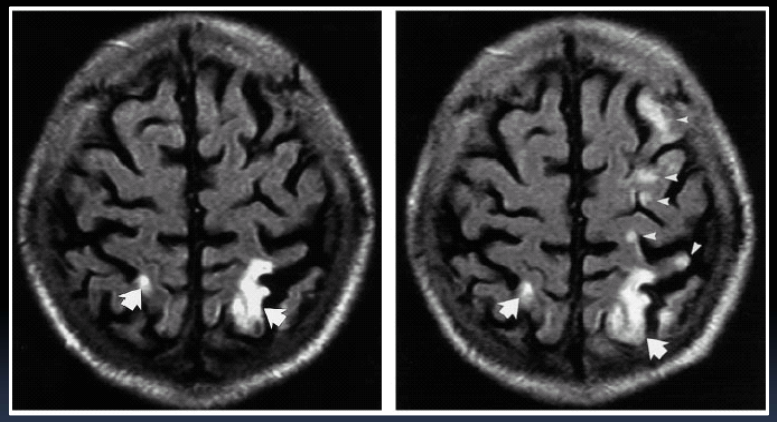
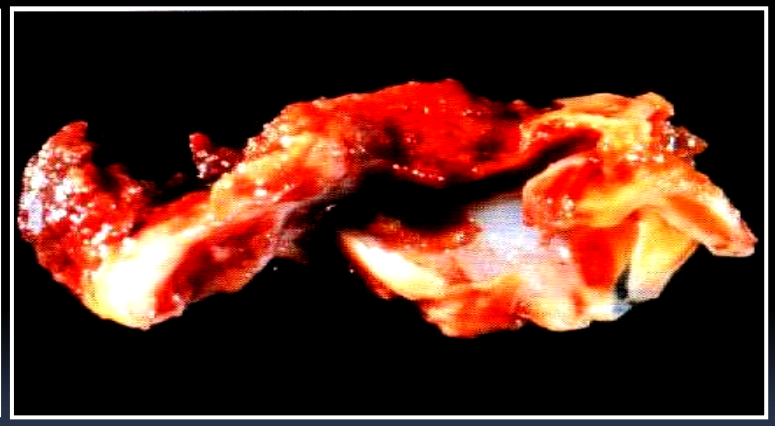
Paul Hsien-Li Kao, MD
National Taiwan University Hospital Yun-Lin Branch

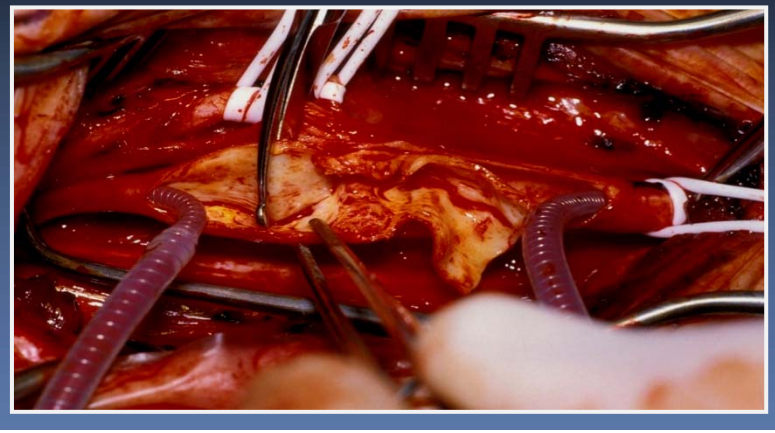
NEURO-COGNITIVE AND PERFUSION IMPROVEMENT AFTER CAROTID STENTING

Carotid stenosis

- Atherosclerotic plaque leading to cerebral embolism







Purpose of carotid procedures

- Prevention of future embolic stroke
- Benchmark for any intervention to be beneficial:
  - <3% death/stroke in asymptomatic lesions
  - <6% death/stroke in symptomatic lesions

But, is this the whole truth?

- Potential patho-physiology of ICA stenosis
  - Embolism
    - Dislodged atheroma fragments
    - In-situ thrombosis and dislodged clots
  - Hypo-perfusion (hemodynamic insufficiency)
    - High grade stenosis causing luminal narrowing or occlusion
    - Thrombotic occlusion

Cerebral perfusion

- Stage 0: CPP normal, CBF matched with resting metabolic demand, no regional variation in OEF
- Stage 1: CPP decreased, but CBF maintained by vasodilatation, CBV increased
- Stage 2: CPP further decreased beyond the capacity of auto-regulation, CBF decreased, regional OEF increased with declined brain function
- Stage 2 perfusion failure is also termed "misery perfusion"

NASCET/ECST carotid symptoms

- Ipsi-lateral stroke/TIA/amaurosis fugax occurring within 180 days
  - These are embolic events!
- But what about other more global but less localized signs?
  - Faintness
  - Blurred/darkened visual fields
  - Mental deterioration
  - Psychomotor retardation

Analogy from coronary procedures

- Plaque rupture leads to myocardial infarction
- Tight stenosis leads to myocardial ischemia at stress, or hibernation
- Does any cardiologist claim that the goal of PCI is only to prevent myocardial infarction?!

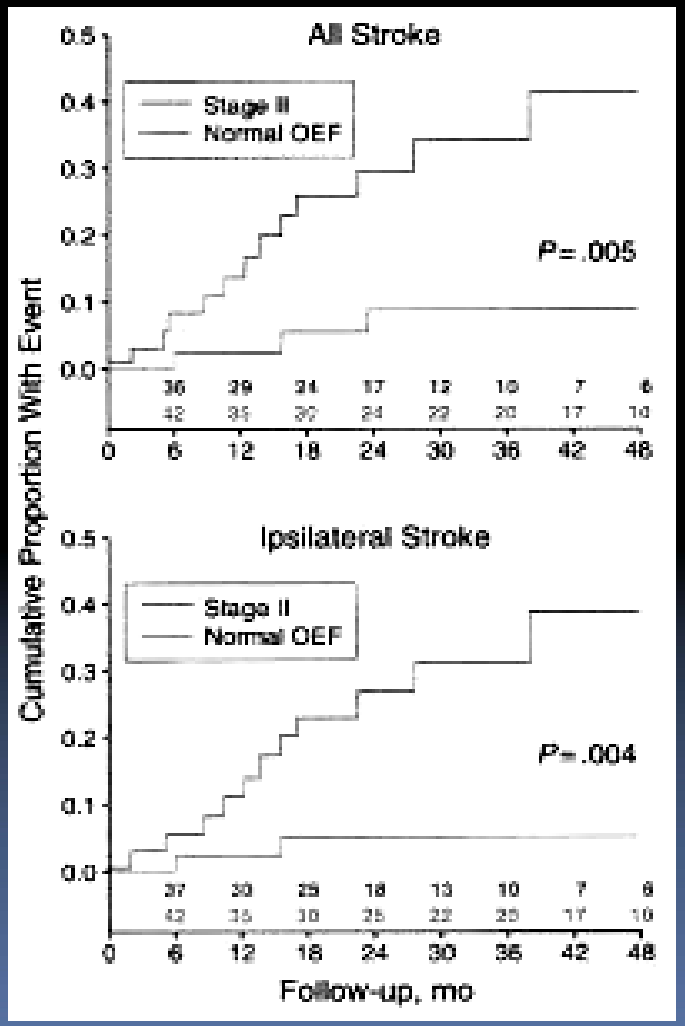
Especially true in ICAO

- 20 studies in patients with TIA or ischemic stroke associated with an ICAO, the annual risk of all and ipsi-lateral stroke were 5.5% and 2.1%
- Patients with a compromised CBF measured by PET, SPECT, TCD, or Xe133 CT have an even higher annual risk of all and ipsi-lateral stroke (12.5% and 9.5%)

Stroke. 1997;28:2084–2093

Objective perfusion does matter!

