*Paul Hsien-Li Kao, MD*
Associate Professor of Medicine
National Taiwan University

CAROTID CTO INTERVENTION: LONG-TERM EFFECT ON NEUROCOGNITIVE FUNCTION

CAO leads to hypoperfusion

- Severe carotid stenosis or occlusion leads to cerebral hypo-perfusion
- Annual stroke risk in patients with carotid CTO and objective cerebral ischemia is as high as 20%

All Stroke

Stage II
Normal OEF

$P = .005$

| 36 | 29 | 24 | 17 | 12 | 10 | 7 | 6 |
| 42 | 35 | 30 | 24 | 22 | 20 | 17 | 10 |

0 6 12 18 24 30 36 42 48

Ipsilateral Stroke

Stage II
Normal OEF

$P = .004$

| 37 | 30 | 25 | 18 | 13 | 10 | 7 | 6 |
| 42 | 35 | 30 | 25 | 22 | 20 | 17 | 10 |

0 6 12 18 24 30 36 42 48

Cumulative Proportion With Event

Follow-up, mo
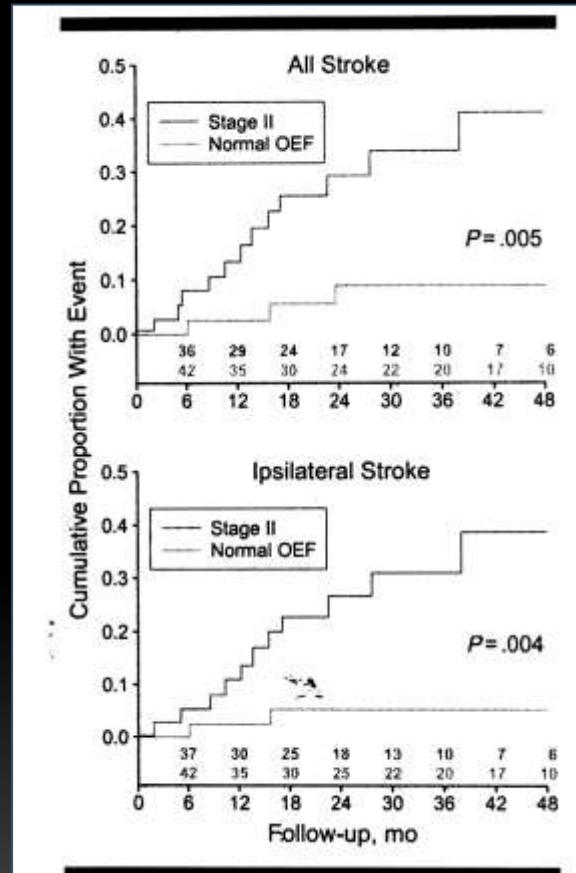
Klijn CJ, et al. Stroke 1997;28:2084
Grubb RL Jr, et al. JAMA 1998;280:1055
Derdeyn CP, et al. Neurology 1999;53:251

Surgery fails in CAO

- Endarterectomy is not possible as the distal end of the occlusion is often located high

- Bypass failed to yield benefit in the EC-IC trial, due to high surgical complication and poor patient selection
  EC/IC Bypass Study Group. N Engl J Med 1985;313:1191

- COSS (Carotid Occlusion Surgery Study) also failed to show benefit
  Powers WJ, et al. JAMA 2011;306(18):1983
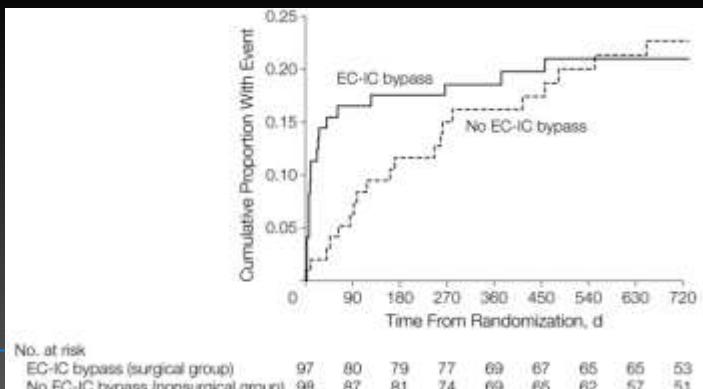
Incidence of CAO

- 1255 CS done since 1998 in NTUH, with 199 CAO attempts since 2002 (15.8%)

- Feasibility and safety has been reported, with 70.9% success and 4.5% 30-day stroke/death

JACC 2007;49:765-771

Circ Cardiovasc Intervent 2008;1:119-125

NTUH data on file

NTUH CAO 30d data

N=199	n	%
Death	3	1.5
Neurological	3*	1.5
Other cause	0	0
Non-fatal ischemic stroke	5	2.5
Major ipsi.	0	0
Major non-ipsi.	0	0
Minor ipsi.	5#	2.5
Minor non-ipsi.	0	0
Non-fatal ICH	1$	0.5

*: 1 immediate SAH+ICH, 1 delayed ICH, 1 delayed CCF with massive nasal bleeding to death
#: includes 3 ipsi retinal infarction with permanent scotoma
$: major motor deficit after craniotomy

The right question

- ## Is preventing embolic stroke the only goal for carotid interventions?

- Coronary bypass or intervention are mainly done to correct insufficient perfusion and ischemia, thus restoring function. So why is brain so different from heart?

