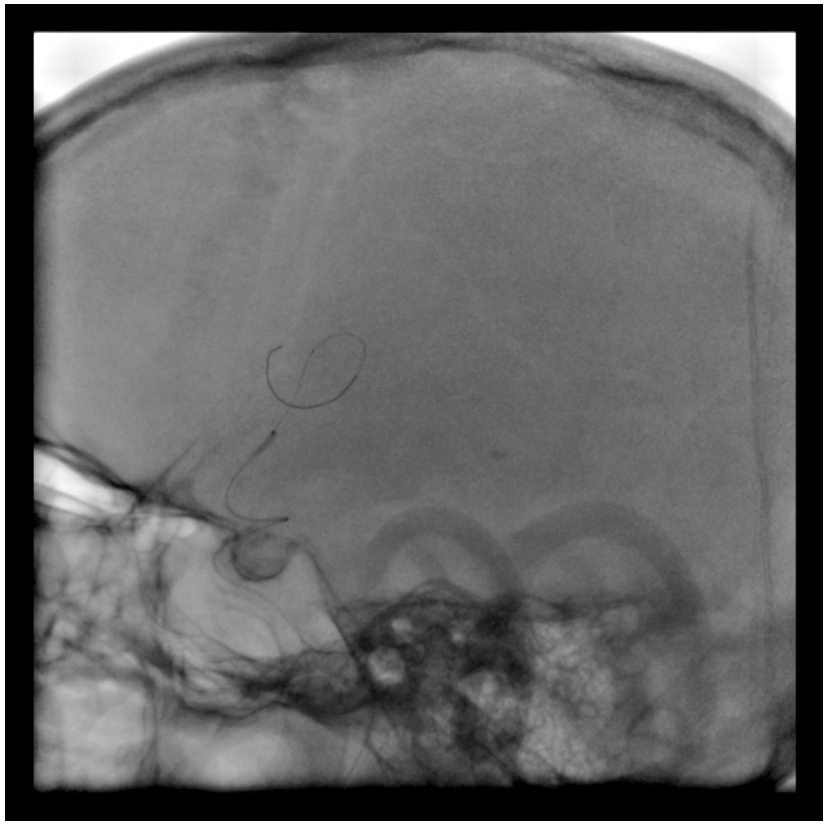


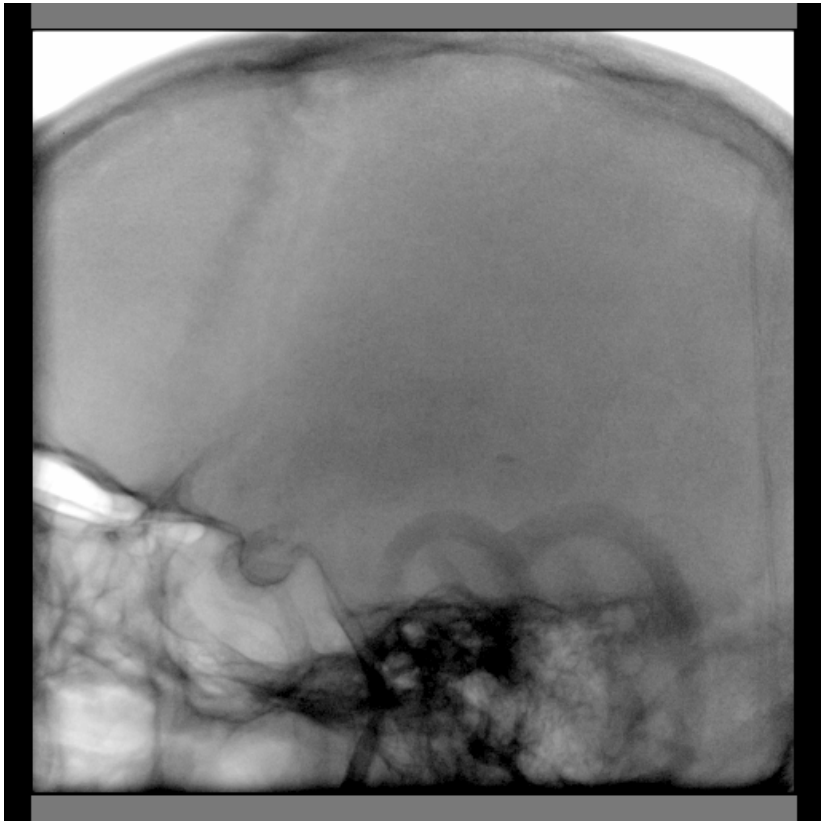
Guidewire advanced and confirmed



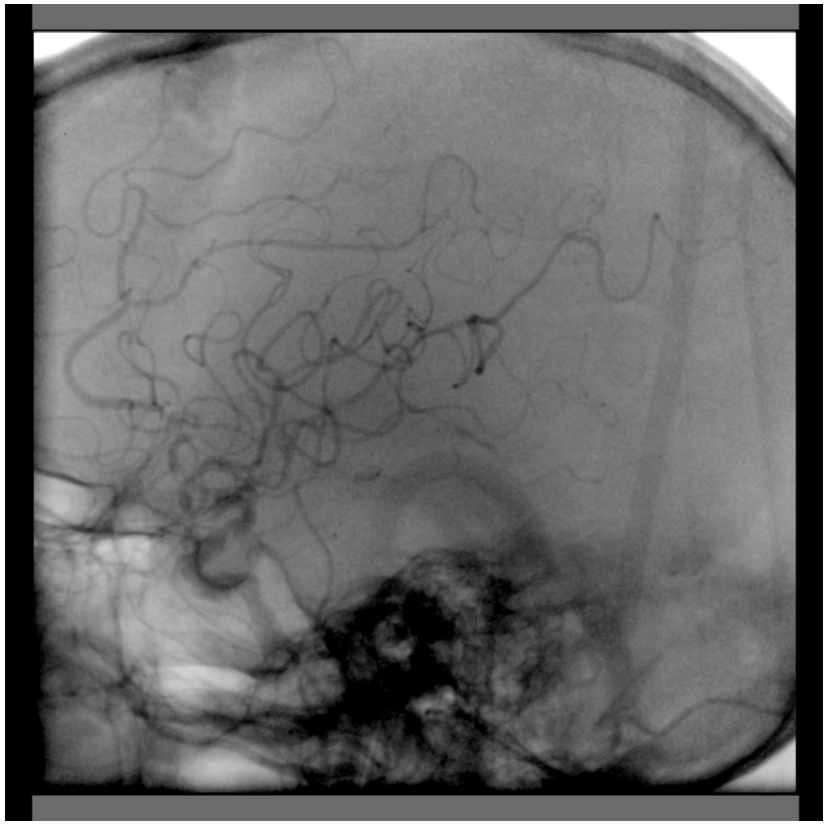


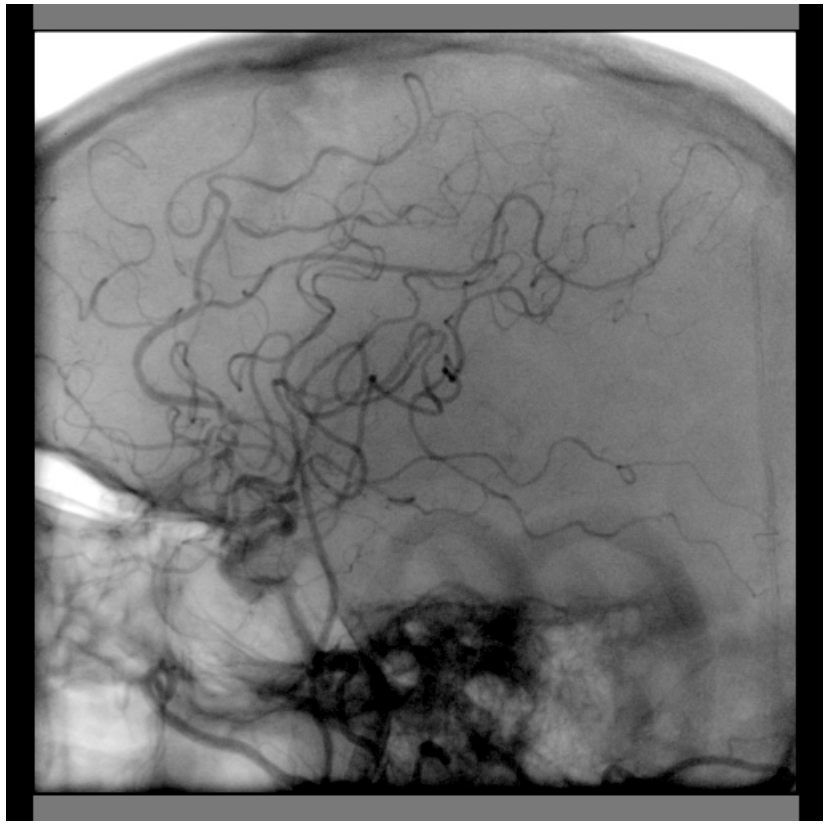
Angioplasty restoring flow after 40’





Comparison of baseline and final



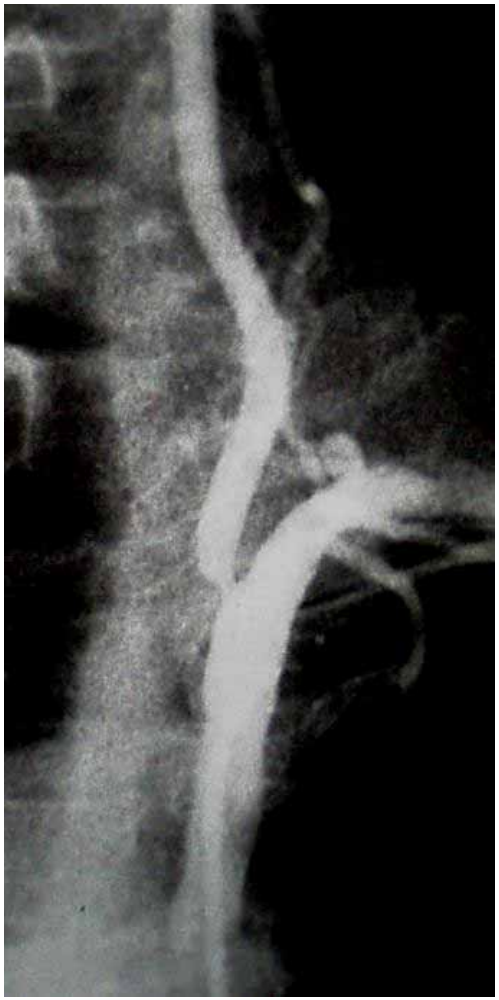


Current practice in NTUH

- Angiography for patients with >50% diameter stenosis (DS) on neck ultrasound
- Indication for stenting
  - Symptomatic DS>50%
  - Asymptomatic DS>80%
- Reimbursed since 7/04