- 81 ICAO patients with old ipsilateral stroke or TIA, evaluated with PET and followed for 3 years
- Stroke occurred in 12/39 and 3/42 (p=0.005, RR= 6) with and without stage 2 perfusion failure, ipsilateral stroke in 11/39 and 2/42 (p=0.004, RR= 7.3)



JAMA. 1998;280:1055–1060

NTUH experience

- From Apr 1998, over 900 ICA stenting procedures have been done
- ICAO were attempted in anecdotal cases since 2002, with dramatic neuro-cognitive recovery
- Systematic attempts were done in 92 chronic ICAO in 90 patients since 2004
  - Perfusion CT for objective ischemia
  - Neuro-cognitive evaluation (NCE)

FIM publication

Interventional Cardiology

Feasibility of Endovascular Recanalization for Symptomatic Cervical Internal Carotid Artery Occlusion

Hsien-Li Kao, MD,* Mao-Shin Lin, MD,† Chia-Sung Wang, MD,* Yen-Hong Lin, MD,* Lung-Chun Lin, MD,* Chia-Lun Chao, MD,* Jiann-Shing Jeng, MD,‡ Ping-Keung Yip, MD,‡ Shih-Chung Chen, MD§

Taipei and Yun-Lin, Taiwan

Objectives This study sought to report technical details and clinical results of the first series of endovascular recanalization for cervical internal carotid artery (ICA) occlusion.

Background Cervical ICA occlusion is associated with impaired cerebral perfusion, which may lead to ischemic cerebral symptoms and hemodynamic infarcts. Neither surgical nor endovascular revascularization has been shown to benefit this population.

Methods Endovascular recanalization was attempted in 30 patients with ICA occlusions (27 men; age 72.1 ± 8.0 years,

Results The overall technical success rate was 73% (22 of 30). No neck hematoma, intracranial hemorrhage, or hyperperfusion was noted. One (3.3%) fatal brainstem infarction occurred 1 day after a successful ICA procedure, with angiographically proven acute basilar artery occlusion and patent ICA stent. Baseline ophthalmic artery flow was reversed in 15 of the 22 successfully recanalized patients, and was normalized in 12 after the procedure. There was no new cerebral ischemic event or neurologic death for a mean follow-up of 16.1 ± 18.5 months.

Conclusions Endovascular recanalization for cervical ICA occlusion is feasible with acceptable midterm clinical results.

(J Am Coll Cardiol 2007;49:765–71)

Predictors for success

	Total	Procedure success		Wiring Success	
	n = 73	n = 47	p	n = 49	p
Age (year)		(2.0, 12.7)	0.0616	(0.9, 12.0)	0.1109
Male	66 (90%)	32 (94%)	0.211	45 (92%)	0.544
Hypertension	61 (83%)	41 (87%)	0.255	42 (86%)	0.478
DM	27 (37%)	20 (43%)	0.185	20 (41%)	0.333
Hyperlipidemia	43 (59%)	29 (62%)	0.514	29 (59%)	0.945
Smoking	36(49%)	24 (51%)	0.688	25 (51%)	0.677
Hx of radiotherapy	3 (4%)	0	0.042	0	0.033
Symptom progression	42 (58%)	32 (68%)	0.014	32 (65%)	0.055
NASCET symptomatic	13 (18%)	8 (17%)	0.813	9 (18%)	0.858
Duration of occlusion (D)		(-534, -70)	0.0003	(-583, -70)	0.0001

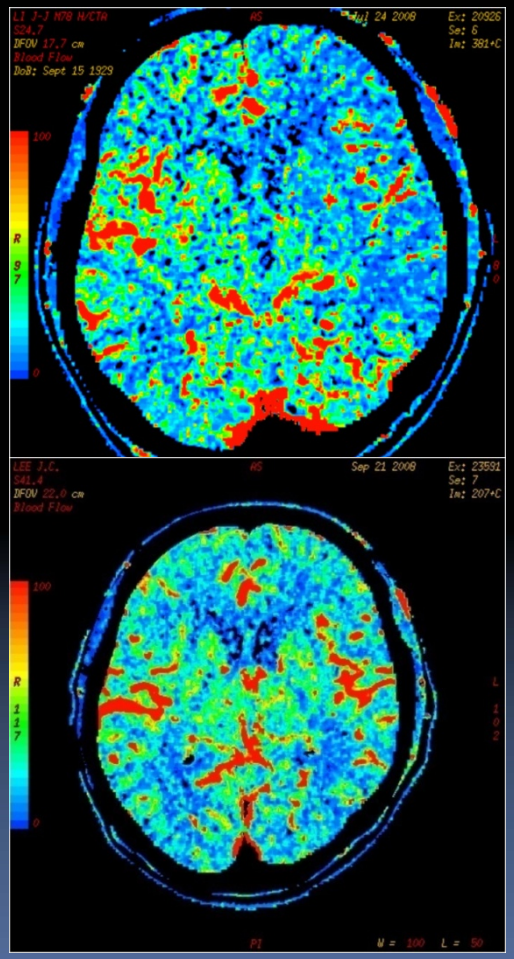
Perfusion CT study

- In 41 ICAO patients with baseline perfusion CT showing ipsi-lateral hemispheric ischemia, 29 had 3 months post-stenting imaging
- Perfusion CT was done with Diamox-stress and read by radiologist blinded to the procedural results

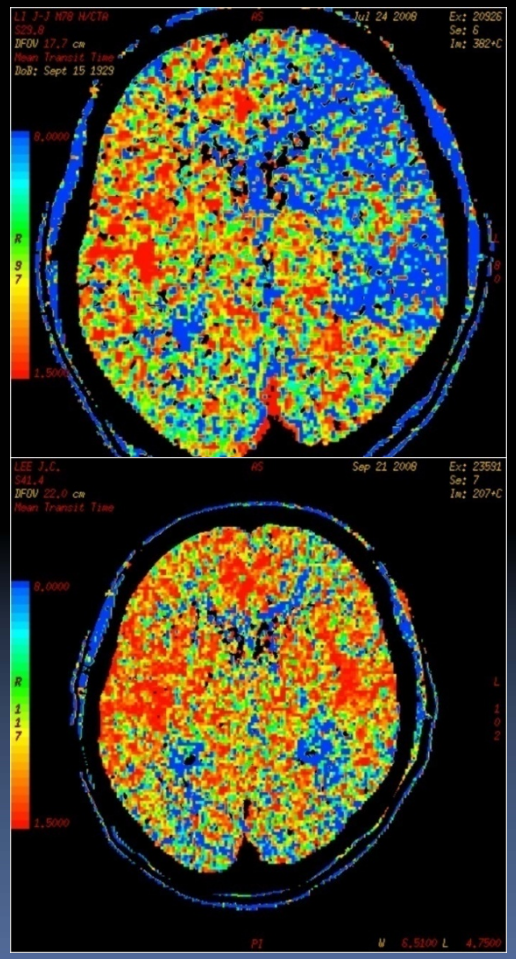
Example images

Baseline

Post stenting



Stress-flow



Stress-MTT

Baseline

Post stenting

Post-procedure perfusion results

	Success (n=20)	Failure (n=9)	P
Improvement	12 (60%)	2 (22%)	<0.01
Stationary	7 (35%)	6 (67%)	Ns
Worsened	1 (5%)	1 (11%)	Ns

Neuro-cognitive evaluation

- All patients undergoing carotid stenting are evaluated by an independent clinical psychologist 1 day before the procedure with standardized NCE form
- Panel contents include ADAS, MMSE, color trailing, and verbal fluency
- NCE will be done 3 months after procedure regardless of the result

Demographics of NCE study

		N	%
Male		24	80
Age (y)		69.7 ± 11.9	
Hypertension		21	70
Diabetes mellitus		8	27
Hyperlipidemia		11	37
Smoking		10	33
Severity of stenosis	100%	11	37
	90-99%	14	47
	70~90%	5	17
Procedure success	ICAO (n=11)	6	55
	ICAS (n=19)	19	100

NCE in 25 successful cases

	Pre	3 months post	P
ADAS	8.1±1.3	6.3±1.0	0.01
MMSE	24.9±0.7	26.2±0.7	0.01
Color trail 1	98.4±10.7	90.5±10.5	0.26
Color trial 2	184.9±20.0	161.2±14.2	0.06
Verbal fluency	27.8±1.0	28.3±1.6	0.70

* No significant changes were found in failed cases, except for a trend toward deterioration

