Intracranial stenosis for ECMINT

Intracranial Stenoses: When to Intervene

ECMINT 3.3 Stroke 19.12.19

St Anne's College Oxford

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Background

- Intracranial arterial stenosis is an important cause of stroke in Asian and Afro-Caribbean patients.
- Trials have shown that stroke frequently occurs even with medical treatment
- The new alternative is to treat the stenosis by angioplasty or stent insertion

How common is intracranial stenosis

- Sacco,Kargman et al Stroke 1995 26
- 14-20 Northern Manhattan Stroke Study
- Population aged over 39.
- 35% black 46% hispanic 19% white
- Proportion extracranial disease similar
- Intracranial more frequent blacks hispanics

Sacco Extracranial

- 10% extracranial
- 11% white
- 8% black
- 9% hispanic

Sacco Intracranial

- 1% white in fact only 1 patient out of 485
- 6% black
- 11% hispanic

How Common is IA

- Goerlick et al
- Large Artery Intracranial Disease
- Stroke 2008 39 2396
- Asian population
- 33 to 50% in Chinese
- 47% Thais
- 40% Korea

Risks

- 11% at one year
- 14% at 2 years
- 70% stenosis risk in territory of artery
- 25% at one year

Warfarin, Aspirin, Symptomatic Intracranial Disease, WASID trial

- 569 patients with a history of TIA or stroke with 50-99% stenosis of a major intracranial artery randomised between warfarin or aspirin
- Warfarin had a high rate of adverse events, particularly haemorrhage compared to the aspirin group, 8.3% vs 3.2%
- No benefit over aspirin in recurrent event rate
- Patients treated with aspirin had a 20% recurrence rate of any stroke at 2 year follow up and 25 % of any stroke at 3 years.

WASID trial

- Sub-analysis of WASID suggested that risk of stroke in the territory of the stenotic artery treated medical were highest with severe stenosis, of greater than 70%, women were at increased risk.
- Age, race, location, length of stenosis, other vascular risk factors, co-morbidities, pre-treatment with antithrombotic agents and type of stroke were not associated with a significant increase in stoke.
- The majority of strokes, 78%, occurred, within the first year of randomisation.

Safety and Efficacy of Stenting

- 7 main case series before the randomised trials
- The rate of successful stent deployment, 90-100%
- In one series of 104 patients post procedural stenosis 18%, compared with 75% pre procedure.
- Mortality related to the procedure , 0-5%, all due to cerebral infarction of haemorrhage, with one fatal anaphylactic reaction
- Few series reported long-term efficacy
- 104 patients, rate of recurrent stroke or TIA during follow up was 31%
- Another case series of 40 patient, no stroke or TIA during 10 months follow up
- Restenosis in 10 months 5-22%.

2006 Cochrane System Review

- Cochrane, 2006. No randomised controlled trials. Authors reviewed 79 published case series in which 3 or more cases were included with the results of intracranial angioplasty with or without stenting
- 1999 patients treated
- Peri-operative stroke 7.9%,
- Peri-operative death 3.4% and combined 9.5%
- Groin haematoma and arterial dissection 9.9%
- With follow up of at least one year the mean risk of stroke or death was 5.6%

- CONCLUSION
- Insufficient evidence to recommend angioplasty with or without stent placement for stroke prevention and a controlled trial is indicated.

Draft NICE Guidelines 2005

- Endovascular stent insertion for intracranial atherosclerotic disease, provisional recommendations
- Evidence of clinical efficacy of endovascular stent insertion for intracranial atherosclerotic disease is currently inadequate and the procedure poses potentially serious safety concerns
- Clinicians should collaborate to organise randomised studies of adequate size to compare endovascular stent insertion against best medical management.
- Until randomised studies are available for recruitment clinicians should inform the clinical governance lead in their Trust and ensure patients understand the uncertainty about the procedure's efficacy and the risk of serious complications, including providing them with written information
- Audit and review of clinical outcomes of all patients.

- Position statement by the American Society of Interventional Therapeutic Neuroradiology: 2005
- Recommendations are:
- For symptomatic patients with greater than 50% intracranial stenosis which have failed medical therapy, balloon angioplasty, with or without, stenting
- Patients who have an asymptomatic intracranial arterial stenosis should be first counselled regarding optimised medical therapy.
- They also state that similar to revascularisation for extracranial artery stenosis patient benefit from revascularisation for symptomatic intracranial arterial stenosis is critically dependent on the low peri-procedural stroke and death rate and should only be performed by experienced Neurointerventionalists.
- We should support randomised trials

- Good editorial by Barnett, as to why randomised trials are essential.
- He looks at the debunking of widespread tonsillectomy, EC-IC bypass and Warfarin for non-cardiogenic ischaemic stroke
- He also makes an excellent point about asymptomatic carotid stenosis, that to be beneficial the peri-operative stroke and death rates must be less than 3% and that in institutions that violate this, carotid endarterectomy can be added at the stroke risk profile.
- He adds that we should not hurry to promote a new technique, such as intracranial stenting, on the back of a few cases, with a limited number of patients when we particularly do not fully understand the natural history.

References

- Intracranial Angioplasty and Stenting for Cerebral Atherosclerosis: a position statement of the American Society of Interventional and Therapeutic Neuroradiology: AJNR 2005: 26: 2323-27
- Conventional wisdom versus reality in stroke prevention. Barnet HJM Neurology 2005: 64: 1122-24

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

N ENGL J MED 365;11 NEJM.ORG SEPTEMBER 15, 2011

Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis

Marc I. Chimowitz, M.B., Ch.B., Michael J. Lynn, M.S., Colin P. Derdeyn, M.D., Tanya N. Turan, M.D., David Fiorella, M.D., Ph.D., Bethany F. Lane, R.N., L. Scott Janis, Ph.D., Helmi L. Lutsep, M.D., Stanley L. Barnwell, M.D., Ph.D., Michael F. Waters, M.D., Ph.D., Brian L. Hoh, M.D., J. Maurice Hourihane, M.D., Elad I. Levy, M.D., Andrei V. Alexandrov, M.D., Mark R. Harrigan, M.D., David Chiu, M.D., Richard P. Klucznik, M.D., Joni M. Clark, M.D., Cameron G. McDougall, M.D., Mark D. Johnson, M.D., G. Lee Pride, Jr., M.D., Michel T. Torbey, M.D., M.P.H., Osama O. Zaidat, M.D., Zoran Rumboldt, M.D., and Harry J. Cloft, M.D., Ph.D., for the SAMMPRIS Trial Investigators*

- Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis
- SAMMPRIS
  - New England Journal of Medicine Sept 2011

- Patients who had recent transient ischaemic attacks or stroke with 70-99% stenosis of an major intracranial artery randomised between aggressive medical therapy or aggressive medical management plus WingSpan Stent

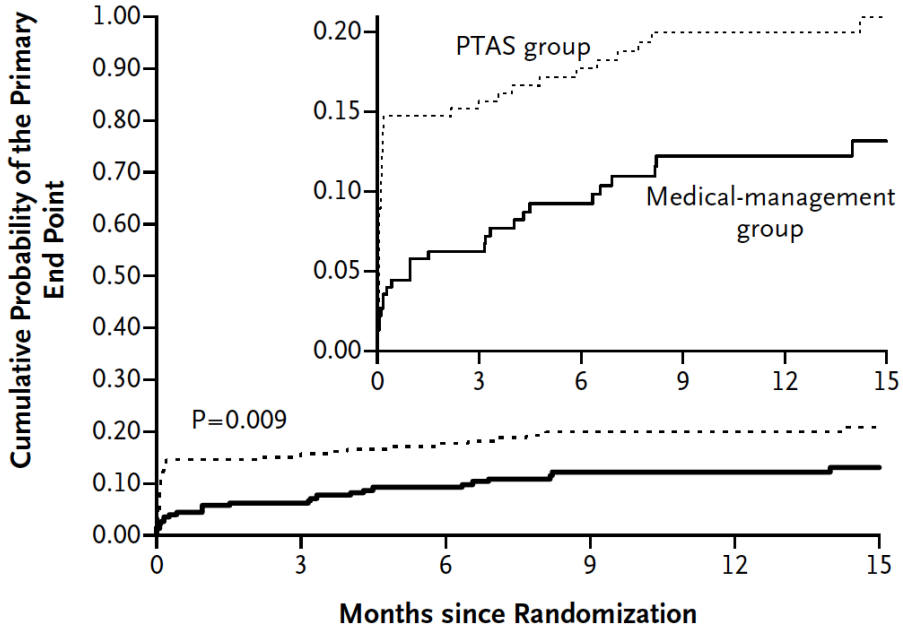
SAMMPRIS: Initial Results

- Ischaemic symptoms within 30 days
- ≥ 70% stenosis VB, M1, ICA

- Medical regimen
  - LDL < 70 (Rousvastatin)
  - SBP < 130
  - Dual antiplatelets for 90 days

- Enrolment was stopped after 451 patients underwent randomisation

- 30 day stroke of death was 14.7% in the PTA group (non fatal stroke 12.5%, fatal stroke 2.5%) and 5.8% in the medical management group (non-fatal stroke 5.3%, non stroke related death 0.4%) P=0.002



No. at Risk

Medical management group	227	196	164	132	115	92
PTAS group	224	182	153	125	98	83

Figure 1. Kaplan–Meier Curves for the Cumulative Probability of the Primary End Point, According to Treatment Assignment.

The primary end point was stroke or death within 30 days after enrollment or after a revascularization procedure for the qualifying lesion during the follow-up period or stroke in the territory of the qualifying artery beyond 30 days. The curves were truncated at 15 months because relatively few patients have been followed beyond this time and there have only been two primary end-point events beyond 15 months, both in the group receiving percutaneous transluminal angioplasty and stenting (PTAS) (one at 26.1 months and one at 26.2 months). The maximum duration of follow-up is 28.9 months for the group receiving medical management only and 28.1 months for the PTAS group. The inset shows the same data on an enlarged segment of the y axis.

SAMMPRIS:FINAL RESULTS Derdeyn et al Lancet Jan 2014

- Median follow up 32.4 months 15% med arm vs 23% stenting arm had a primary end point.
- Absolute risk reduction 8.9% at 30 days and 9 % at 3 years.
- Medical management lower risk than in WASID ? Due to aggressive antiplatelet and medical therapy BP Lipids.

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Effect of a Balloon-Expandable Intracranial Stent vs Medical Therapy on Risk of Stroke in Patients With Symptomatic Intracranial Stenosis The VISSIT Randomized Clinical Trial

Zaidat et al

OBJECTIVE: To evaluate the efficacy and safety of the balloon-expandable stent plus medical therapy vs medical therapy alone in patients with symptomatic intracranial stenosis (70%).

112 patient randomised,
59 stent group, 53 medical group

Trial stopped due to negative results from another trial

112 out of 250, stent group 24.1% stroke or TIA at 30 days vs 9.4% in medical group

8.6% intracranial haemorrhage in the stent group vs none in the medical group

1 year primary outcome, stroke or TIA 36.2% in the stent group vs 15 % in the medical group

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Conclusion

- These findings do not support the use of a balloon expandable stent for patients with symptomatic intracranial stenosis.
- JAMA 2015 313 (12) 1240-1248

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Editorial
Endovascular Therapy for Atherosclerotic Intracranial Arterial Stenosis: Back to the Drawing Board

Marc Chimowitz

JAMA March 24/31, 2015 Volume 313, Number 12

- Criticisms of SAMMPRIS, self expanding stent techniques were criticised however VISSIT trial addresses this
- Lower than expected stroke rate in the medical group in VISSIT strengthens the treatment recommendations from SAMMPRIS, ie patients with symptomatic intracranial stenosis should be treated with aggressive medical management consisting of antiplatelet therapy, dual antiplatelets for the first 90 days and intensive risk factor management
- No proven role for endovascular therapy for any subgroup of patients with intracranial stenosis.

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- Unexpected finds in SAMMPRIS and VISSIT with high rate of parenchymal brain haemorrhage after stenting.
- Identifying a cause of these haemorrhages will be important
- In addition to unacceptably high procedural complication in both VISSIT and SAMPRISS there was also persistent risk of ischaemic stroke beyond the 30 day peri-operative procedure thus technically successful stenting was not protective against future stroke risk
- Further trials are needed for stenting but it is difficult to see how these will happen any time now.

Detailed Analysis of Periprocedural Strokes in Patients Undergoing Intracranial Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis: SAMMPRISS

- Fiorella et al Stroke 43: 2682-2688

- 224 patients randomised to angioplasty or stenting
- 213 underwent angioplasty alone (5) or with stenting (208)
- 13 haemorrhagic strokes (7 parenchymal, 6 subarachnoid)
- 19 ischaemic stroke
- 2 TIAs

- Ischaemic events categorised as
- Perforator occlusion 13
- Embolic 4
- Mixed perforator and embolic 2
- Delayed stent occlusion 2

- Multivariate analyses showed that higher percentage stenosis, lower modified Rankin score and clopidogrel load associated with activate clotting time above the target range were associated with haemorrhagic stroke.
- Nonsmoking, basilar artery stenosis, diabetes and older age were associated with ischaemic events

Conclusion

- In SAMMPRIS periprocedural stroke have multiple causes, most common being perforator occlusion
- Excluding patients with these features from undergoing percutaneous transluminal angioplasty and stenting to lower procedural risk would limit percutaneous transluminal angioplasty and stenting to a small subset of patient
- Given the small number of events the present data should be used for hypothesis generation rather than a guide t o patient selection in clinical practice

Smokers' Paradox

- Smokers had dramatically lower periprocedural events in SAMMPRIS than non-smokers
- Also observed after coronary interventions
- Related to the fact that nonsmokers are likely to be female, diabetic and hypertensive may increase their risk
- Smokers are also more responsive to clopidogrel than nonsmokers due to induction of hepatic cytochrome p450 system involved in conversion of clopidogrel to its active metabolite

Conclusion

- Perforators most common cause of ischaemic events after PTAS, especially after basilar PTAS as reported previously
- Due to atherosclerotic debris being displaced or snow-ploughed over the perforator origins during angioplasty or stent placement
- However perforator rich MCA artery was associated with the lowest risk of periprocedural ischaemic artery stroke of all arteries stented in the trial

SAMMPRIS Update: Current Indications

- SAMPRISS limited to stable patients with recent (within 30d) symptoms.
- Reasonable to consider angioplasty and / or stenting
  - Unstable or progressing symptoms
  - Recurrent stroke on SAMPRISS medical regimen - chronic fixed lesions
- Avoid perforator rich segments, particularly the basilar

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WEAVE Trial

Stroke 2019; 50: 889-894 Alexander MJ et al

WEAVE trial - (Wingspan stent system post market surveillance) mandated by FDA to assess periproecdural safety of the Wingspan stent system in the treatment of symptomatic intracranial atherosclerotic disease.

