

Current Endovascular Management of Arteriovenous Malformations



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Disclosures

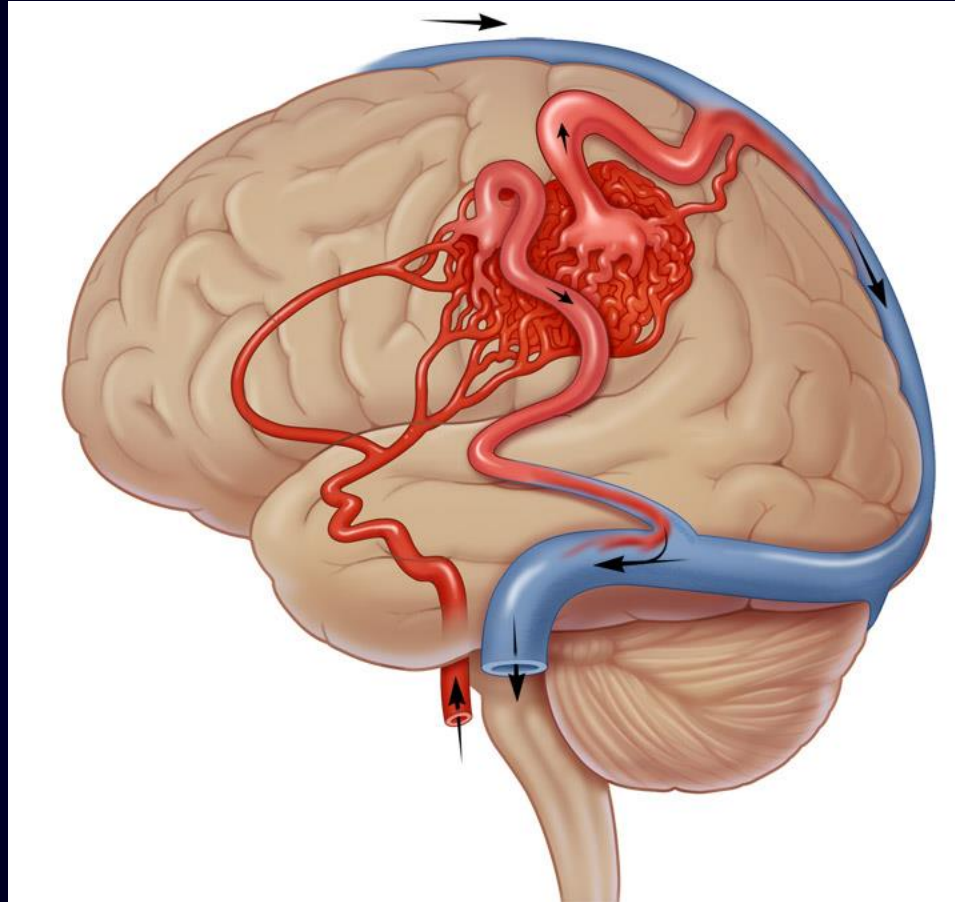
- Microvention/Terumo - consultant
- Medtronic - consultant and proctor
- Penumbra - consultant
- Surpass Medical/Stryker - shareholder
- Medina Medical/Medtronic - shareholder
- InNeuroCo - shareholder



Baptist NeuroIR Team



Definition - AVM



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Background

- 2% of intracranial hemorrhages
- Incidence of AVMs: 1.2/100 000 person-years
- AVM hemorrhage is 0.42/100 000 person-years
- Supratentorial location 85 %
- Posterior Fossa 15%
- Spontaneous thrombosis in 2-3%
- Incidence of multiple AVMs: rare outside of HHT or Wyburn-Mason Syndrome



Background

- Level V evidence multiple observational studies 1966-1997.
- Annual bleeding risk 2-4%
- Each bleed:
 - 20-30% neurological morbidity
 - 10-30% mortality

Cockroft KM, *Stroke* 2006; 37:1148-1149



Background - Hemorrhage

- 678 consecutive, prospectively patients for 1931.7 patient-years
- Hemorrhage rates were 4.61% per year
- 7.48% per year for bAVMs with initial hemorrhagic presentation
- 4.16% per year for initial seizure presentation
- 3.99% per year for patients not harboring aneurysms
- 6.93% per year for patients with associated aneurysms
- 5.42% per year for bAVMs with deep venous drainage
- Hemorrhagic presentation was a significant independent predictor of future hemorrhage ($P < 0.01$)
- Associated aneurysms ($P = 0.07$) and deep venous drainage ($P = 0.07$) showed a trend toward significance

da Costa, et al. Stroke 2009



Background – Risk Factors for Bleed

- Vertebrobasilar system
- Location (basal ganglia)
- Deep venous drainage
- Perforators as feeders
- Intranidal aneurysms
- Multiple aneurysms

Turjman et al. Neurosurgery 1995



Background - Hemorrhage

- N = 115 hemorrhage presenting symptoms
- N= 27 second hemorrhage during f/u
- Mean f/u time 16.2 months
- 23% ICH
- 31% ICH + IVH
- 16% IVH
- 30% SAH

Hartmann et al. Stroke 1998



Treatment Options

- Surgery
- Embolization + Surgery
- Radiosurgery
- Embolization + Radiosurgery
- Embolization

Big Question: should we treat unruptured AVM?



Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial

J P Mohr, Michael K Parides*, Christian Stapf*, Ellen Moquete, Claudia S Moy, Jessica R Overbey, Rustam Al-Shahi Salman, Eric Vicaut, William L Young†, Emmanuel Houdart, Charlotte Cordonnier, Marco A Stefani, Andreas Hartmann, Rüdiger von Kummer, Alessandra Biondi, Joachim Berkefeld, Catharina J M Klijn, Kirsty Harkness, Richard Libman, Xavier Barreau, Alan J Moskowitz, for the international ARUBA investigators‡*

ARUBA

A Randomized trial of Unruptured
Brain Arteriovenous
Malformations



Lancet. 2014 February 15; 383(9917): 614-621

Study Descriptions

ARUBA

- Multicenter, randomized BAVM trial
- Medical management of BAVM
 - Med tx plus intervention (standard tx)
 - Med tx alone (experimental tx)
- Trial aimed to prove superiority or non-inferiority of med tx alone
- Recruiting April 4, 2007-April 15 2013
 - NIH halted randomization

Mohr JP, et al, *Lancet* 2014; 383:581-583

Salman RA-S, et al, *JAMA* 2014; 311(16):1661-1669

1^o Outcome Endpoints

ARUBA

- Time to composite event of death from any cause or symptomatic stroke
- “Symptomatic Stroke”: Any new focal neurological deficit, seizure, or new headache
- Imaging findings of hemorrhage or infarct

2^o Outcome Endpoints

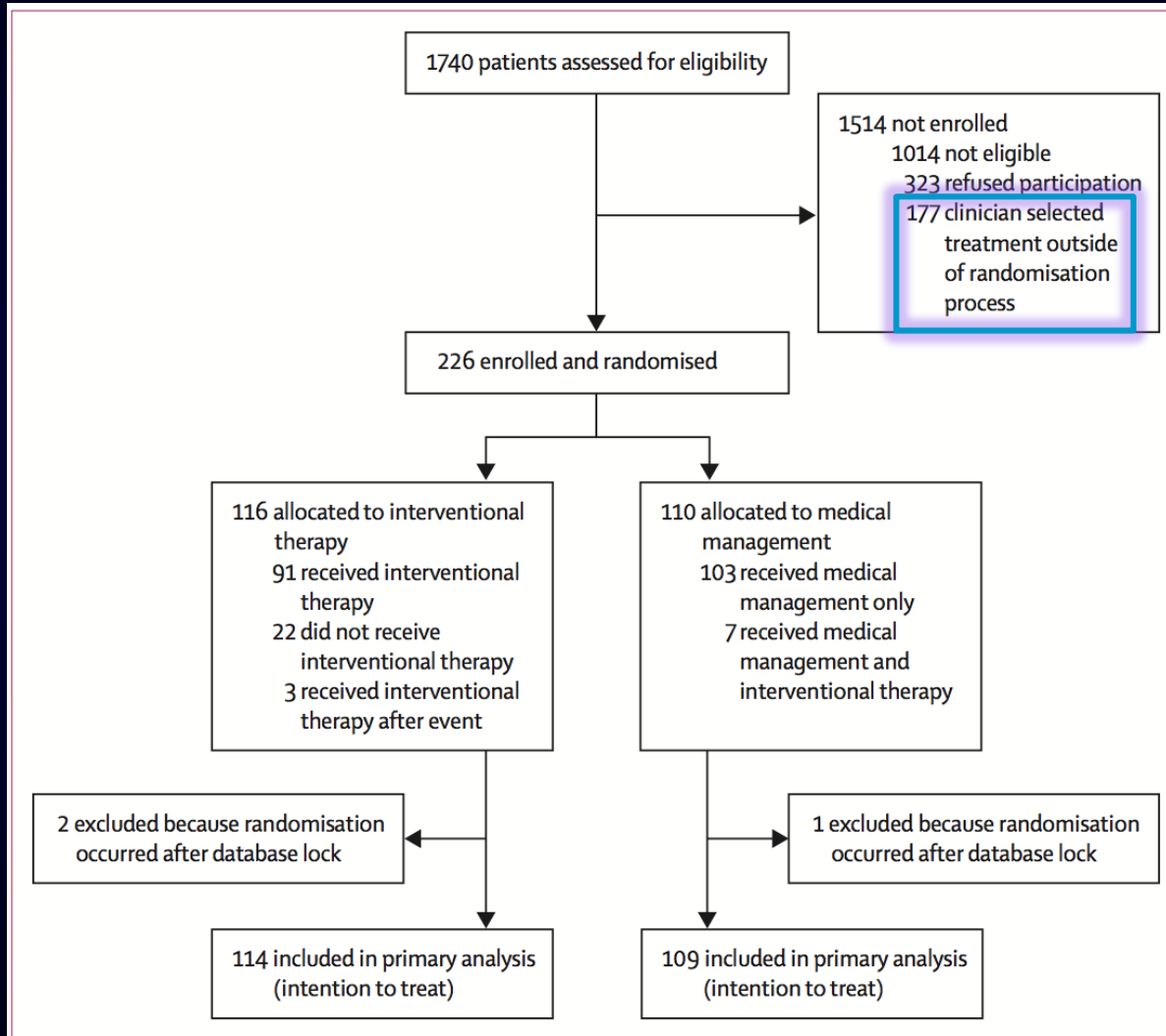
ARUBA

- Clinical impairment at 5 years
- Modified Rankin scale score of 2 or higher

Salman RA-S, et al, *JAMA* 2014; 311(16):1661-1669

Mohr JP, et al, *Lancet* 2014; 383:581-583

ARUBA Recruitment



****Number of pts selected for tx outside trial = 74 intervention 61 medical 42 managed at ctrs with no randomized pts**

ARUBA AVM Characteristics

AVM Characteristic	Interventional (n=114)	Medical (n=109)	
Spetzler Martin Grade			
I	32 (29%)	33 (30%)	→ 55-70%
II	44 (39%)	27 (25%)	
III	28 (25%)	34 (31%)	18/94 pts (19.1%) treated with surgery
IV	8 (7%)	15 (14%)	
AVM Size <3cm	78 (68%)	60 (55%)	
Lobar Location	104 (91%)	99 (91%)	
Eloquent Location	54 (47%)	51 (47%)	
Associated Aneurysm	15 (13%)	21 (19%)	
Superficial Venous Dr.	78 (70%)	69 (63%)	

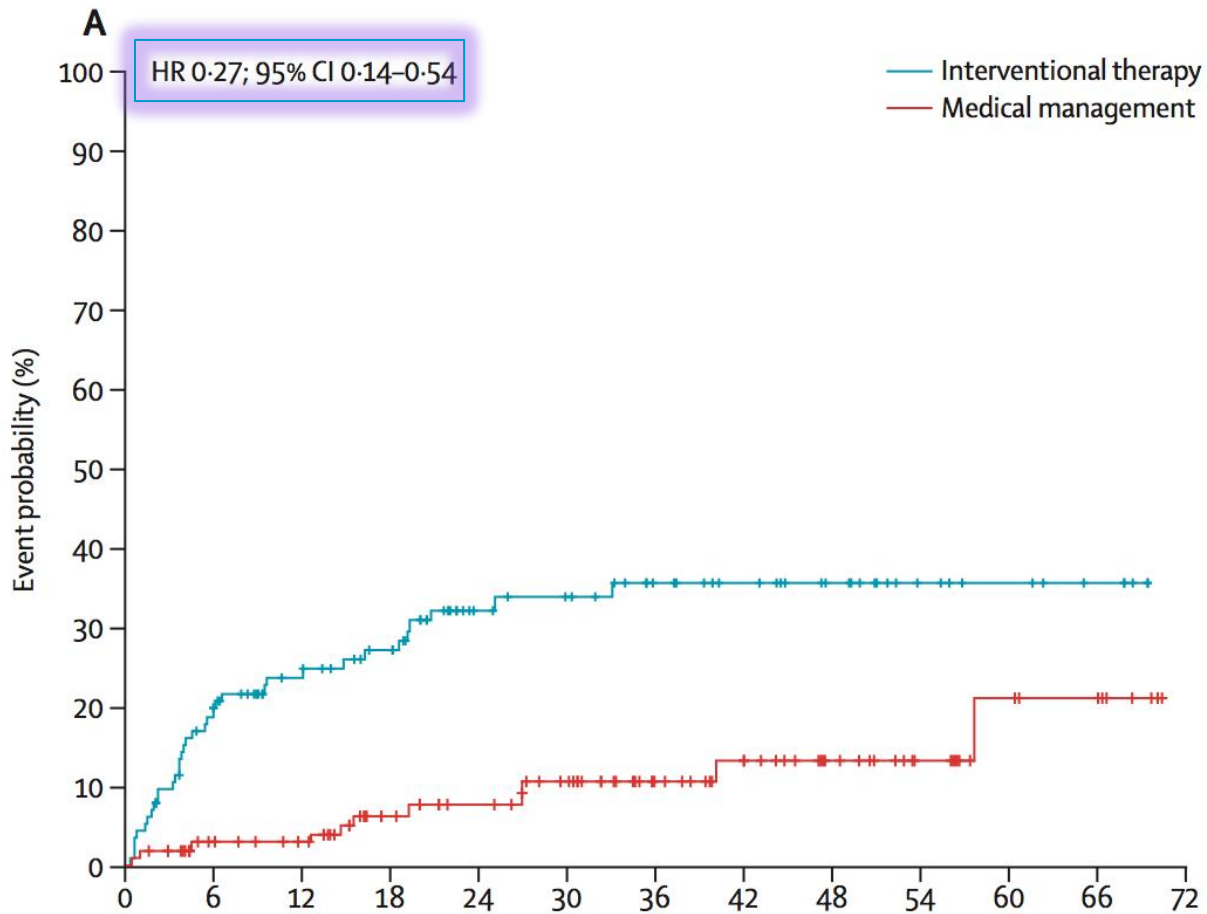
Treatment Heterogeneity

Treatment Modality	ARUBA/SIV MS Tx 2007-2013	UTSW 2005-2010	van Rooij 2008-2011
Embo Alone	30/22	10	24
Surg Alone	5/18	20	6
SRS Alone	31/28	61	72
Embo/Surg	12/12	50	
Embo/SRS	15/20	17	
Embo/Comb o	1/1	3	42
SRS/Surg	0/2	7	
Total	94/103	168	144
% Embo Alone	31%/21%	5.95%	16.7%

Mohr JP, et al, *Lancet* 2014; 383:581-583

Van Rooij WJ, et al, *AJNR* 2012; 33:1299-1304

ARUBA Results-1^o Endpoint



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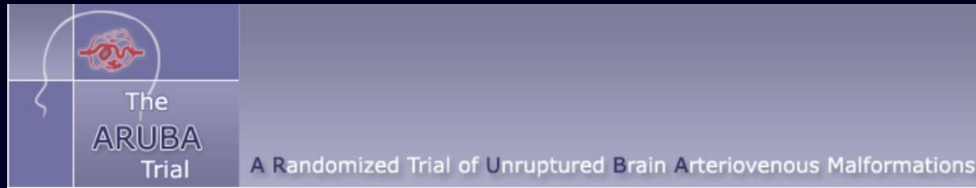
ARUBA Results-2⁰ Endpoint

Functional Outcome	Interventional (n=114)	Medical (n=109)	Risk Ratio (95% CI)
MRS \geq 2 30 mo F/U	46.2% (24/52)	15.1% (8/53)	0.33 (0.16-0.66)
MRS \geq 2 36 mo F/U	38.6%(17/44)	14.0% (6/43)	0.36 (0.16-0.83)

ARUBA Adverse Events

AE	Interv. # N=114	Rate per pt-yr	Medical # N=109	Rate per pt-yr	p-value
Stroke*	45	0.144	12	0.039	<0.0001
Hemor.	33	0.106	8	0.026	
Ischem.	12	0.038	4	0.013	
Focal def					
All	14	0.045	1	0.003	0.0008
Persist.	4	0.013	1	0.003	
Revers.	10	0.032	0	0	

* Includes recurrent stroke



<http://www.arubastudy.org>

ARUBA Medical Group

**ANNUALIZED HEMORRHAGE
RISK 2.2% (95% CI 0.9-4.5)**

SIVMS Hemorrhage rate 18%/12 yrs

ARUBA Trial Debate

A Perfect Storm

How A Randomized Trial of Unruptured Brain Arteriovenous Malformations' (ARUBA's) Trial Design Challenges Notions of External Validity

Kevin M. Cockroft, MD, MSc; Mahesh V. Jayaraman, MD; Sepideh Amin-Hanjani, MD; Colin P. Derdeyn, MD; Cameron G. McDougall, MD; John A. Wilson, MD

Cockroft KM, et.al. *Stroke* 2012; 43(7):1979-81

Hull Down on the Horizon

A Randomized Trial of Unruptured Brain Arteriovenous Malformations (ARUBA) Trial

J.P. Mohr, MD, MS; Alan J. Moskowitz, MD; Michael Parides, PhD; Christian Stapf, MD; William L. Young, MD

Mohr JP, et.al. *Stroke* 2012; 43(7):1744-45

What is an AVM?
Frequently asked questions

For Physicians

Description of Trial
Background and Rationale (pdf)
Contact the PIs

Participating Sites



The ARUBA study is a clinical trial to find out better ways of caring for people who have been discovered to have an arteriovenous malformation (AVM) in the brain that has never bled. It is sponsored by the National Institutes of Health.