Successful vs. failed cases

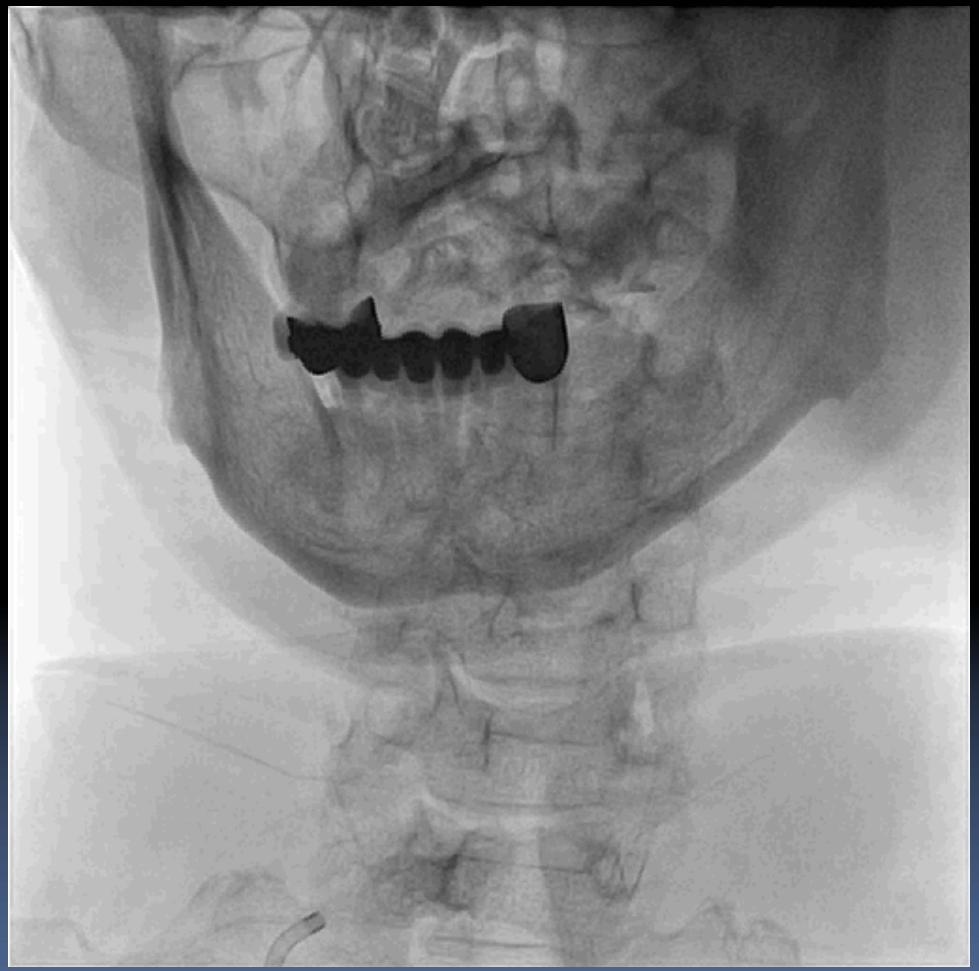
	Success (n=25)	Failed (n=5)	P
Age	70.9±2.2	63.6±7.4	0.214
Contra-lateral >50% stenosis	9/25	0/5	0.286
Male	19/25	5/5	0.553
HTN	16/25	5/5	0.286
DM	7/25	1/5	1.000
Hyperlipidemia	11/25	0/5	0.129
Smoking	10/25	0/5	0.140
Baseline ADAS	8.1±1.3	9.2±4.8	0.75
MMSE	24.9±0.7	24.2±2.7	0.6669
Color trail 1	98.4±10.7	84.5±26.1	0.6208
Color trial 2	184.9±20.0	136±32.6	0.3405
Verbal fluency	27.8±1.9	28.2±4.6	0.9234
△ ADAS	-1.8±0.6	1.4±1.2	0.0324

Exemplary case

76 y/o man with history of left hemi paresis 2 years ago

Carotid dissection was diagnosed and he was put on long-term anticoagulant

Neck Duplex showed occluded RICA with reversed right OA flow



ICAO with ischemia documented

Family reported worsening mental capacity for 1 year but definitely no recurrent carotid symptom