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On label use

- 70-99% stenosis intracranial atherosclerotic lesion
- Greater than 7 day post stroke
- 22-80 years old
- mRS 3 or less
- Difficult to manage medically
- Recurrent 2 or more strokes

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Experienced interventionalists

- INRs had mean case experience greater than 37 wingspan stents
- Primary end point stroke or death within 72 hours of procedure
- On label patients (off label patients also analysed, those outside the criteria)

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- 24 sites in the USA, 152 patients
- Lower than expected periprocedural stroke rate 2.6%, 4 out of 152
- 148 out of 152 event free at 72 hours
- 1.3%, 2 out of 52 non fatal strokes, 1.3%, 2 out of 52 died
- However off label branch stroke or death rate after 72 hours was 23.9%
- Most common reason being treated off label, being treated early within 7 days of stroke
- Comments : wide variation 2.6% vs 23.9% really need a randomised trial

- INTRACRANIAL STENTING FOR ATHEROSCLEROTIC DISEASE

Technical Aspects

- Intracranial stenting and angioplasty,
- General anaesthesia,
- Dual antiplatelet therapy
- Intra-procedural Heparin
- Either angioplasty with slow inflation and under dilatation or using the Micrus balloon expandable Pharos stent(if you can get one or just use a cardiac stent) or the Boston self-expanding WingSpan stent.

Technical Aspects

- Patients should be pre-medicated with antiplatelet agents
  - Recommended with aspirin 75mg a day for at least 7 days prior to the procedure, or a 600mg loading dose the day before the procedure and 75mg on the day,
  - plus clopidogrel 75mg a day for at least 7 days before the procedure, or a 600mg loading the dose the day before the procedure and 75mg on the day of the procedure.
- 75mg of both agents continued for 6 months (much debate about length of time) and one agent, usually clopidogrel, 75mg a day for life.
- If a platelet functional analyser such as VerifyNow is available antiplatelet function should be tested prior to the procedure and dosages adjusted accordingly.
- If inadequate suppression with clopidogrel use prasugrel 60mg loading 10mg a day

Intracranial Stenting

- Premedication as above. Heparinisation as above.
- Procedure is ideally preformed under general anaesthesia.
- Both balloon mounted Cardiac or Pharos and self expanding stents are used. Self expanding stents usually require pre-dilatation of the lesion using a gateway balloon to approximately 75% of the diameter of the normal vessel before deployment of the stent.

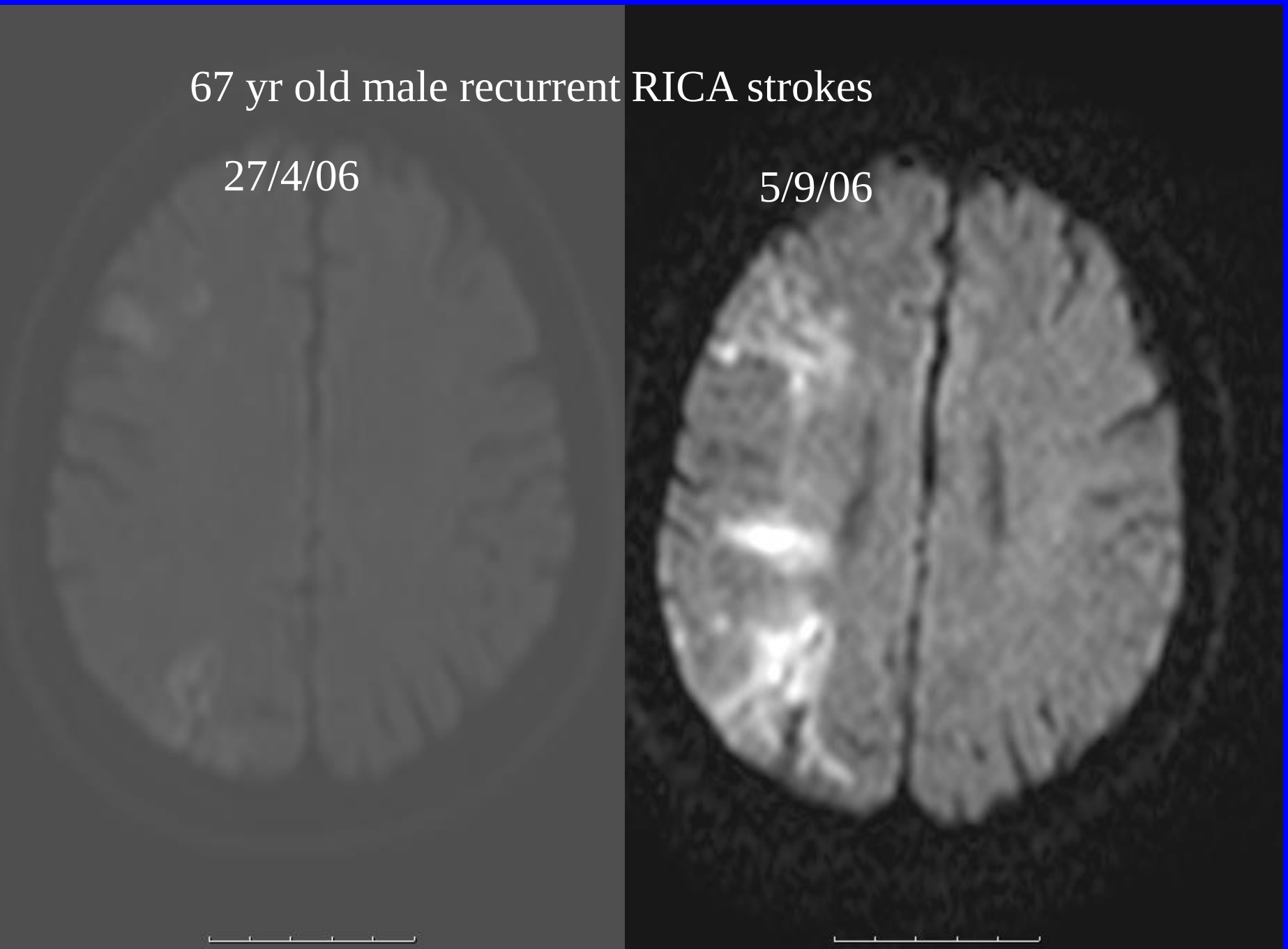
Post procedure care

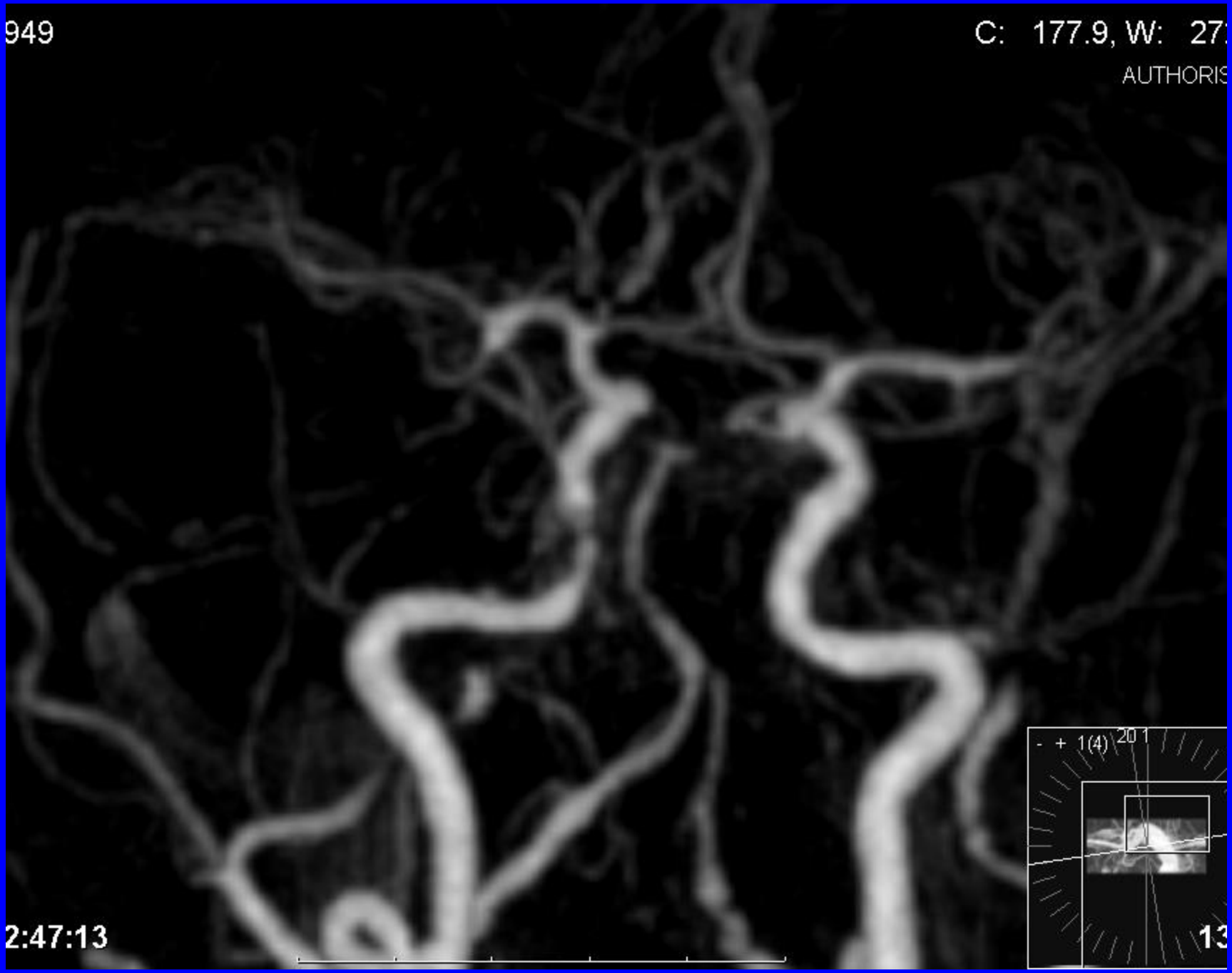
- Post procedure care:-
- Extracranial can be managed in a high dependency unit over night. Heparinisation is not necessary for extracranial stents.
- Intracranial stenting:- essential the patient has access to an HDU or even an ITU bed overnight for close monitoring of blood pressure and other neurological parameters. Heparinisation is usually continued for 24 hours after the procedure.
- It goes without saying that all these patients have atheromatous disease and will be managed by a Neurologist or Stroke Physician with control of risk factors such as hypertension, glucose, cholesterol etc.