If you are an AVM patient, the information provided here may be helpful. For more information, please contact your physician or the ARUBA study coordinator in your country.

Unruptured Brain Arteriovenous Malformations Should Be Treated Conservatively

No

Kevin M. Cockroft, MD, MSc, FACS

Cockroft KM, *Stroke* 2007; 38(12):3310-11

Editorial

Unruptured Cerebral Arteriovenous Malformations To Treat or Not to Treat

Kevin M. Cockroft, MD, MSc, FACS

Cockroft KM, *Stroke* 2006; 37(5):1148-49

ARUBA Trial Debate

- Follow-up Duration
- Disease/Treatment Heterogeneity
- Selection/External Validity
- Complication Rate/Stroke Definition

Treatment Options

- Surgery
- Embolization + Surgery
- Radiosurgery
- Embolization + Radiosurgery
- Embolization

Totally dependent on center expertise and AVM features

BAVM Meta-analysis

137 articles 142 cohorts 1972-2009

Modality	*Case Fatality	*Bleed Rate	**Proc. Complic	**Severe Complic	**Oblit. Rate	**F/U (Mo)
Overall	0.68 (.61-.76)	1.4 (1.3-1.5)	-	-	-	30 (2-123)
Surgery	1.1 (.87-1.3)	0.18 (0.1-0.3)	29% (1.5-54)	7.4% (0-40)	96% (0-100)	17 (2-98)
SRS	0.50 (.43-.58)	1.7 (1.5-1.8)	13% (0-63)	5.1% (0-21)	38% (90-75)	35 (8-94)
Embo	0.96 (.67-1.4)	1.7 (1.3-2.3)	25% (7.6-55)	6.6% (0-28)	13% (0-94)	27 (5.3-78)

13,698 pts, 46,314 pt/yr F/U

* Estimate per 100 Person-Years (95% CI)

“Severe” = perm. neuro deficit or death

Van Beijnum J, et al, *JAMA* 2011; 306(18):2011-2019

“We were not able to provide reliable estimates of the risk of multimodality treatment. Multimodality treatment may be the safest approach for some brain AVMs, but it may also result in accumulation of risks of the various treatments involved.”

BAVM Embo 1995-2002

Complications of preoperative embolization of cerebral arteriovenous malformations

**CHRISTOPHER L. TAYLOR, M.D., KIM DUTTON, R.N., GEORGE RAPPARD, M.D.,
G. LEE PRIDE, M.D., ROBERT REPLOGLE, M.D., PHILLIP D. PURDY, M.D.,
JONATHAN WHITE, M.D., COLE GILLER, M.D., PH.D., THOMAS A. KOPITNIK JR., M.D.,
AND DUKE S. SAMSON, M.D.**

Department of Neurological Surgery and Department of Radiology, The University of Southwestern Texas Medical Center, Dallas, Texas

339 Embos 201 pts (mean 1.7 embo/pt)

Neuro Deficit/Death per Procedure 7.7%

Neuro Deficit/Death 11%

Taylor CL, et.al., *J Neurosurg* 2004; 100(5):810-812



BAVM Embolization

ORIGINAL RESEARCH

E.F. Hauck
B.G. Welch
J.A. White
P.D. Purdy
L.G. Pride
D. Samson

Preoperative Embolization of Cerebral Arteriovenous Malformations with Onyx

BACKGROUND AND PURPOSE: Preoperative embolization facilitates the surgical management of complex cerebral arteriovenous malformations (cAVMs). This analysis aims to investigate the risks for preoperative cAVM embolization with Onyx.

MATERIALS AND METHODS: We retrospectively analyzed clinical data of all patients who underwent embolization with Onyx as a preoperative treatment of cAVMs at our institution since 2005 (US Food and Drug Administration [FDA] approval). Patients with arteriovenous fistulas were excluded. A total of 107 patients were treated for cAVMs during the study period. Of those patients, 41 underwent cAVM embolizations with Onyx in 82 procedures.

RESULTS: After the embolization, the cAVM diameter was reduced from 3.71 ± 1.55 cm to 3.06 ± 1.89 cm ($P < .05$). Median volume reduction was 75%. Complete occlusion with embolization alone was achieved in 4 (10%) cAVMs. The recurrence rate for completely occluded cAVMs was 50% (2 patients). A total of 71% of the 41 patients treated with Onyx underwent surgery, and 15% underwent radiosurgery. There were 9% who have not yet received definitive treatment of their residual cAVMs. A new permanent neurologic deficit occurred in 5 patients (6.1% per procedure or 12.2% per patient).

CONCLUSIONS: A considerable risk for a permanent neurologic deficit remains for cAVM embolization with Onyx. The risk has to be carefully weighted against the benefit of volume reduction in the treatment of cAVMs.

Hauck EF, et.al., *AJNR* 2009; 30(3):492-495



BAVM Embo 2002-2008

ORIGINAL RESEARCH

V. Panagiotopoulos
E. Gizewski
S. Asgari
J. Regel
M. Forsting
I. Wanke

Embolization of Intracranial Arteriovenous Malformations with Ethylene-Vinyl Alcohol Copolymer (Onyx)

BACKGROUND AND PURPOSE: Endovascular therapy of intracranial arteriovenous malformations (AVMs) is increasingly used. However, it is still under discussion which embolic material is optimal. We report our experience in the treatment of AVMs with ethylene-vinyl alcohol copolymer (Onyx).

MATERIALS AND METHODS: Between July 2002 and January 2008, brain AVMs were embolized with Onyx in 82 consecutive patients in our department. There were 41 females and 41 males with a mean age of 44.2 years (range, 15–85 years). Clinical presentation included symptoms due to intracerebral hemorrhage ($n = 37$), seizures ($n = 18$), nonhemorrhagic neurologic deficits ($n = 8$), headaches ($n = 9$), or incidental symptoms ($n = 10$). According to the Spetzler-Martin scale, 59 AVMs were grades I–II, 16 were grade III, and 7 were grades IV–V.

RESULTS: Complete obliteration at the end of all endovascular procedures was achieved in 20/82 patients (24.4%), with an average of 75% (range, 30%–100%) volume reduction. A mean of 2.9 (range, 1–10) feeding arteries was embolized per patient, whereas an average of 2.6 ml of Onyx was used per patient. Procedure-related permanent disabling morbidity was 3.8%, whereas mortality was 2.4%.

CONCLUSIONS: The overall initial complete obliteration rate of intracranial AVMs with Onyx embolization is relatively high, compared with other embolic agents, with evidence of stability with time. Morbidity and mortality rates due to AVM embolization as a single treatment method or as a part of a multimodality treatment should be further assessed regarding the natural course of the disease.

Panagiotopoulos V, et al., *AJNR* 2009; 30(1):99-106



Embolization

- 11- year period, 295 embolization procedures (761 pedicles embolized) in 168 patients
- Embolization as the primary treatment modality (16) or as an adjunct to surgery (124) or radiosurgery (28)
- There were a total of 27 complications, of which 11 were clinically significant.
- Excellent or good outcomes (GOScale 4) 152 (90.5%) patients.
- Unfavorable outcomes (GOS 1 to 3) 3.0% at discharge
- 1.2% embolization-related mortality

Ledezma CJ. et al *Neurosurgery*. 2006;58



Embolization

- Predictors of unfavorable outcome by univariate analysis were:
 - (1) deep venous drainage ($P0.05$)
 - (2) Spetzler-Martin Grade III to V ($P0.05$)
 - (3) periprocedural hemorrhage ($P0.0001$)

Ledezma CJ. et al *Neurosurgery*. 2006;58



Saatci et al J Neurosurgery

Endovascular treatment of brain arteriovenous malformations with prolonged intranidal Onyx injection technique: long-term results in 350 consecutive patients with completed endovascular treatment course

Clinical article

ISIL SAATCI, M.D., SERDAR GEYIK, M.D., KIVILCIM YAVUZ, M.D.,
AND H. SARUHAN CEKIRGE, M.D.

Department of Interventional Neuroradiology, Hacettepe University Hospitals, Ankara, Turkey

Object. The purpose of this study was to present the authors' clinical experience and long-term angiographic and clinical follow-up results in 350 patients with brain arteriovenous malformations (AVMs) treated using prolonged intranidal Onyx injection with a very slow "staged" reflux technique described by the authors.

Methods. Three hundred and fifty consecutive patients with brain AVMs treated using Onyx between 1999 and 2008 and in whom definitive status for endovascular treatment was reached are presented. There were 206 (59%) male and 144 (41%) female patients, with a mean age of 34 years. There were 607 endovascular sessions performed. Onyx was the only agent used for intranidal injections in all patients, but in 42 patients high-concentration *N*-butyl cyanoacrylate glue was used adjunctively to close high-flow dural arteriovenous intra- or perinidal fistulas, or when a feeding vessel or nidus perforation and/or dissection occurred.

Results. Angiographically confirmed obliteration was achieved in 179 patients (51%) with only endovascular treatment; 1 patient died due to intracranial hemorrhage after the treatment. Twenty-two patients underwent resection, and 136 patients were sent to radiosurgery after endovascular treatment. In 4 patients embolization therapy was discontinued, and 5 additional patients refused the suggested complementary surgery. In all 178 surviving patients who had angiographically confirmed AVM obliteration by embolization alone, 1–8 years of control angiography (mean 47 months) confirmed total obliteration in 178 patients, in whom a very small recanalization was noted in the 1st year in control angiography studies, despite initial apparent total obliteration (recanalization rate 1.1%). In the entire series, 5 patients died; the mortality rate was 1.4%. The permanent morbidity rate was 7.1%.

Conclusions. With the prolonged intranidal injection technique described herein, Onyx allows the practitioner to achieve higher rates of anatomical cures compared with the cure rates obtained previously with other embolic agents. More importantly, due to this technique's much more effective intranidal penetration, it allows high-grade AVMs to be made radiosurgically treatable in a group of patients for whom there has been no treatment alternative.
(DOI: 10.3171/2011.2.JNS09830)

Saatci I, et al, *J Neurosurg* 2011; 115:78-88



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Hemorrhagic Complications

ORIGINAL RESEARCH
INTERVENTIONAL

Hemorrhagic Complications after Endovascular Treatment of Cerebral Arteriovenous Malformations

H. Baharvahdat, R. Blanc, R. Termechi, S. Pistocchi, B. Bartolini, H. Redjem, and M. Piotin

“EVT (with the goal of complete obliteration of the nidus in 1 or multiple sessions) being the first-choice treatment for cerebral AVMs”

Complete obliteration 40.8% overall

70% of AVMs 92% embolization (100%)

8.7% SM1, 5.2% SM2, 5.5% SM3, 5.7% SM4, 5.0% SM5

Overall perm. deficit:

5% SM1, 6% SM2, 14% SM3, 19% SM4, 21% SM5

Mortality 1.6%

Baharvahdat R, et al, *AJNR* 2014; 10.3174/ajnr.A3906



Other published series of AVM embolization with 100 or more patients

Series	Patients (n)	Permanent D &D	Notes
Ledezma ⁷³	168	6.5%	Described as clinically significant complication,
Haw ⁷⁴	306	3.9%	Eloquence, presence of fistula or venous glue embolization related to morbidity.
Kim ⁷²	153	11.8%	Did not distinguish between transient or permanent, disabling or non-disabling,
Jayaraman ⁴⁹	192	1.6%	No factors reached statistical significance for complications
Katsaridis ⁴¹	101	11%	
Gao ⁷⁵	115	3.5%	
Starke ²	202	5%	5% rate improved to 0.5% at long-term follow-up

Embolization on Acutely Ruptured AVM

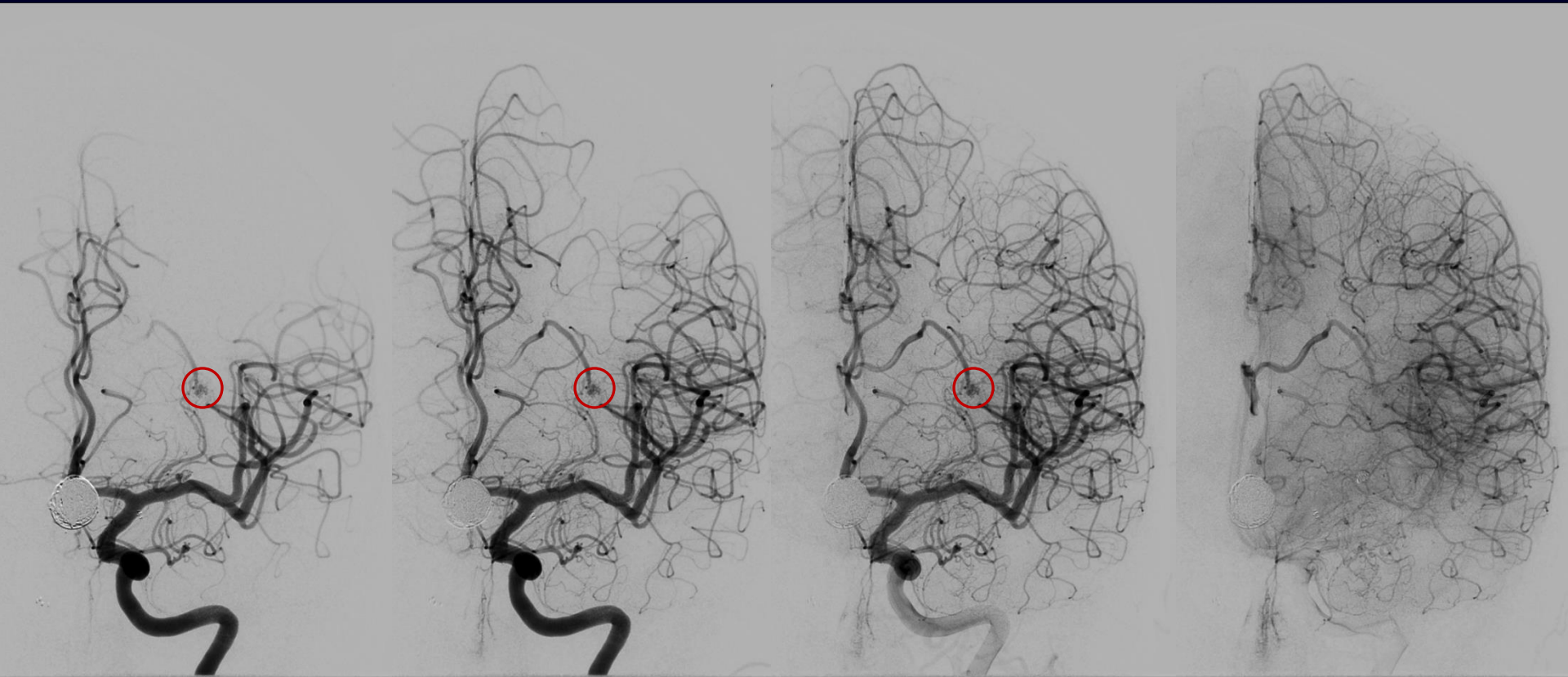
- Stemer et al. JNIS 2013
 - 21 patients
 - 62% one session
 - cure rate 33% with one session embo
 - 2 patients had asymptomatic procedural complications
 - mean GOS at presentation was 4 and at discharge was 4.4 (improved)