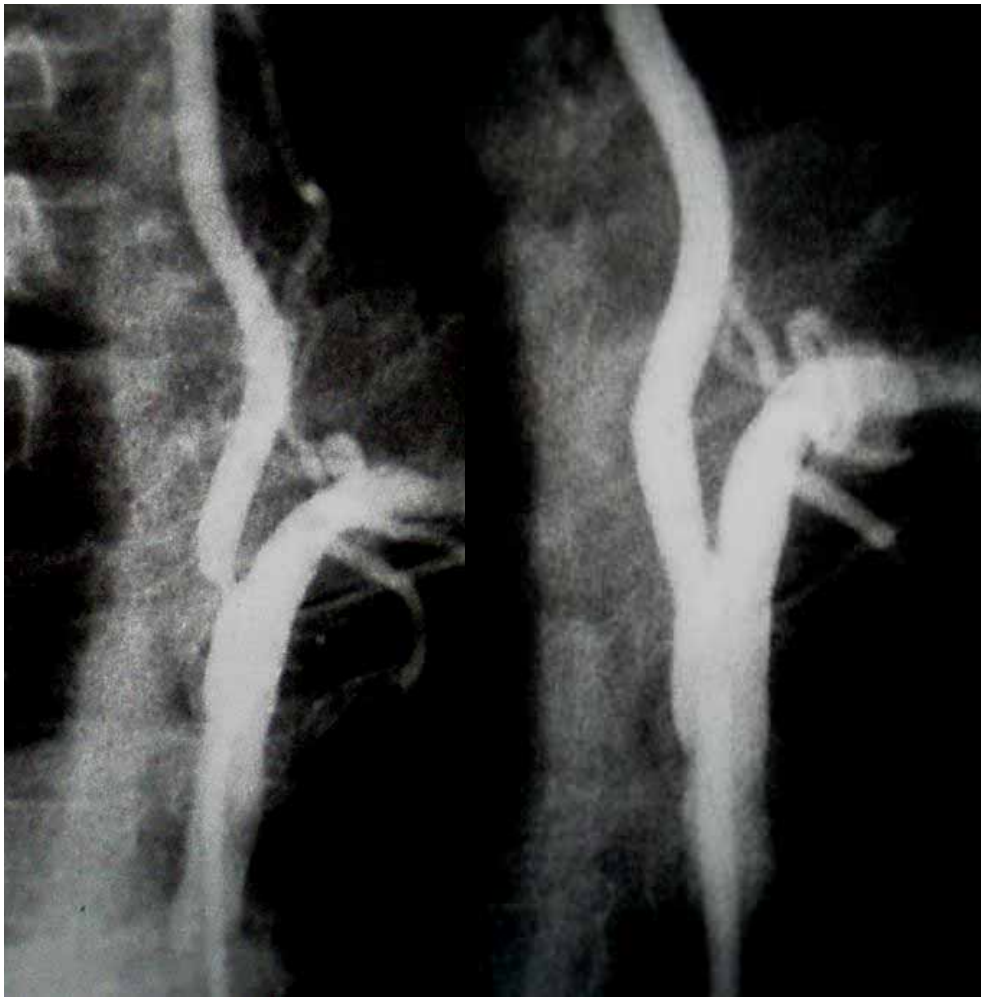
Vertebral artery (VA) stenosis

- Atherosclerotic narrowing, most frequently at ostium
- Extracranial vertebral stenosis may be found in 25-40% of the symptomatic patients
- 5-year survival is 27% lower and stroke rate 8.5-fold higher than control
- Also a major reason for vertebro-basilar insufficiency
- Surgical correction is technically difficult, with high complication rates



Ostial VA stenting

- Technique and device similar to coronary orifice stenting
- Mechanical scaffolding offers luminal patency, with reasonable restenosis rate
- NTUH program started in 3/99



Published VAS stenting case series

Author	Publication	Lesion/pt	30d DS	f/u	Recurrence	ISRS
Chastain et al	J Neurosurg 1999	55/50	4%	25m	4%	10%
Piotin et al	AJNR 2000	7/7	0	NA	14%	NA
Jenkins et al	CCI 2001	38/32	3%	11m	3%	3%
Mukherjee et al	J Invasive cardiol 2001	12/12	0	NA	8.3%	8.3%
Albuquerque et al	Neurosurg 2003	33/33	3%	16m	10%	43%
Overall		**145/134**	**2.8%**		**5.5%**	**14.5%**

Ostial VA stenting

- **58 patients with 67 vertebral artery stentings since 3/99 in NTUH were analyzed**

Angiographic Measurements in 67 Vertebral Arteries

Location right/left	30/37 (45%/55%)
Predilation	15 (22%)
Balloon diameter, mm	3.1±0.8
Reference vessel diameter, mm	4.2±0.6
Lesion length, mm	6.0±2.7
Initial diameter stenosis, %	92±5
Stent diameter, mm	4.2±0.5
Stent length, mm	11.6±3.4
Maximum deployment pressure, atm	16±3
Residual stenosis, %	1±3

Lin, Kao et al. JEVT 2004

Demographics

Patient	N=105 (%)
Age (y)	72.0±8.6
Male/female	85/20 (81/19)
Qualifying symptoms VBI	88 (84)
post stroke	17 (16)
Lesion	**N=118 (%)**
RD (mm)	4.2±0.7
Lesion length (mm)	6.6±3.0
DS (%)	91±10
Final DS (%)	1±4

Clinical results

30d outcome	N=118 (%)
Technical success (%)	118 (100)
MACE	3 (2.5)
Ischemic stroke	3 (2.5)
Death	0
Long-term (>6m) outcome	**N=105 (%)**
New posterior/any stroke	1/2 (1/2)
Death	3 (3)
Neuro death	0
Angio restenosis	12/53 (22.6)

Restensis analysis

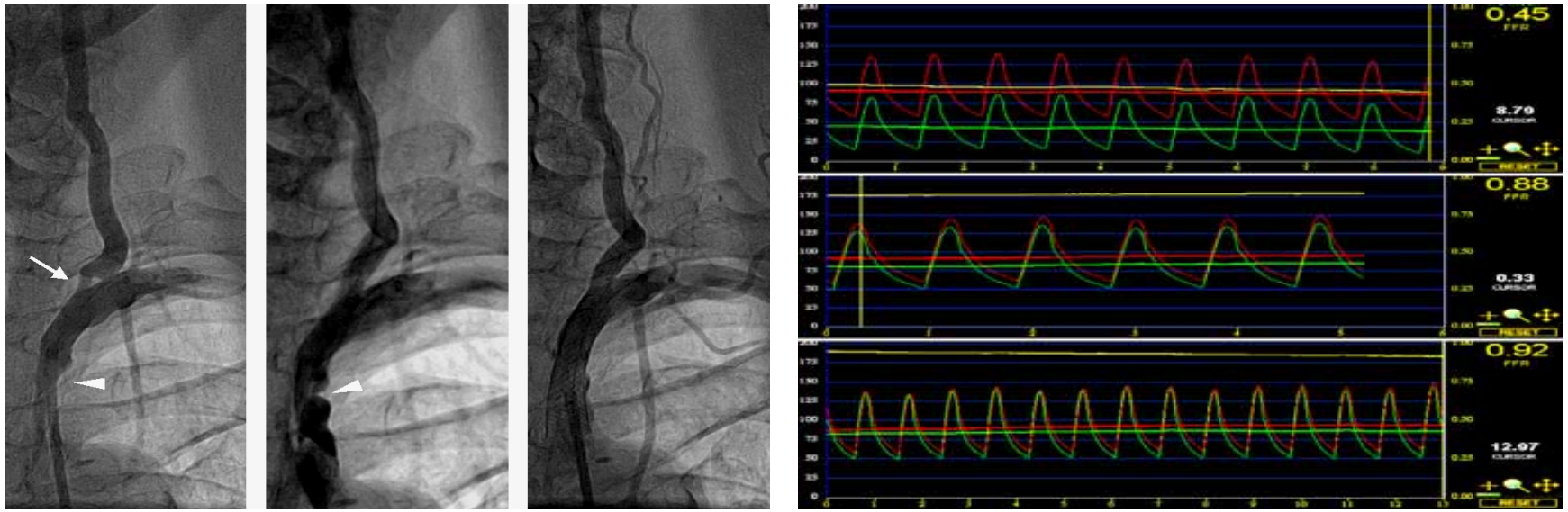
Multivariant Cox Model for Restenosis Risk Factor Identification

	Hazard Ratio (95% CI)	p
Reference vessel diameter, mm	0.03 (0.00 to 0.46)	0.011
Predilation	0.02 (0.00 to 1.93)	0.091
Lesion length, mm	1.64 (0.91 to 2.94)	0.099
Smoking	0.17 (0.02 to 1.58)	0.119
Male sex	0.11 (0.01 to 2.62)	0.172
Stent length, mm	0.75 (0.45 to 1.25)	0.270

- **Reference vessel diameter was the only predictor of restenosis**

Lin, Kao et al. JEVT 2004

PressureWire-guide intervention strategy



Liu, Kao et al. AJNR 2005

Current practice in NTUH

- Angiography for symptomatic patients with >50% DS on CTA or MRA
- Indication for stenting
  - DS>50% in single existing VA supplying basilar artery
  - DS>70% in VA greater than 3.5mm in diameter
- Investigational treatment

Conclusion

- Brain is more vascular than heart, and a paradigm shift is taking place in the treatment of steno-occlusive cerebral vascular diseases
- Interventional concepts, techniques, and devices are now being explored, and “cardiologist” should be actively involved in this process