67 yr old male recurrent RICA strokes

27/4/06

5/9/06

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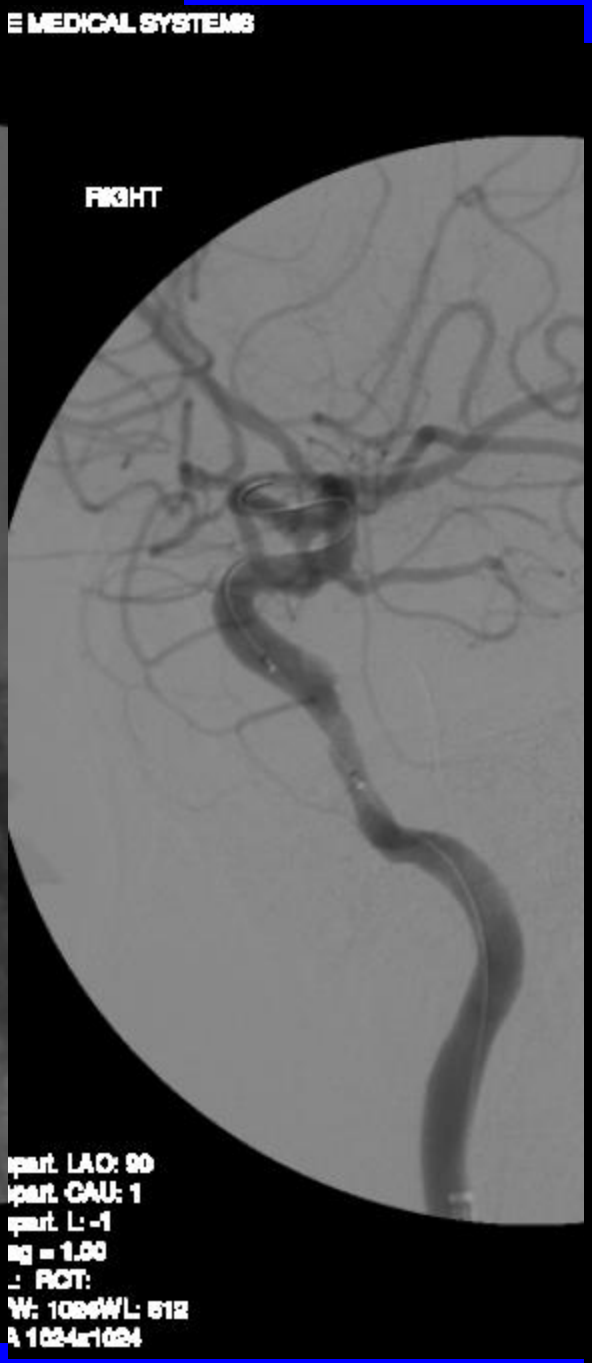
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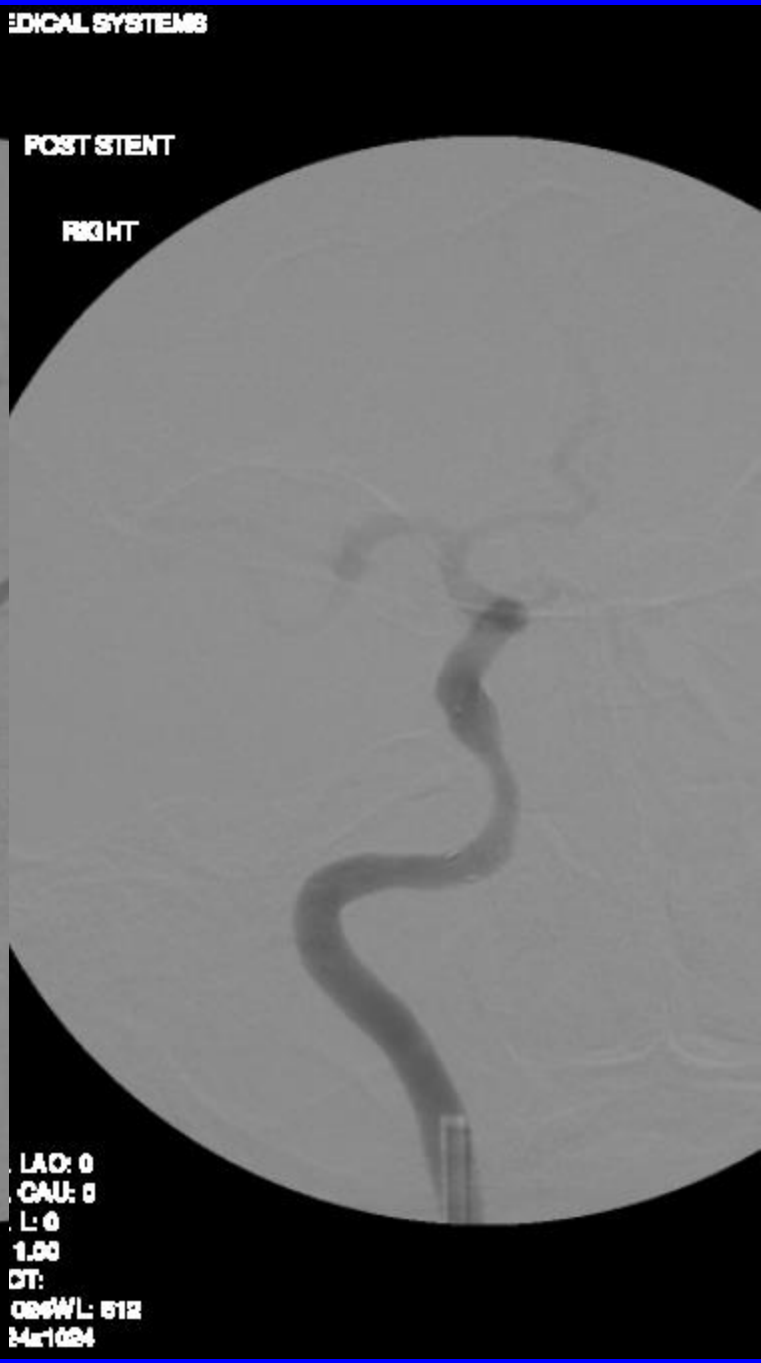
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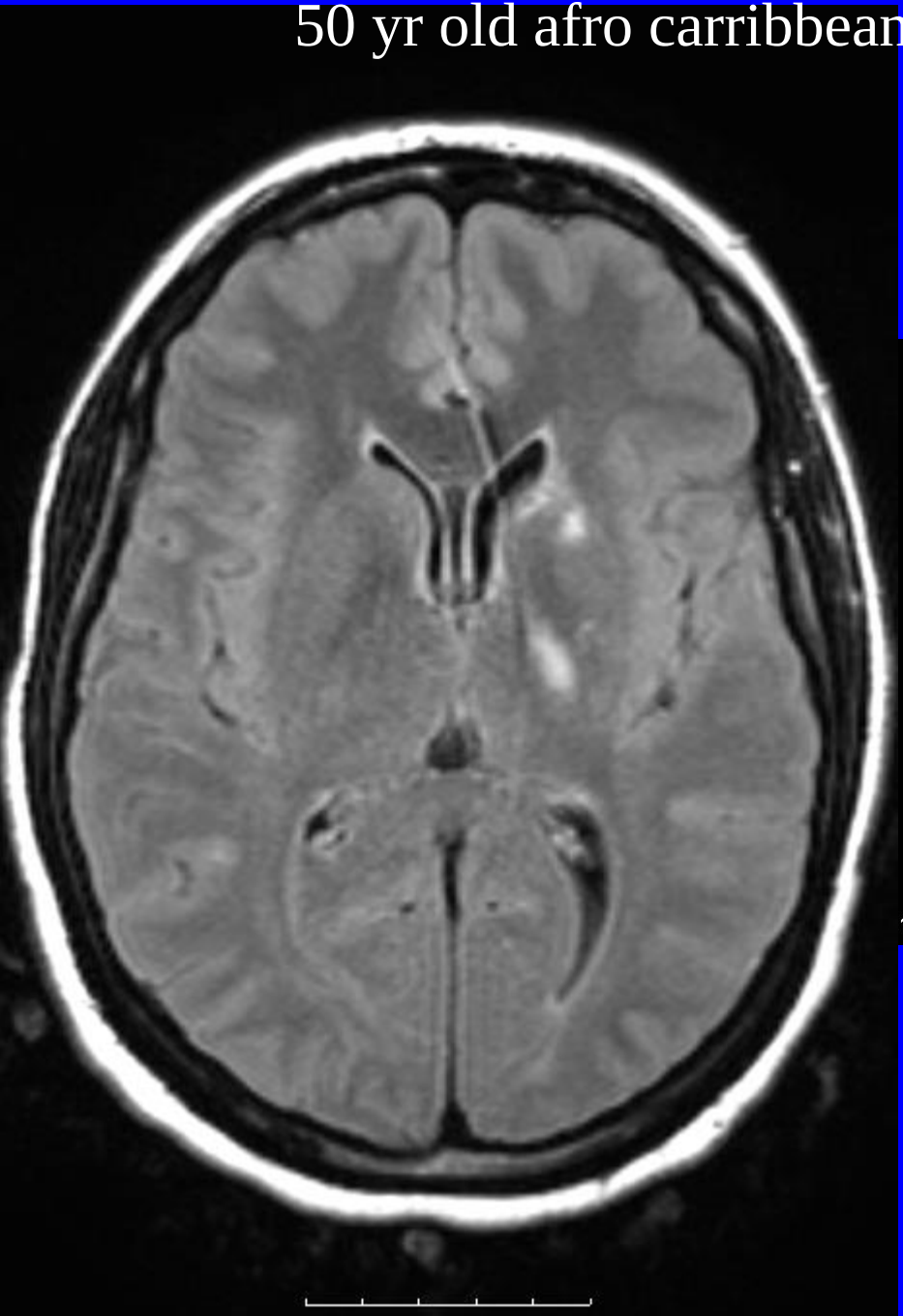
6 month follow up

50 yr old afro carribbean female recurrent stroke/TIAS

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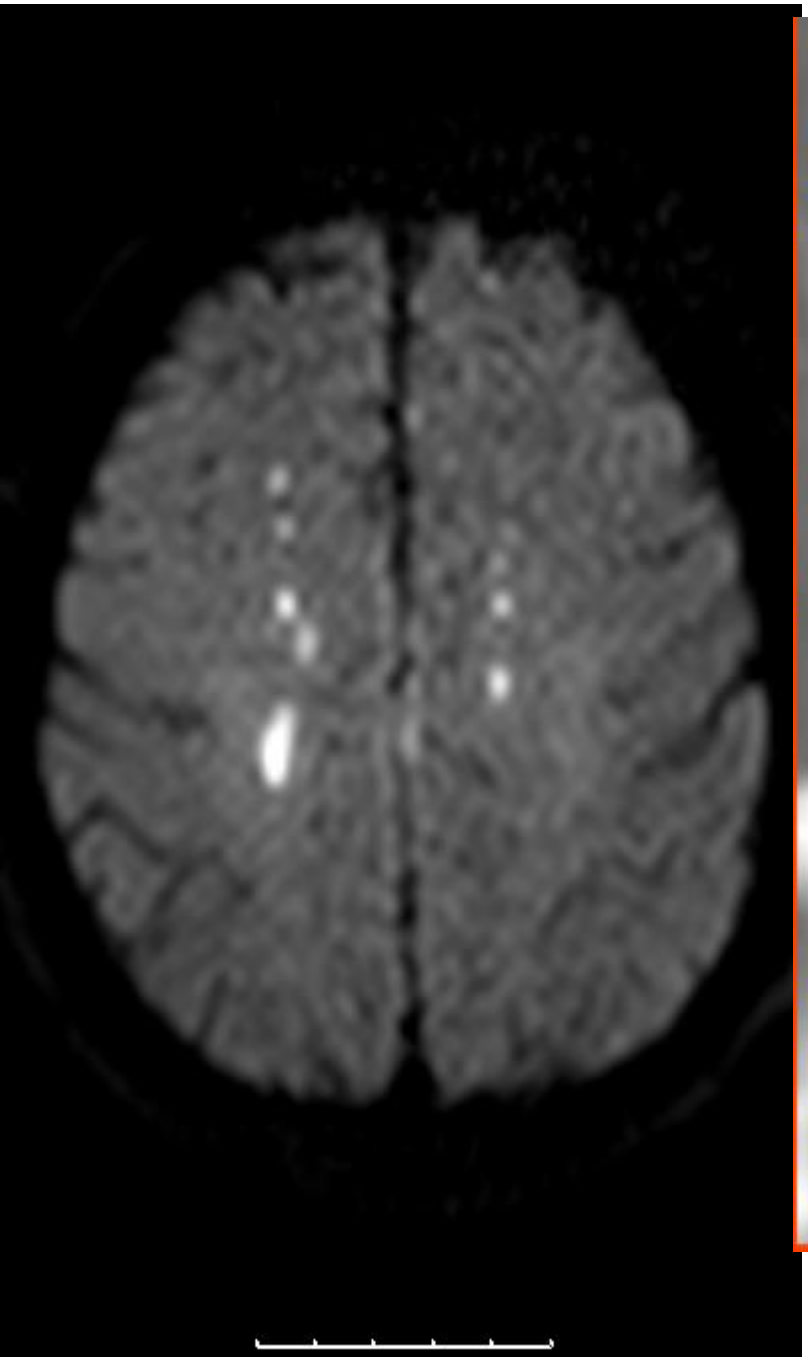
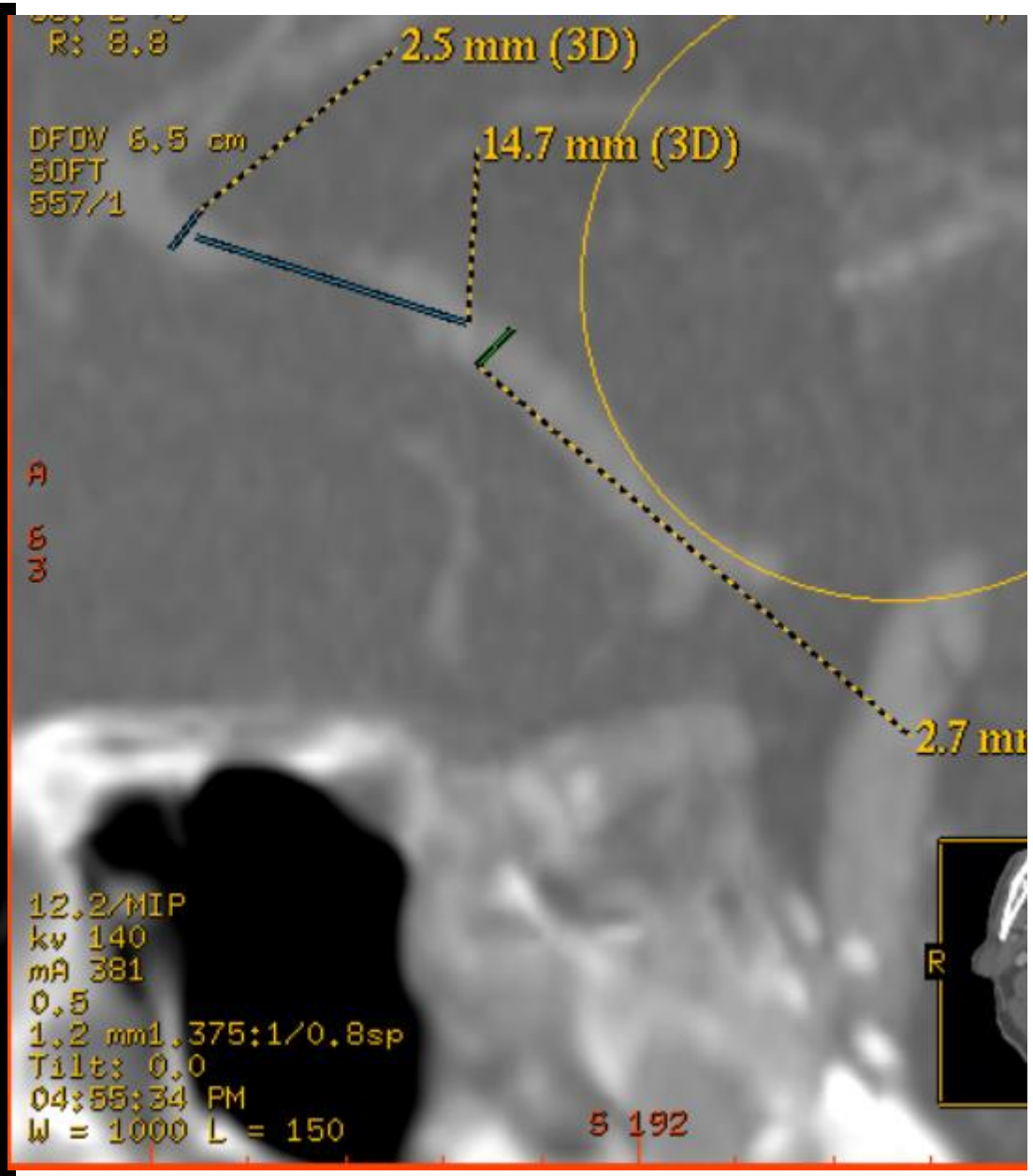
POST STENT DEPLOYMENT - 10 minutes