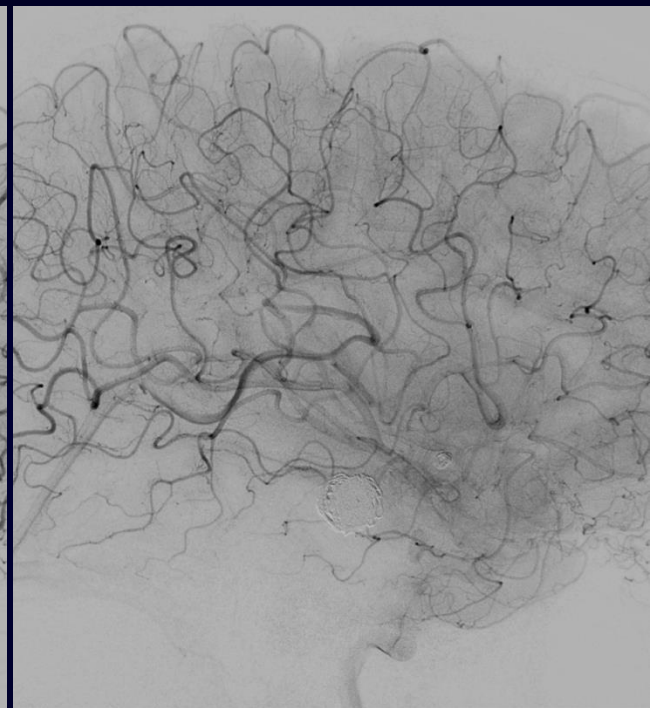
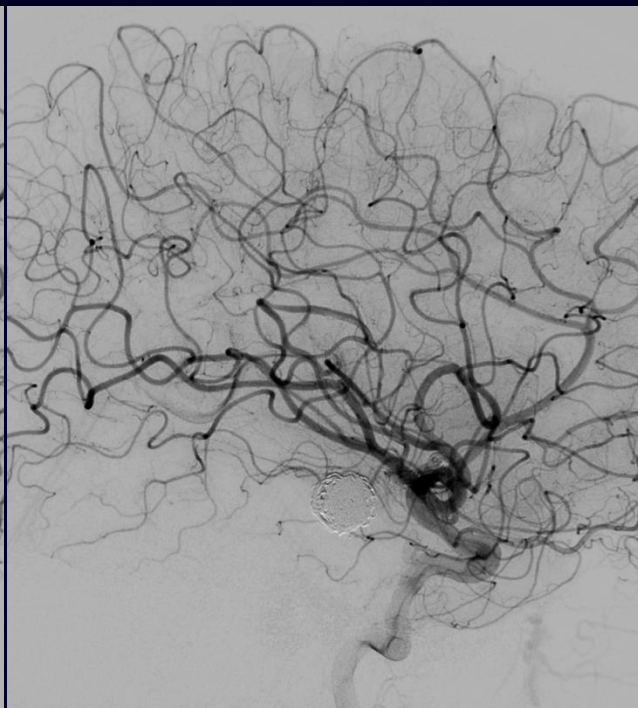
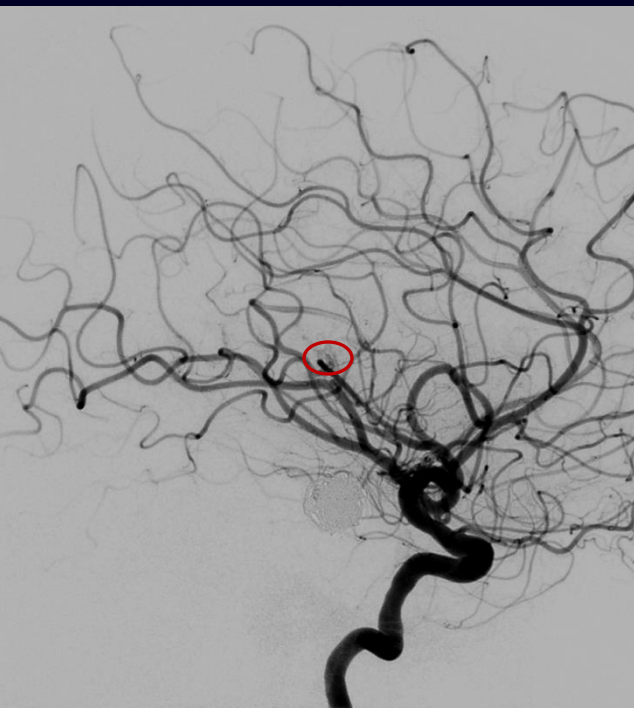
How do we approach AVM

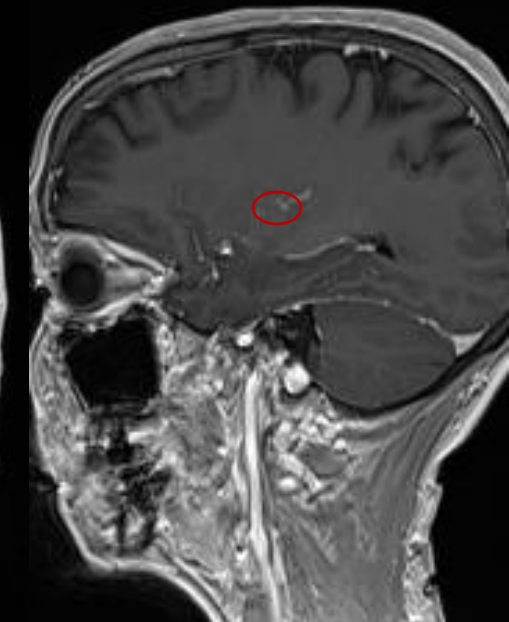
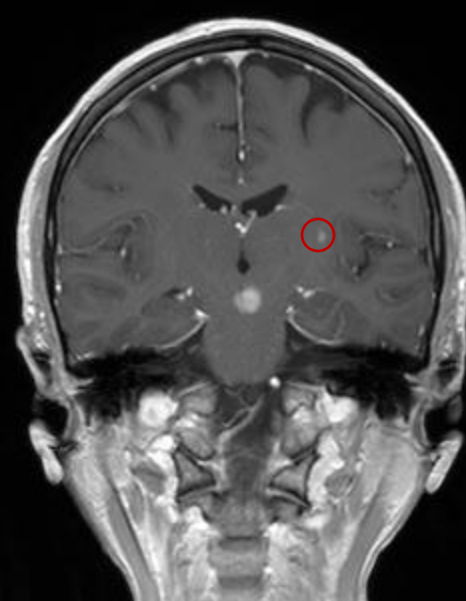
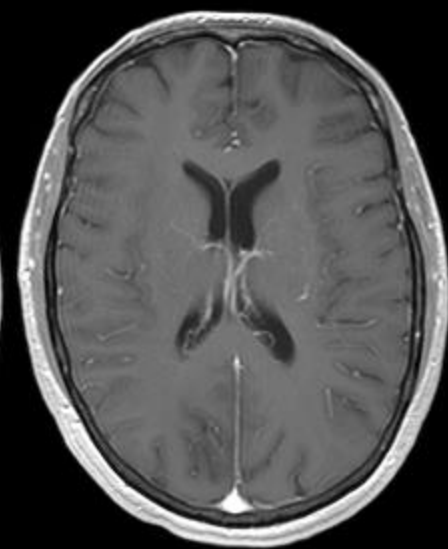
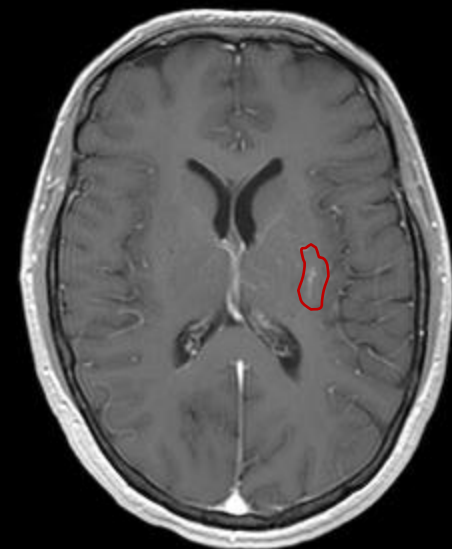
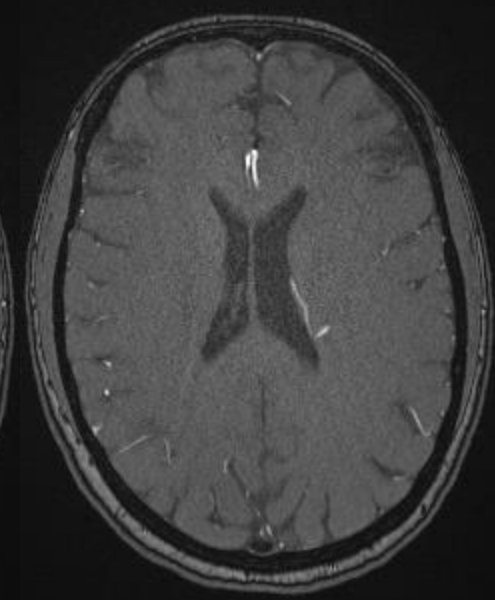
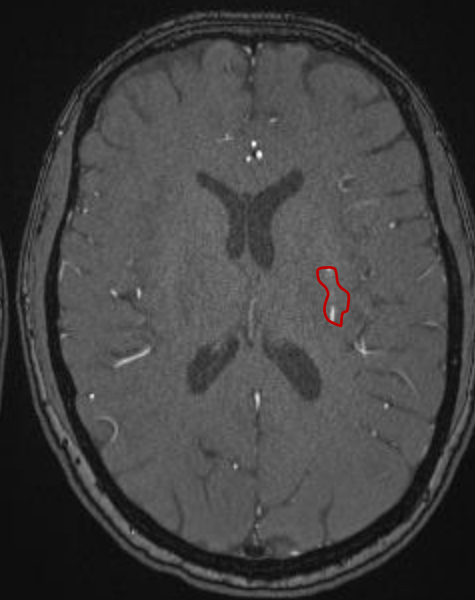
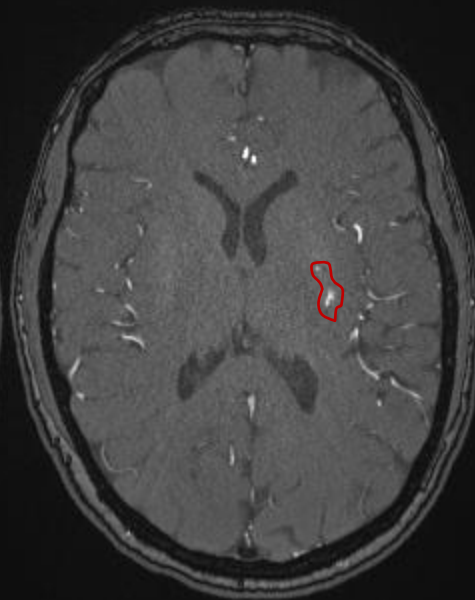
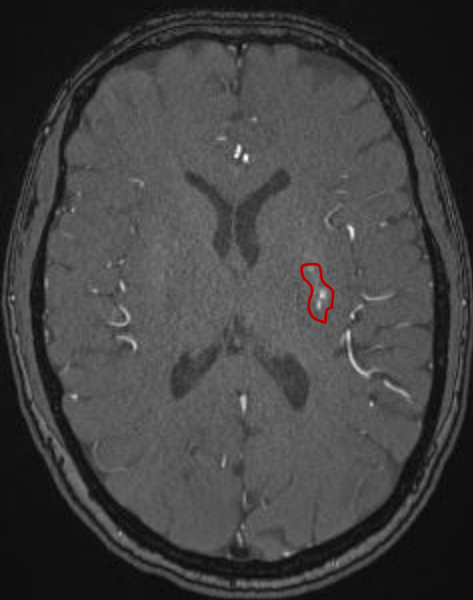
- Unruptured deep lesion – SRS
- Unruptured lesion SM 1 to 3: embo+surgery
- Unruptured/Ruptured lesion SM 4 to 5: embo
angioarchitectural defect
- Ruptured lesion SM 1 to 2: embo to cure with or
without surgery
- Ruptured lesion SM 3: embo+surgery