Objective cerebral ischemia

baseline
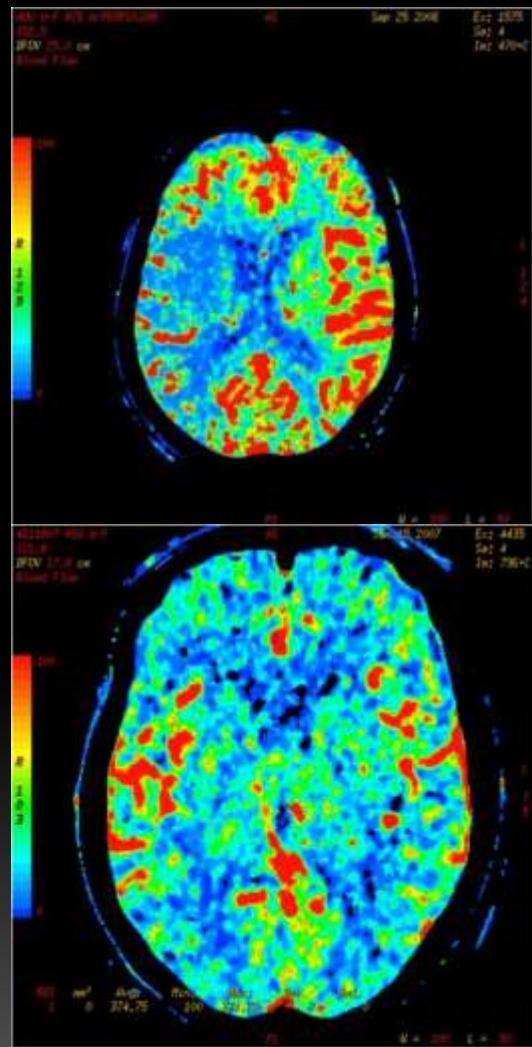
post stenting

stress blood flow   stress mean transit time
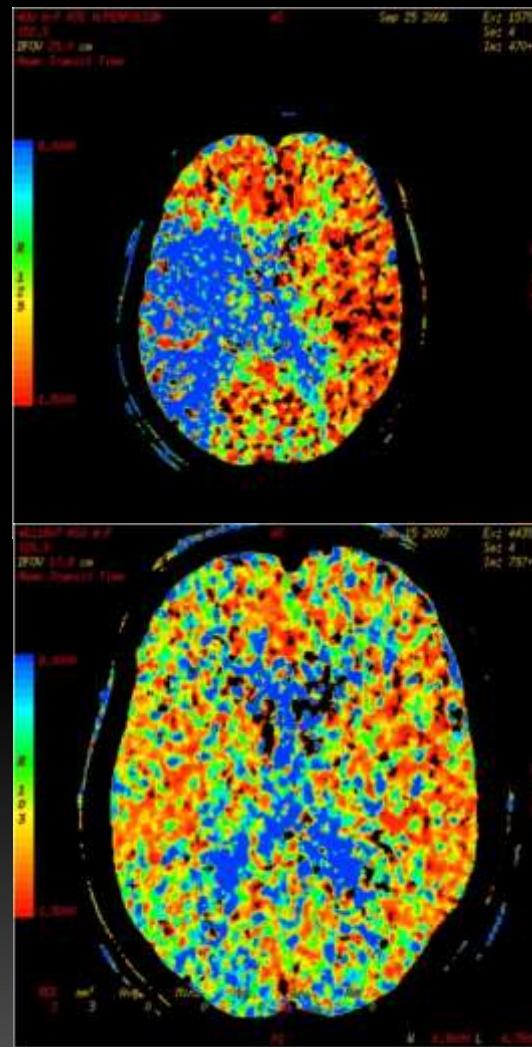
Example case
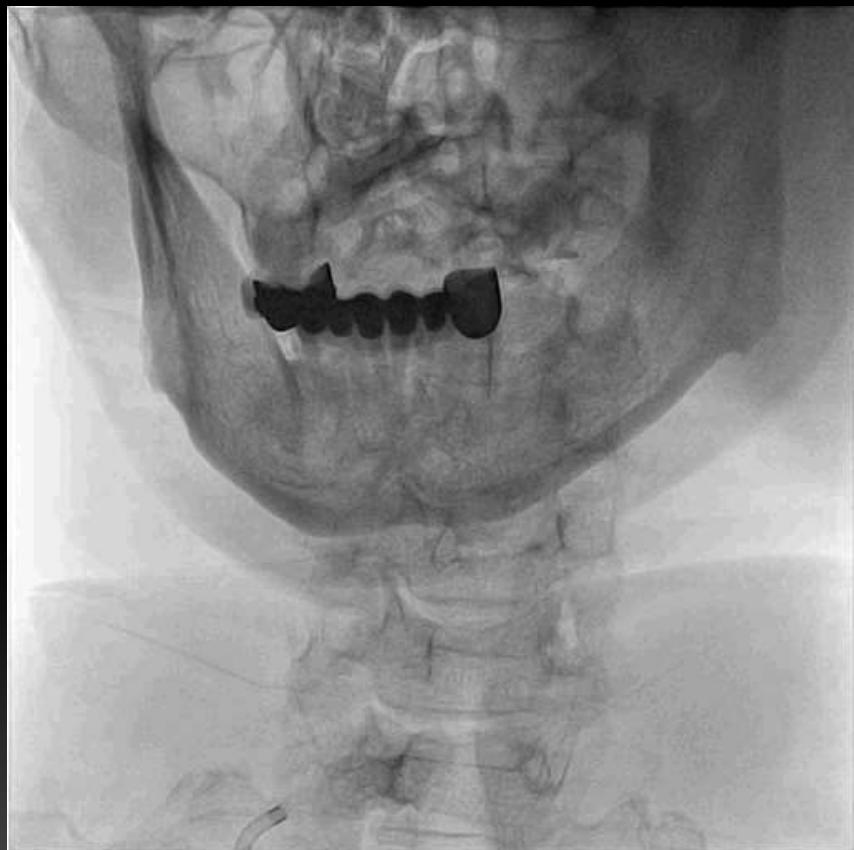
Progressive "dementia"

Wiring across
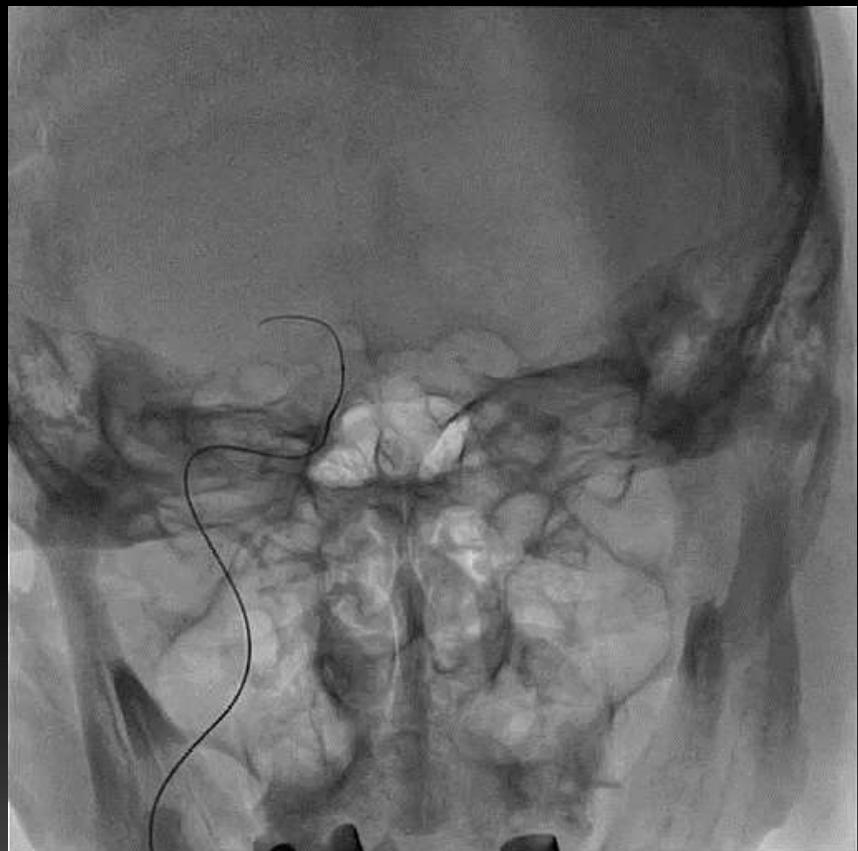
Final angiograms

Indications for recanalization

- Current indications at NTUH (consensus between neurologist, radiologist, and interventionist)
  - Classic NASCET carotid symptoms on optimal medical treatment after documentation of CAO, or
  - Objective ischemia by CTP, MRP, or PET