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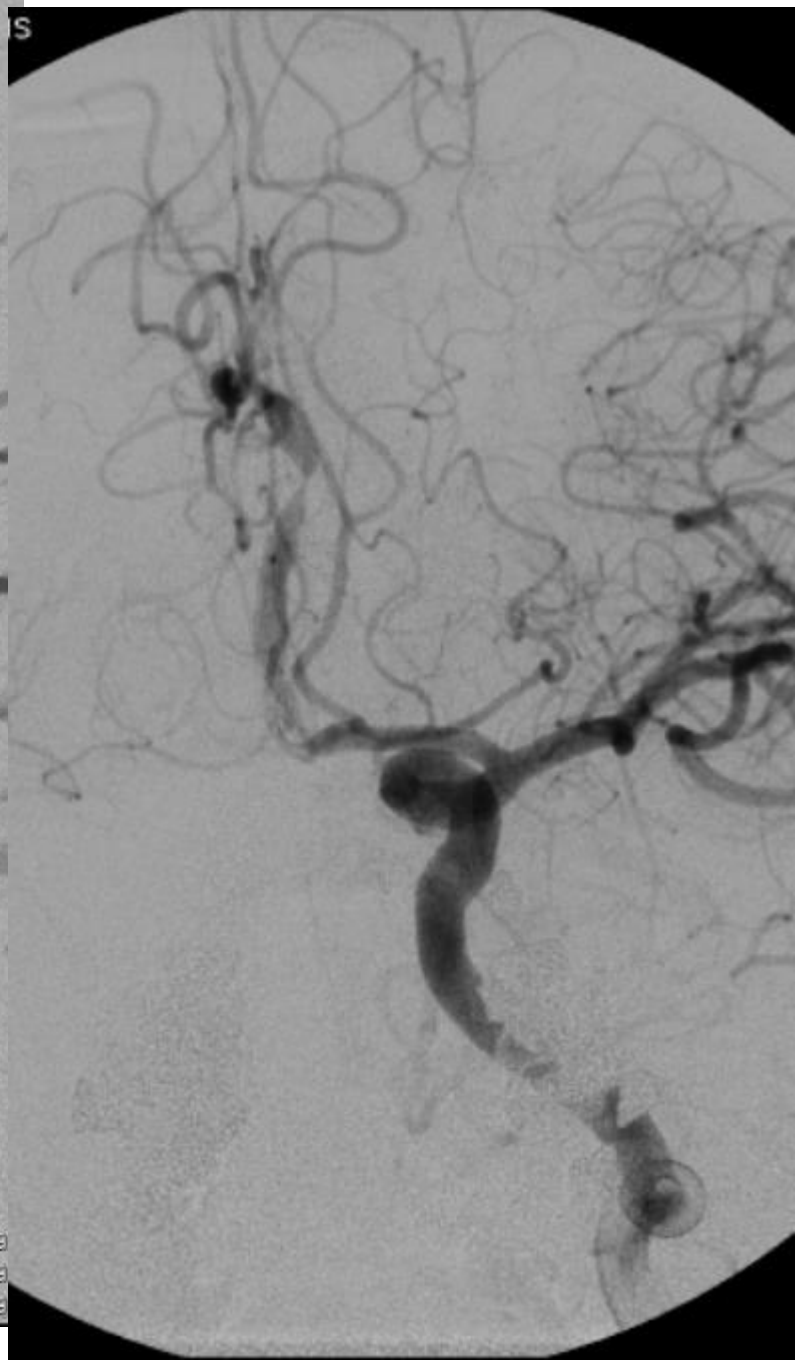


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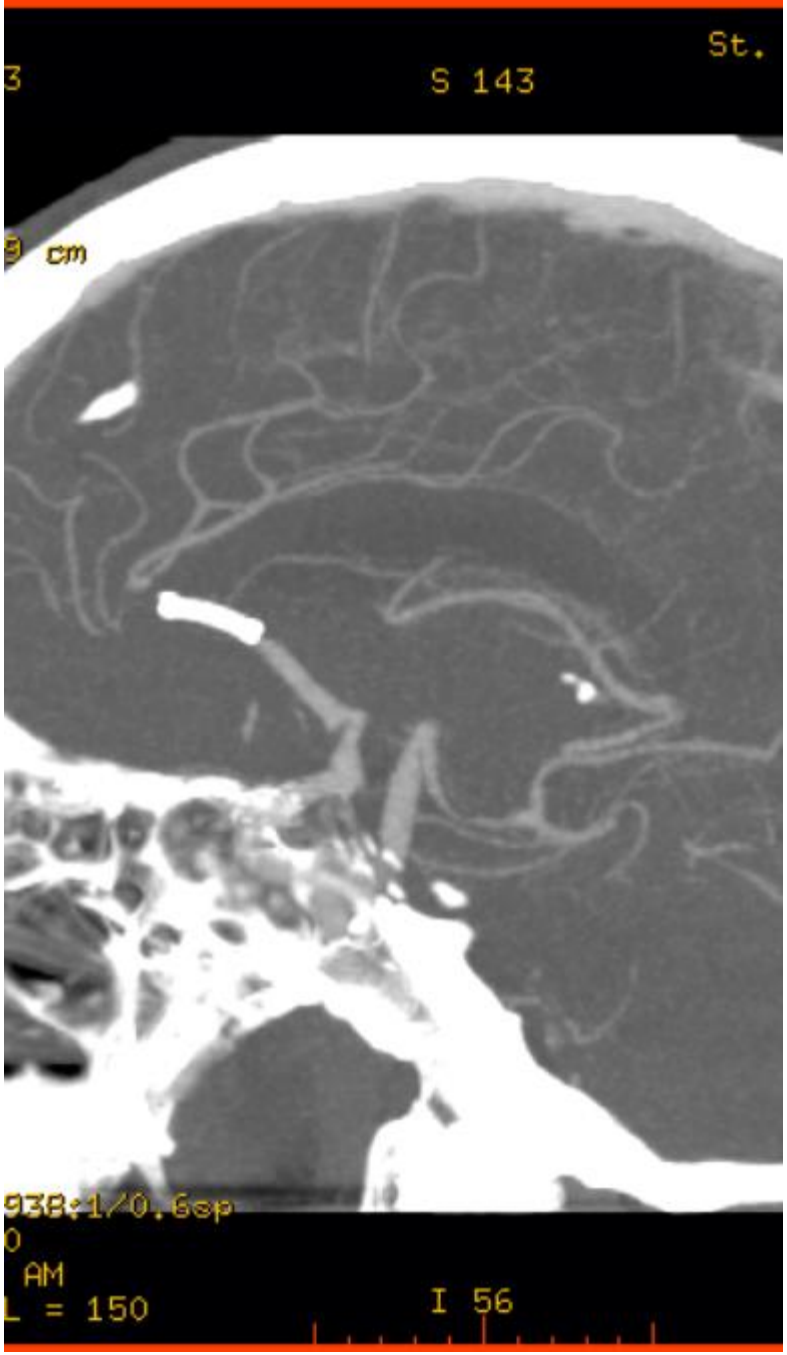
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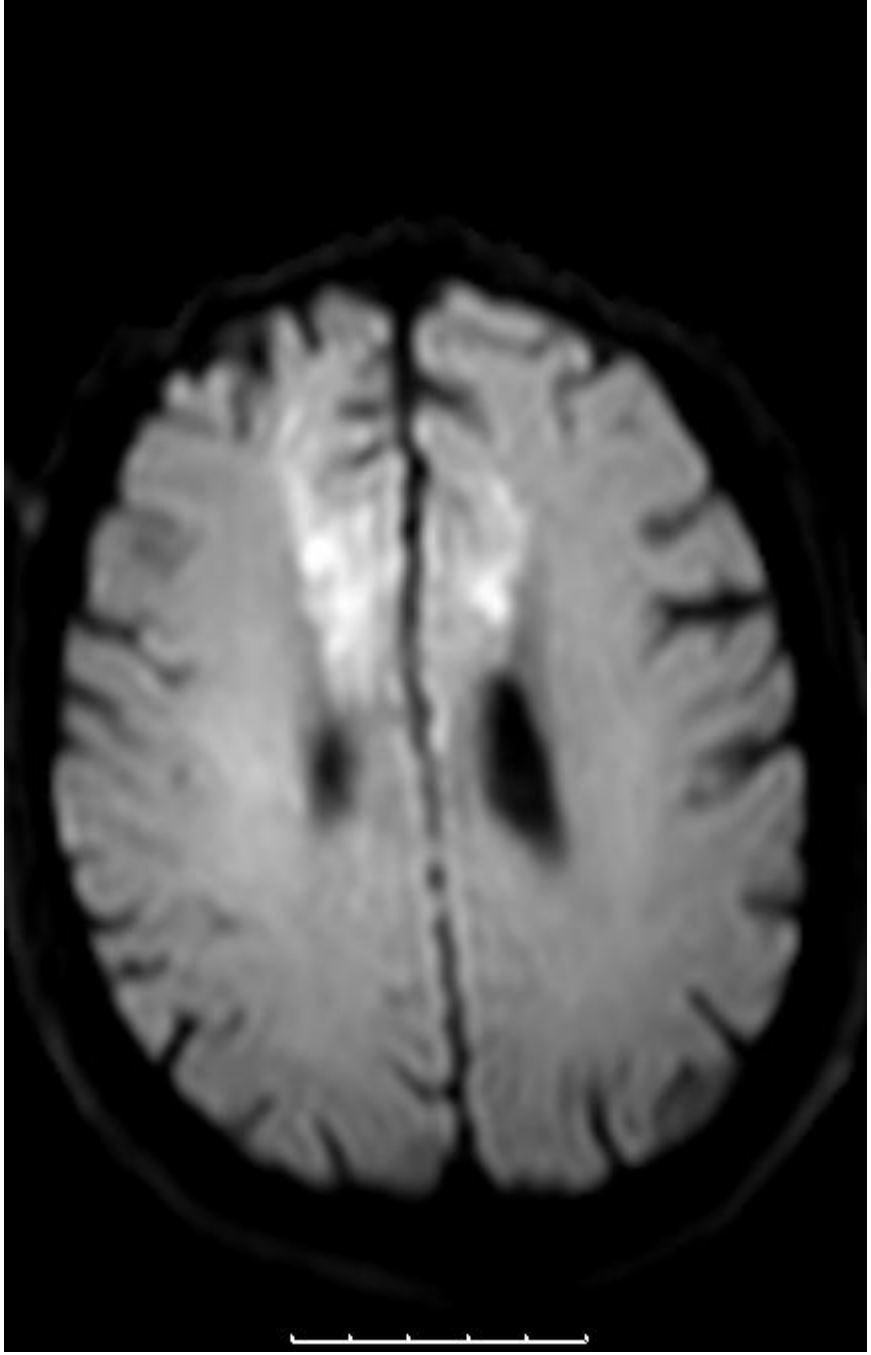
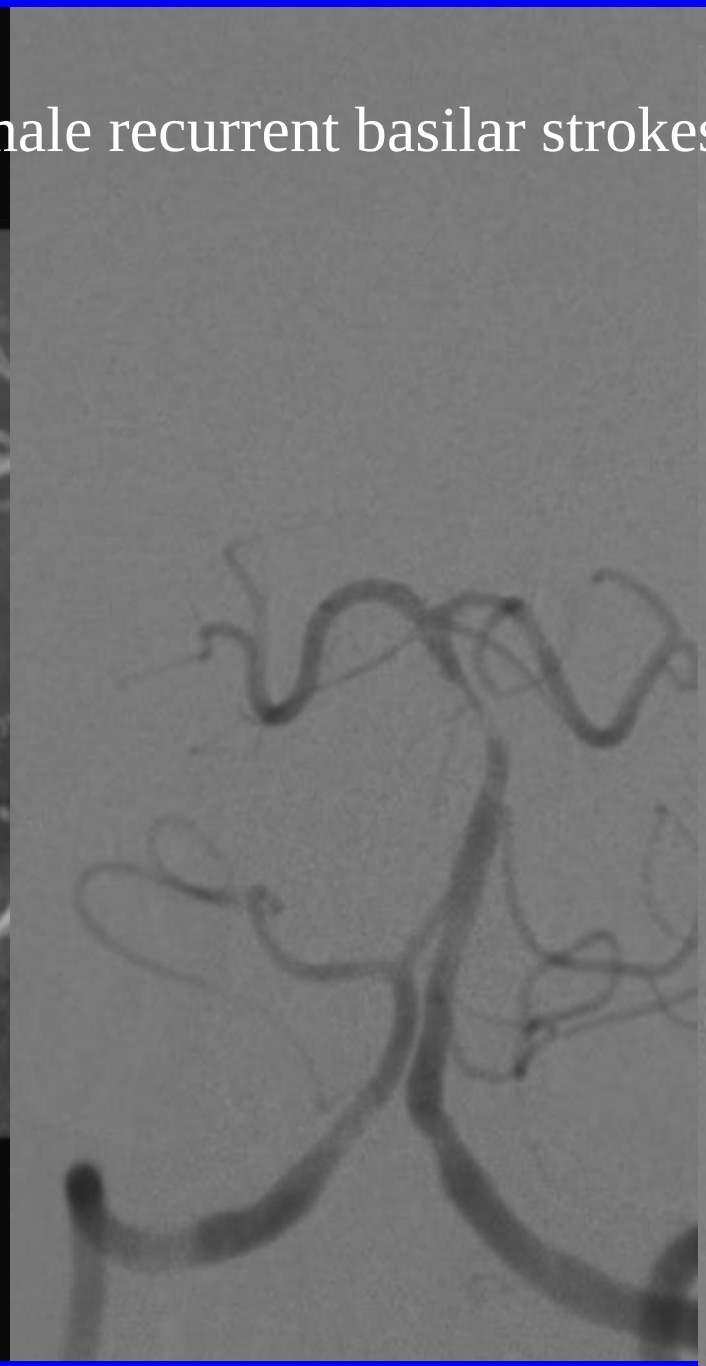
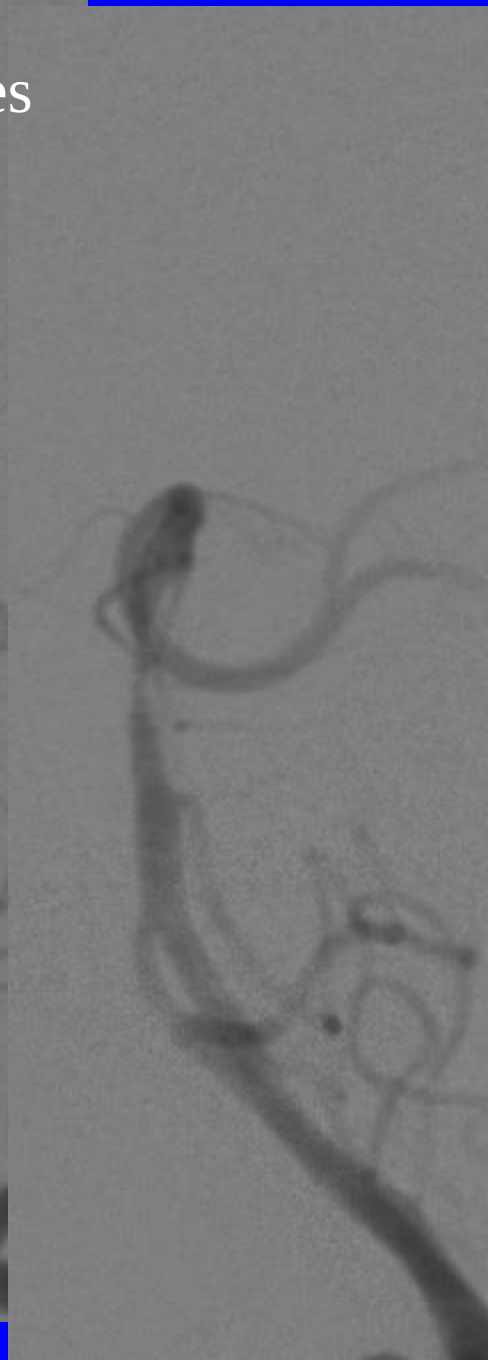
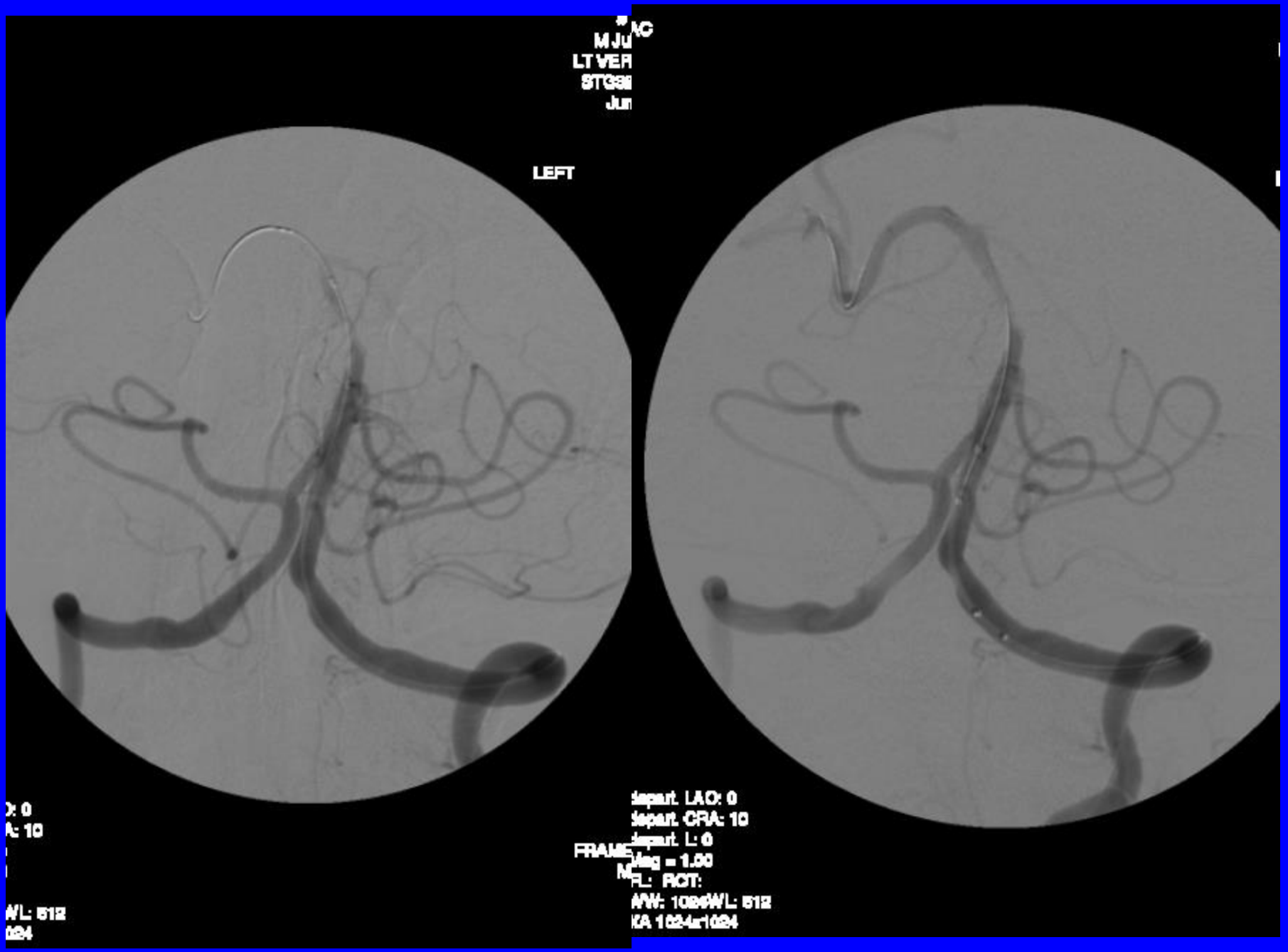