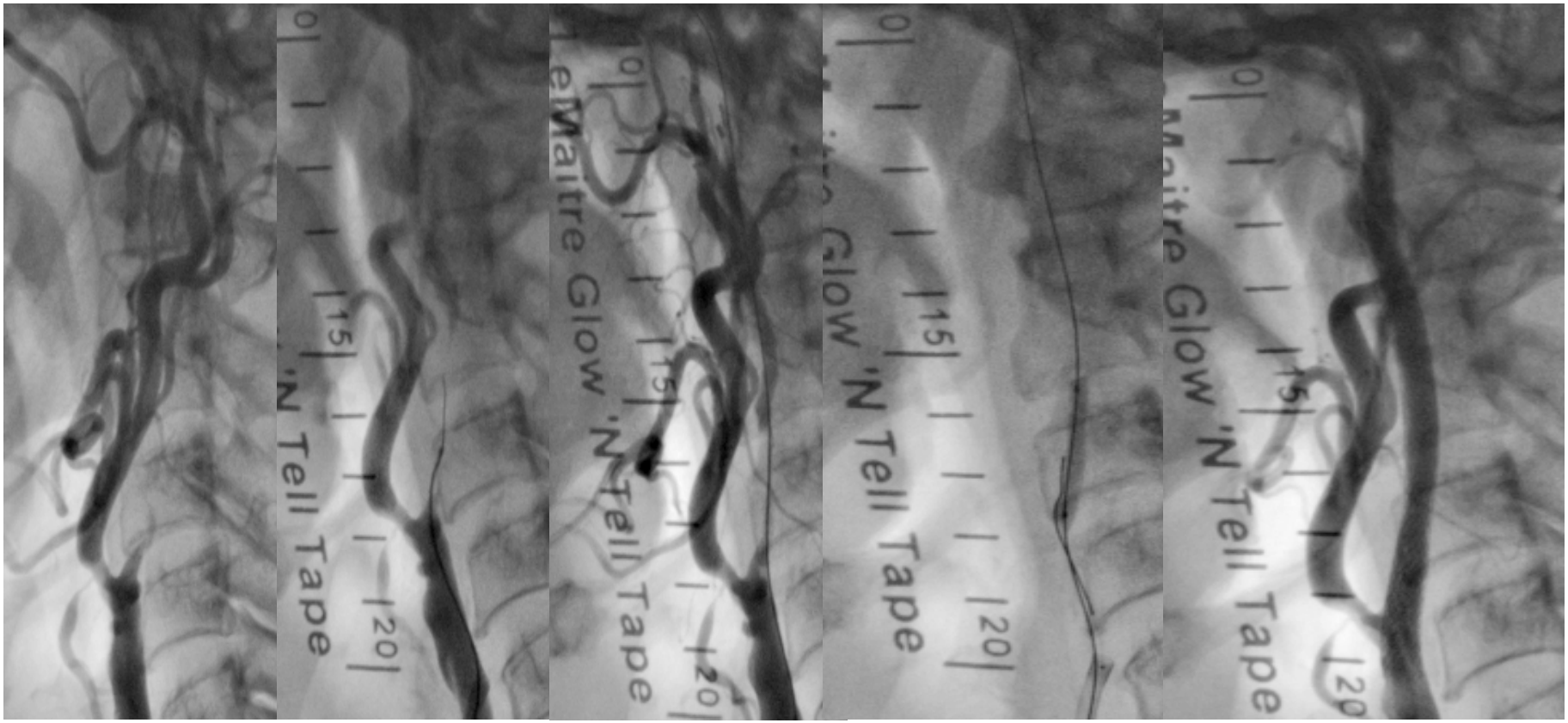
A mind once stretched by a new idea will never regains its original dimension

Oliver W. Holmes

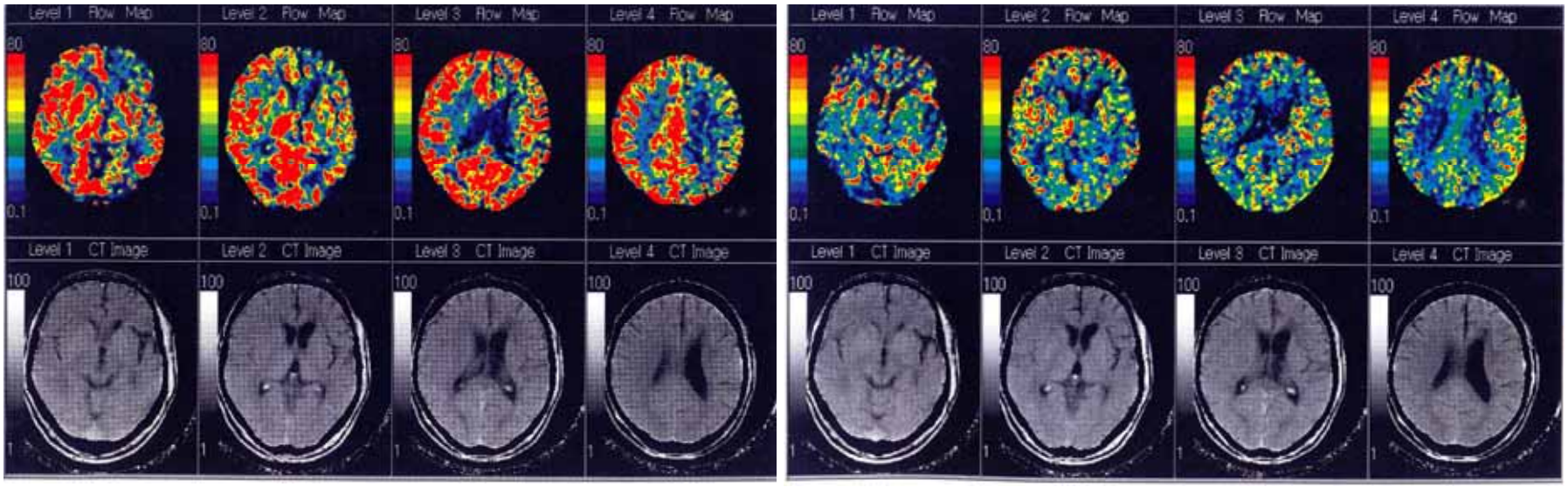
The future – at present tense

- Understanding the carotid plaque
  - Fusion imaging of MR/PET/IVUS
  - Inflammatory markers
- Understanding the cerebral hemodynamics
  - Intravascular pressure wire study
  - Elective recanalization of chronic occlusion
- Acute “cerebral” syndrome
  - Dissection
  - Primary intervention/thrombolysis
- Intracranial diseases