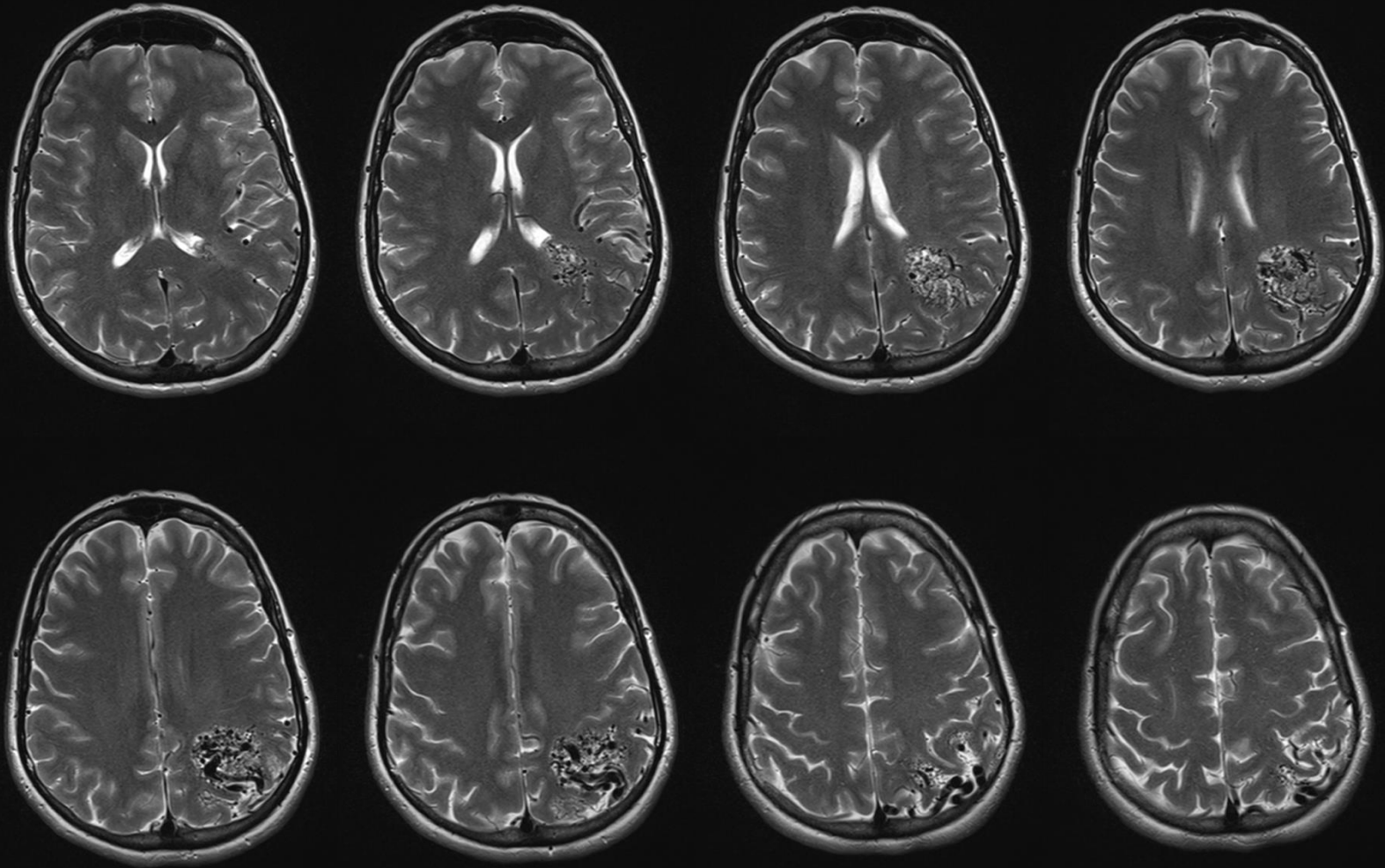
Left BG AVM GK planning

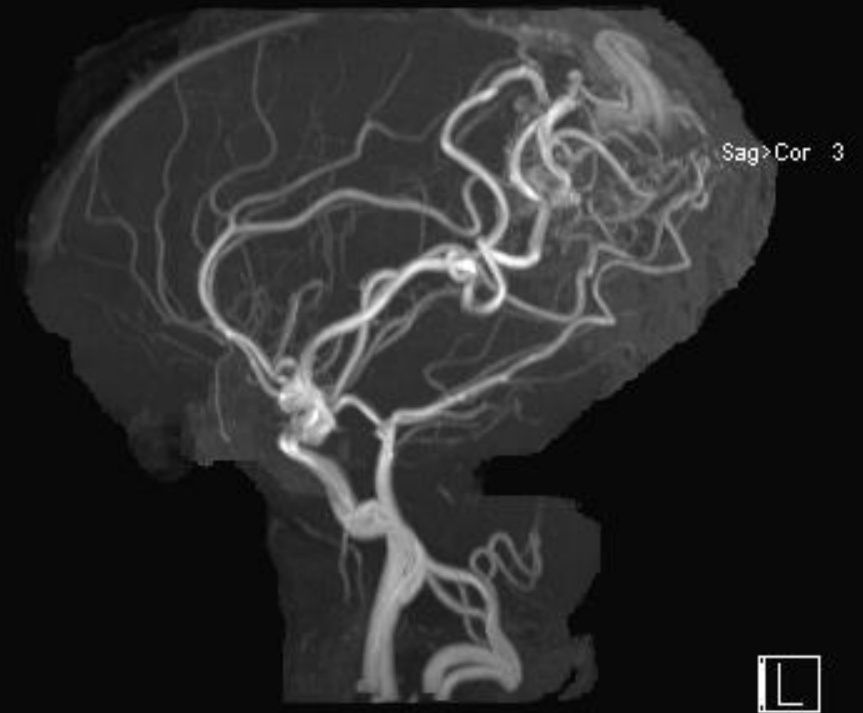


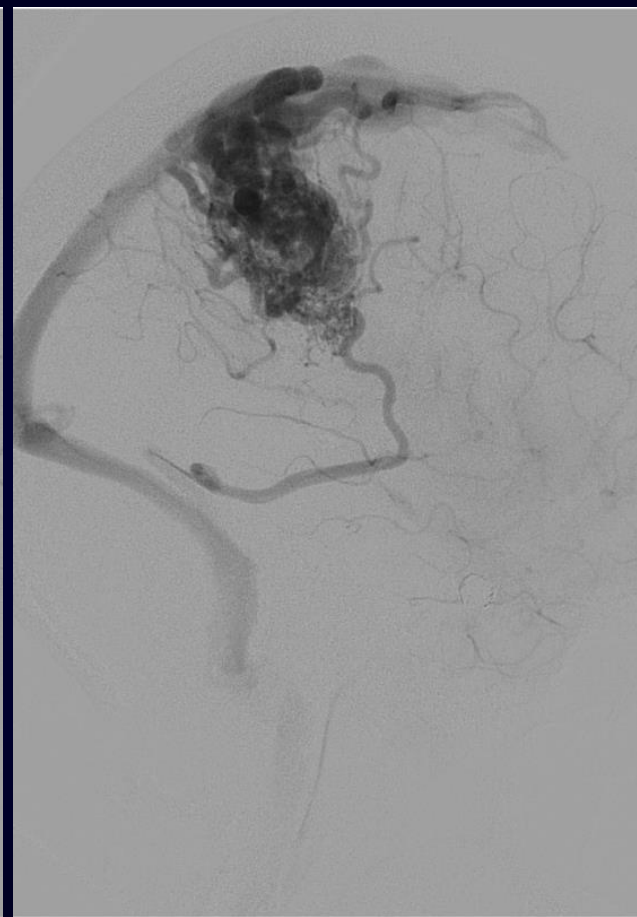
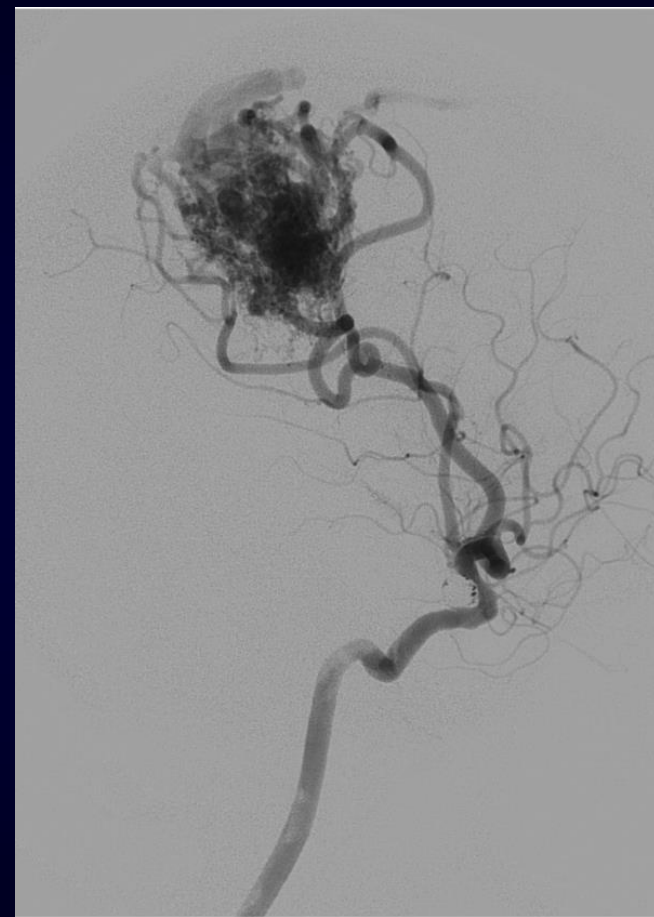
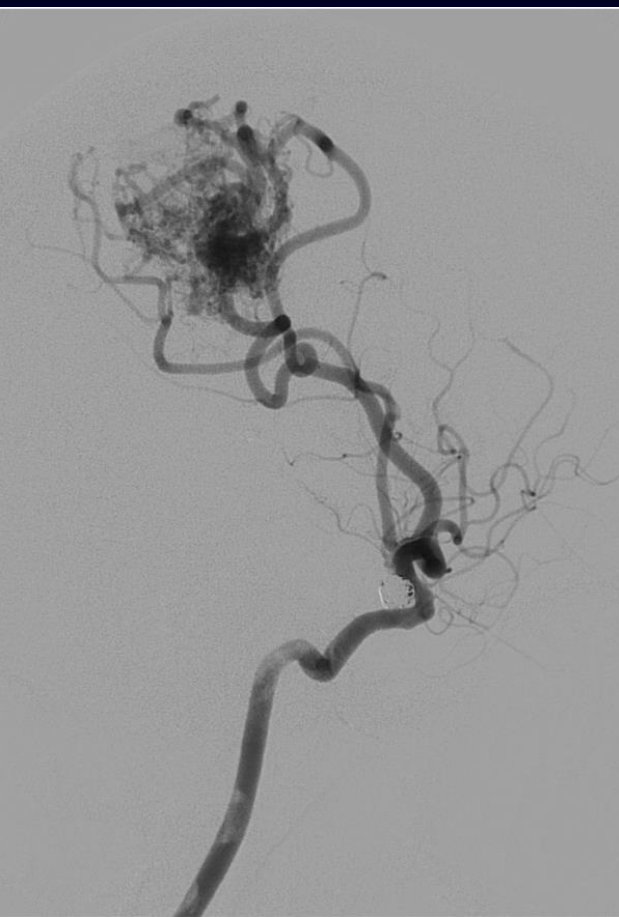




30F severe headaches







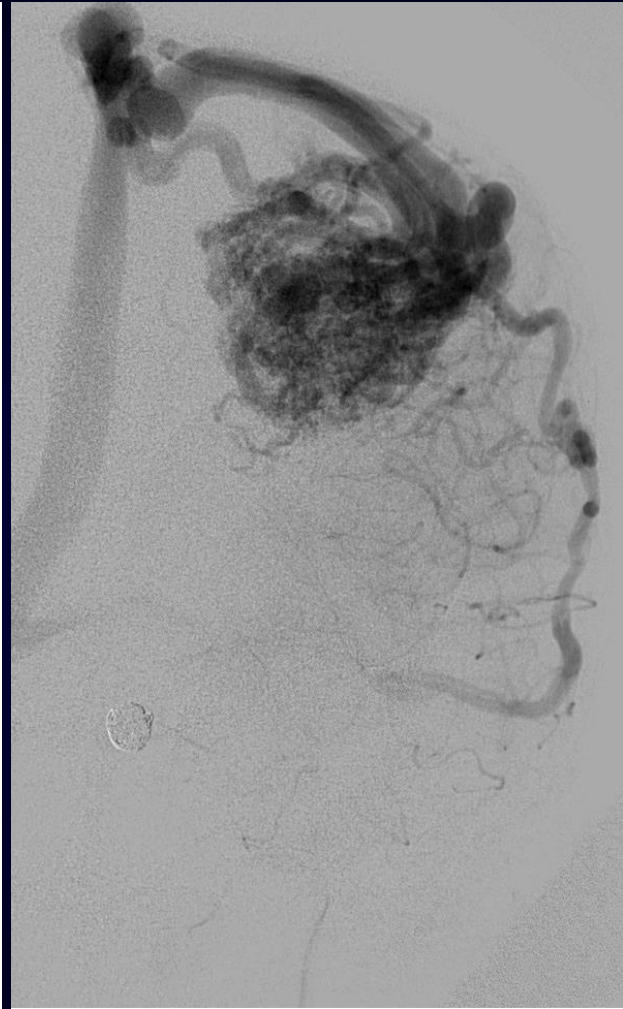
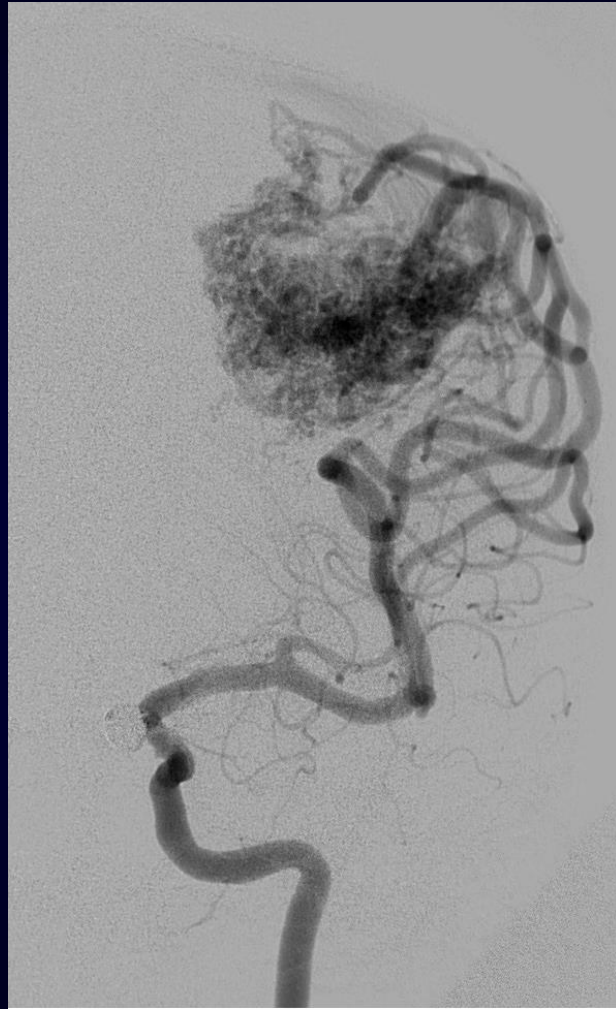
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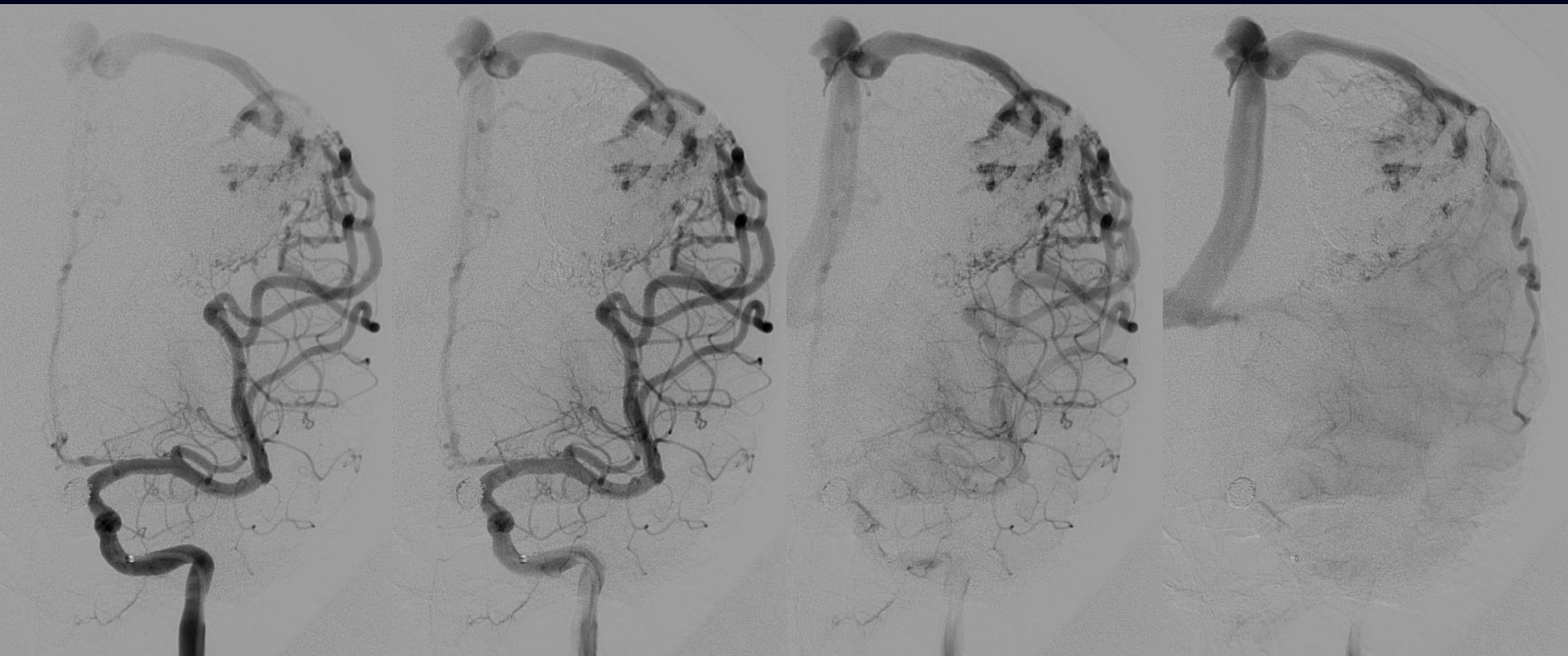