Perfusion CT showed significant right hemisphere ischemia

ADAS 12

MMSE 14

Worsened NCE during follow-up

Anticoagulant was shifted to dual anti-platelet agents for 2 months

Duplex showed same findings

ADAS 12 → 14

MMSE 14 → 15

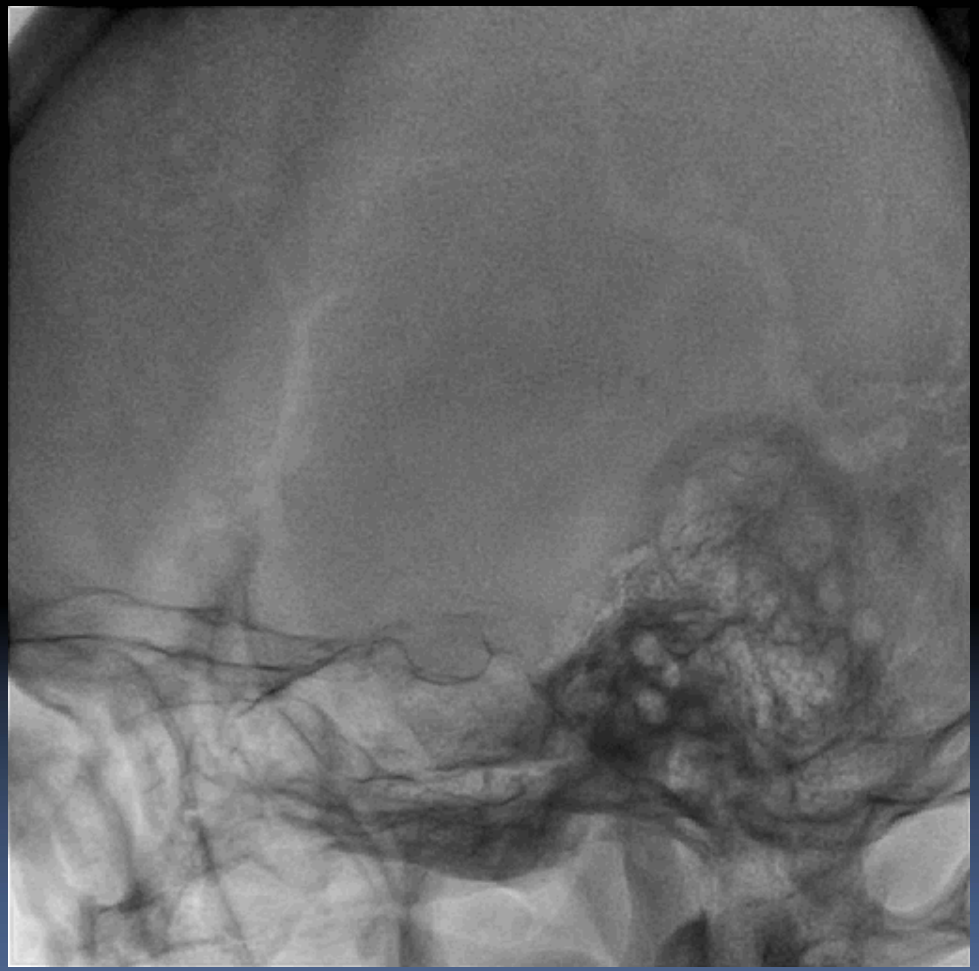
Angiography summary

Angiography showed cervical RICA occlusion 20mm from orifice

OA reconstituted distal RICA with good ACA/MCA run-off

Willis circle is intact

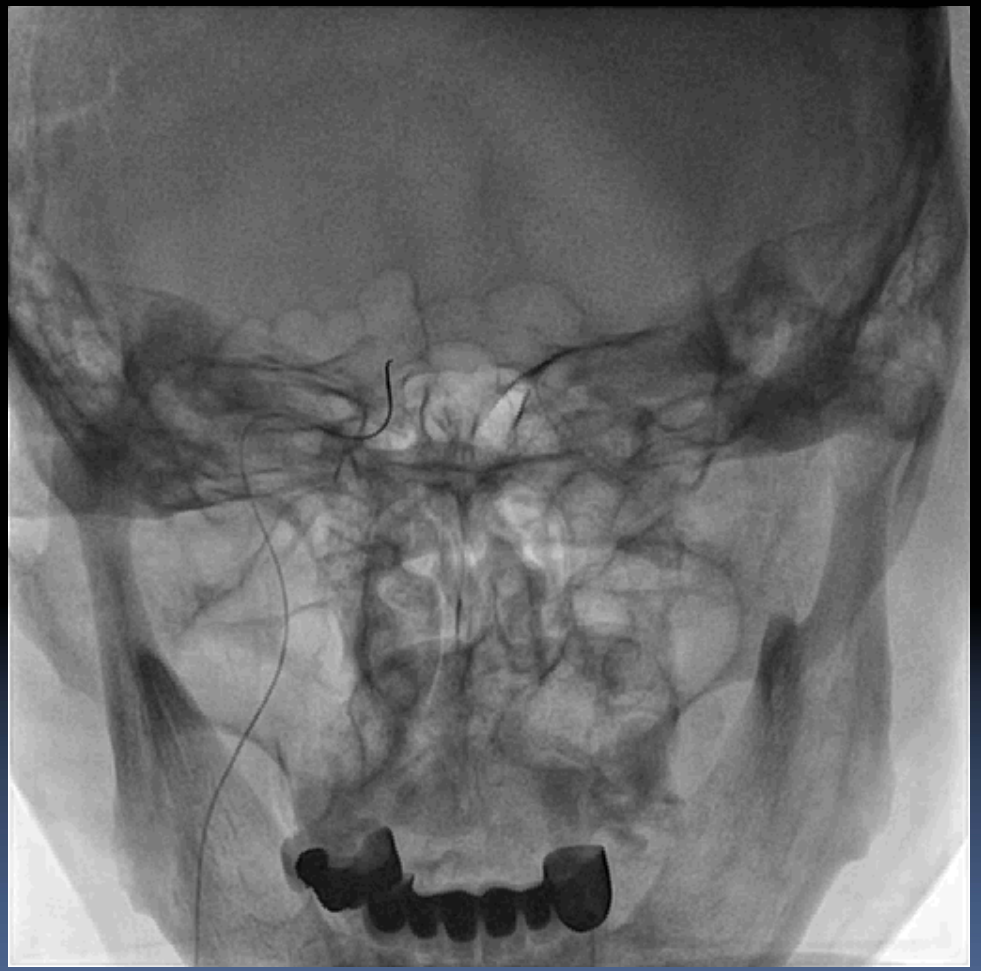
The findings were the same as CTA



Initial wiring attempt

Fielder FC through Finecross can be manipulated into distal ICA just proximal to OA take-off

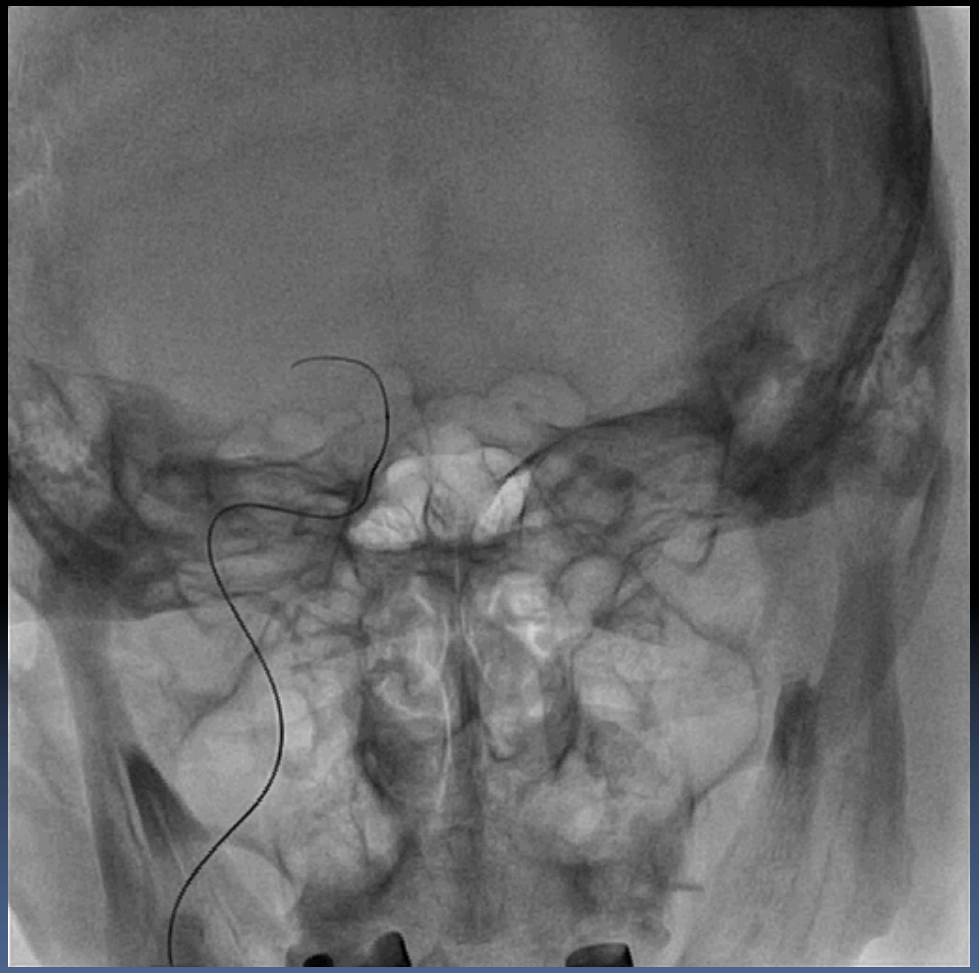
Further advancement was impossible



Dedicated CTO wiring

Fielder FC was exchanged to Conquest Pro

With careful and delicate manipulation Conquest Pro entered MCA

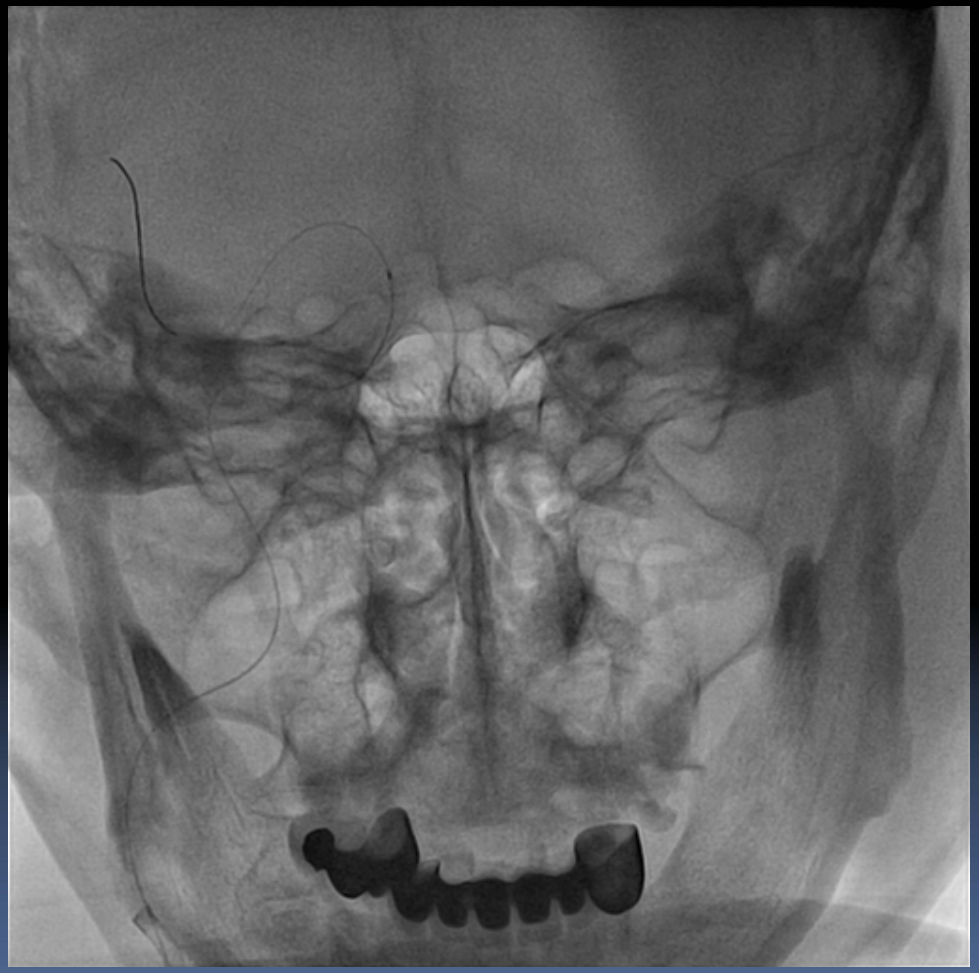


Balloon dilatation

Finecross was advanced over Conquest Pro and microinjection through the wire lumen confirmed true lumen position