62 yr old thai male recurrent basilar strokes



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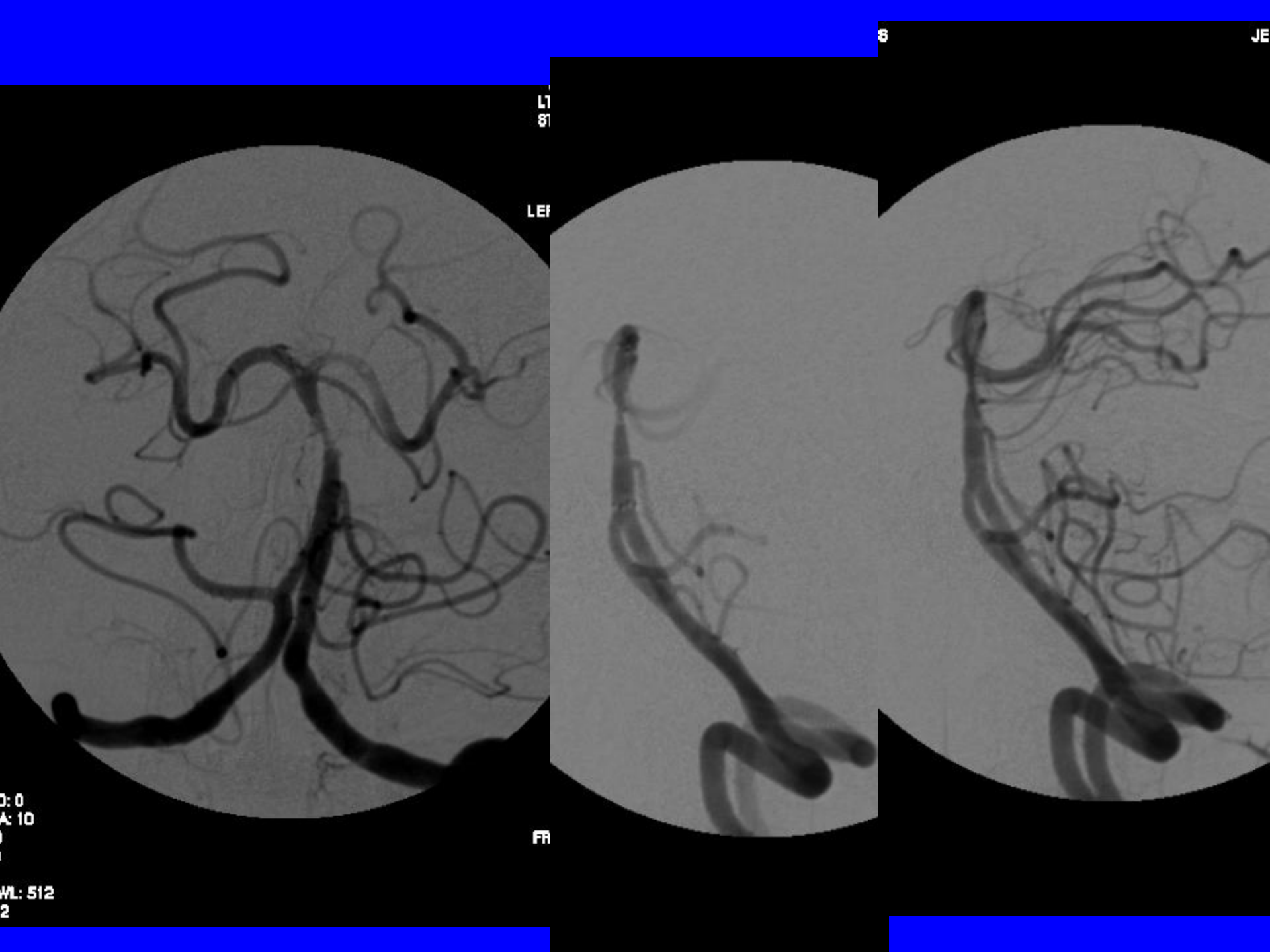
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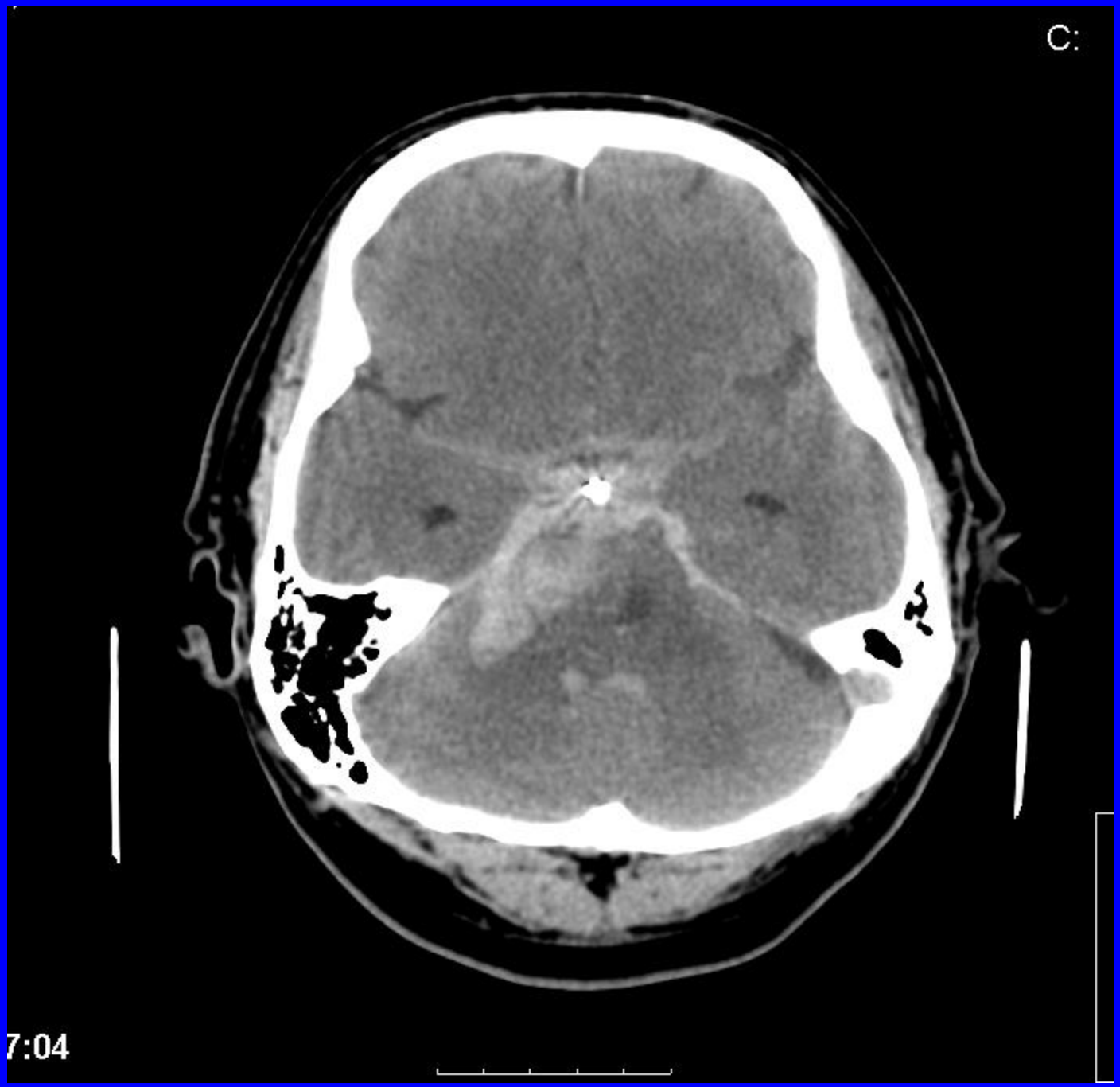
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Figure 2

- Left intradural vertebral stenosis treated with a balloon mounted stent

Intradural vertebral stenosis pre and post stenting

Thrombectomy and intracranial stent.