Effect on neurocognitive function

- Impaired cerebral perfusion impairs neurocognitive function

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Stroke 2003;34:1491-1424

J Neurol 2003;250:1340-1347

Ann Intern Med 2004;140:237-247

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- Our have demonstrated improvement 3 months after CAO intervention, and its correlation to cerebral perfusion improvement

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Stroke 2011;42:2850-2854

Int J Cardiol 2012;157:104-107

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Improved NCF in successful CAO

	Successful (n=12)			Unsuccessful (n=7)		
	baseline	3m	p	baseline	3m	p
ADAS	7.7±8.9	5.7±7.1	0.024	8.7±9.7	9.7±11.1	0.268
MMSE	25.8±3.8	27.7±2.7	0.015	24.7±5.6	25.7±4.9	0.422
Color trail A	123.2±68.6	99.3±51.5	0.017	141.3±101.0	138.3±103.7	0.799
Color trail B	196.2±99.3	175.1±85.5	0.169	176.8±82.1	182.0±92.3	0.397
Verbal fluency	26.3±14.0	27.3±10.2	0.937	27.5±9.4	25.3±6.5	1.0
NIHSS	0.6±0.9	0.4±0.7	0.157	0.6±0.8	0.6±0.8	
Barthel index	97.5±8.7	98.8±4.3	0.317	95.7±7.3	97.1±3.9	0.310

Correlation of NCF with CTP

	Ischemia(+) failed			Ischemia(+) success			Ischemia(-) success		
	Baseline	3m	p	Baseline	3m	p	baseline	3m	p
NIHSS	0.17±0.41	0.17±0.41	1.0	0.24±0.56	0.12±0.33	0.32	0	0.18±0.60	0.32
BI	99.2±2.0	99.2±2.0	1.0	100	99.4±2.4	0.32	100	100	1.0
ADAS	5.2±1.7	4.7±2.1	0.52	6.2±3.6	4.9±2.8	0.033	6.5±4.8	5.6±5.1	0.07
MMSE	26.7±2.1	27.8±2.3	0.066	25.8±3.8	27.4±3.5	0.007	27.1±3.1	27.4±2.7	0.73
Color A	97.2±67.4	110.0±63.9	0.17	120.4±73.9	95.8±57.6	0.004	82.7±51.3	84.0±58.7	0.66
Color B	168.0±74.4	169.3±88.2	0.83	193.1±104.3	184.6±95.2	0.352	135.3±70.2	136.6±78.1	0.96
Verbal	32.5±8.0	29.2±6.7	0.34	25.7±8.5	27.1±6.9	0.92	30.4±10.0	33.6±7.5	0.08

Re-defining "carotid symptoms"

- NCF improvement can be demonstrated in "asymptomatic" patients (stenosis or CTO) after successful stenting, as long as there is objective baseline ischemia

Improved CTP and NCF in "Asx" CAS

Table 3 Differences of Neurocognitive and Neurological Function Between Baseline and 3-Month Follow-Up Among Groups

	Group 1 (n = 8)			Group 2 (n = 33)			Group 3 (n = 18)		
	Baseline	3 Months Post-Procedure	p Value	Baseline	3 Months Post-Procedure	p Value	Baseline	3 Months Post-Procedure	p Value
ADAS	4.5 (3-6.5)	5 (3.5-6)	0.669	6 (4-9)	5 (3-7)	0.002	5 (4-8)	6 (3~7)	0.301
MMSE	28 (27-29)	28.5 (26.5-30)	0.309	27 (25-28)	28 (25-29)	0.004	28 (25-29)	28 (25~29)	0.605
Color Trails Test Part 1, s	70.5 (52.5-127.5)	63.5 (56.5-136)	0.944	100 (78.5-136.5)	97 (60-128.5)	0.003	74.5 (55-109)	77 (51~120)	0.296
Color Trails Test Part 2, s	115.5 (105.5-192)	130 (96-206.5)	0.726	180 (143-215.5)	174.5 (138-218.5)	0.507	151 (102-189)	145.5 (105~197)	0.794
Verbal fluency	27.5 (24-37)	31.5 (27-37)	0.623	24 (20-30)	28 (21-32)	0.681	28 (25-32)	29 (25~36)	0.256
NIHSS	0 (0-1)	0 (0-1)	1.000	0 (0-0)	0 (0-0)	0.564	0 (0-0)	0 (0~0)	1.000
Barthel Index	100 (97.5-100)	100 (97.5-100)	1.000	100 (100-100)	100 (100-100)	0.564	100 (100-100)	100 (100~100)	0.317

Values are median (interquartile ranges).
Abbreviations as in Table 2.

JACC 2013;61(25):2503-2509

- Editorial: Asymptomatic Carotid Stenosis: The Not-So-Silent Disease – Changing perspectives from thromboembolism to cognition

JACC 2013;61(25):2510-2513

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Long-term effect on NCF

- Group 1: failed CS (n=8, all CAO)

- Group 2: ipsi ischemia/successful CS (n=49, 18 CAO/31 CAS)

- Group 3: no ischemia/successful CS (n=29, all CAS)