Runthrough NC Floppy was advanced into M3 branch

1.25x10 Ottimo was inflated to 6atm, then 2.5x15 Ottimo 6atm

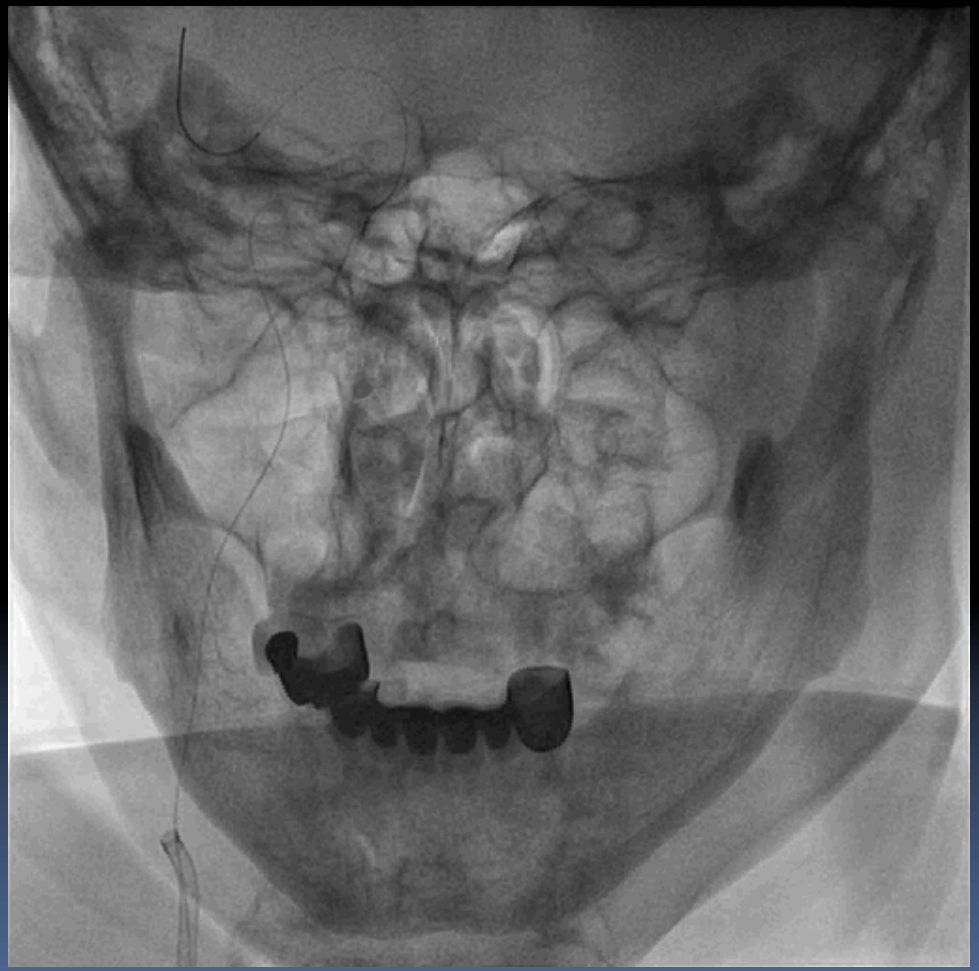


Stenting planning

RICA was recanalized successfully

SBP was lowered to 140mmHg by nitroglycerin infusion

ACT checked at 240”



Intracranial stenting

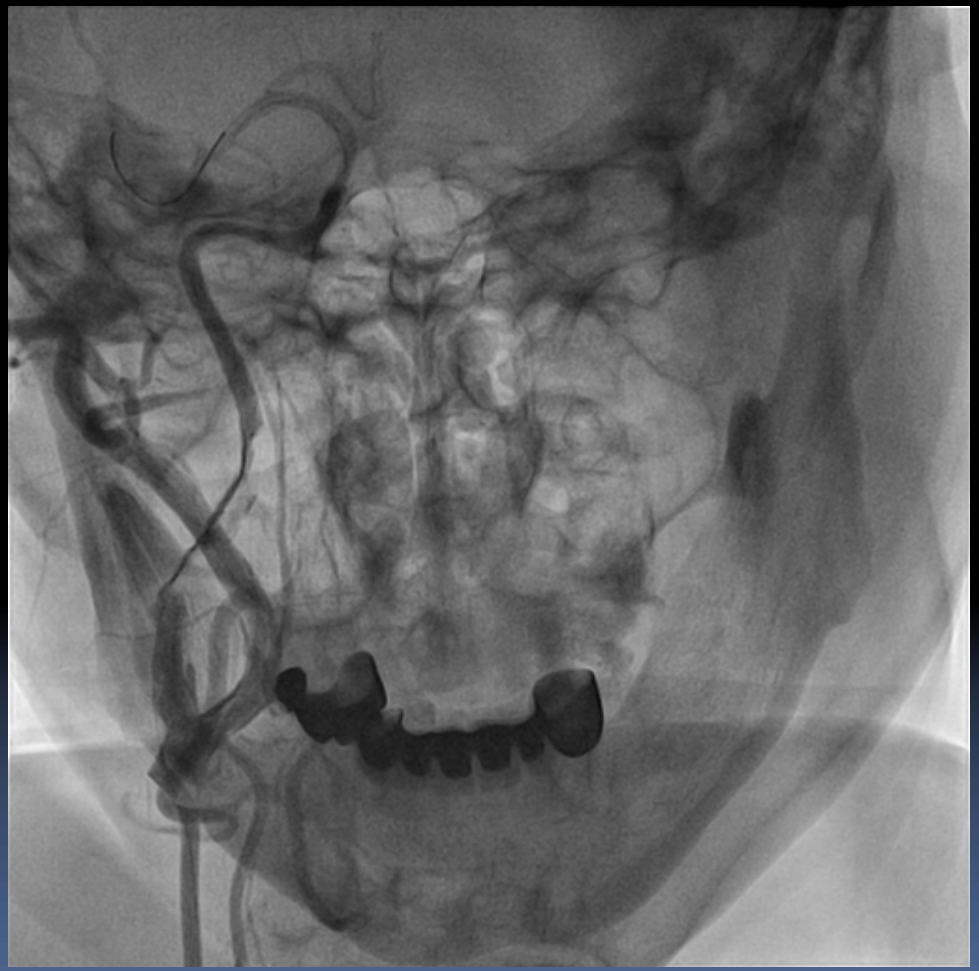
Tsunami 3x30mm stent delivered and implanted at 10atm