CTO

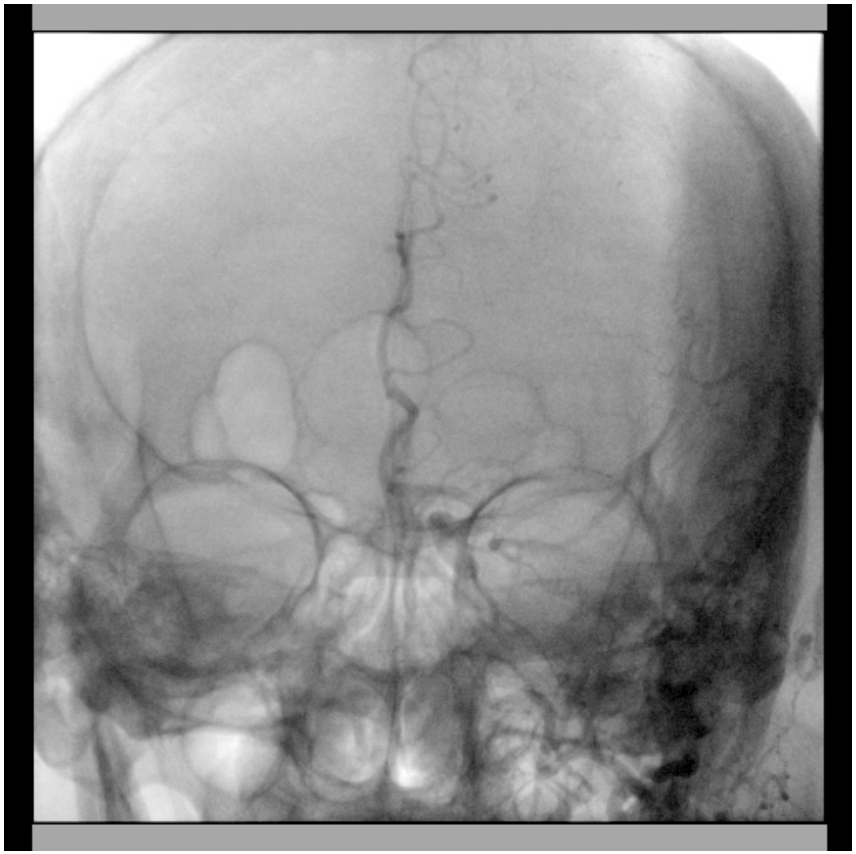


Xe133 perfusion CT

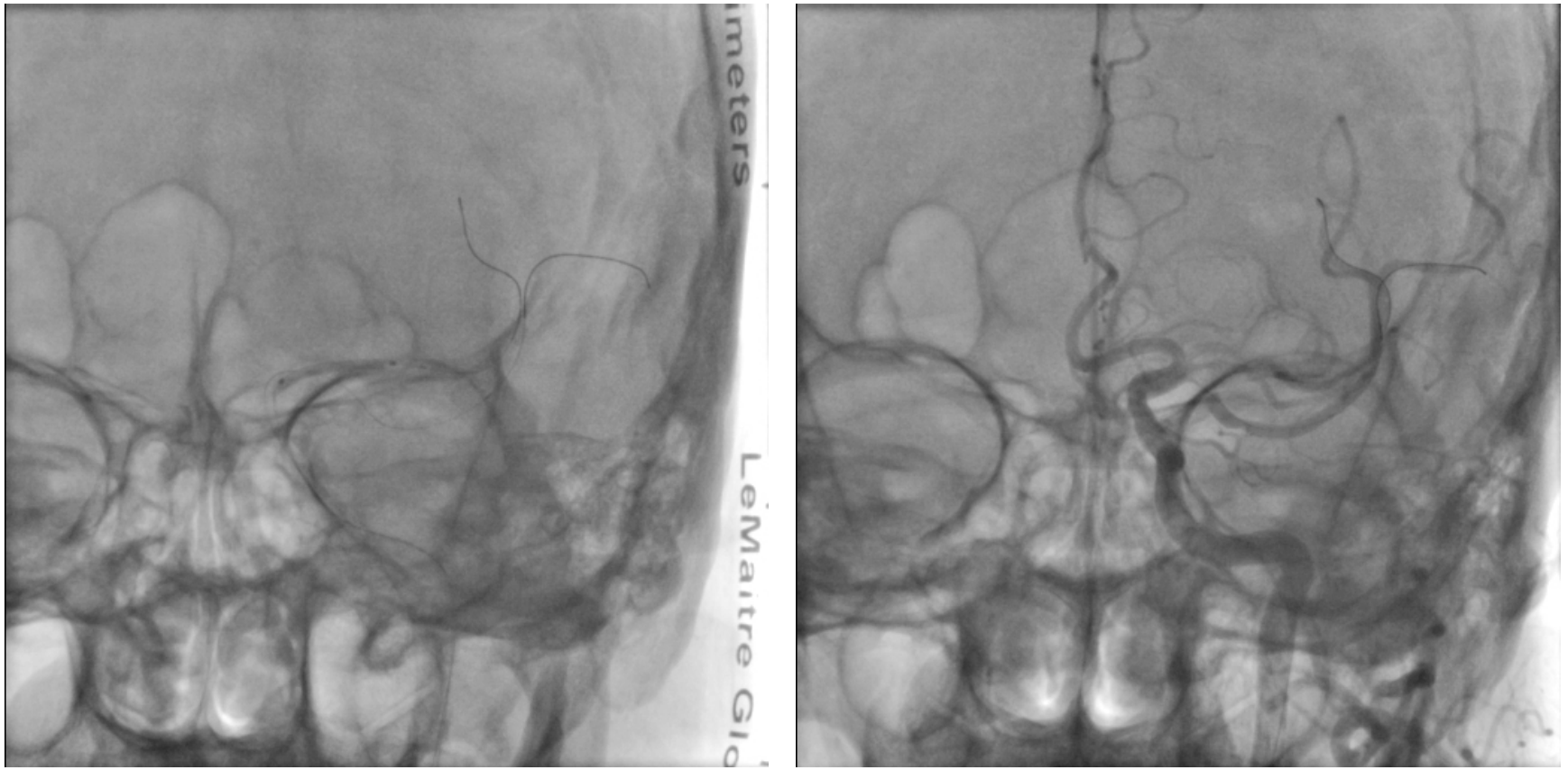


pre post

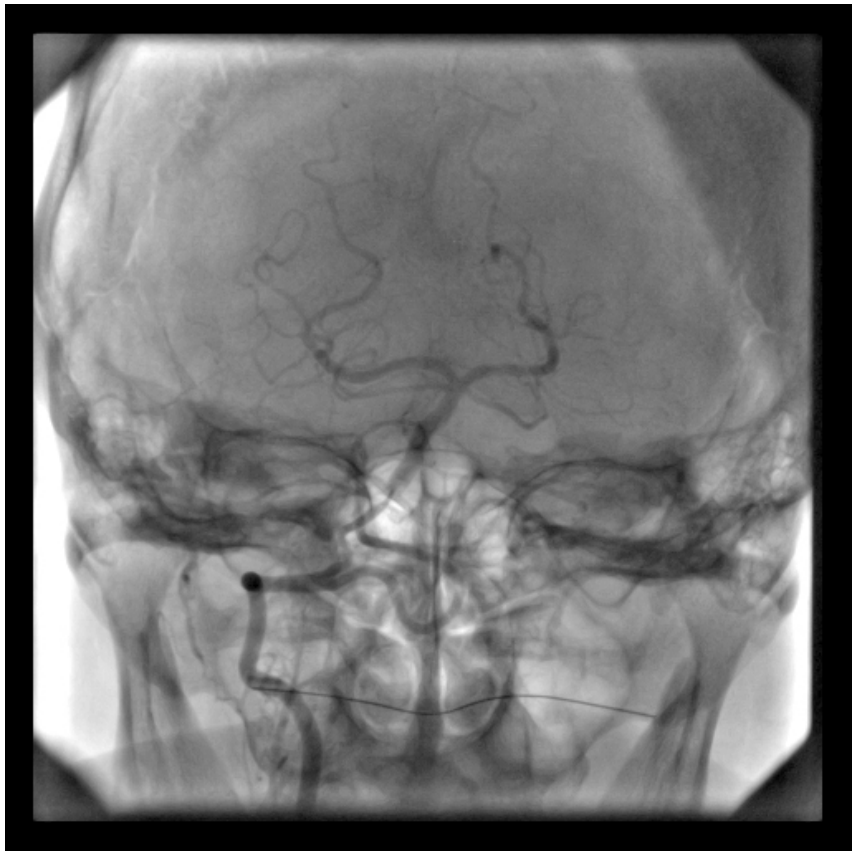
Intracranial disease



Intracranial disease

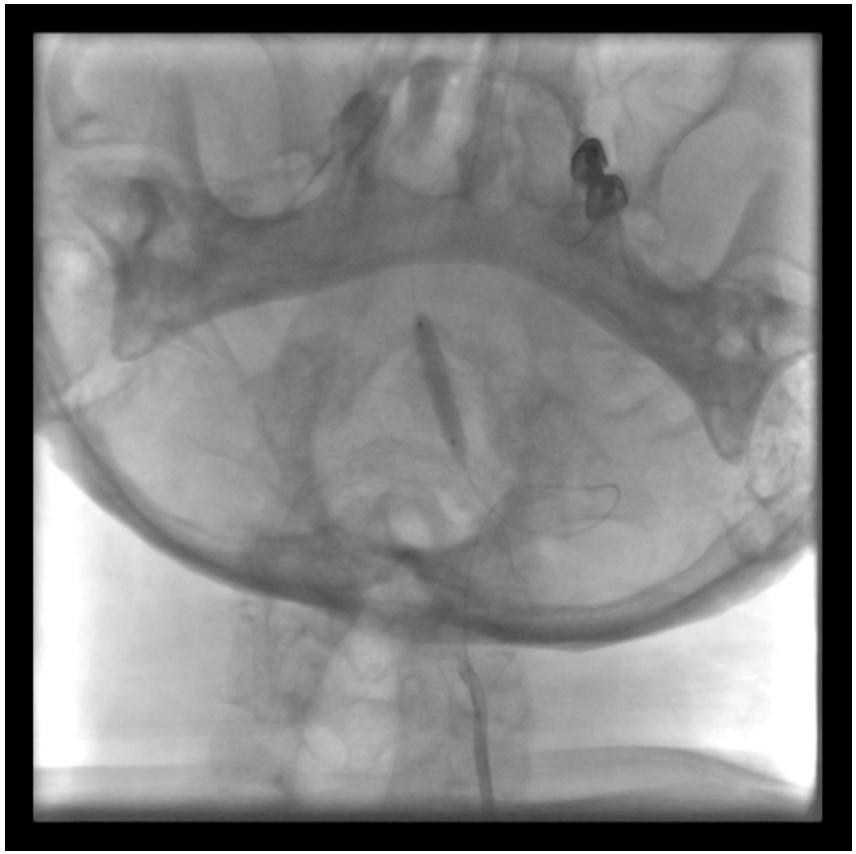


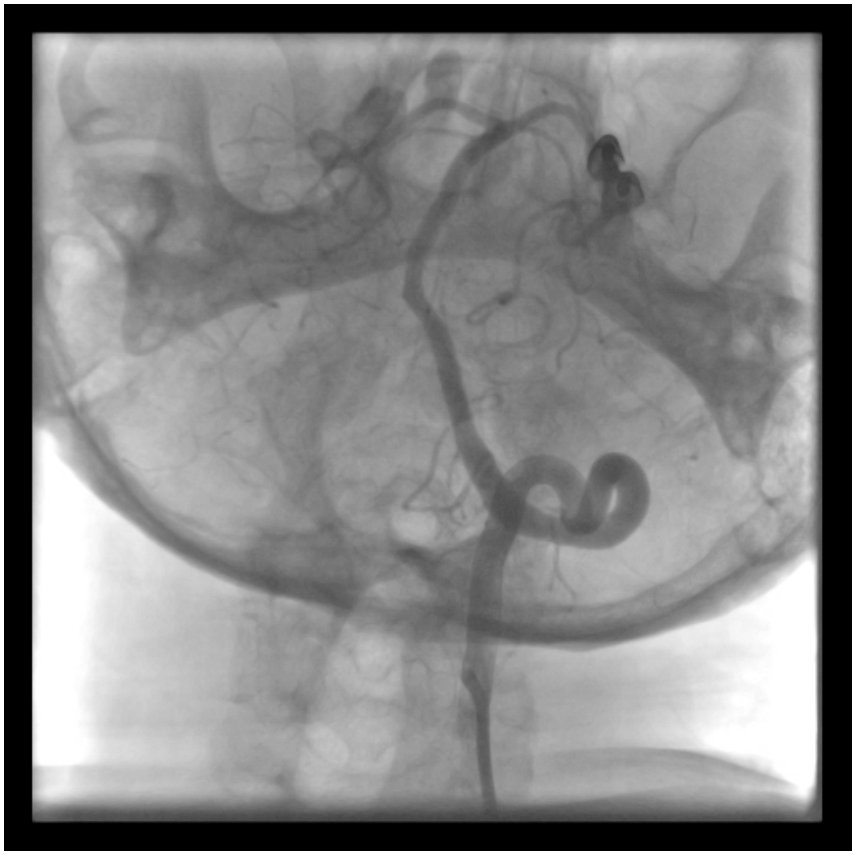
57M with severe VBI



Dissection after balloon

Final result after stenting





Long-term outcome

- 118 consecutive patients from Apr. '98 to Oct. '00 in NTUH

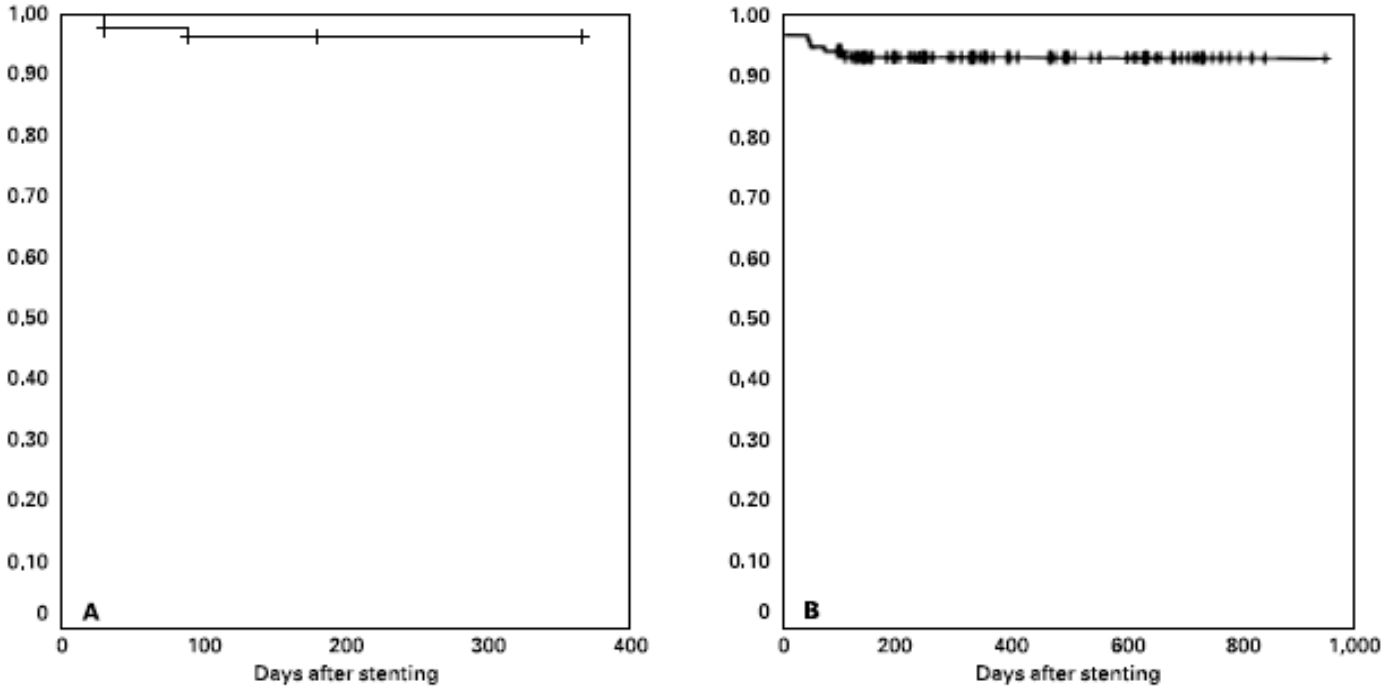


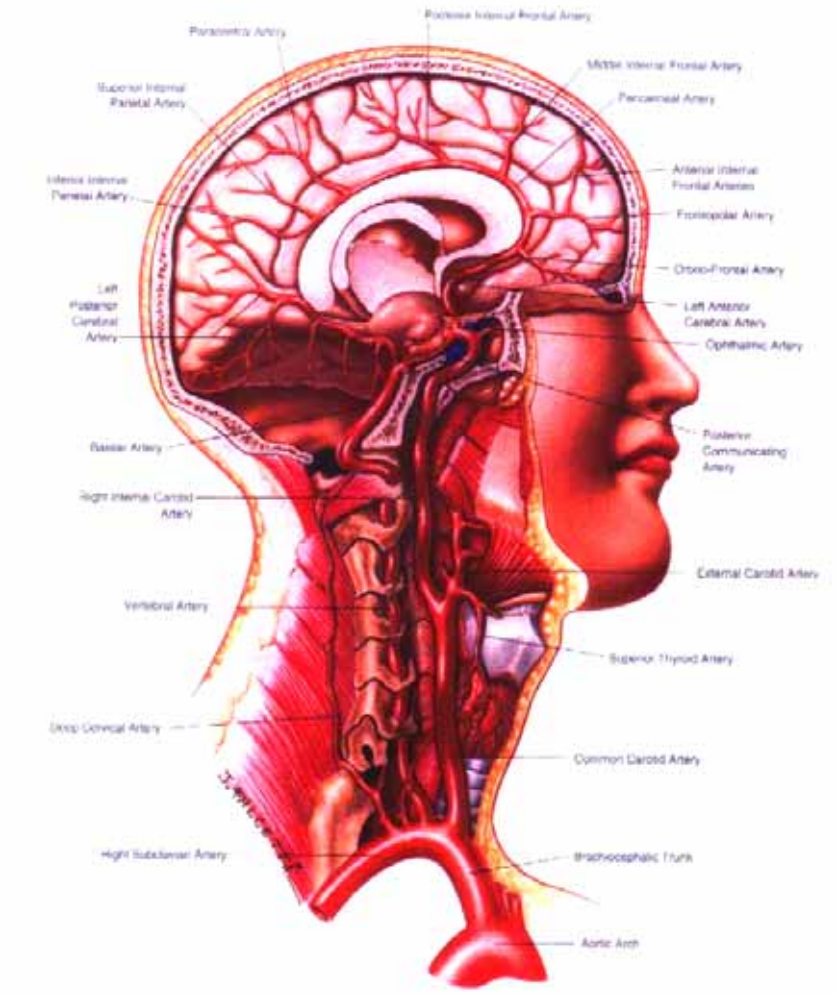
Fig. 2. Survival distribution curve of patients without restenosis (**A**) and any stroke/death during clinical follow-up (**B**).

Paul HL Kao 05

Long-term results of elective stenting for severe carotid artery stenosis in Taiwan. Kao HL, et al. Cardiology 2002;97:89

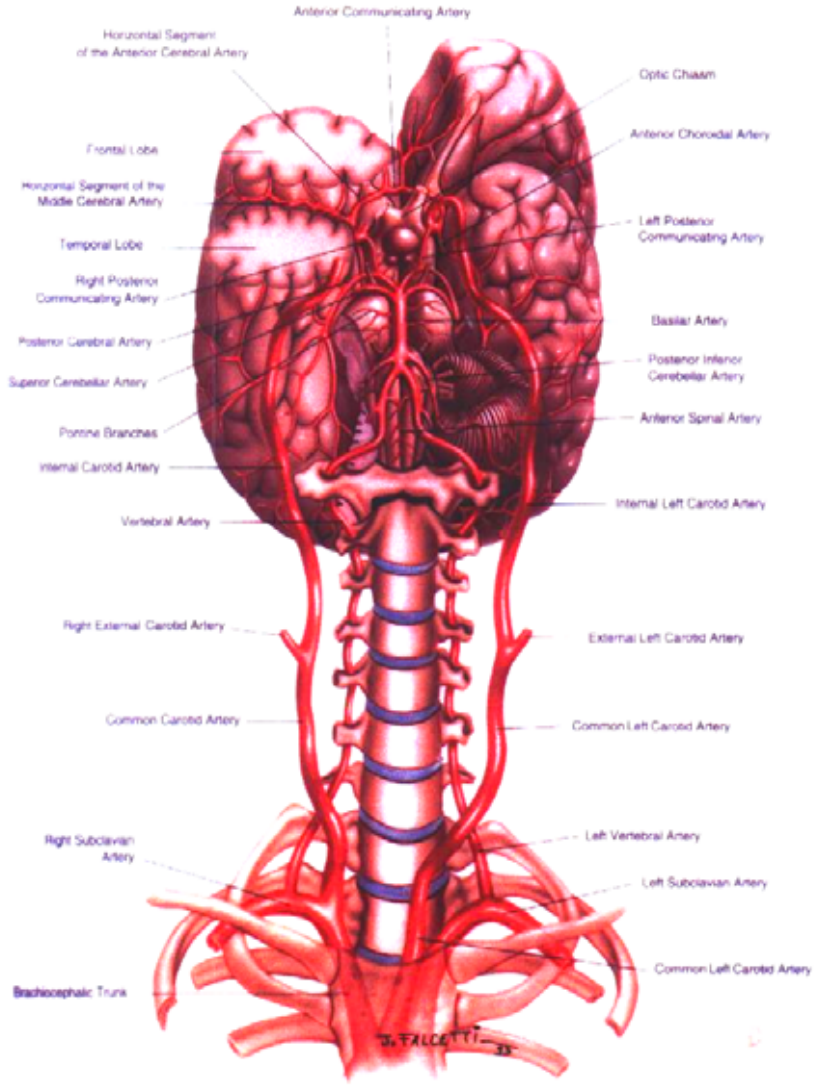