Intracranial Stenting in acute stroke

- Intracranial stenting is possible
- If vessel recanalised and then reoccludes
- May need to leave a stent
- Detachable solitaire little metal
- May just get away with iv aspirin
- Balloon mounted may need dual
- More data needed.
-


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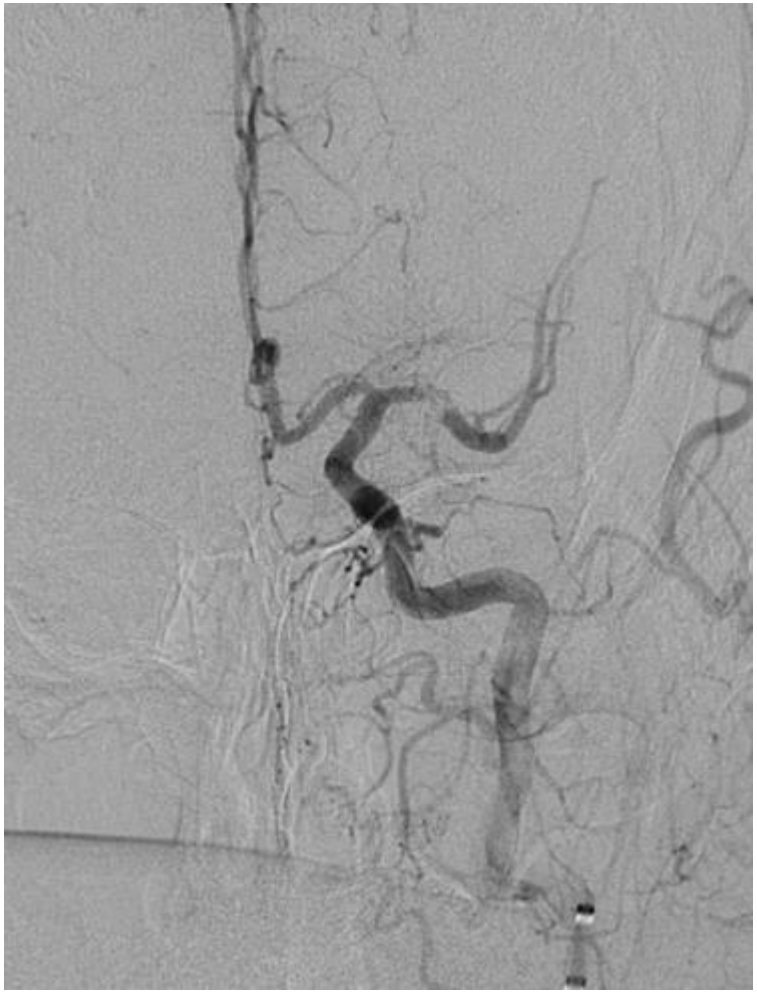
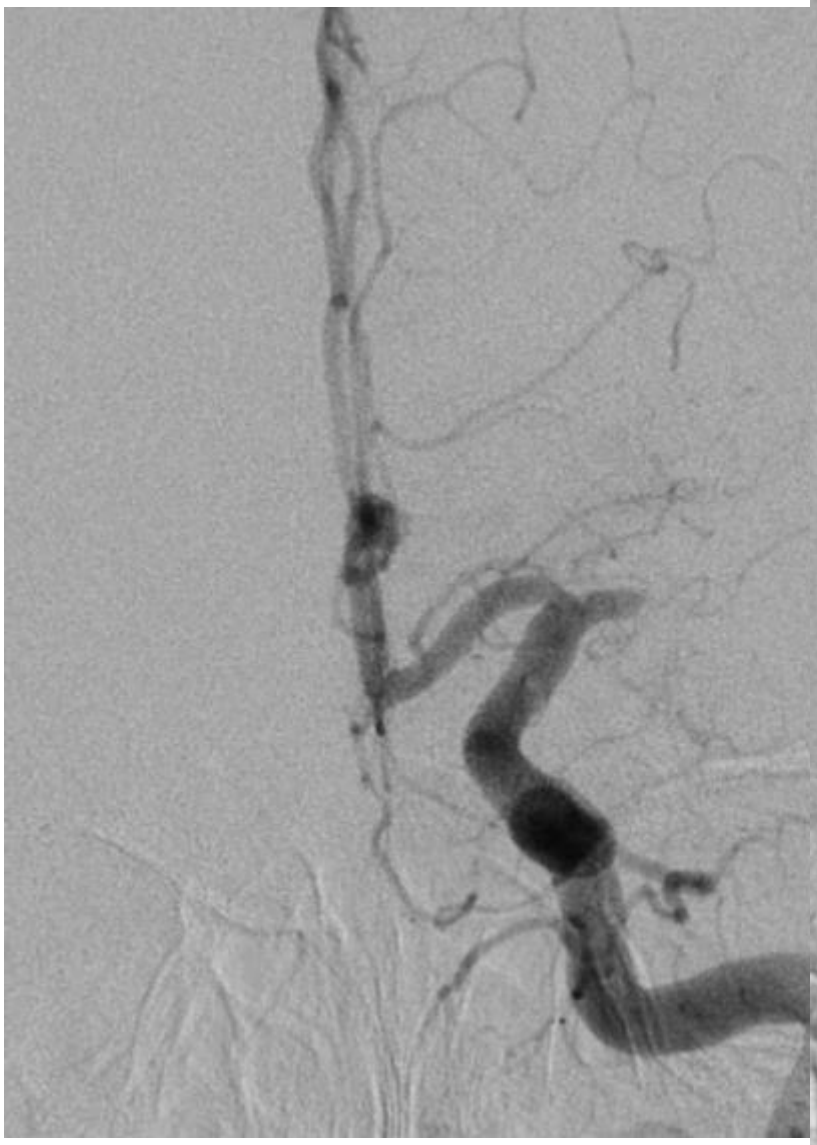
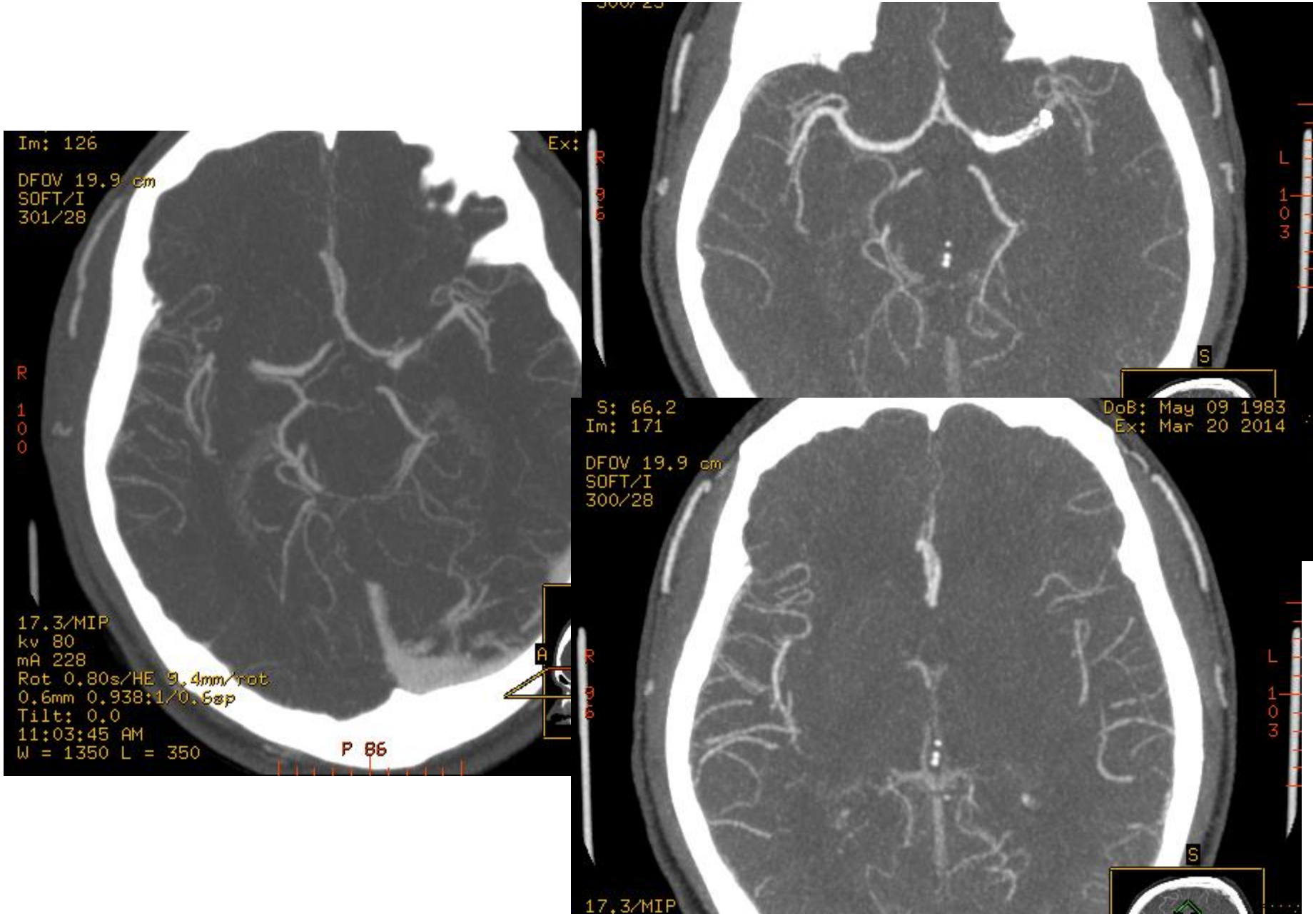
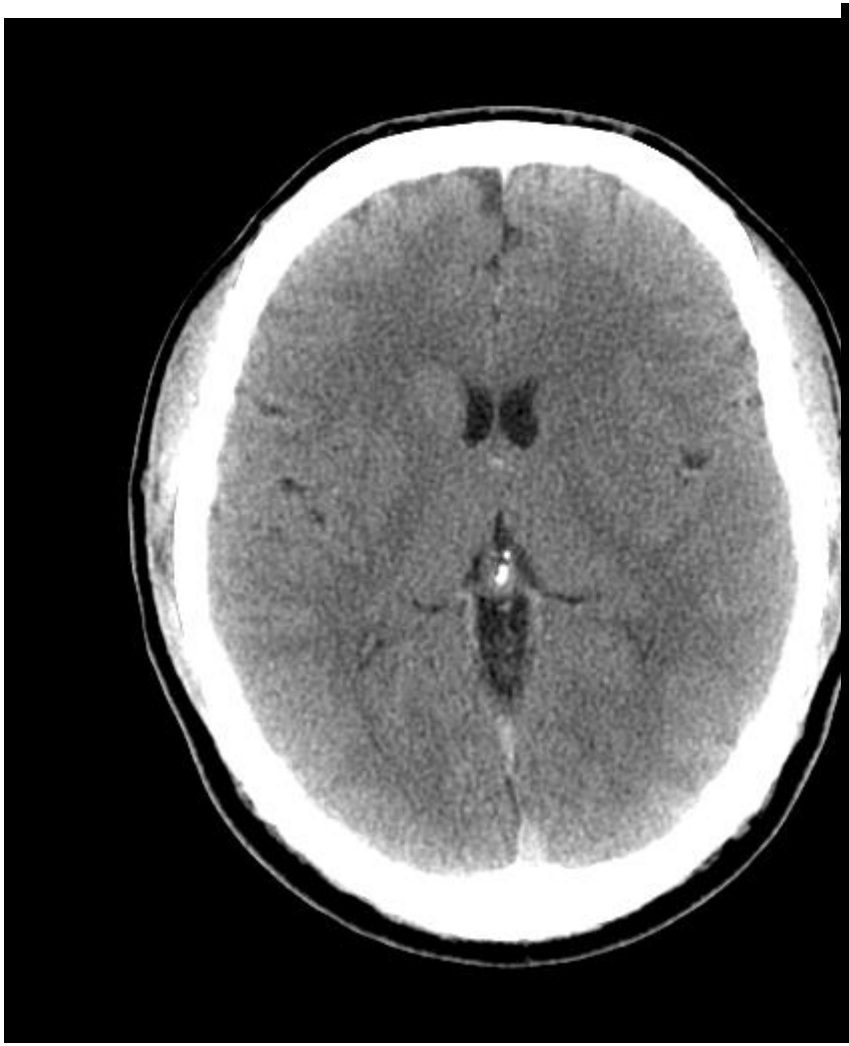
FRAME = 7 / 18
MASK = 3