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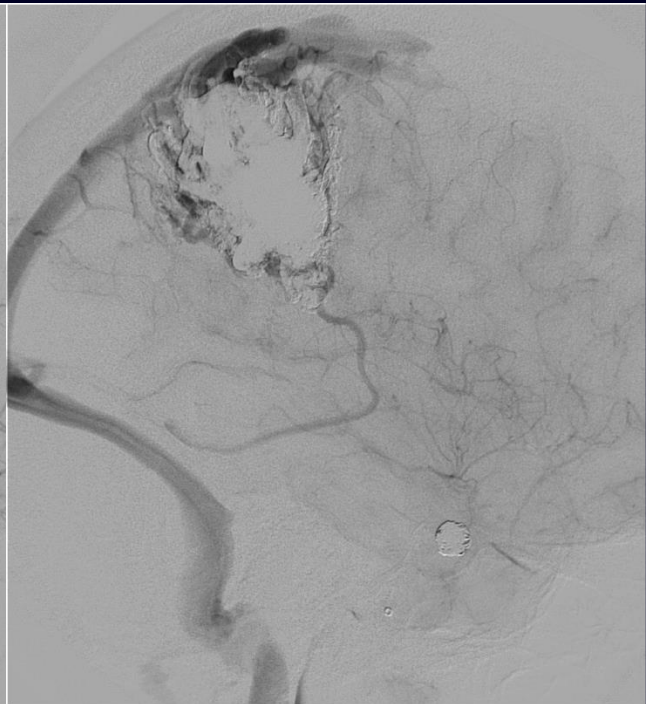
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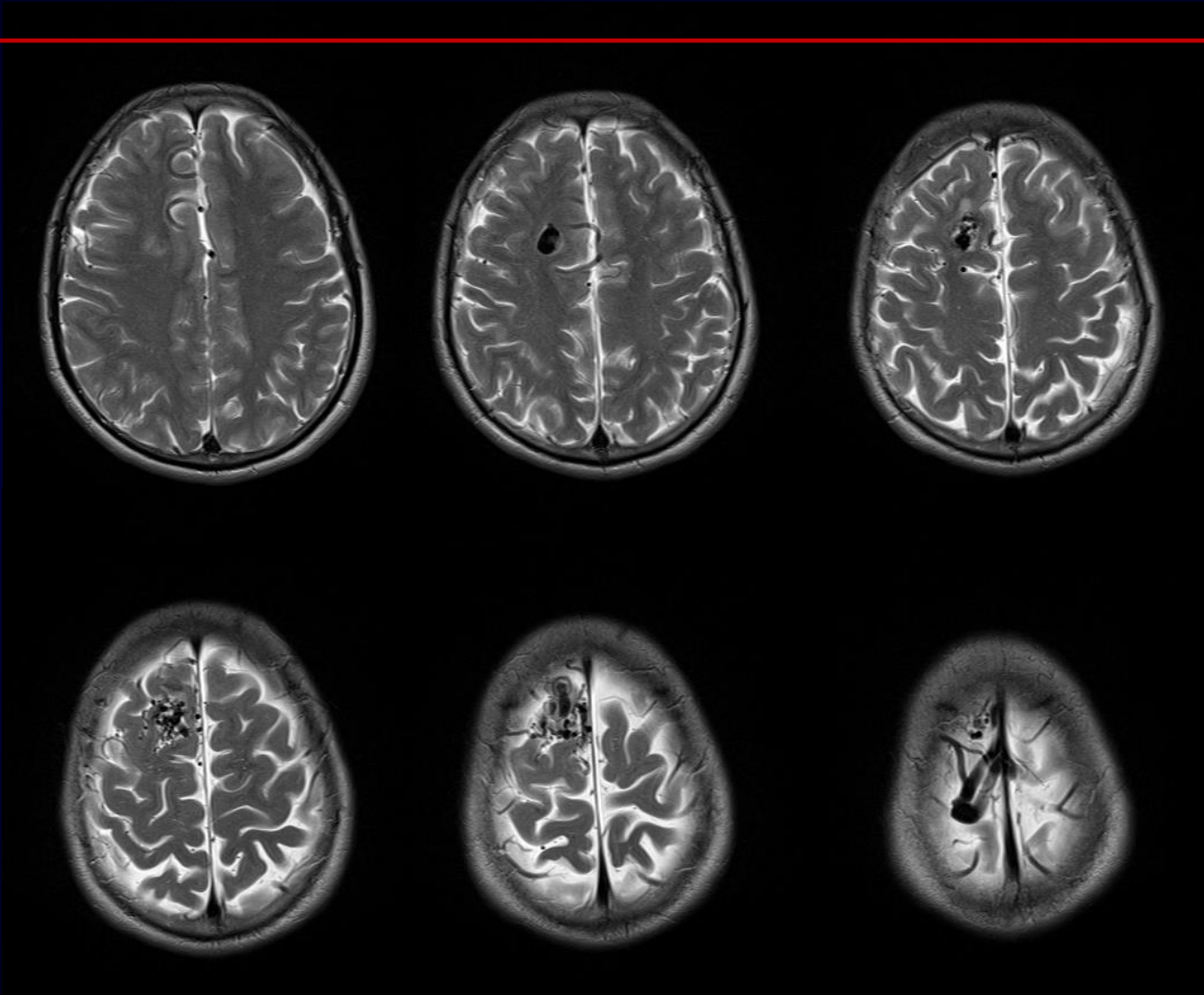
Baptist Neuroscience Center
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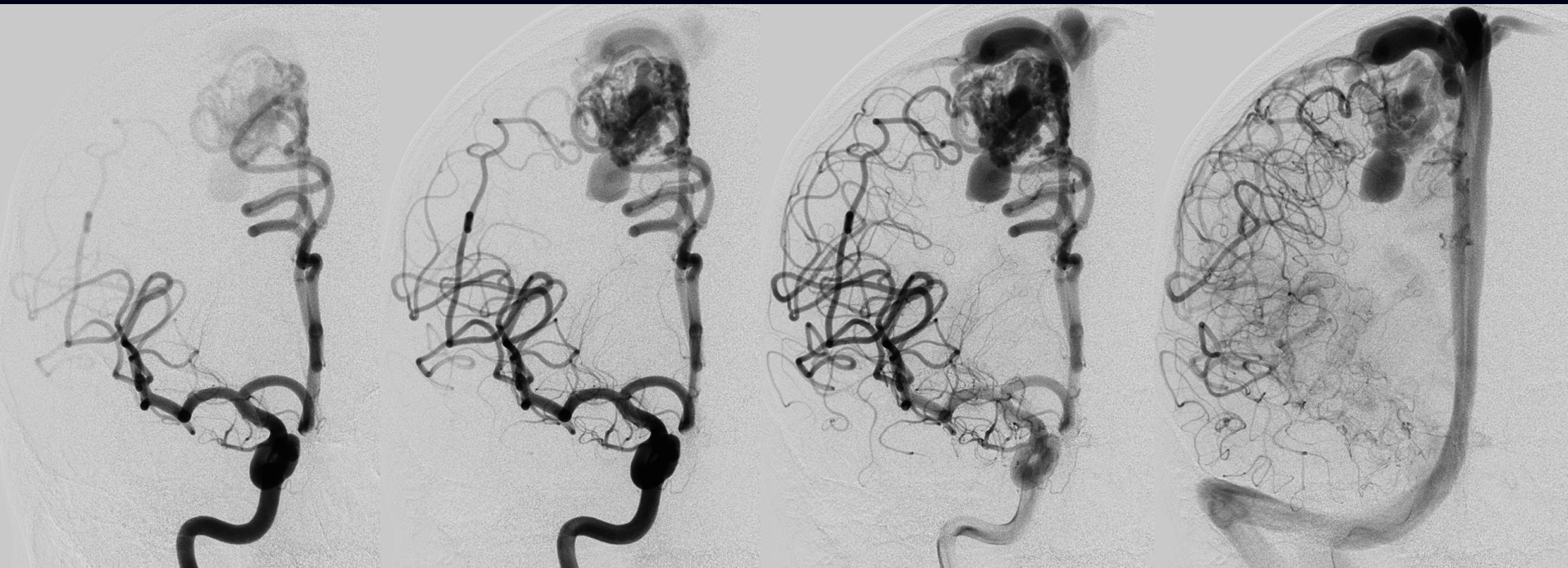


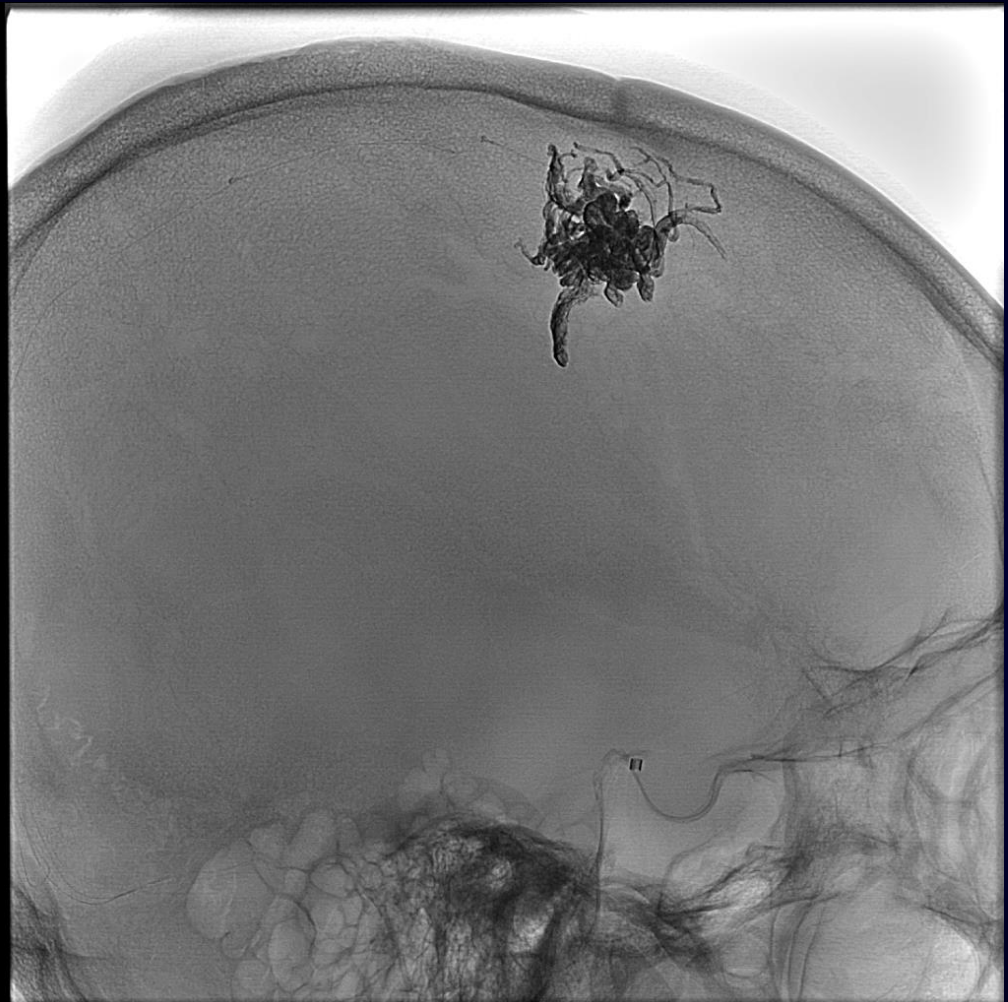
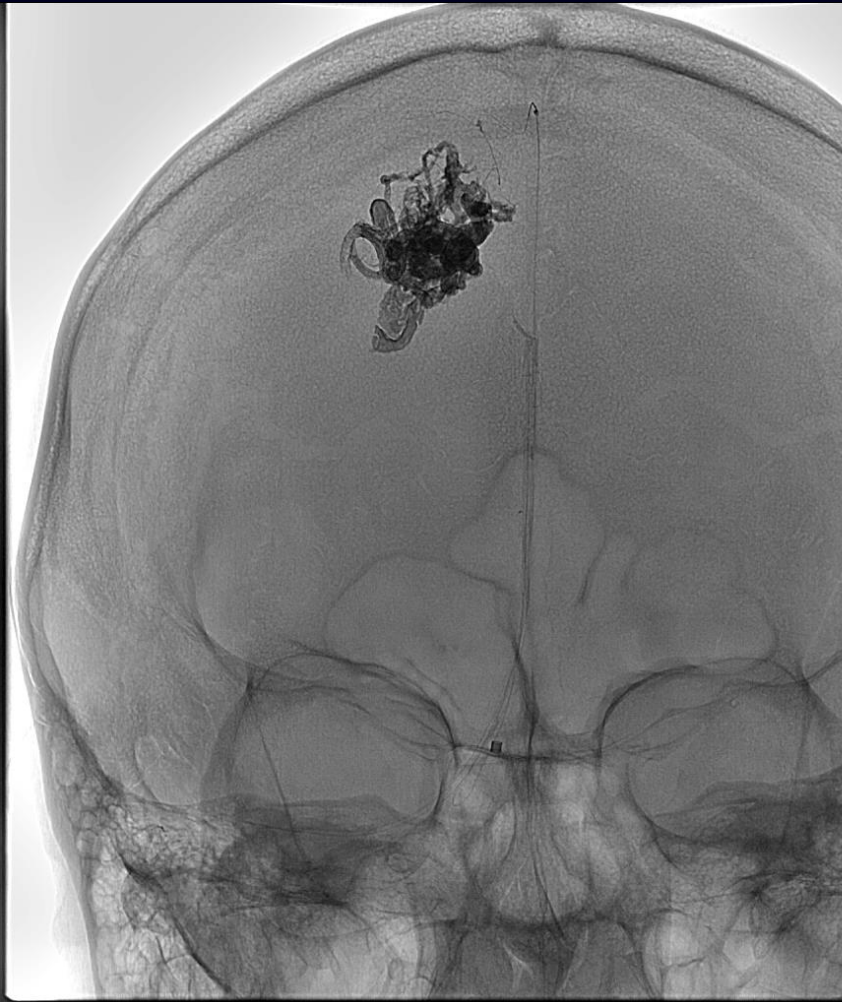
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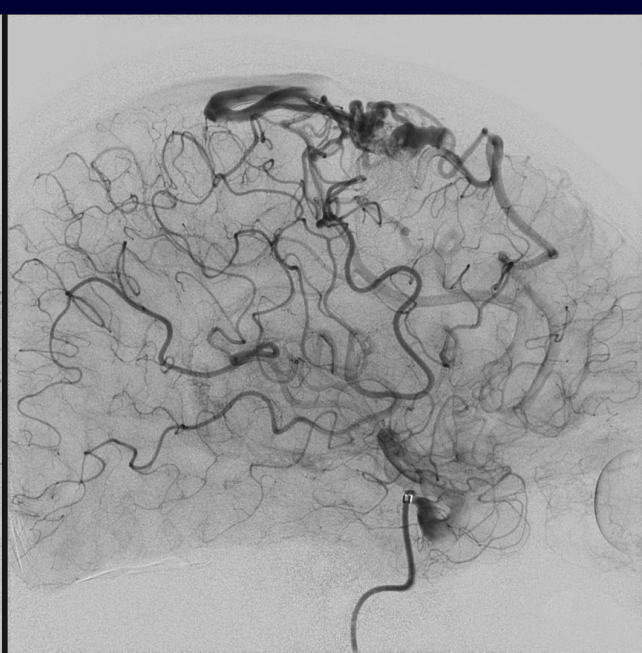
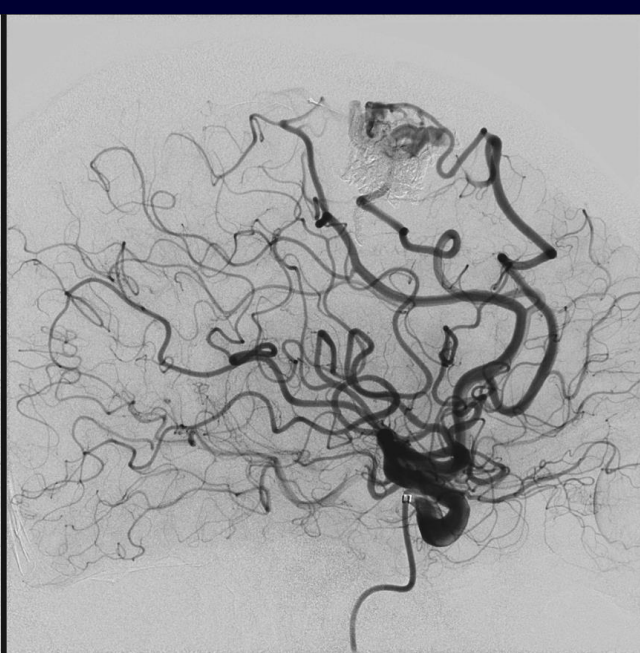
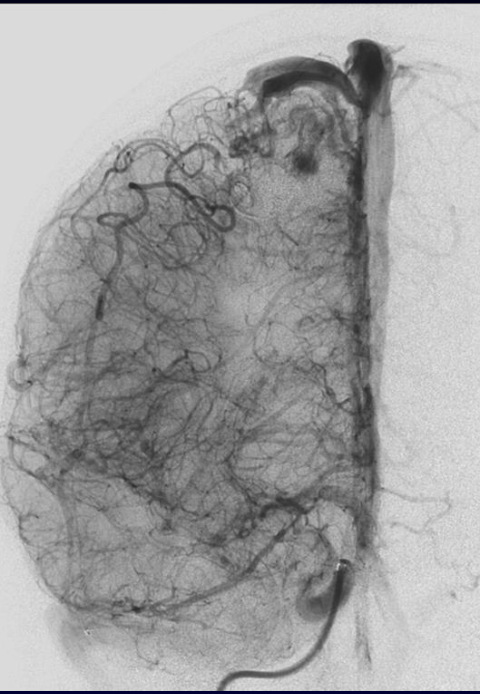