Vasculature of the brain

- Carotid artery system
- Vertebrobasilar system
- Both systems connected mainly via Willis circle



Cerebrovascular disease

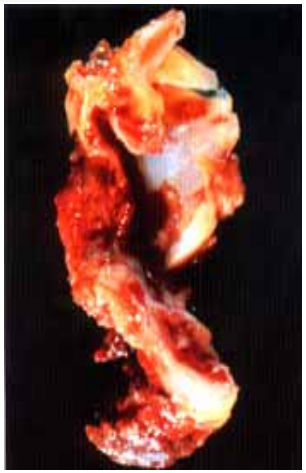
- Congenital
  - Agenesis
  - Persistent embryological vessel
  - AVM
- Acquired
  - Aneurysm
  - AVM
  - Fistula
  - Steno-occlusive lesion
  - Dural sinus thrombosis



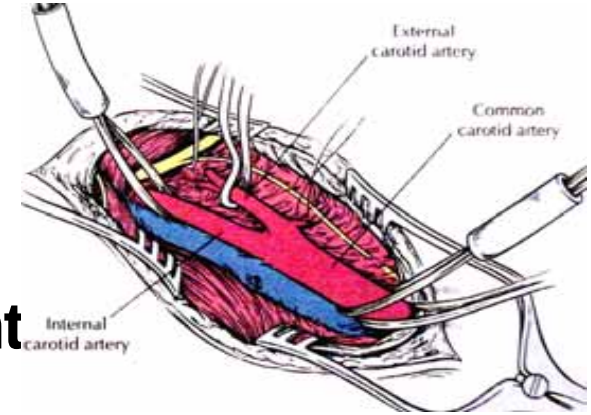
Epidemiology

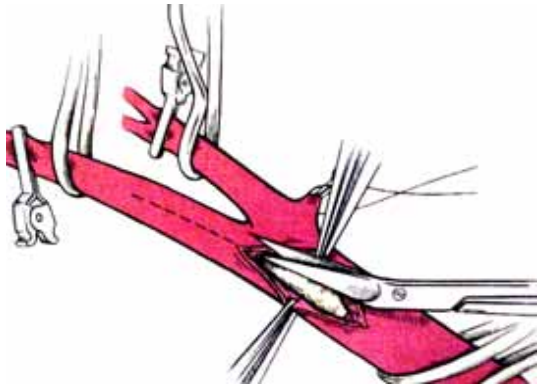
- Annual incidence of first-ever ischemic stroke in Taiwan is approximately 500-600/100000
- Extracranial carotid stenosis is found in 12% of all ischemic strokes, and 20-30% of cerebral infarctions in Taiwan
- Annual stroke rate in patients with symptomatic severe carotid stenosis is 15-30%
- Incidence of asymptomatic severe carotid stenosis in population older than 35 years in Taiwan is 3.7%