Distal cervical stenting

Tsunami 3.5x30 stent overlapping the first stent by 1mm and implanted at 10atm

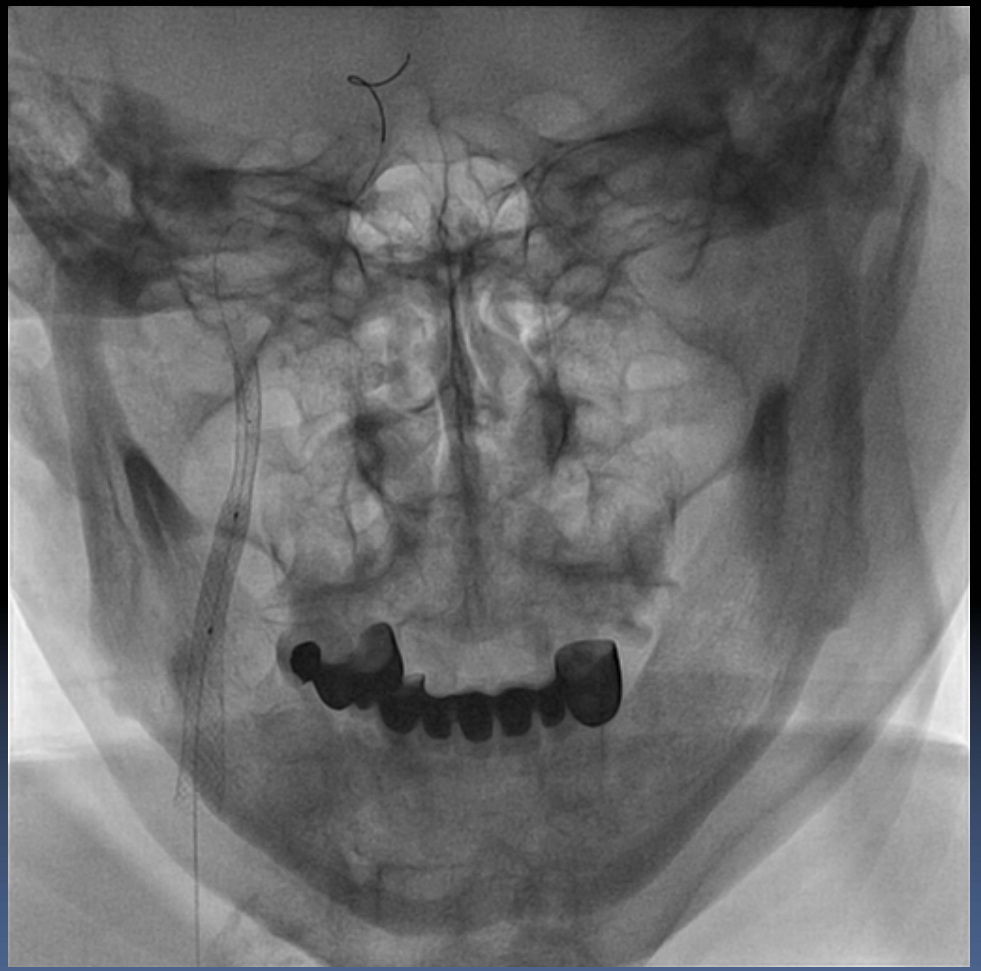
After 2 balloon expandable stents

Obviously 1 more stent was needed to cover the whole occlusion segment



Final self expanding stent

Carotid Wallstent 8x29 was deployed and post-dilated with 4x15 Maverick at 10atm



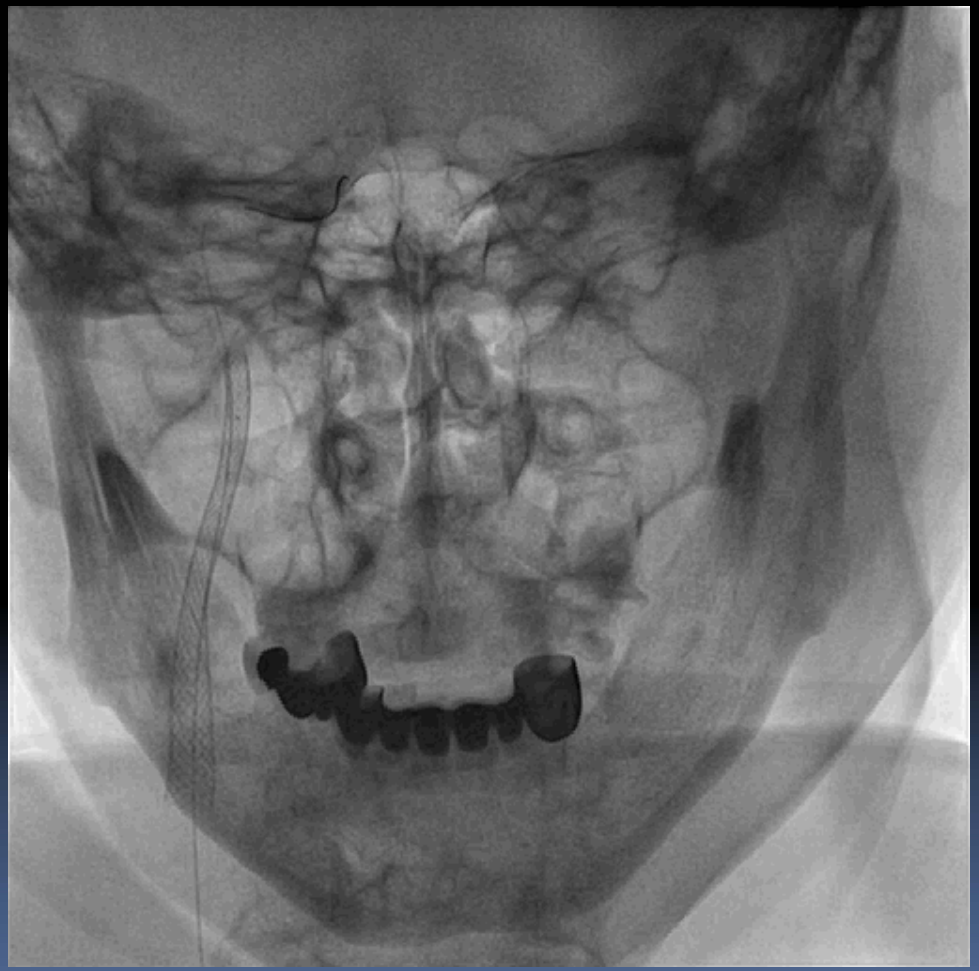
Complete recanalization

Complete reperfusion of the RICA territory

Patient was sent to CCU for overnight hemodynamic management

No post-procedure anticoagulation

Dual anti-platelet agents for 3 months



Objective improvement

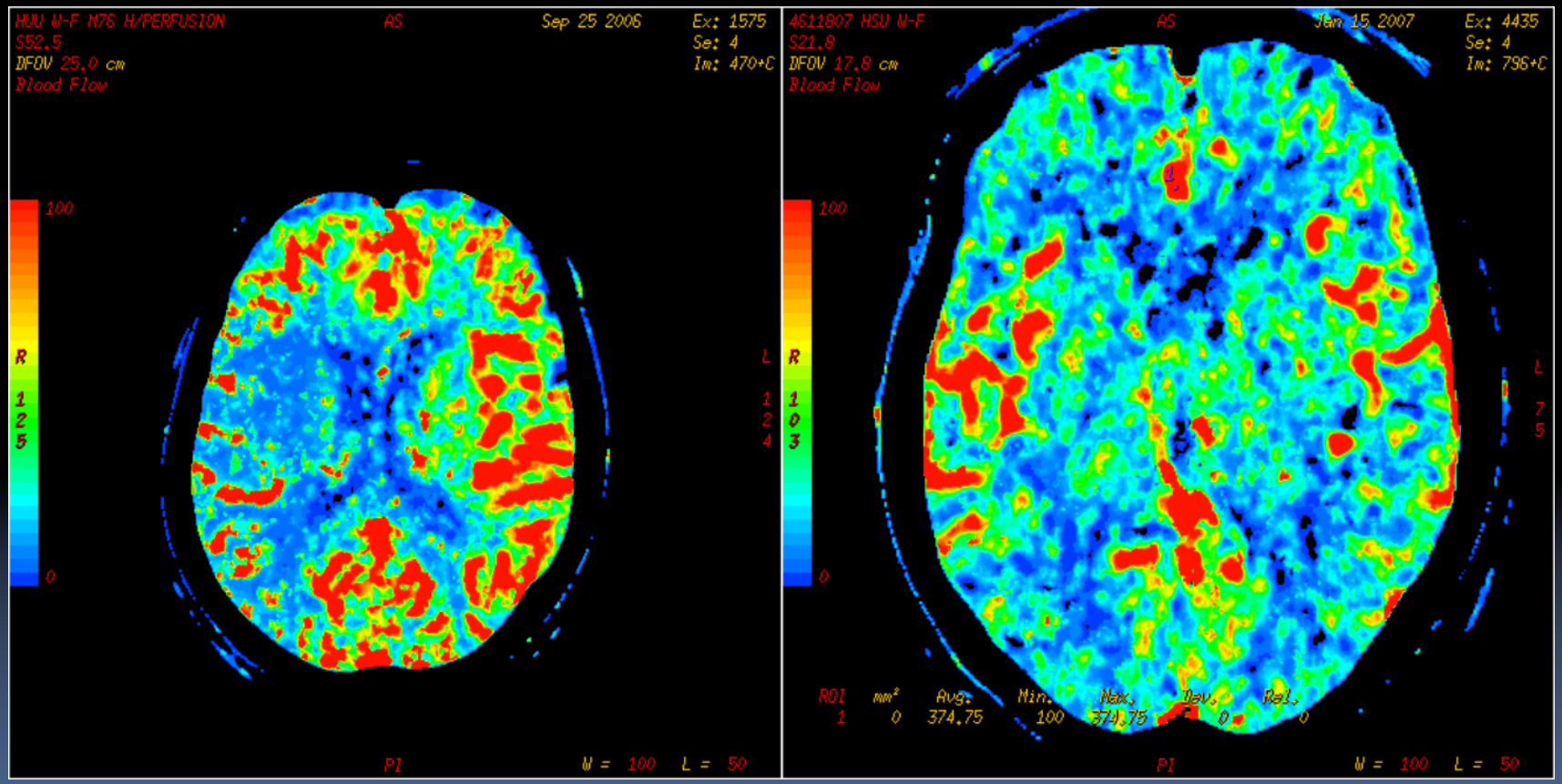