29M seizures

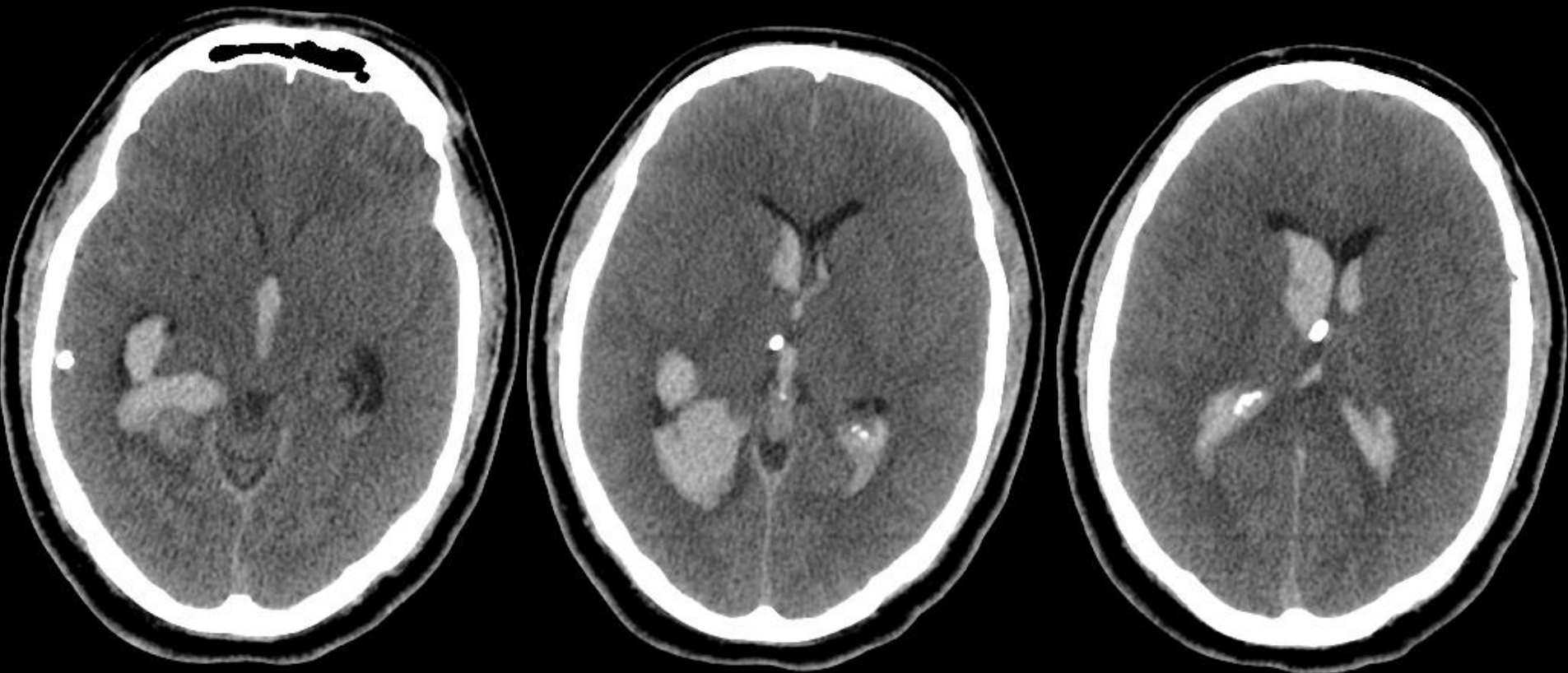


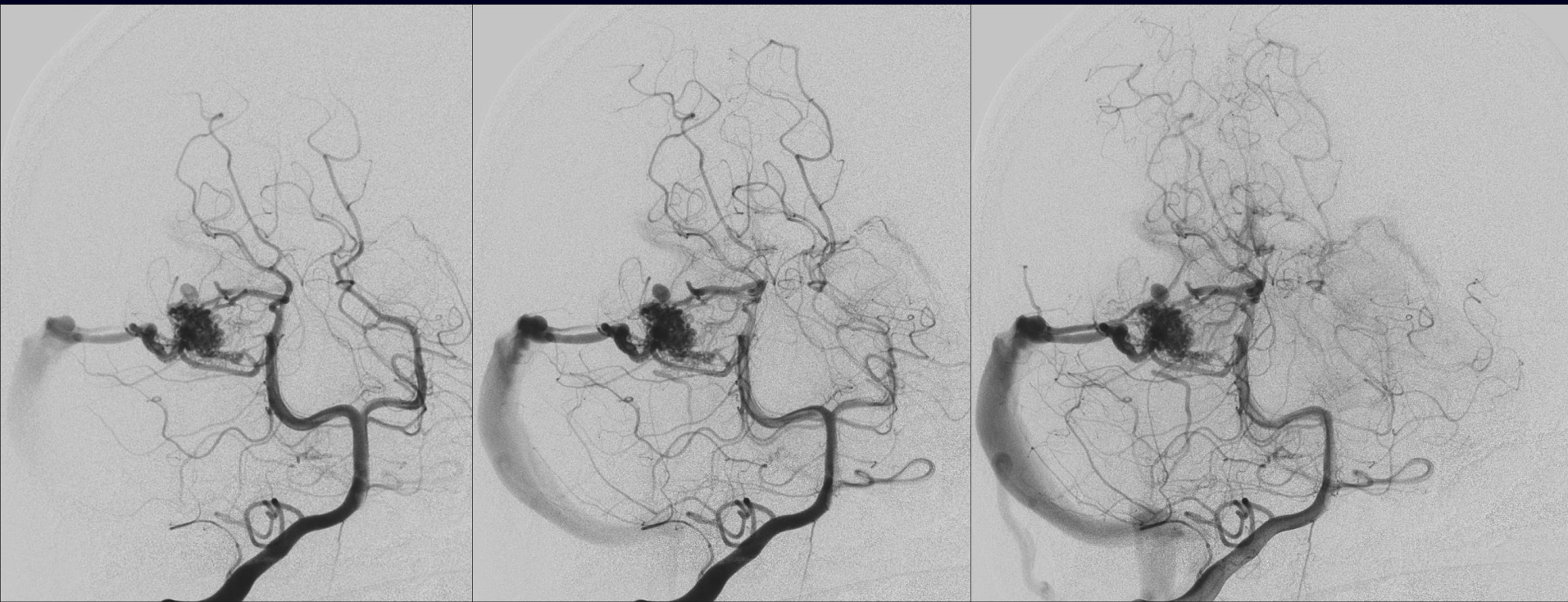






32M severe HA and LOC





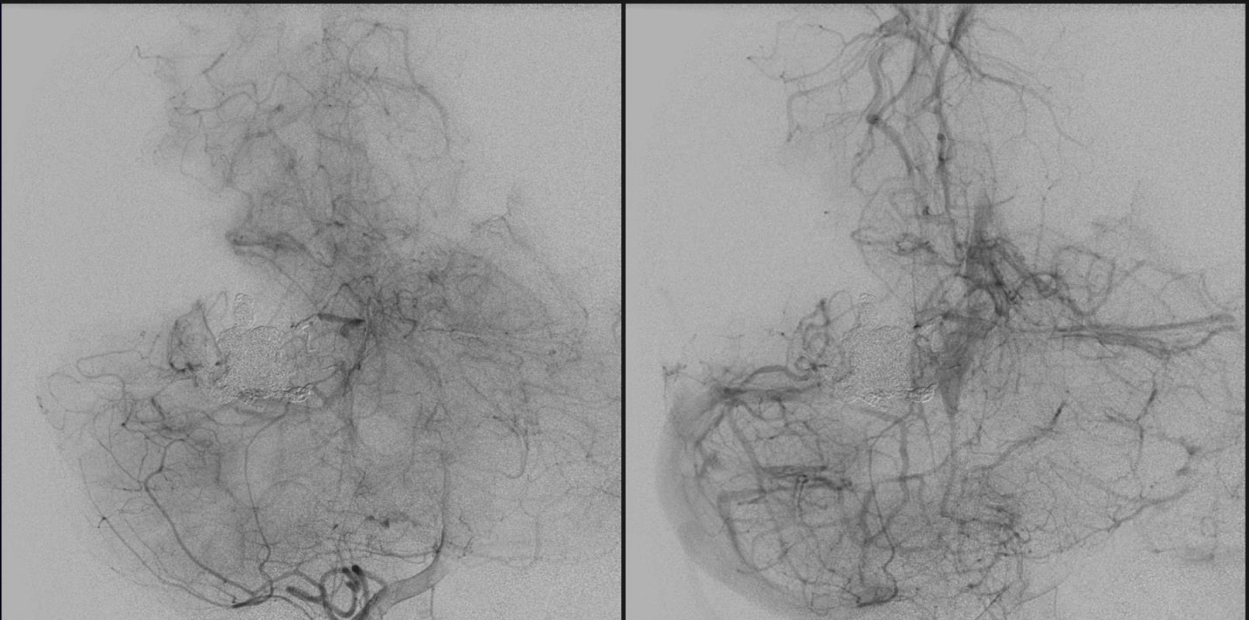
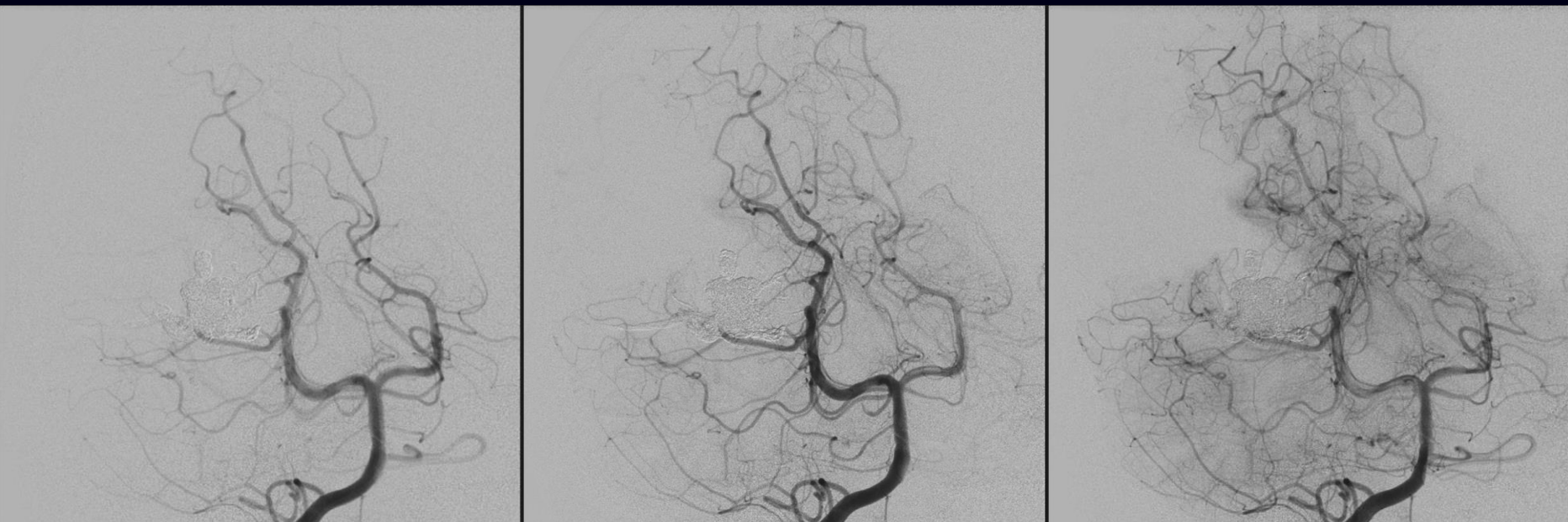
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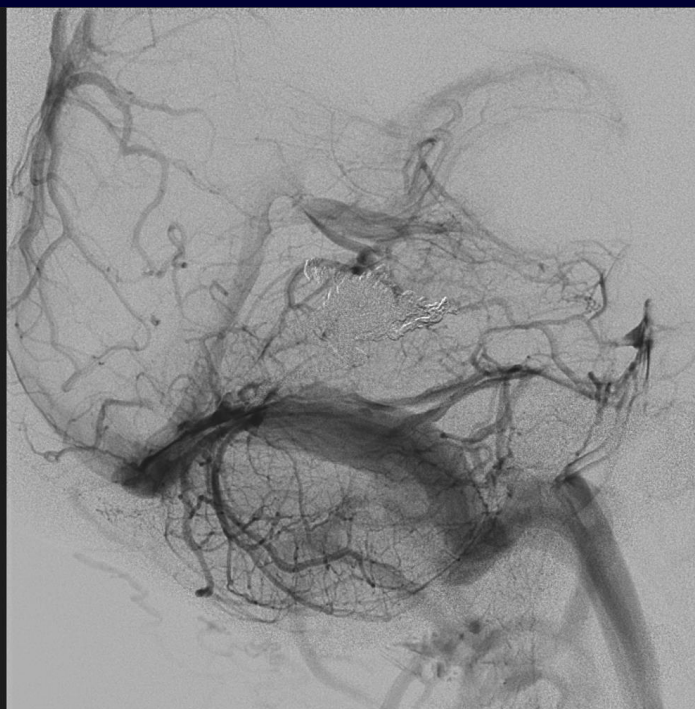