- 94% (46/49) in group 2 showed improved ipsi. perfusion, none in groups 1 & 3

ADAS up to 1 year

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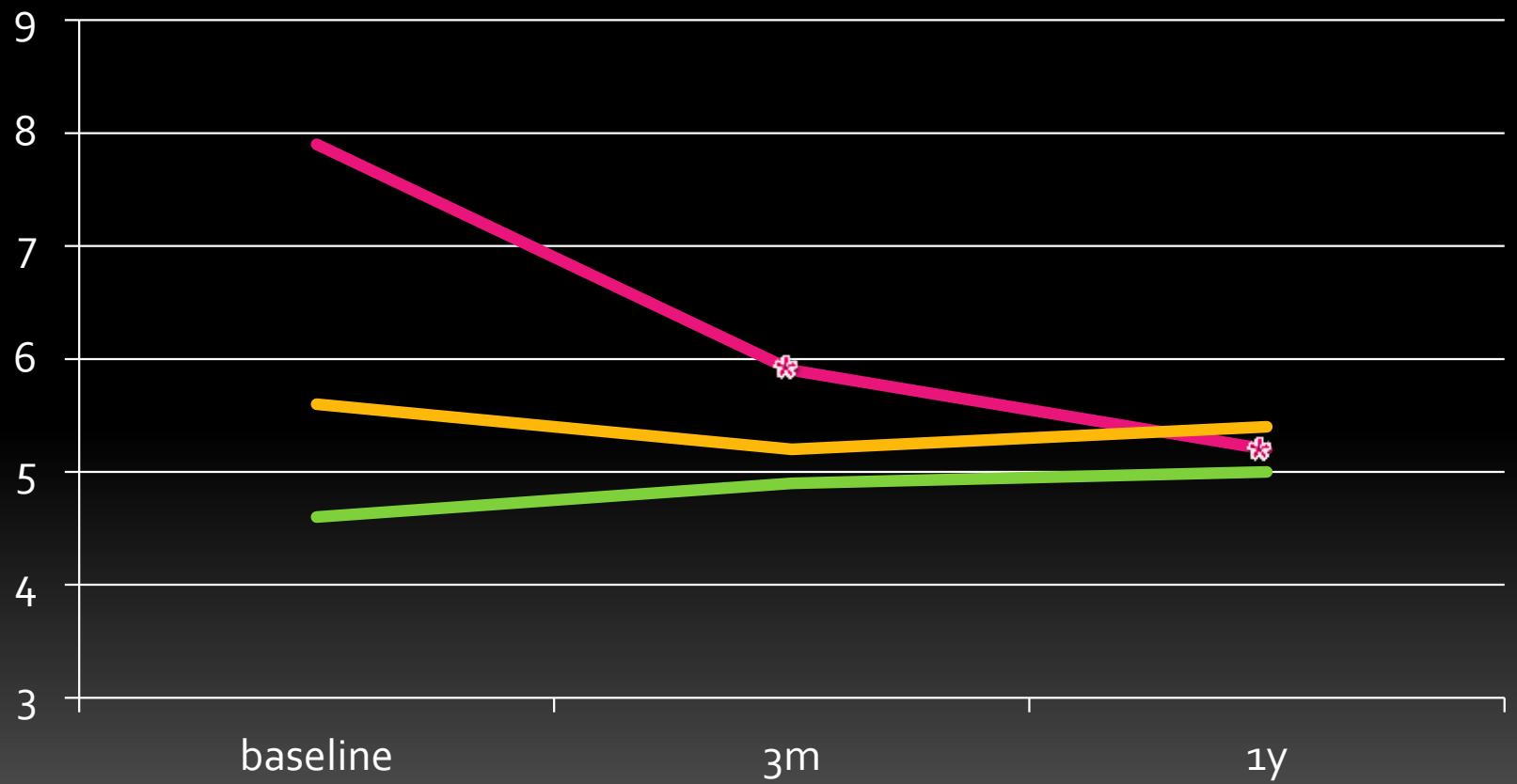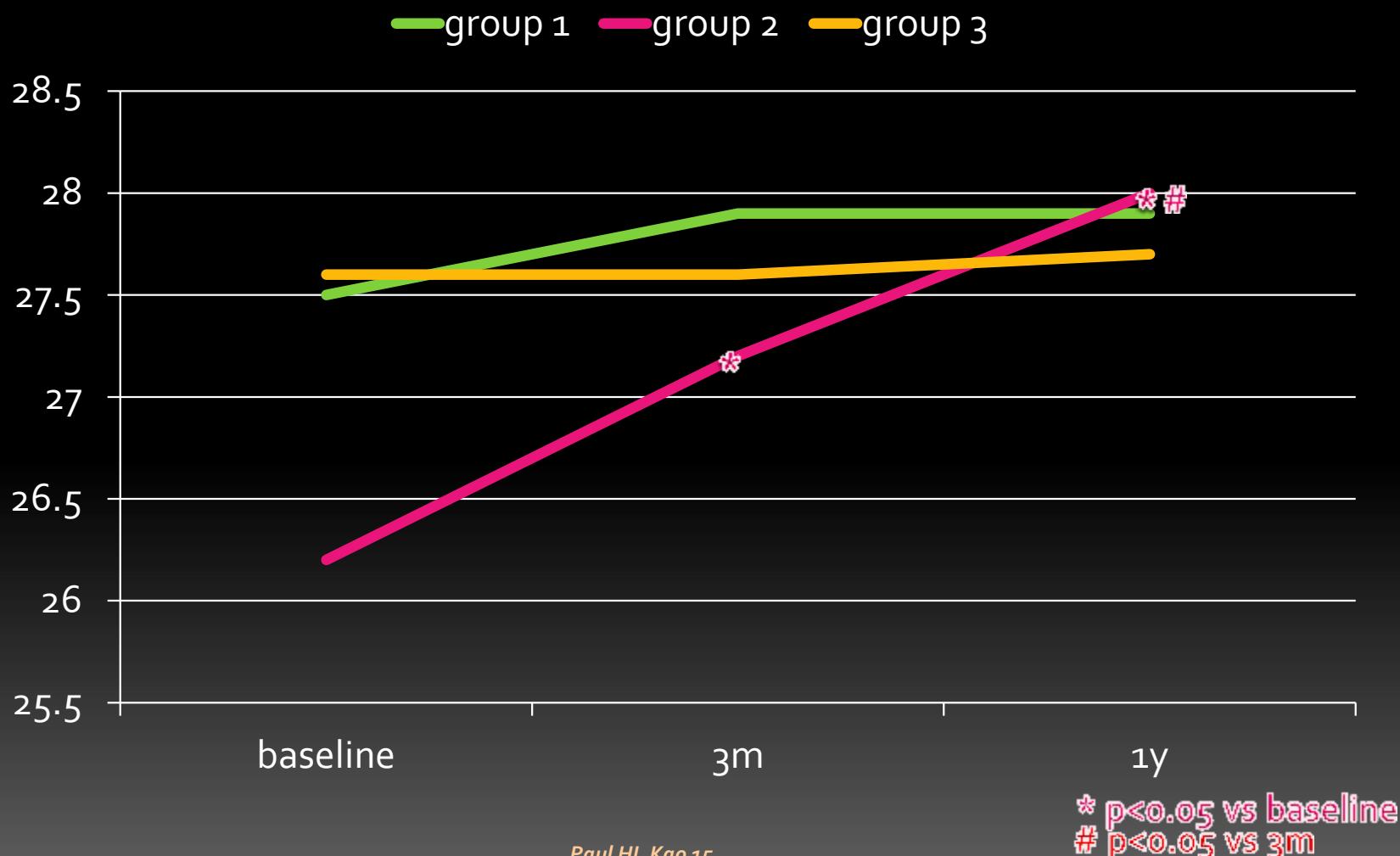
MMSE up to 1 year