Discharged on D3

Perfusion CT showed complete recovery of right hemisphere ischemia

ADAS 14 → 5

MMSE 15 → 26

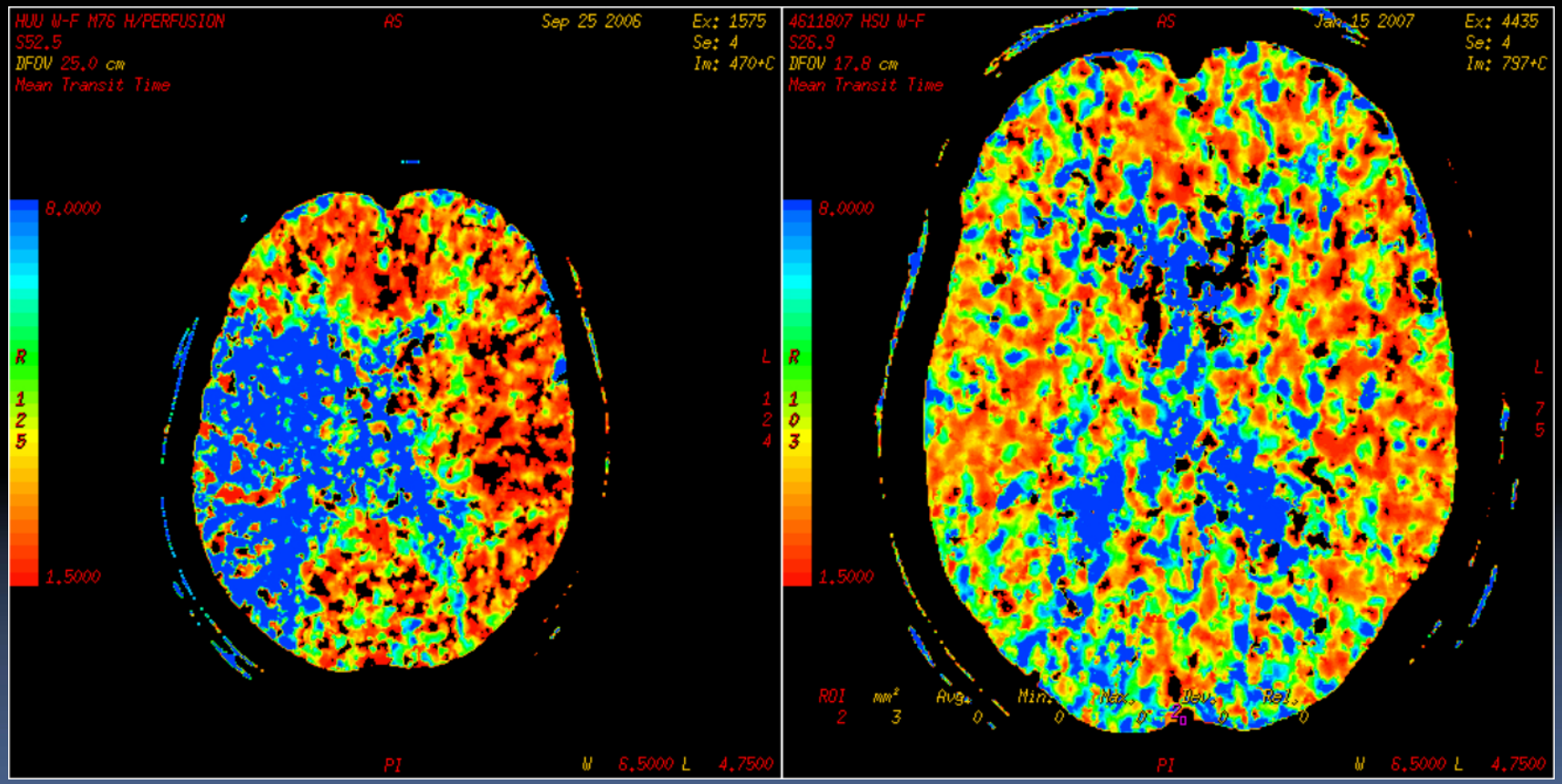
Improved stress-flow



baseline

After stenting

Improved stress-MTT



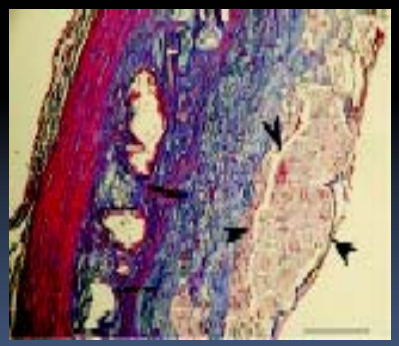
baseline

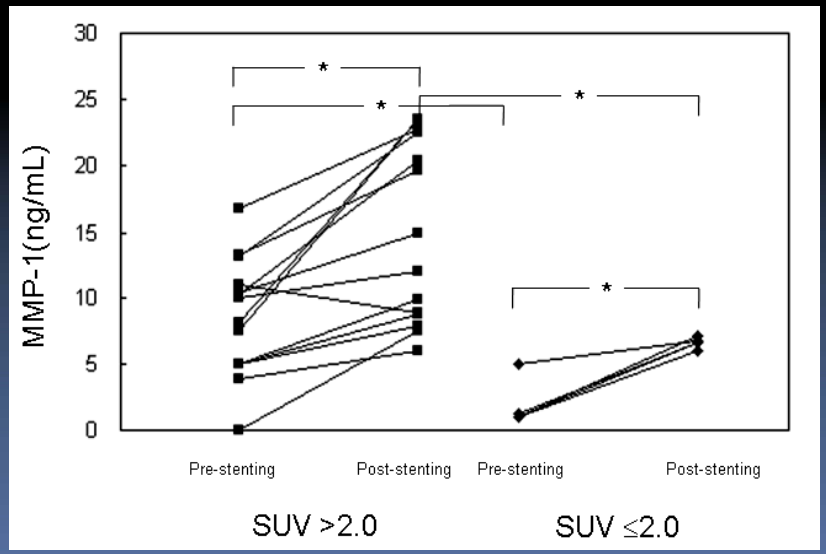
After stenting

Future directives in NTUH

- Vulnerable plaque imaging using FDG-PET/CT fusion imaging correlating with high circulating inflammation marker
- Quantification of brain perfusion in ICAS based on dynamic susceptibility contrast-enhanced MRI
- Cerebral glucose metabolism assay using FDG-PET with statistical parametric mapping