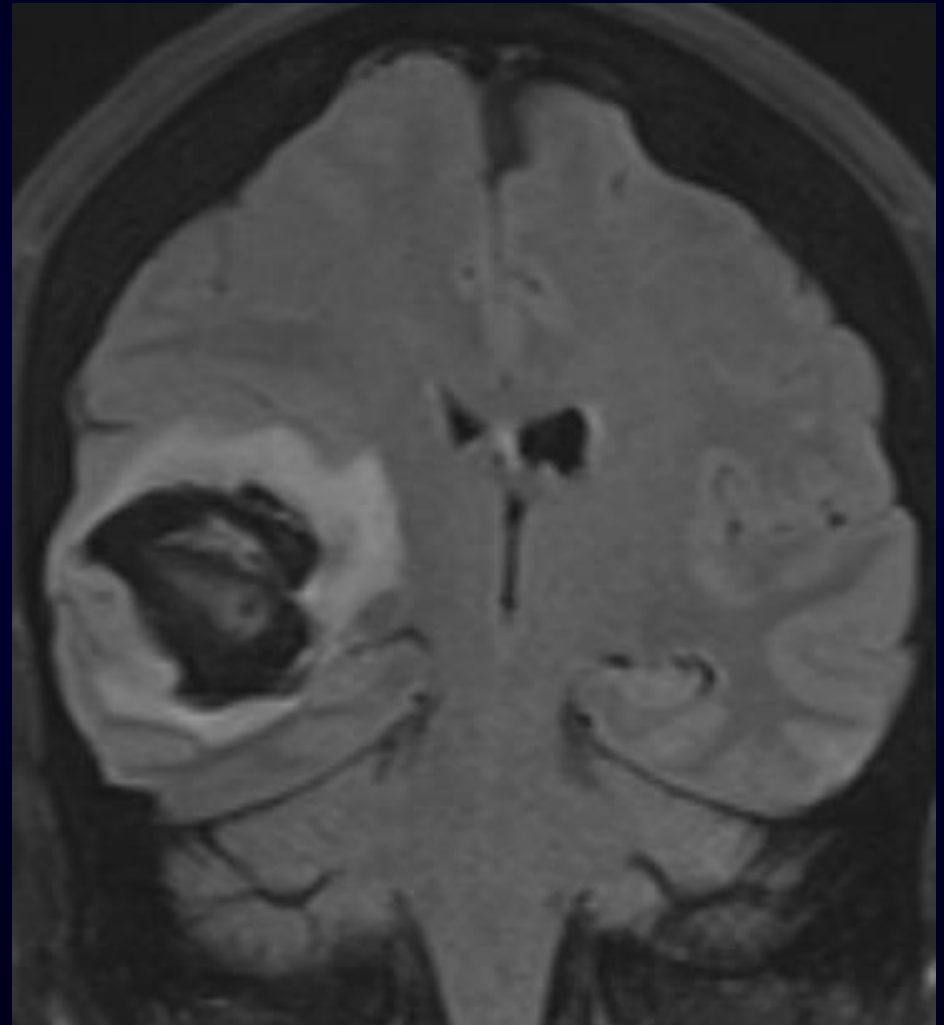
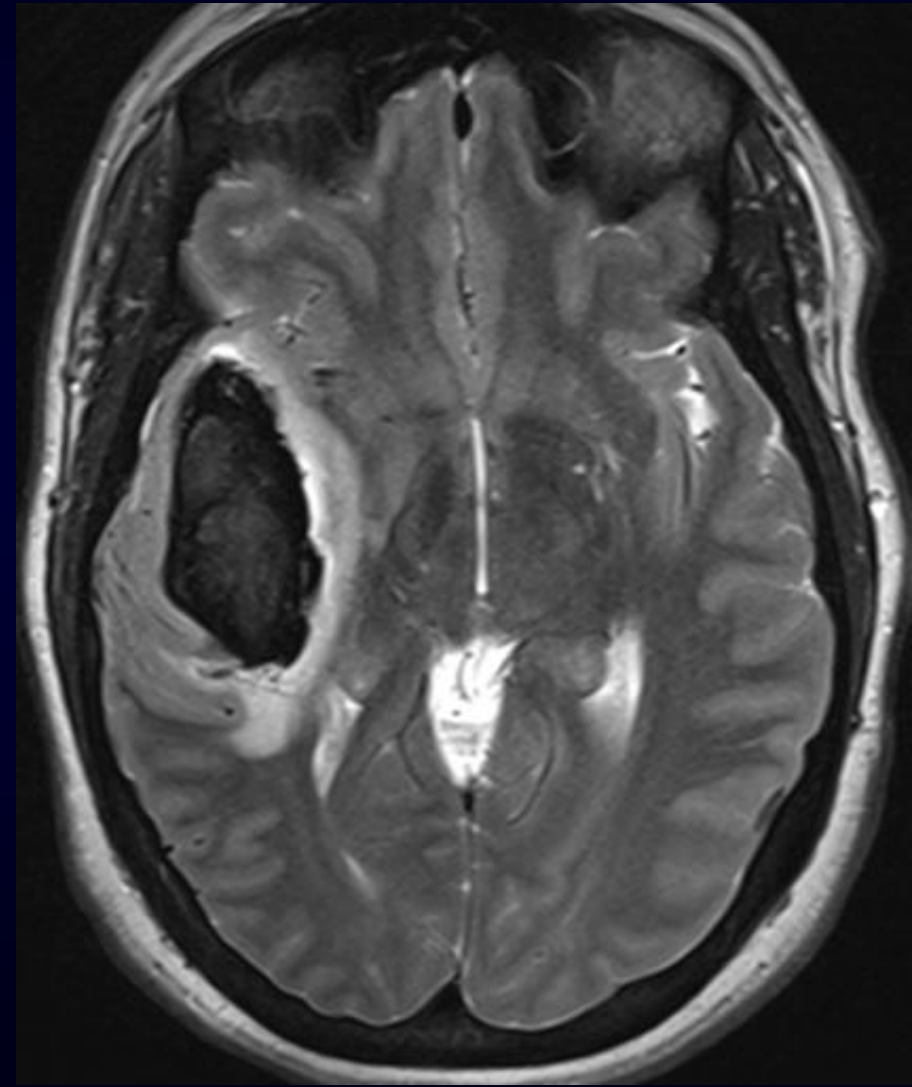
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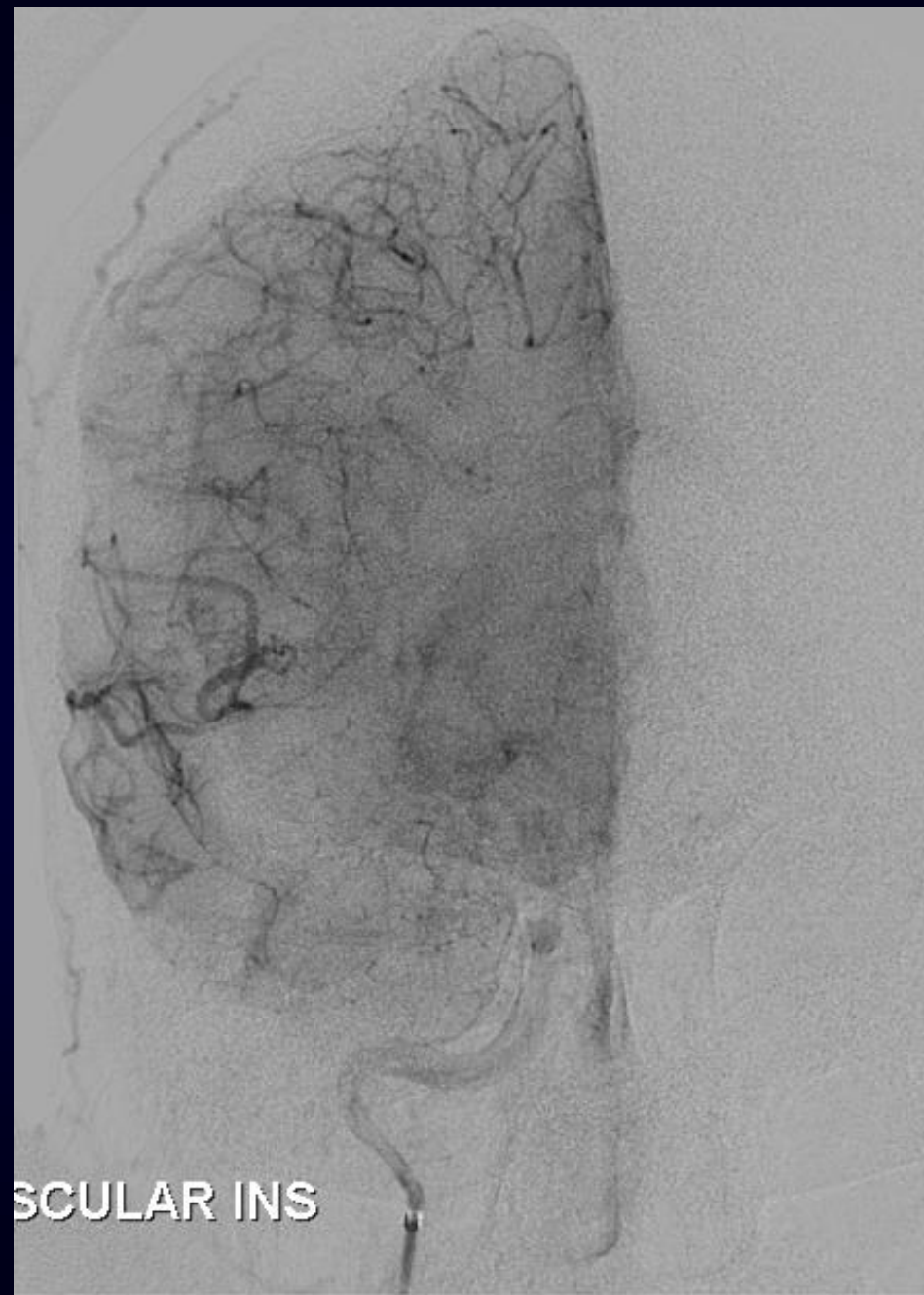


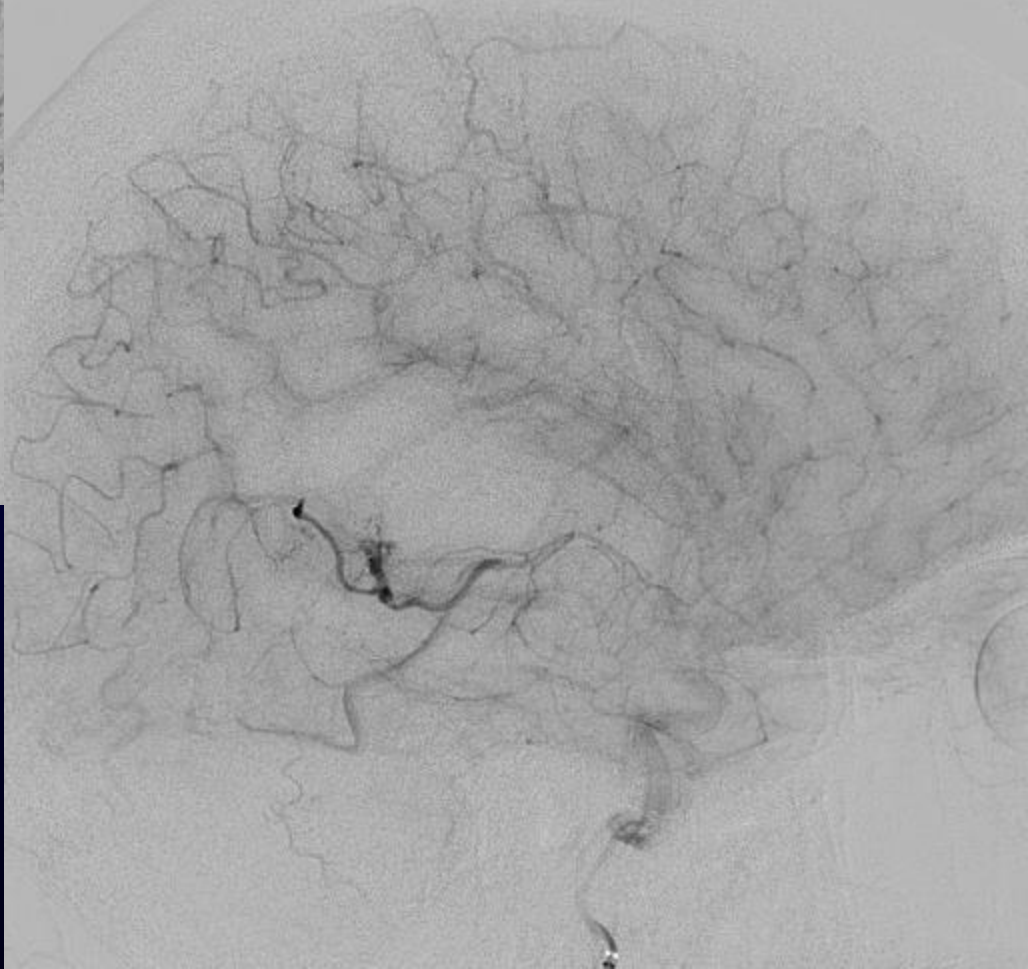
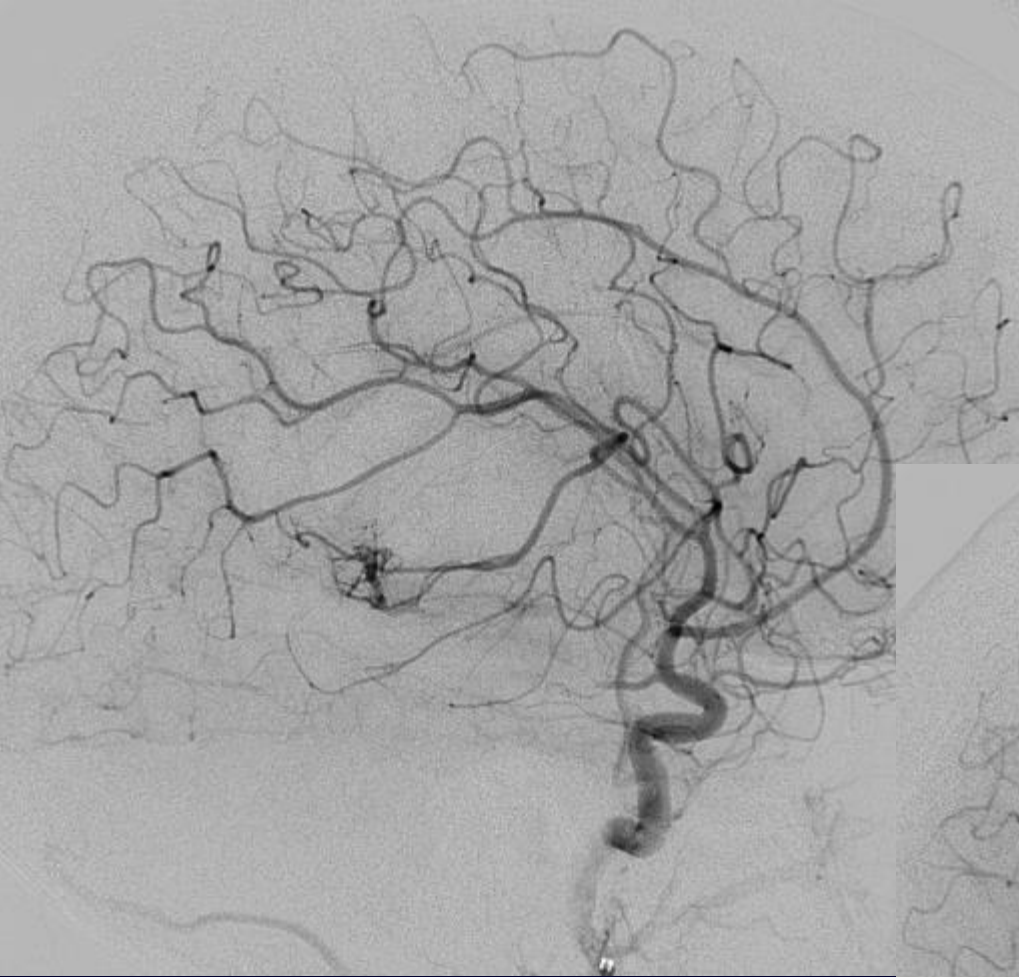
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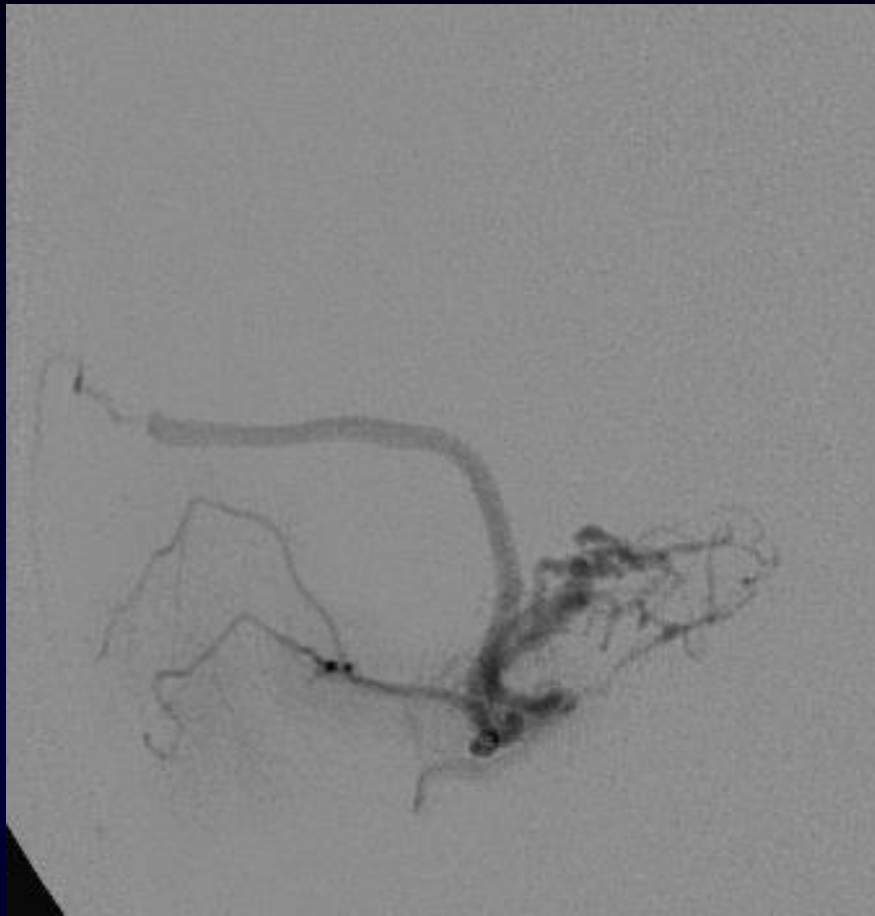