Color trail making A up to 1 year

* p<0.05 vs baseline
# p<0.05 vs 3m

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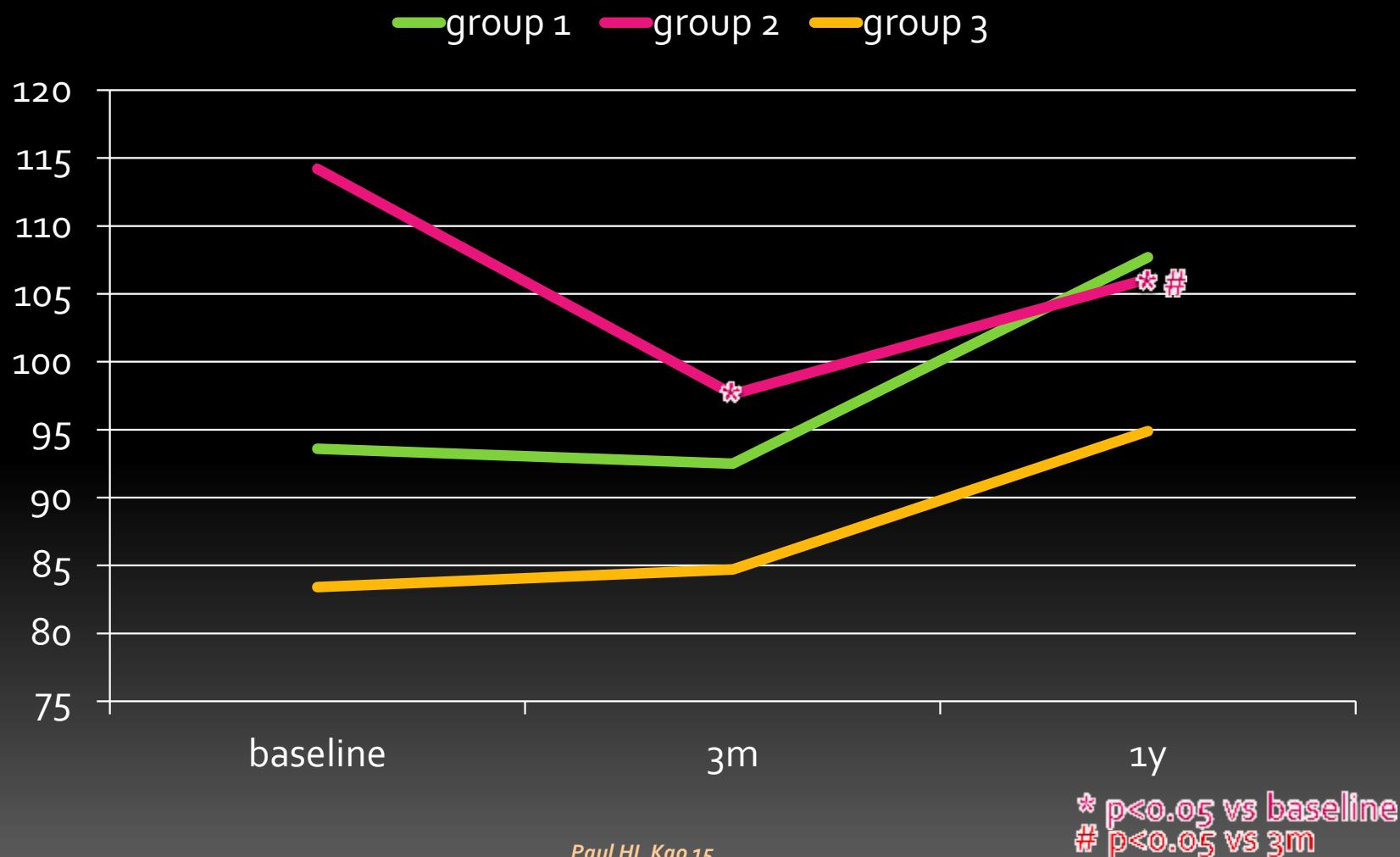
Color trail making B up to 1 year

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* p<0.05 vs baseline
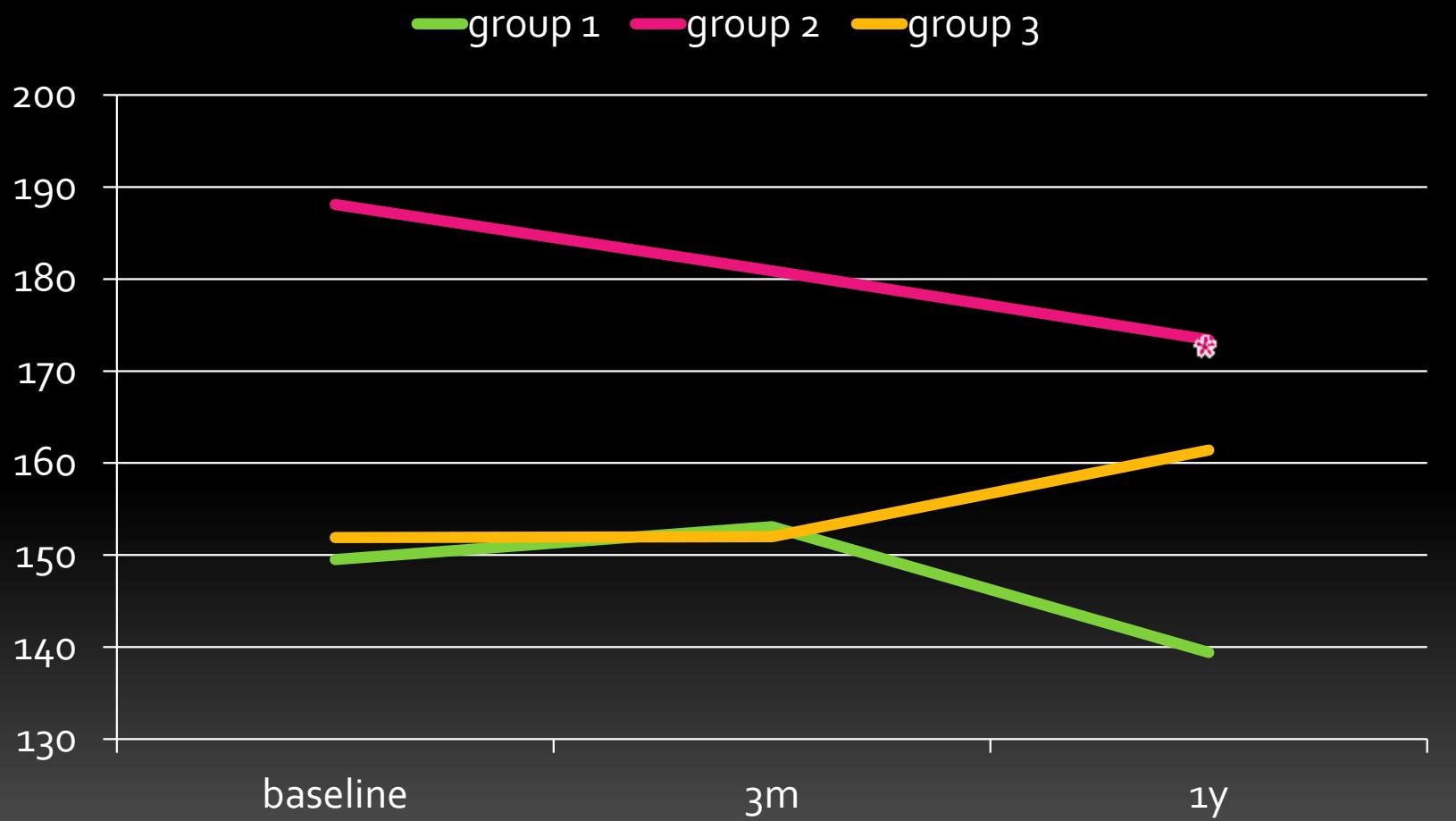
Verbal fluency up to 1 year