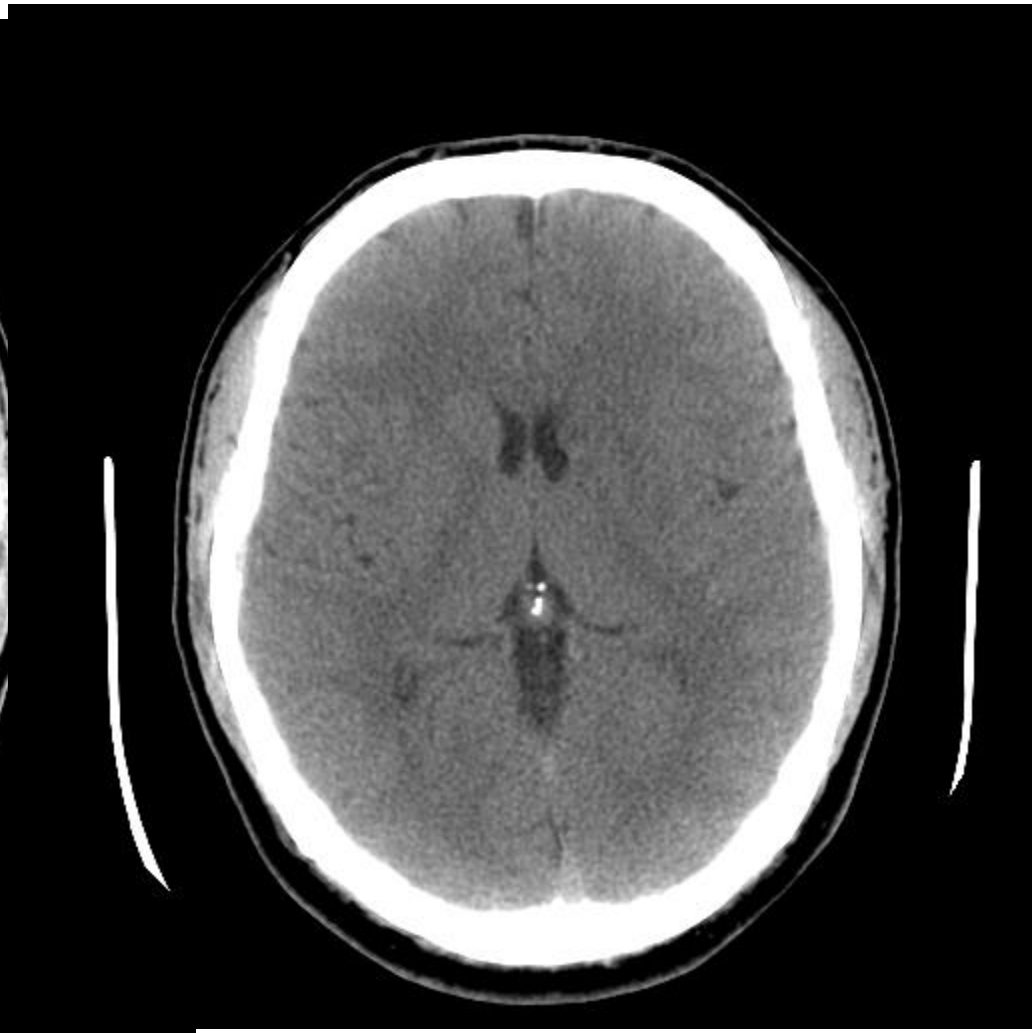




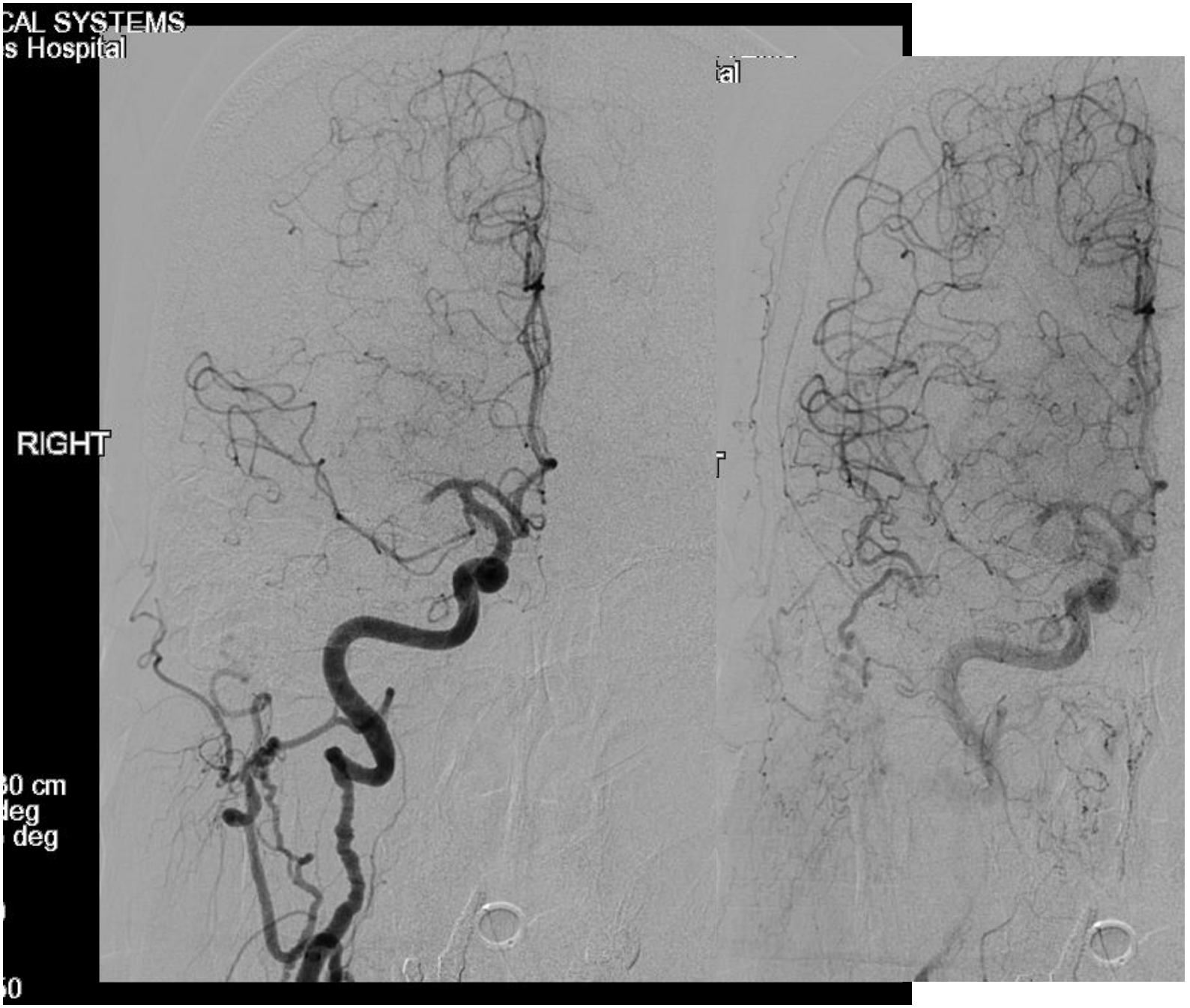

Mar 19 2014
13:45:22
LEFT
(Filt. 3)
(Shut.)
FRNT
FOV: 30x30 cm
LAO: 0.0 deg
CRA: 19.8 deg


Im: 126
Ex:
DFOV 19.9 cm
SOFT/I
301/28
R
100
17.3/MIP
kv 80
mA 228
Rot 0.80s/HE 9.4mm/rot
0.6mm 0.938:1/0.5sp
Tilt: 0.0
11:03:45 AM
W = 1350 L = 350
P 86
A
S: 66.2
Im: 171
DFOV 19.9 cm
SOFT/I
300/28
DoB: May 09 1983
Ex: Mar 20 2014
17.3/MIP