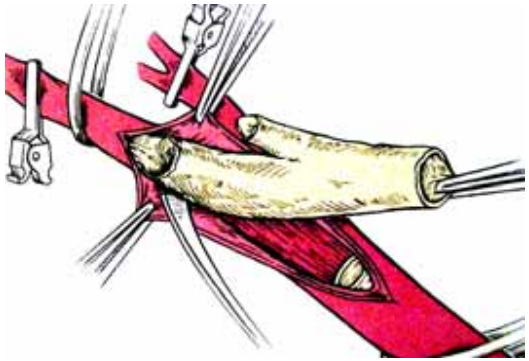
Endarterectomy

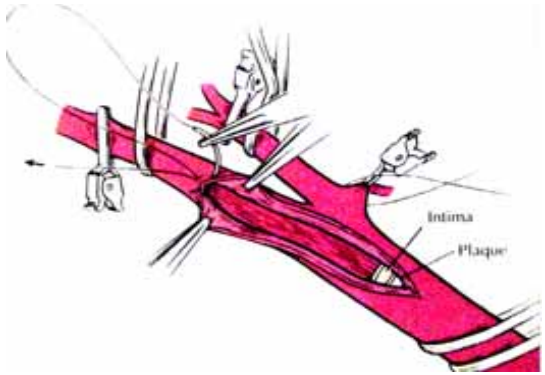


- Offers effective stroke prevention
- 5-8% peri-procedural complication rates in selected patients
- Not proven in all patient subsets
- Impossible in certain clinical or anatomical conditions









Global experience

- 12,393 procedures in 11,243 patients at 53 centers worldwide since '97
- Registry with "real world" demographics
- Technical success rate 98.9%
- 53.2% lesions symptomatic
- Peri-procedural event (%)
  - Minor stroke 2.14
  - Major stroke 1.20
  - Procedure-related death 0.64
  - Non-related death 0.77
  - Total stroke/death 4.75

Wholey MH, et al. CCI 2003;60:259

Demographics

	N=404 (%)
Male/female	323/81 (80/20)
Age (y)	72.5±8.4
HTN	329 (81)
DM	129 (32)
HLP	188 (47)
Smoker	192 (48)
Symptomatic (N=461)	287 (62)
Concurrent CAD	272 (67)
NASCET exclusion	250 (62)

Angiographic data

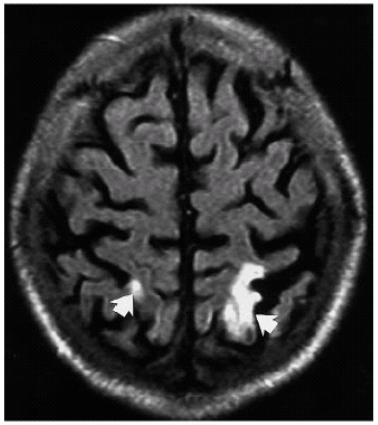
	N=461 (%)
Right/left	233/228 (51/49)
CCA (mm)	7.6±1.0
ICA (mm)	5.5±0.7
Lesion length (mm)	20.0±8.5
DS (%)	89±9
Pre-dilatation	207 (45)
Post-dilatation	409 (89)
Final DS (%)	11±7
Stent per lesion	1.09

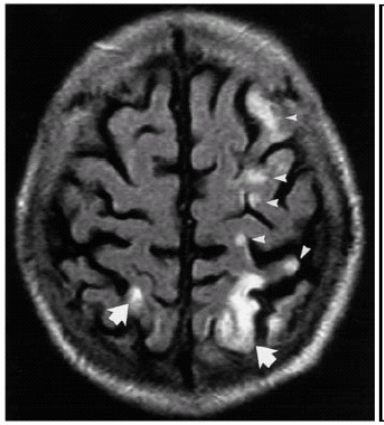
Procedural results

30-day outcome	N=461 (%)
Technical success	455 (98.7)
MACE	16 (3.5)
ipsi stroke	9
ipsi ICH	1
non-ipsi stroke	5
non-ipsi ICH	1
death	2
myocardial infarction	0

Why embolic protection necessary?

- CS registries have shown procedural complication rate of 5%, and procedural embolism is the main cause
- Embolic materials are released in all steps of CS
- Embolism may be silent or symptomatic, identification and salvage may be difficult





Postprocedural Clinical Signs and MR Imaging Findings

Clinical Signs	MR Imaging Findings: No New Lesions	MR Imaging Findings: New Lesions	Total
No clinical signs	55	6	61
Transient monocular blindness	3	...	3
TIA	2	2	4
Major stroke	...	2	2
Minor stroke	1	1	2
Total	61	11	72

Note.—Data are numbers of patients.

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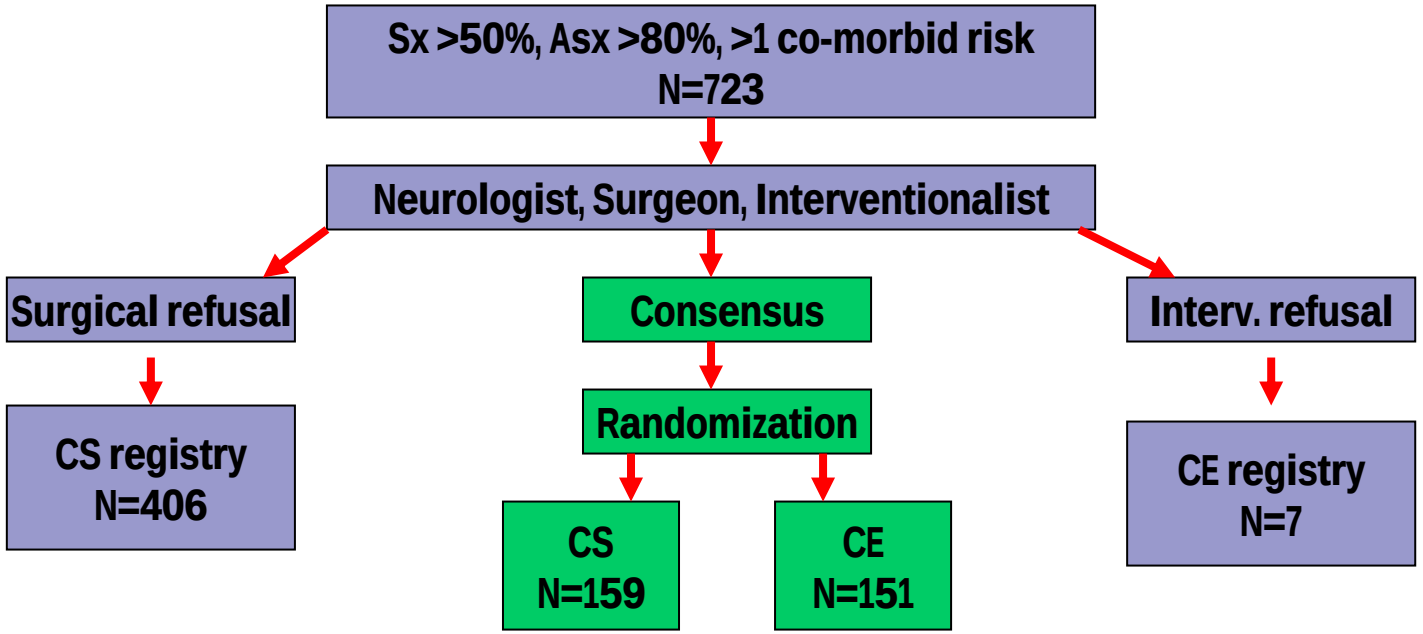
SAPPHIRE trial

Yadav et al. N Engl J Med 2004

- Parallel randomized comparison and registries of CS under protection vs. CE in 29 US sites
- Designed to look at real-world and randomization-eligible patients



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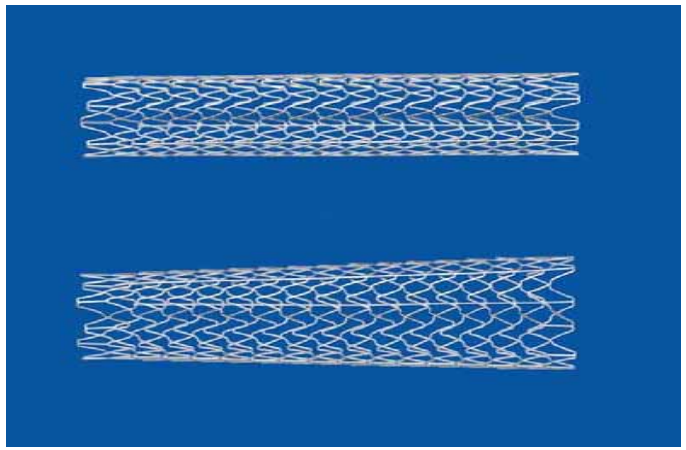
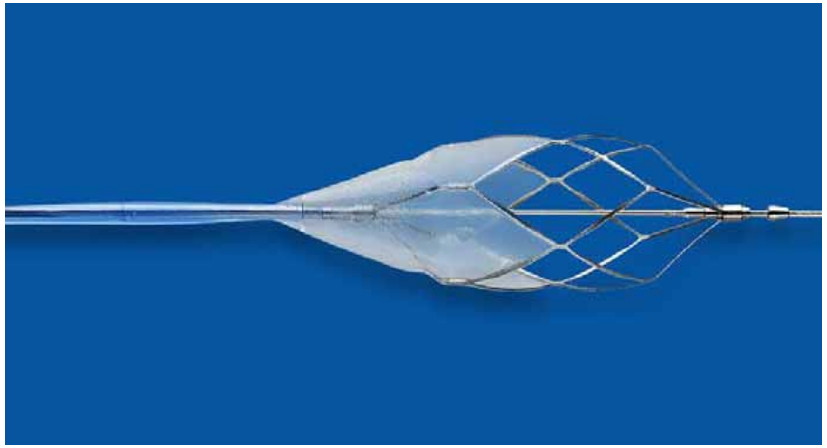
CAPTURE