Legend: group 1, roup 2, group 3

* p<0.05 vs baseline

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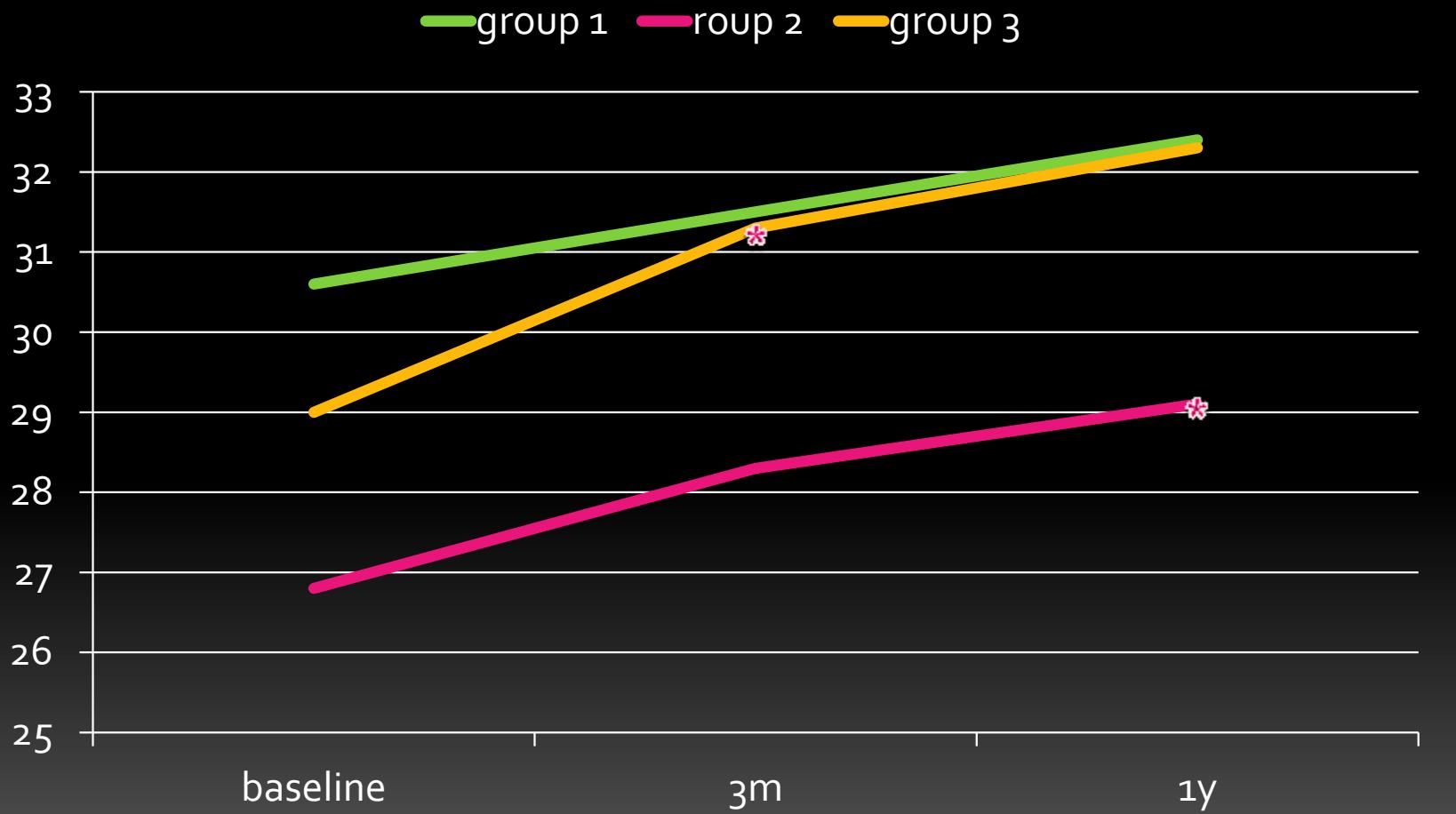
# Cervical RICAO baseline CTA/P