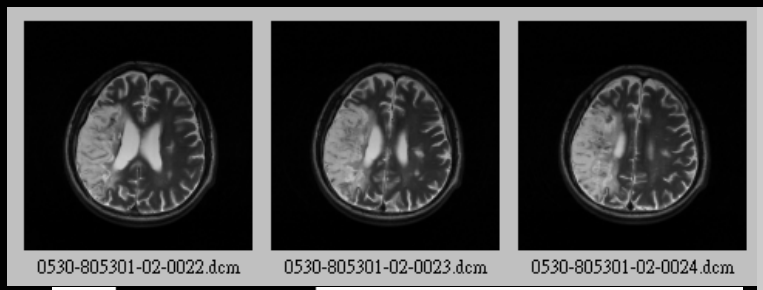
FDG-PET/CT fusion

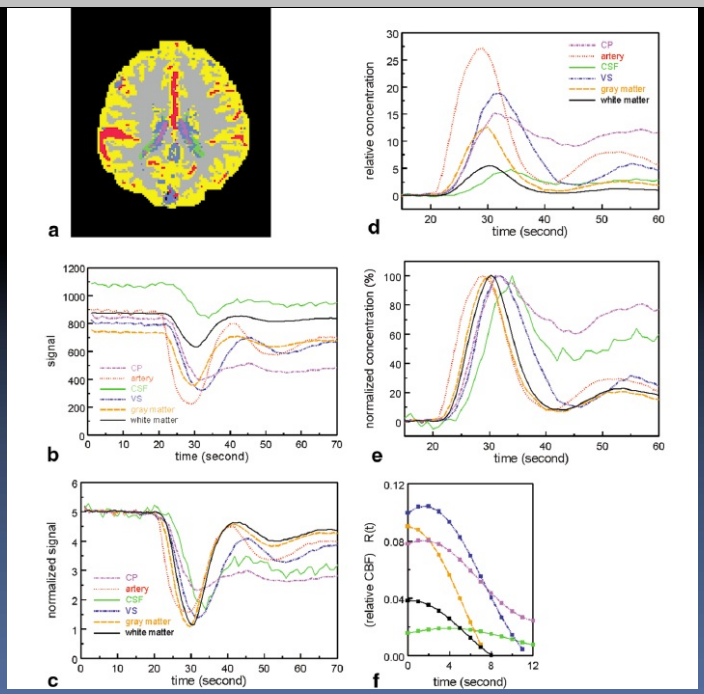


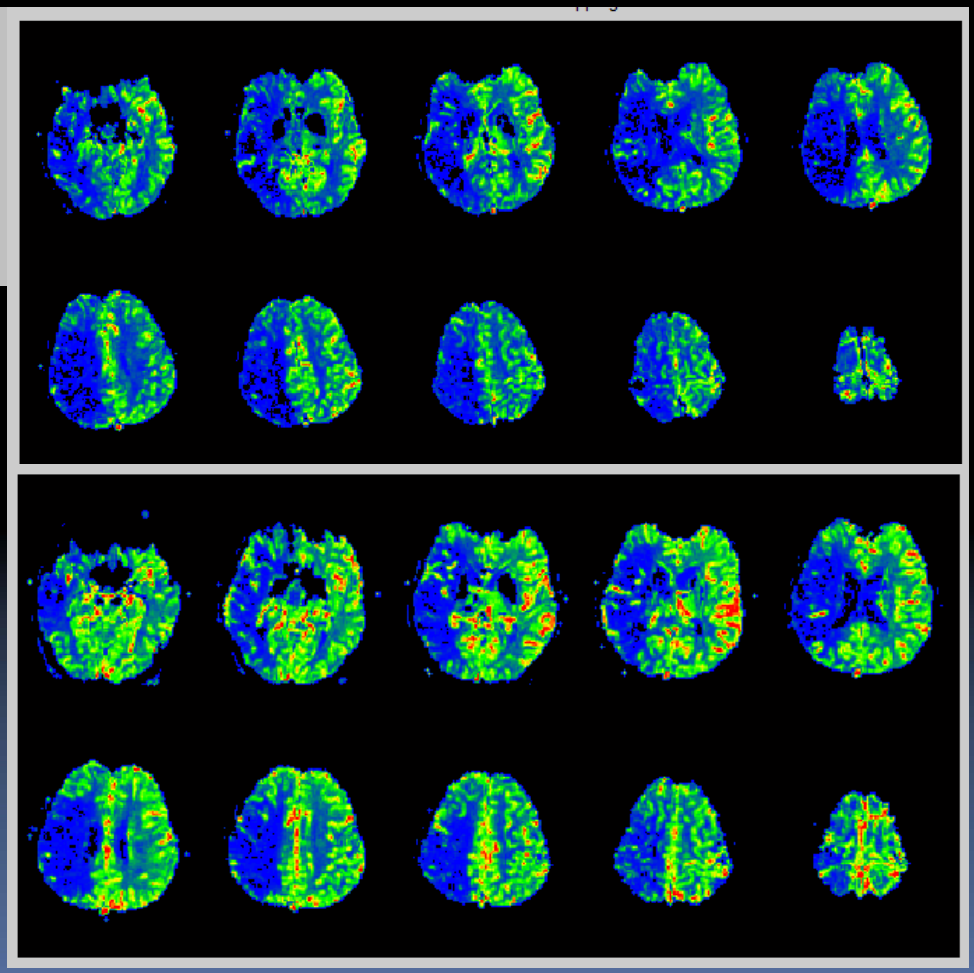


Wu YW, Kao HL, et al. JNM 2007;48: 227-233

MRI-CBF changes after stenting

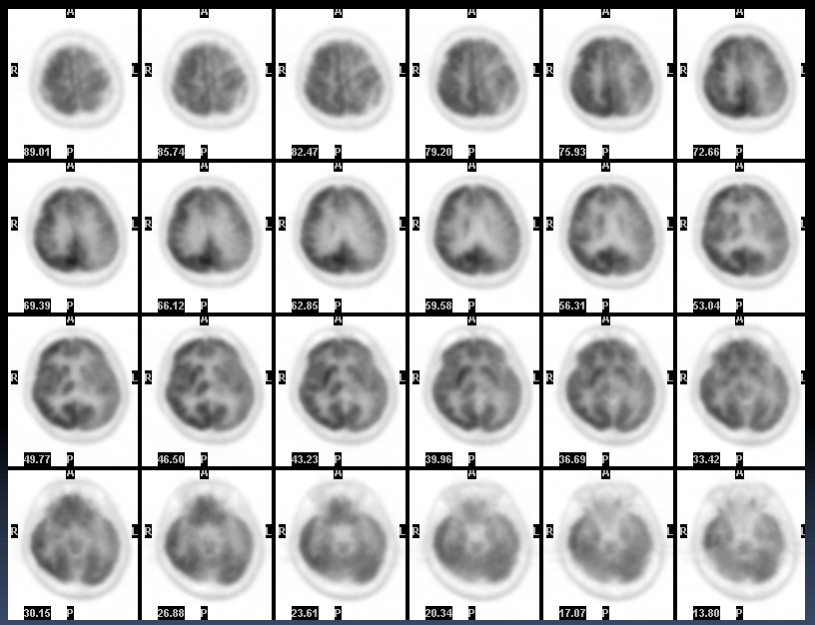




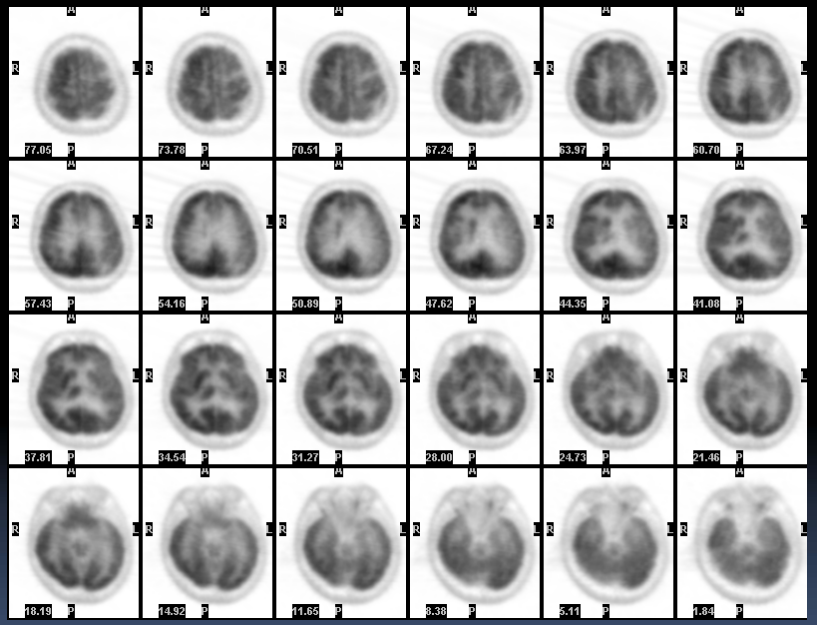


Su MY, Tseng WY, Kao HL, et al. ISMRM 2009

FDG-PET changes after stenting



baseline



After stenting

Paradigm shift in carotid procedures

- The goal of carotid interventions should not be limited to stroke prevention only, but also correction of cerebral ischemia
- Tools including functional (NCE) and imaging (CT, MRI. PET) modalities will be more important than anatomical ones (Duplex, angiography)
- Vulnerable plaques and tight stenoses are two different sets of targets, and treatment philosophy should be different