- FDA-mandated post-approval surveillance
- 2500 patients in 137 US sites
- Devices used: Guidant Accunet and Acculink
- Reported in ACC 06

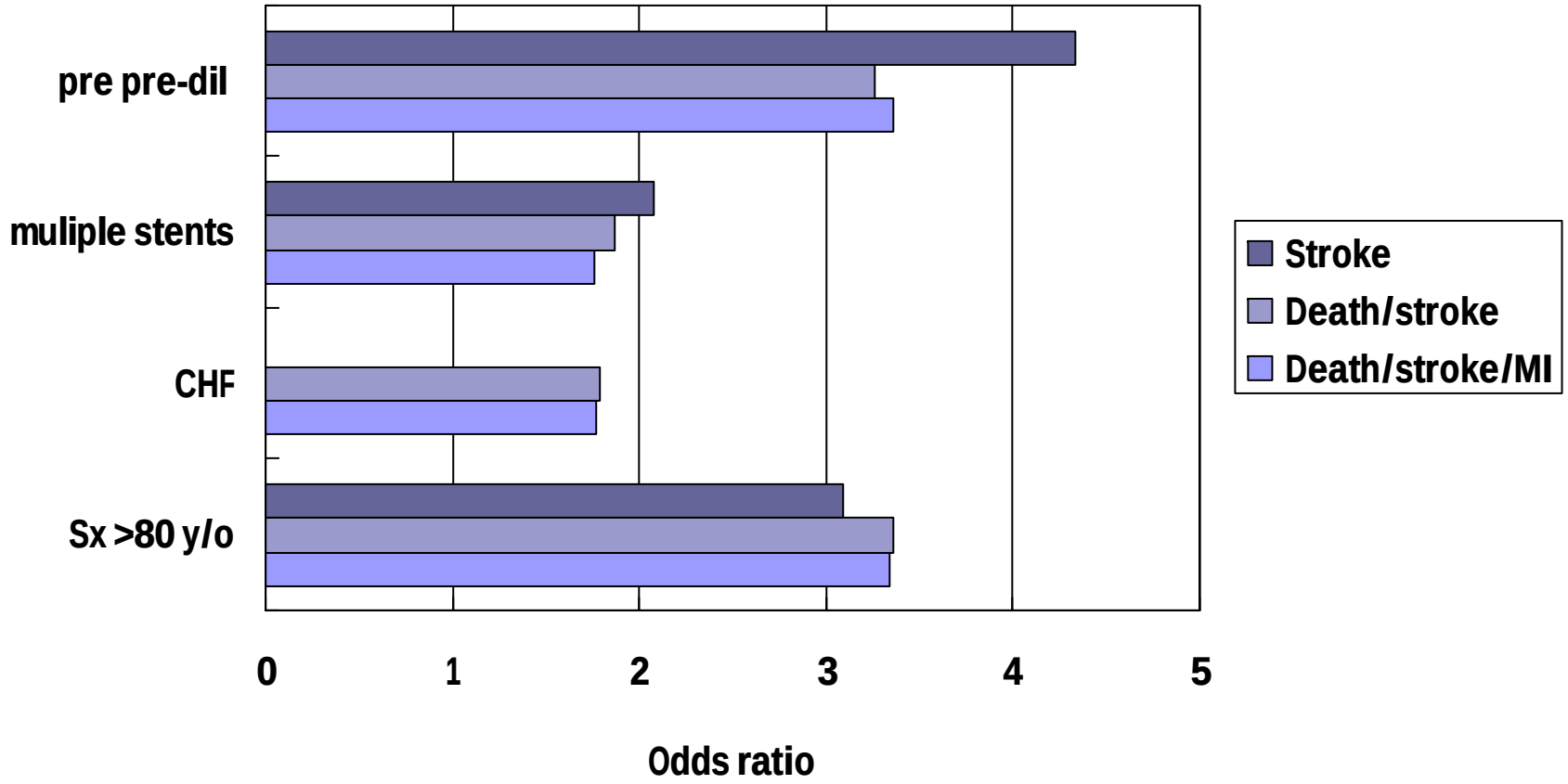




Patient demographics

	CAPTURE N=2500	ARCHeR N=581
Age *	72.8	70.3
>80 y/o *	23.8	15.5
>65 y/o *	81.0	72.5
Symptomatic *	9.3	23.8
Male *	61.1	67.1
DM	34.7	37.9
HTN *	88.5	83.8
HLP *	78.9	72.6
CHF *	14.9	33.6
Anatomic *	7.7	19.3
Smoker	20.0	19.3
PVD	34.7	36.3
Renal failure *	5.7	2.9

CAPTURE predictors for events



30d event rates in symptomatic patients

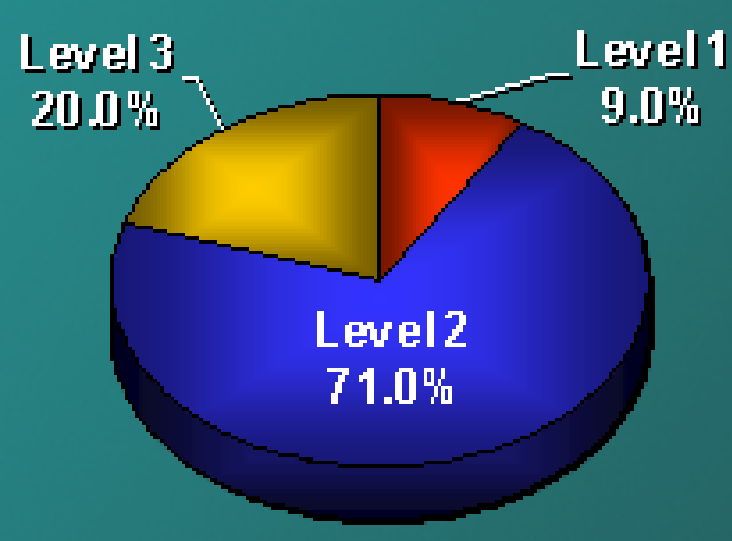
	CAPTURE	ARCHeR
Death/stroke/MI	14.2	13.0
Death	4.3	2.2
Stroke-related death	3.4	1.4
All stroke	11.2	10.9
Major stroke	5.2	4.3
Minor stroke	6.4	6.5
MI *	2.6	2.2
All stroke and death	12.0	11.6
Major stroke and death	6.0	5.1

30d event rates in asymptomatic patients

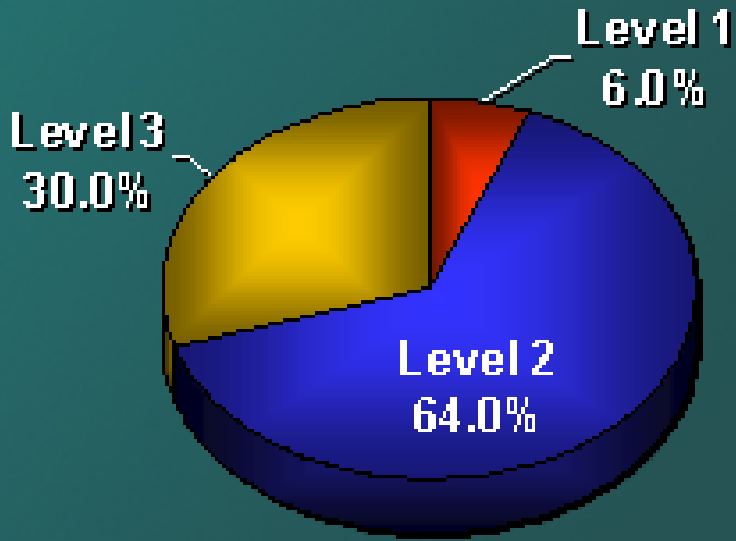
	CAPTURE	ARCHeR
Death/stroke/MI	4.9	6.8
Death	1.3	2.0
Stroke-related death	0.5	0.2
All stroke	3.5	3.8
Major stroke	1.3	0.7
Minor stroke	2.2	3.2
MI *	0.7	2.5
All stroke and death	4.4	5.4
Major stroke and death	2.2	2.3

CAPTURE 2500

Physician & Hospital Prior Experience



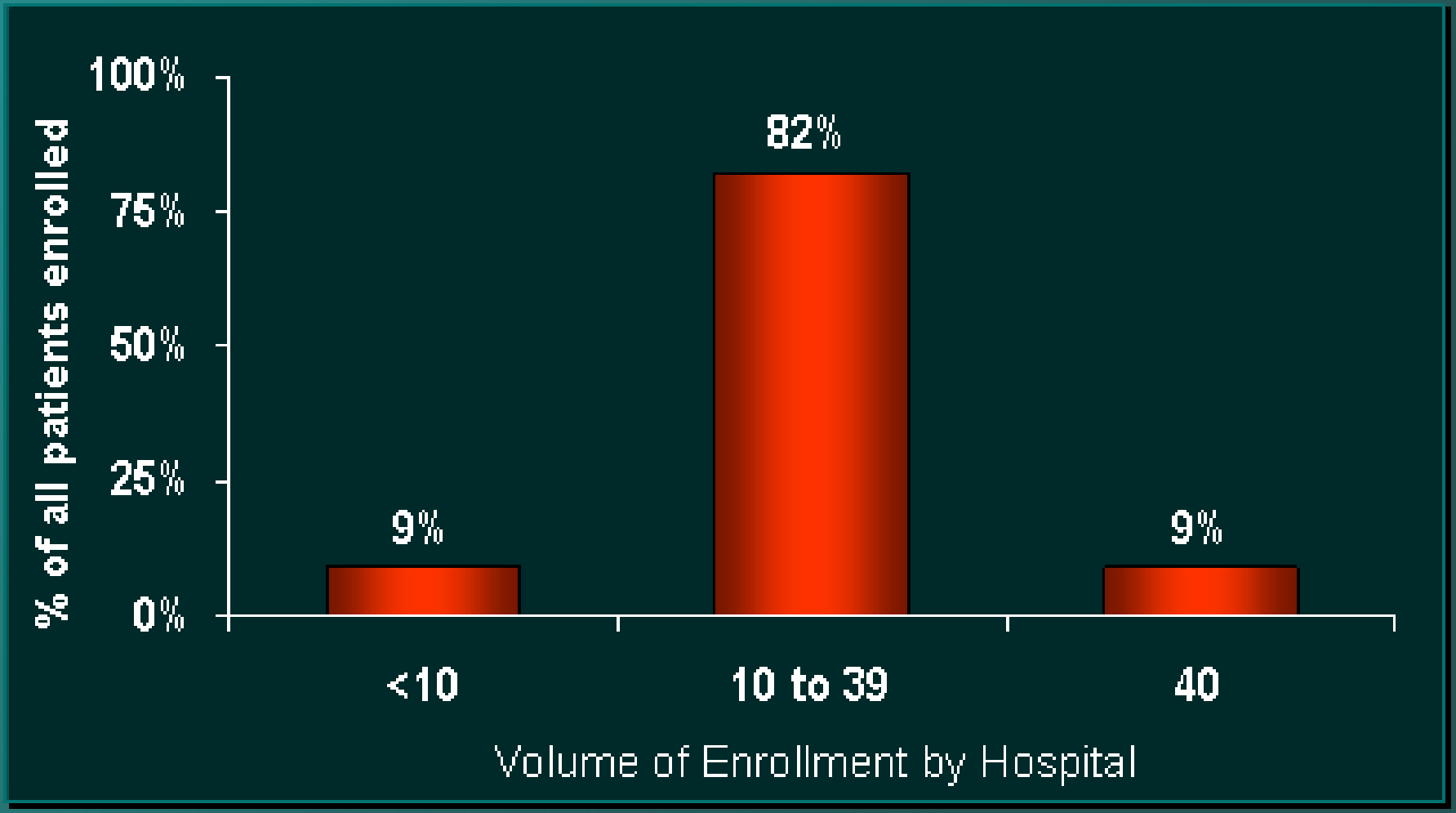
Enrollment by Physician Prior Experience