Right
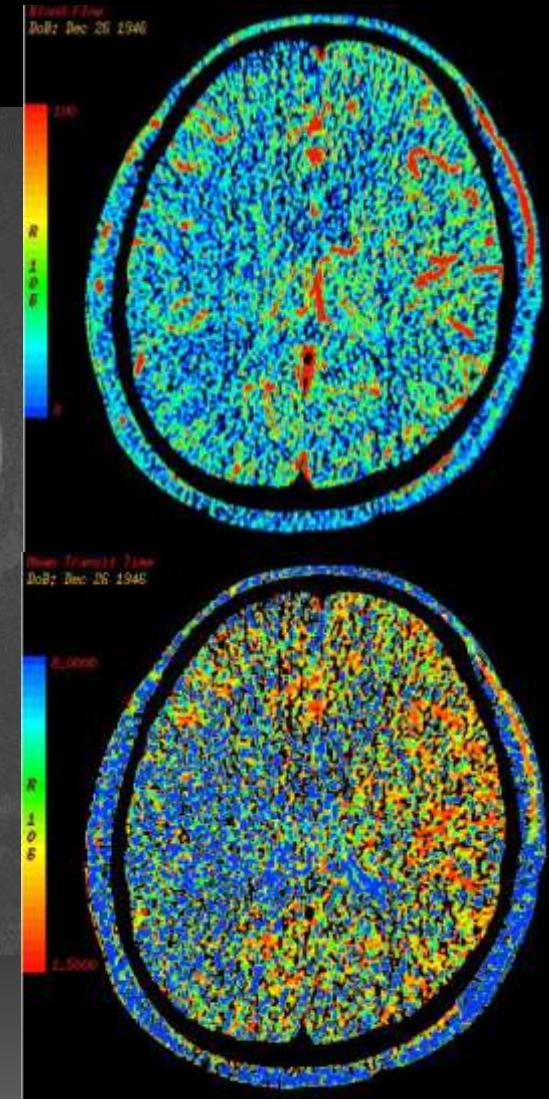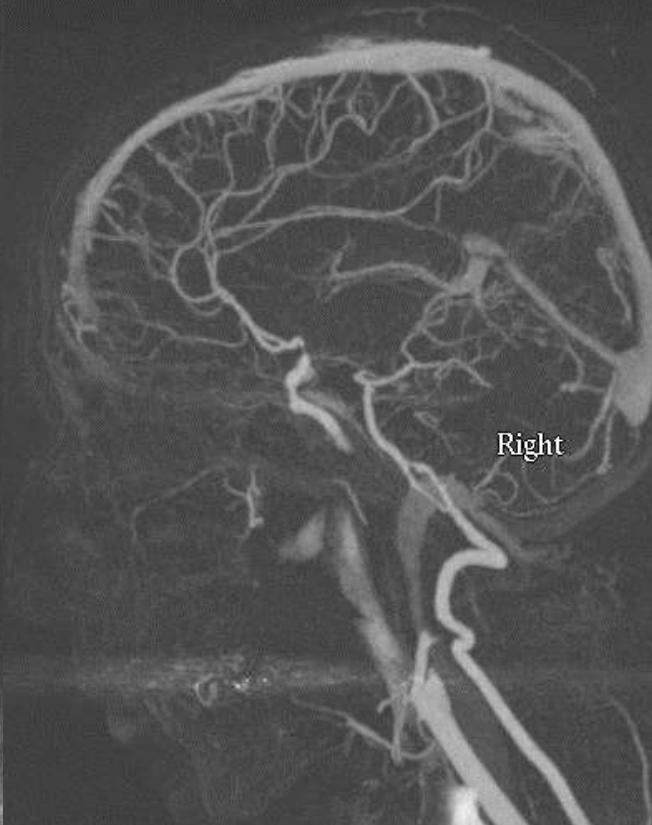
3m after successful stenting
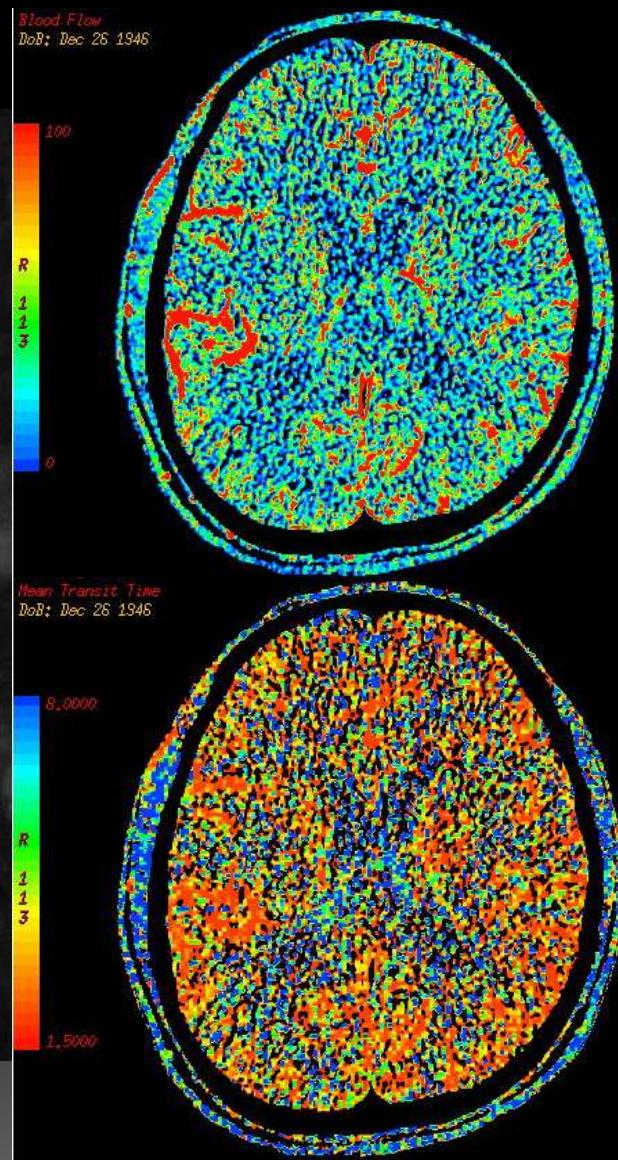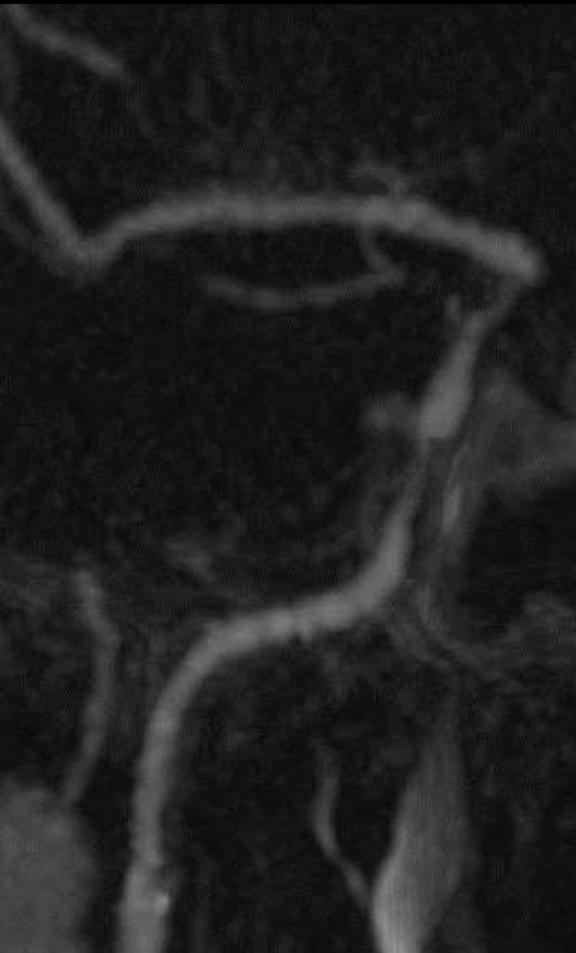
Re-occlusion 15m after stenting
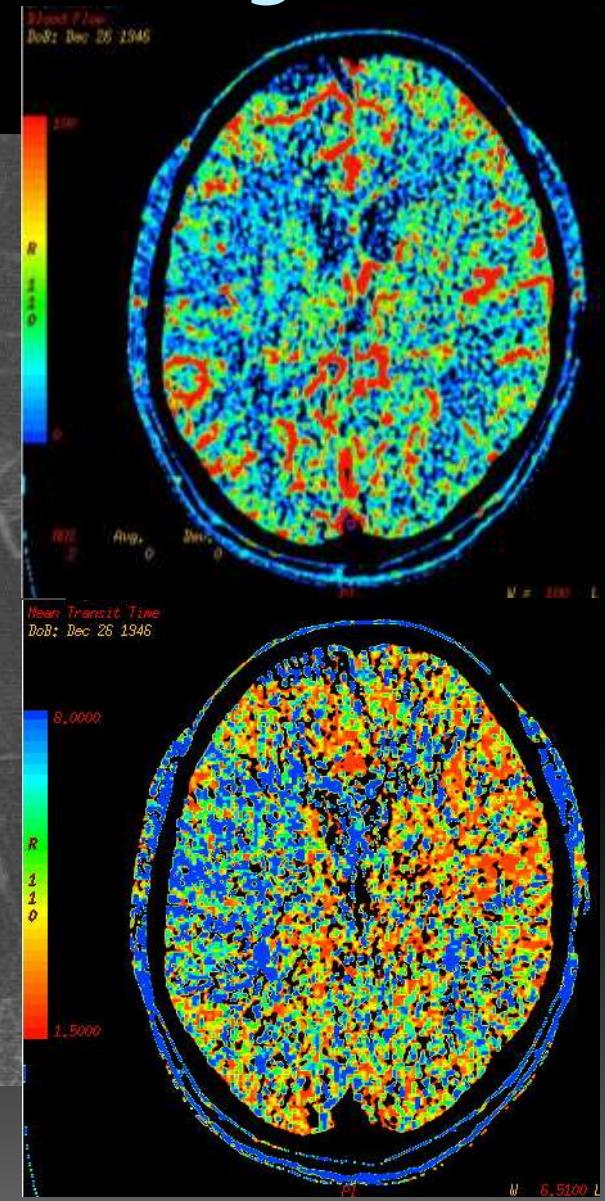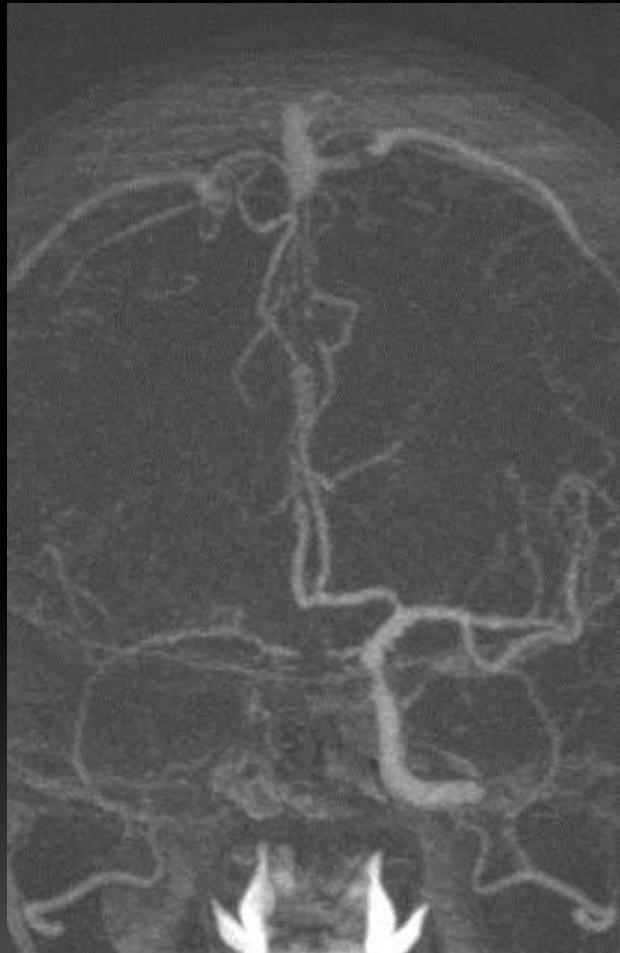
3m after re-intervention
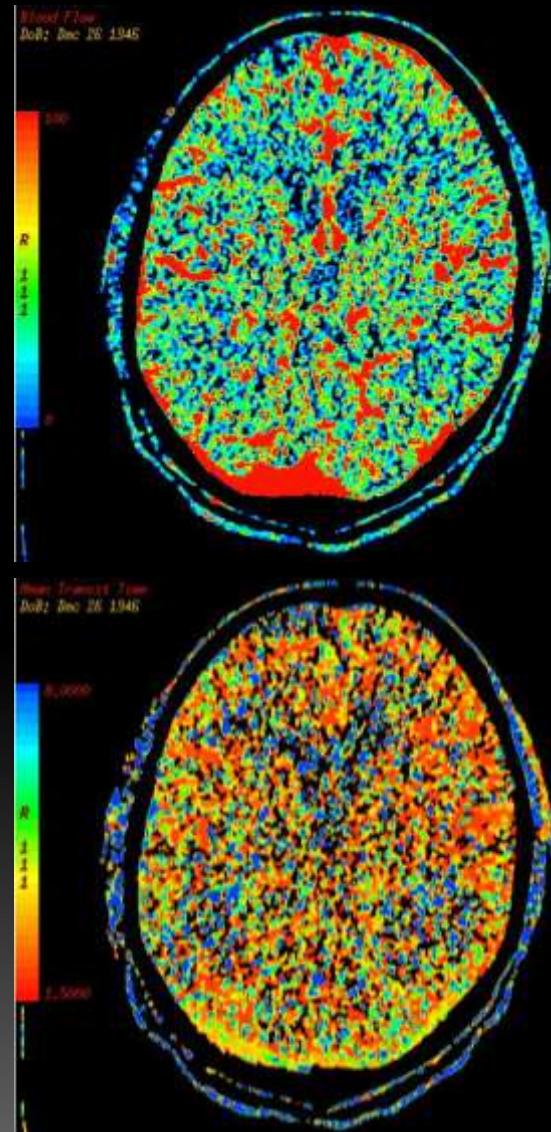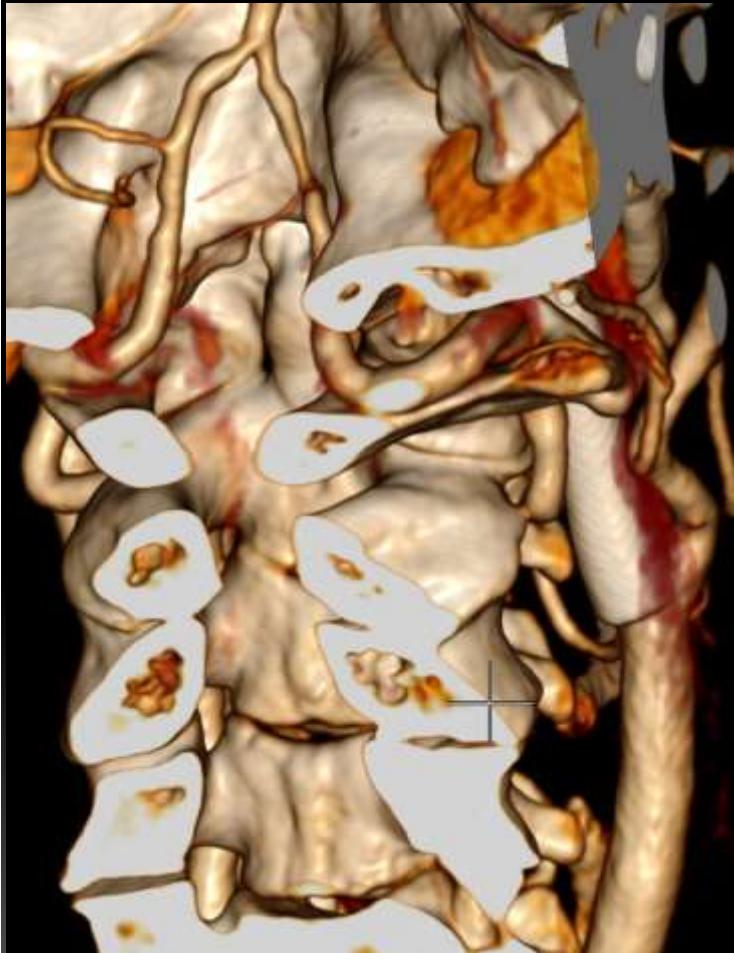
Conclusions

- CAO recanalization improves mid-term and long-term cerebral perfusion and NCF

- Indications should include persistent sx or objective viable ischemia

- The term "asymptomatic carotid disease" needs serious re-consideration

- The treatment goal of carotid intervention should be expanded from embolic prevention to perfusion/NCF restoration