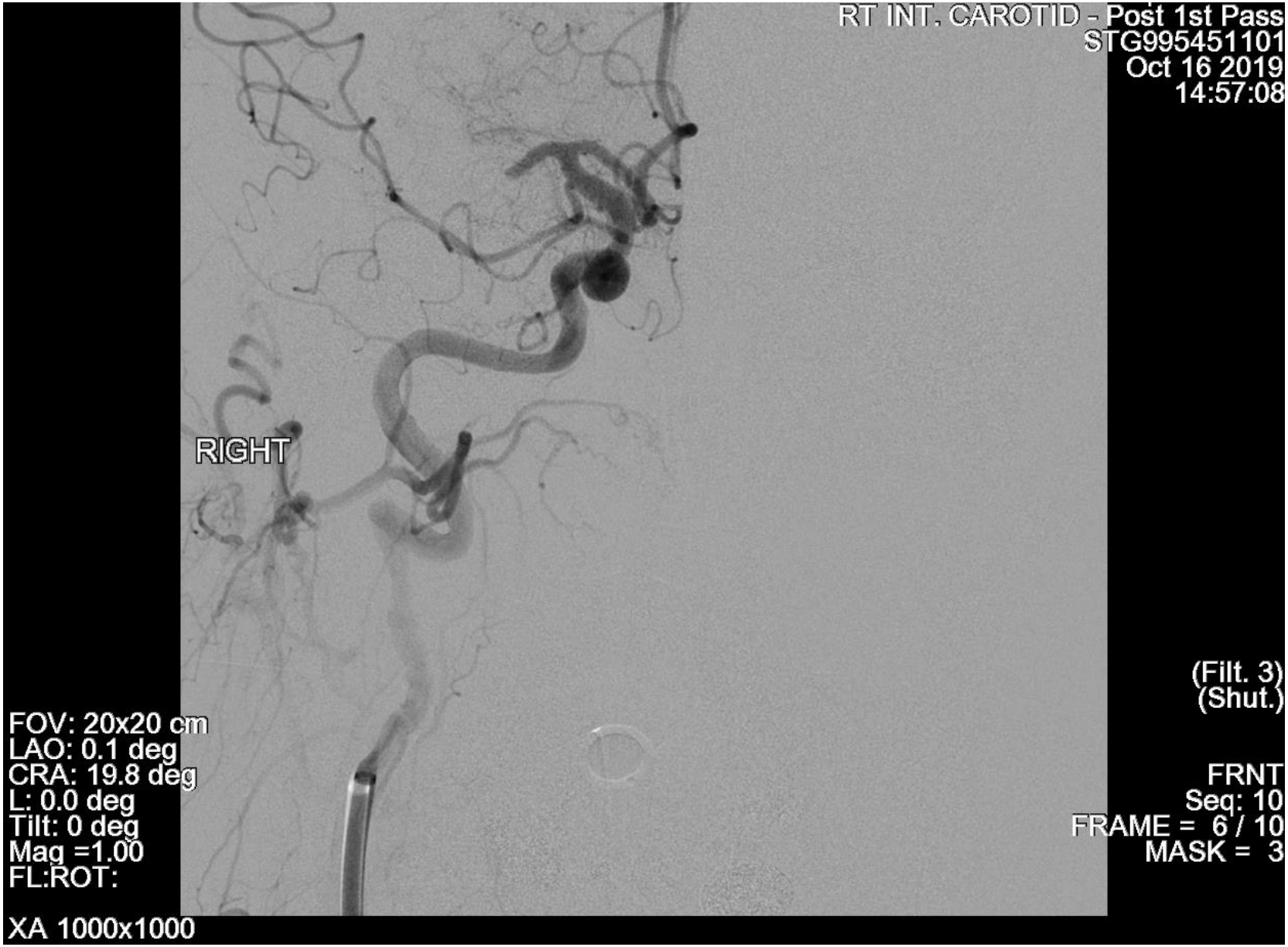


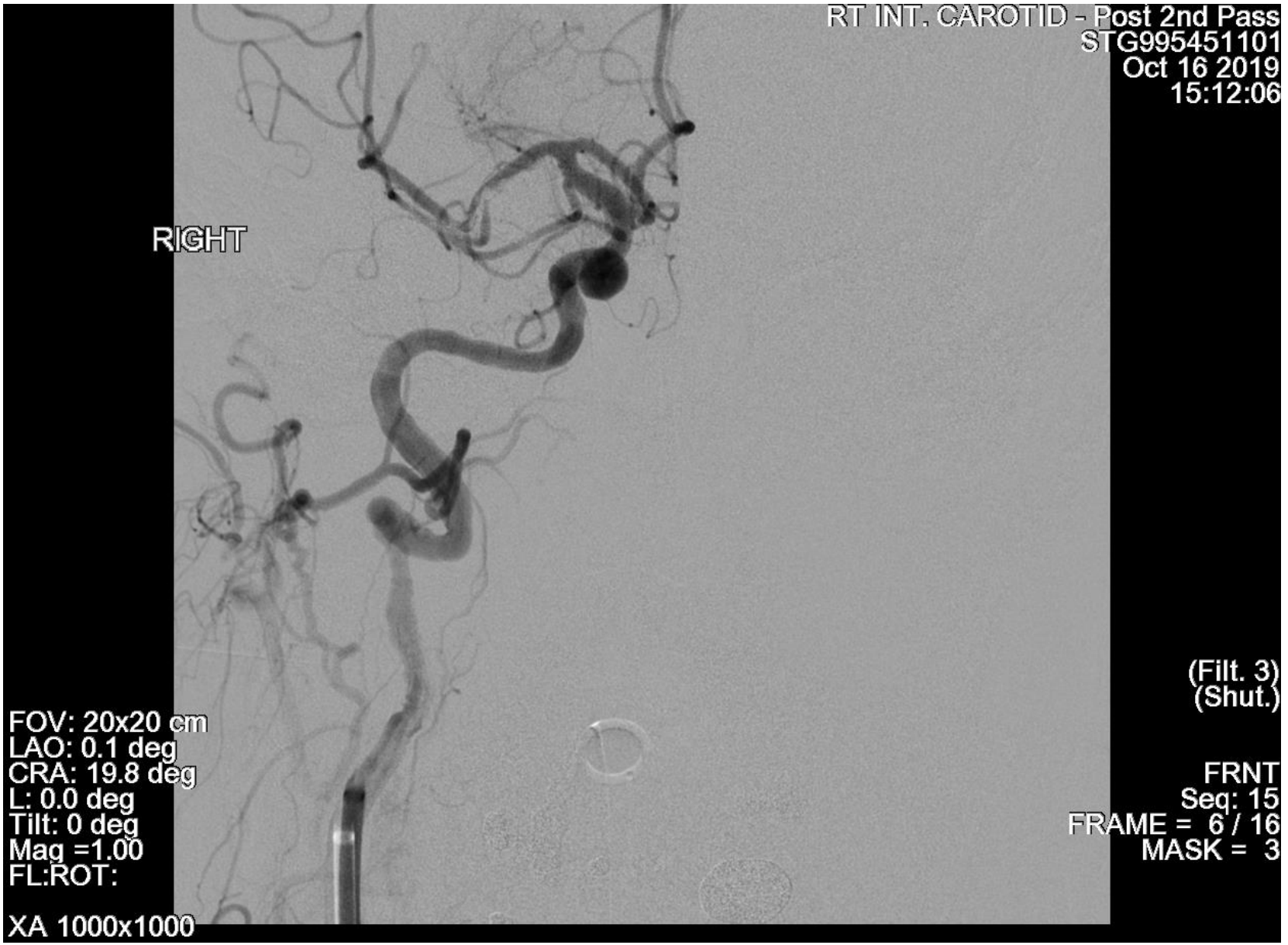
FMD plus ? Intracranial stent

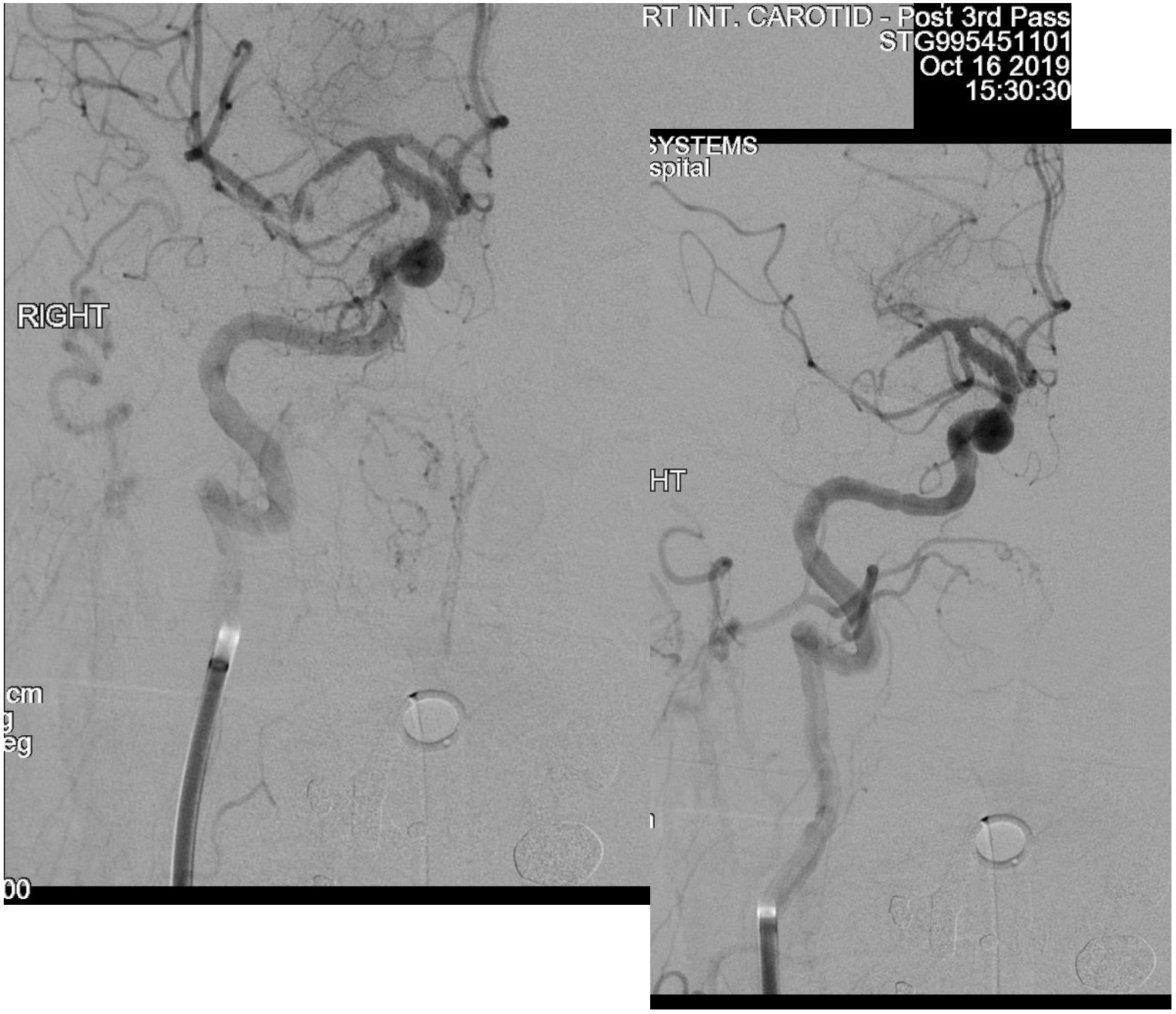

CAL SYSTEMS
s Hospital
al
RIGHT
0 cm
leg
deg
0


SYSTEMS
RIGHT


SYSTEMS
RIGHT


RT INT. CAROTID - Post 1st Pass
STG995451101
Oct 16 2019
14:57:08
RIGHT
(Filt. 3)
(Shut.)
FOV: 20x20 cm
LAO: 0.1 deg
CRA: 19.8 deg
L: 0.0 deg
Tilt: 0 deg
Mag =1.00
FL:ROT:
FRNT
Seq: 10
FRAME = 6 / 10
MASK = 3
XA 1000x1000


RT INT. CAROTID - Post 2nd Pass
STG995451101
Oct 16 2019
15:12:06
RIGHT
(Filt. 3)
(Shut.)
FOV: 20x20 cm
LAO: 0.1 deg
CRA: 19.8 deg
L: 0.0 deg
Tilt: 0 deg
Mag =1.00
FL:ROT:
XA 1000x1000
FRNT
Seq: 15
FRAME = 6 / 16
MASK = 3


RT INT. CAROTID - Post 3rd Pass
STG995451101
Oct 16 2019
15:30:30
SYSTEMS
spital
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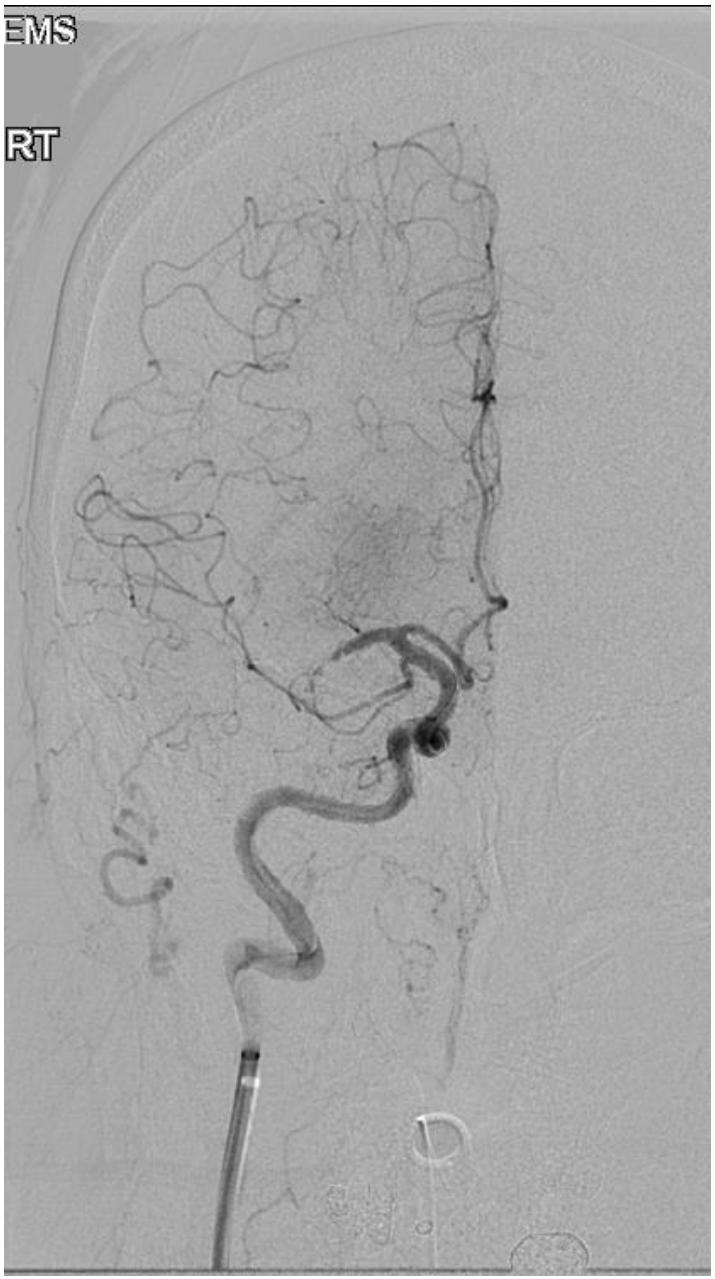
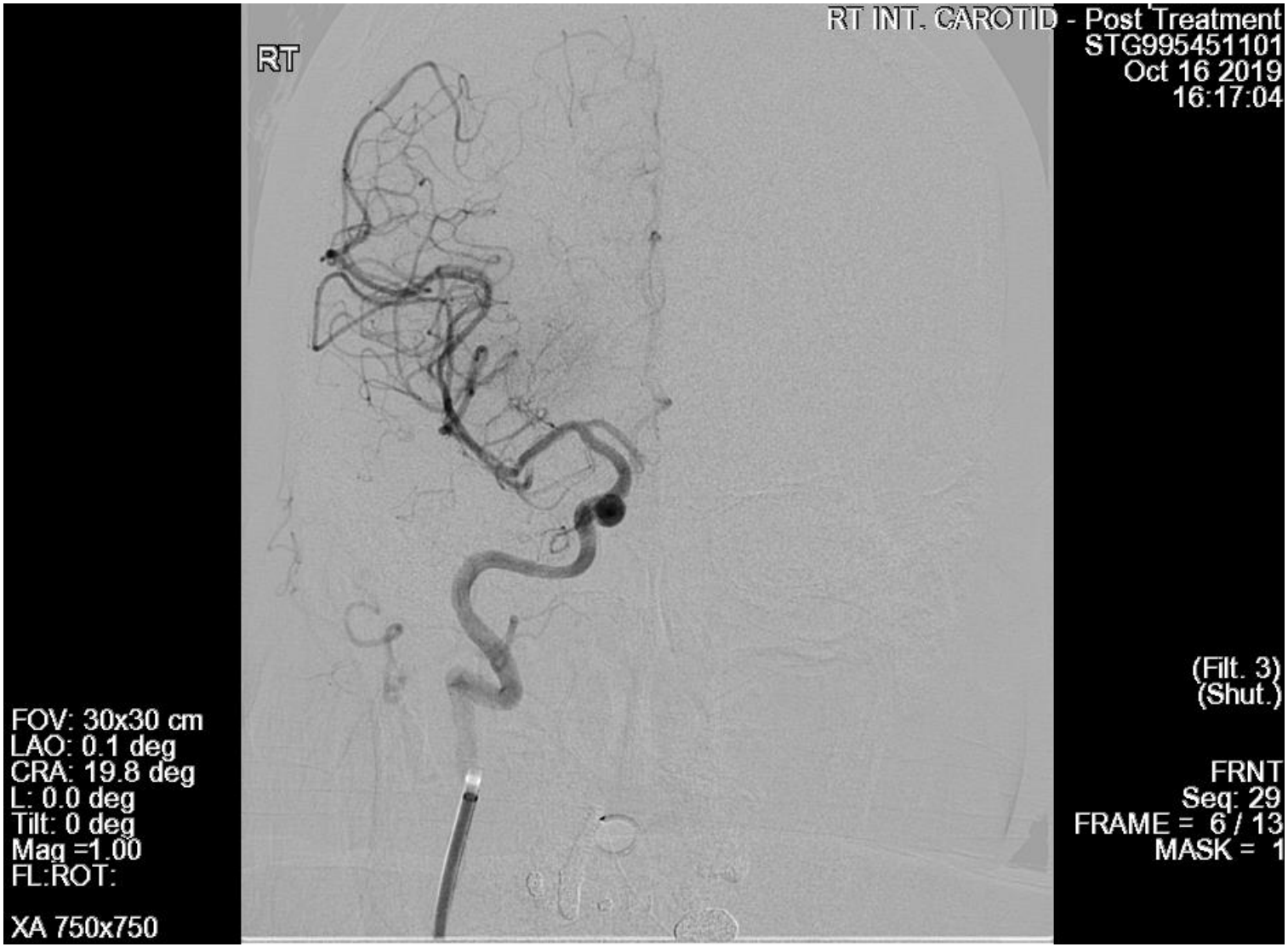
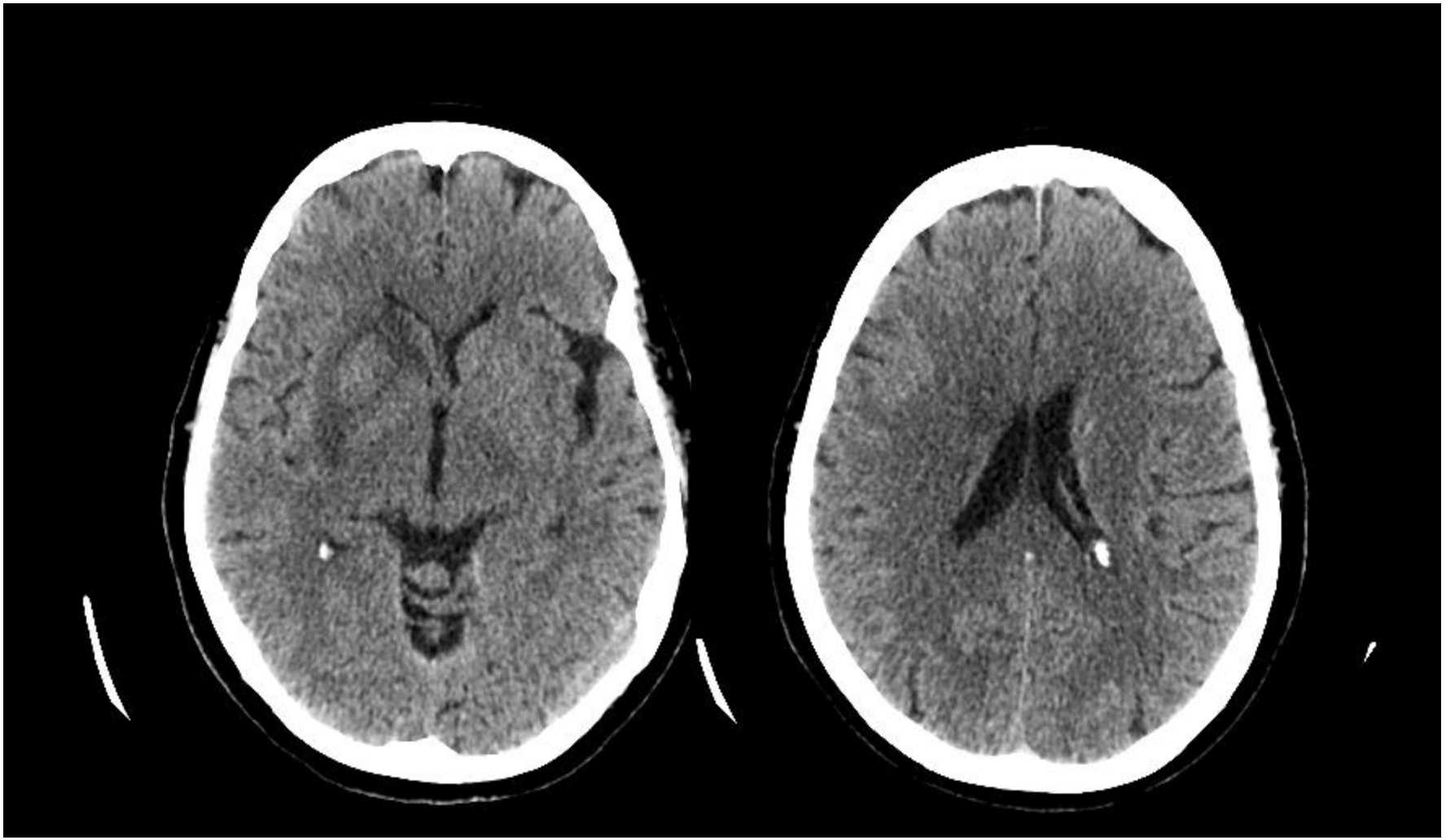

EMS
RT


RT
RT INT. CAROTID - Post Treatment
STG995451101
Oct 16 2019
16:17:04
(Filt. 3)
(Shut.)
FRNT
Seq: 29
FRAME = 6 / 13
MASK = 1
FOV: 30x30 cm
LAO: 0.1 deg
CRA: 19.8 deg
L: 0.0 deg
Tilt: 0 deg
Mag =1.00
FL:ROT:
XA 750x750



SAMMPRIS Update: Current Indications

- SAMPRISS limited to stable patients with recent (within 30d) symptoms.
- Reasonable to consider angioplasty and / or stenting
  - Unstable or progressing symptoms
  - Recurrent stroke on SAMPRISS medical regimen - chronic fixed lesions
- Avoid perforator rich segments, particularly the basilar

- Patient selection for endovascular stent insertion for intracranial atherosclerotic disease should involve a multidisciplinary team experienced in the management of stroke
- The procedure should be carried out by a clinician experienced in interventional neuroradiology.