Enrollment by Hospital Prior Experience

Level	Physician Prior Experience
1: High	Previous investigational experience, 5 as primary operator, using the RX ACCULINK® Carotid Stent System and RX ACCUNET™ Embolic Protection System
2: Medium	10 carotid stent procedures as the primary operator
3: Low	Adequate interventional experience as a primary operator: 25 carotid angiograms (selective, 4 vessel) AND 10 peripheral procedures with self-expanding stents AND 10 procedures with 0.014" RX systems

CAPTURE 2500: Enrollment Profile

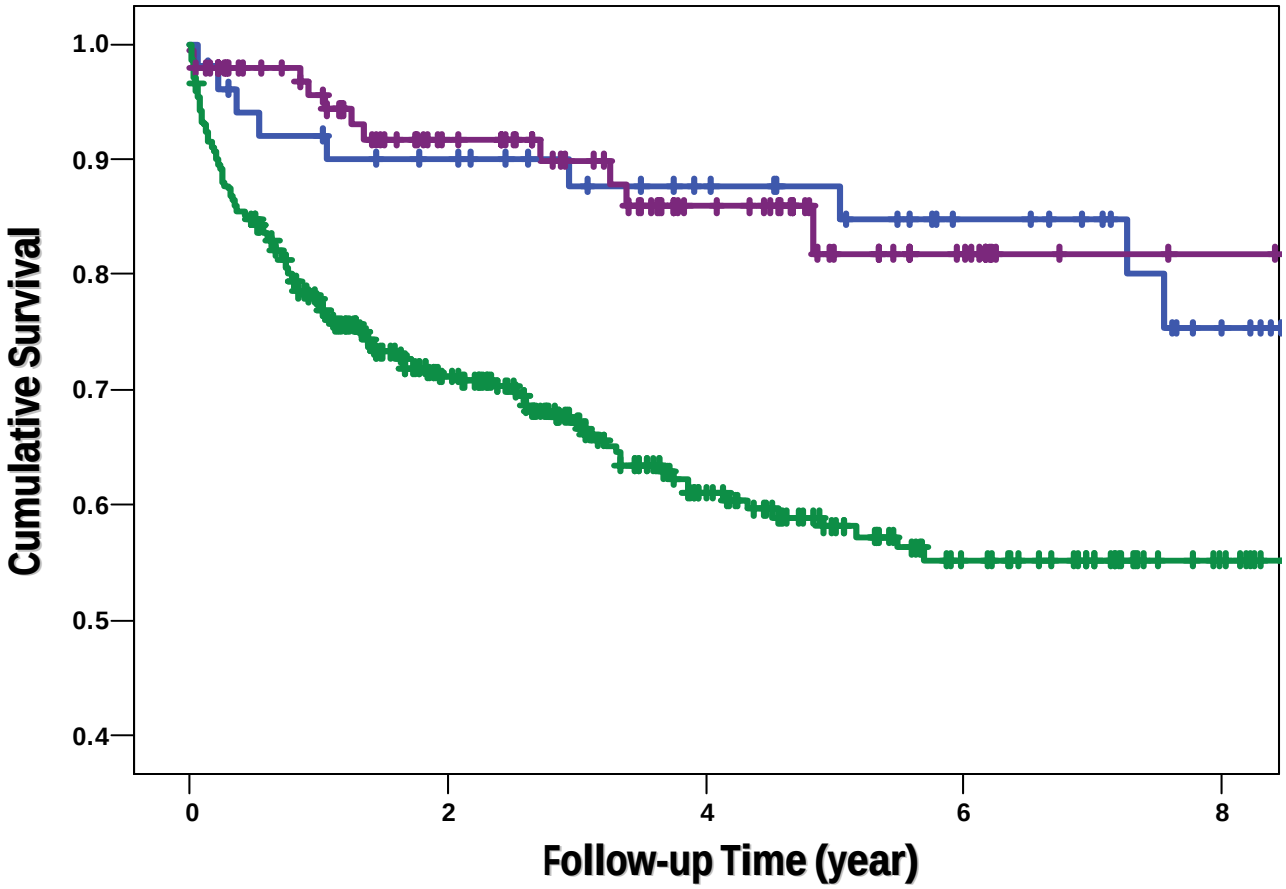


82% of patients at hospitals enrolling 11-39 patients

Difference between surgery and stenting

- Real-world endarterectomy results are far worse than those reported in trials, which recommendations are based upon
- But the post-marketing real-world stenting registry yielded results as good as those seen in trials
- Adequate training (probably with simulation) and refined equipments can cut the learning curve short

Long-term stroke-free survival (sx)



Carotid stenting

Carotid endarterectomy

$p < 0.001$

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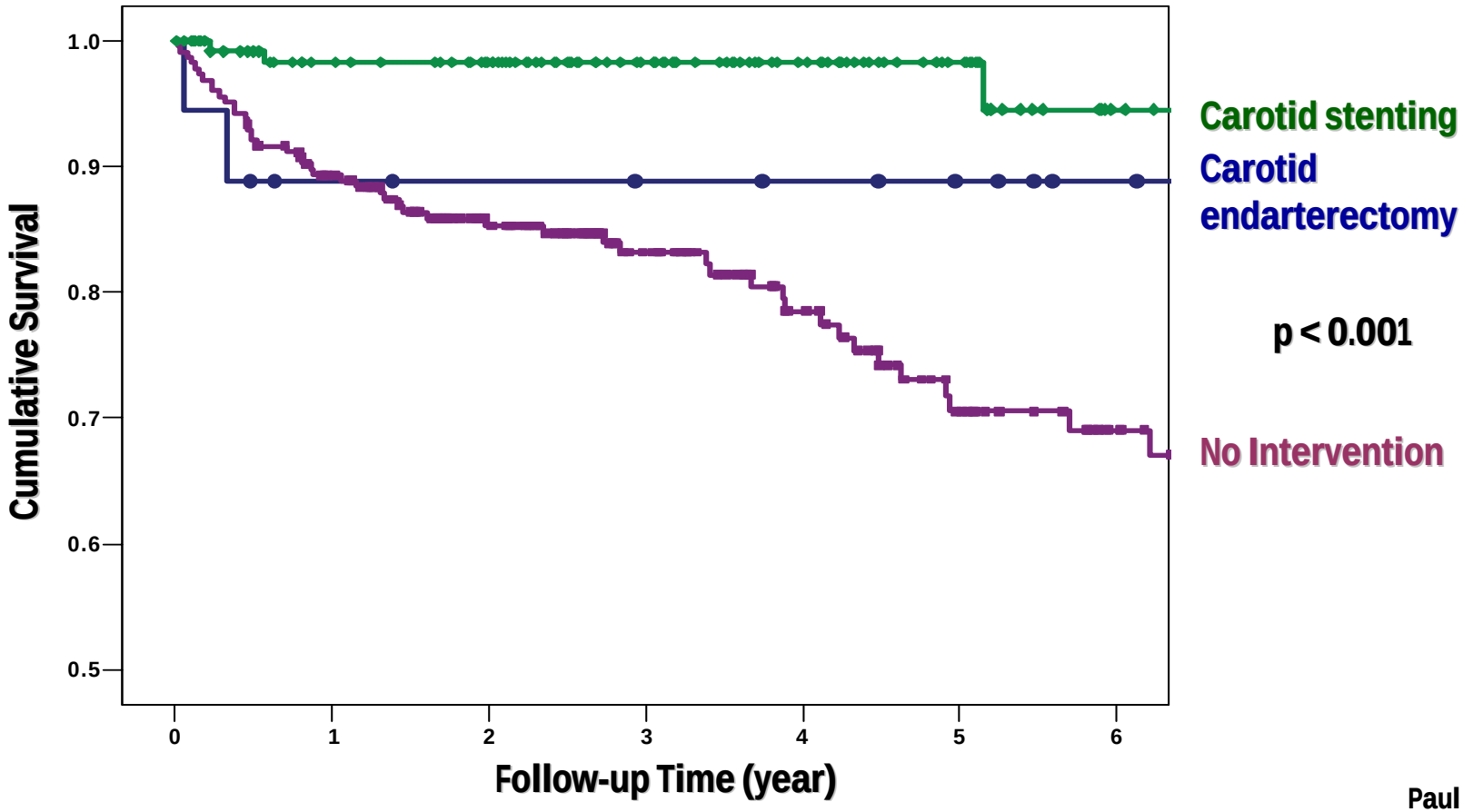
Long-term stroke-free survival (asx)



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Cerebral circulation

- Brain is a highly vascular organ, receives 55 cc/min/100g of blood and consumes 3.3 cc O_2/min/100g of oxygen
- Receives 15% of cardiac output, and 20% of total body oxygen consumption, but weighs only 2% of body mass
- Neurons and glial cells are very susceptible to ischemia
- No clinical relevant regeneration can be seen after damage
- Perfused with carotid and vertebrobasilar system