40y F presenting with HA and mild left side weakness

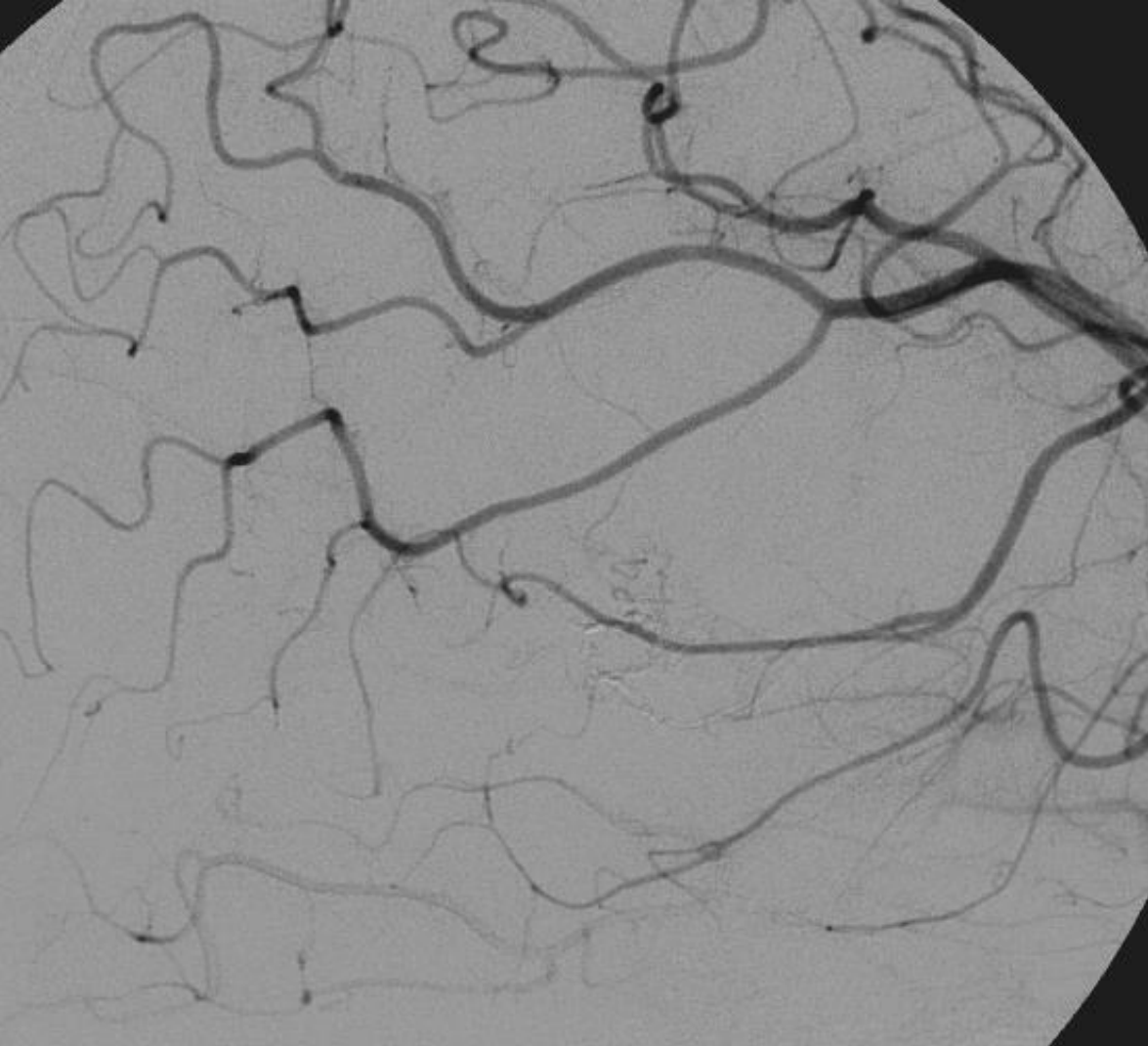


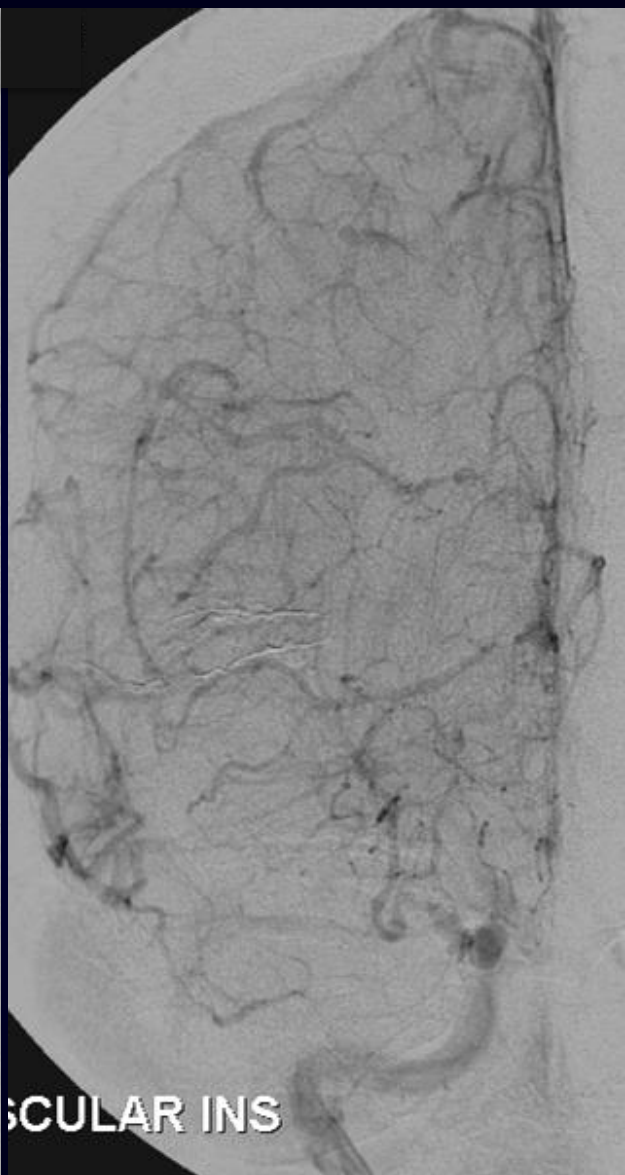
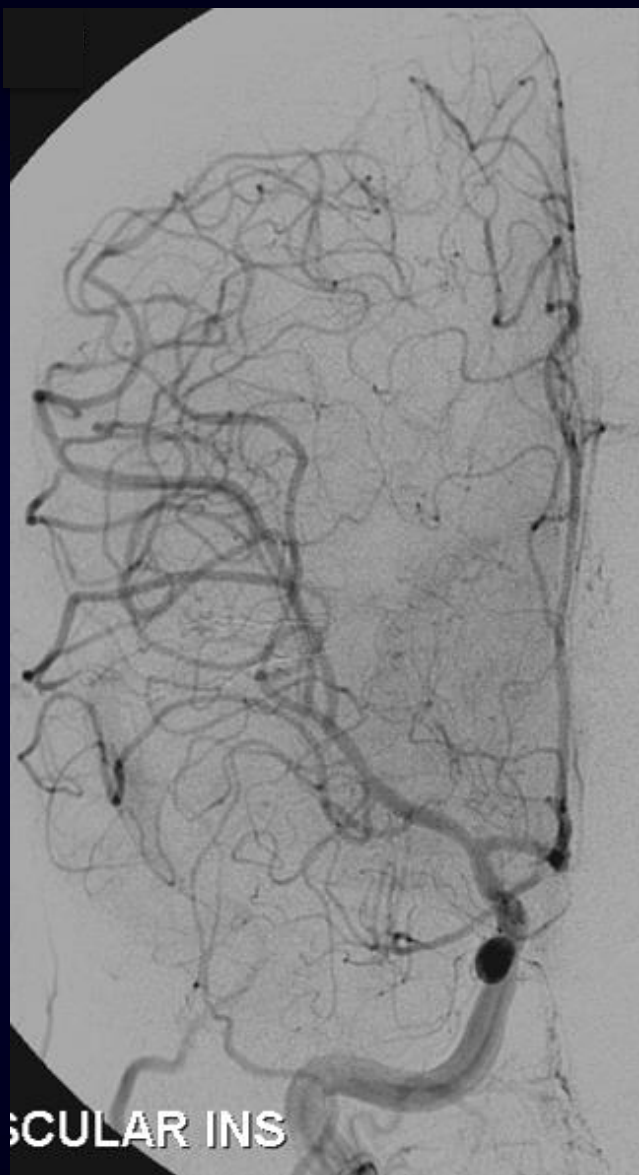
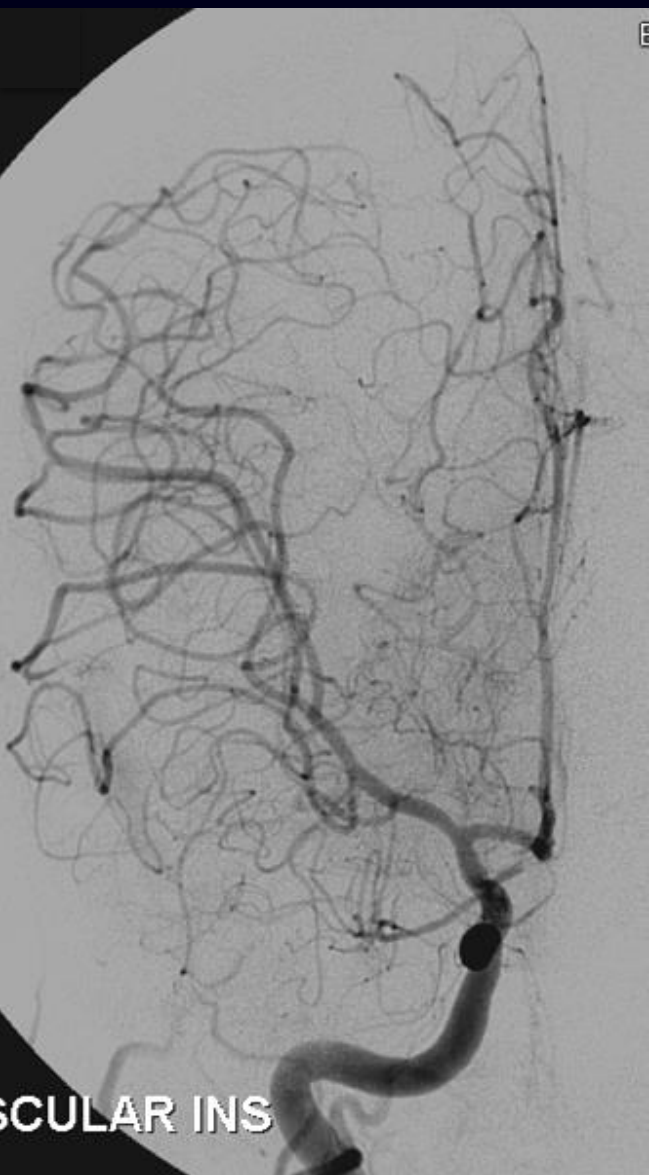


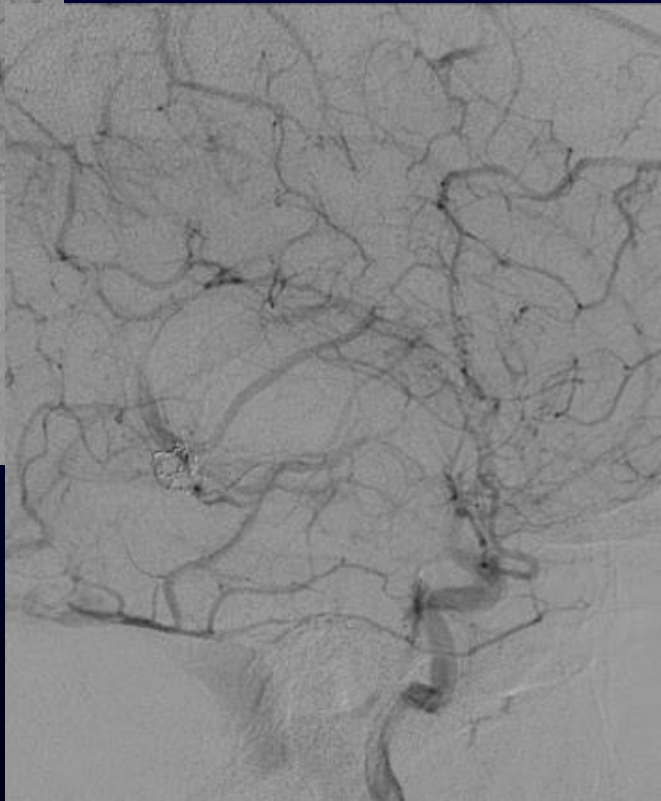
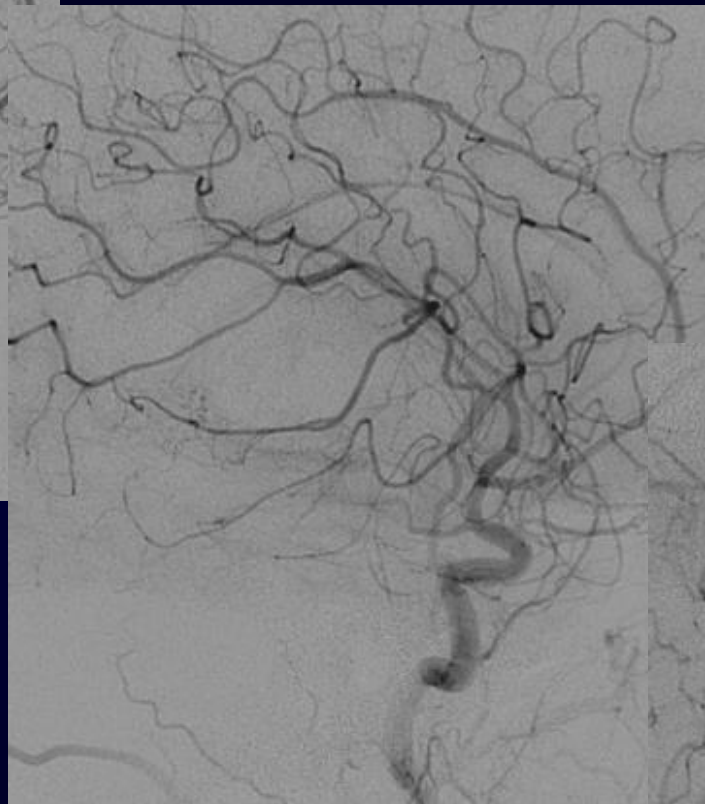
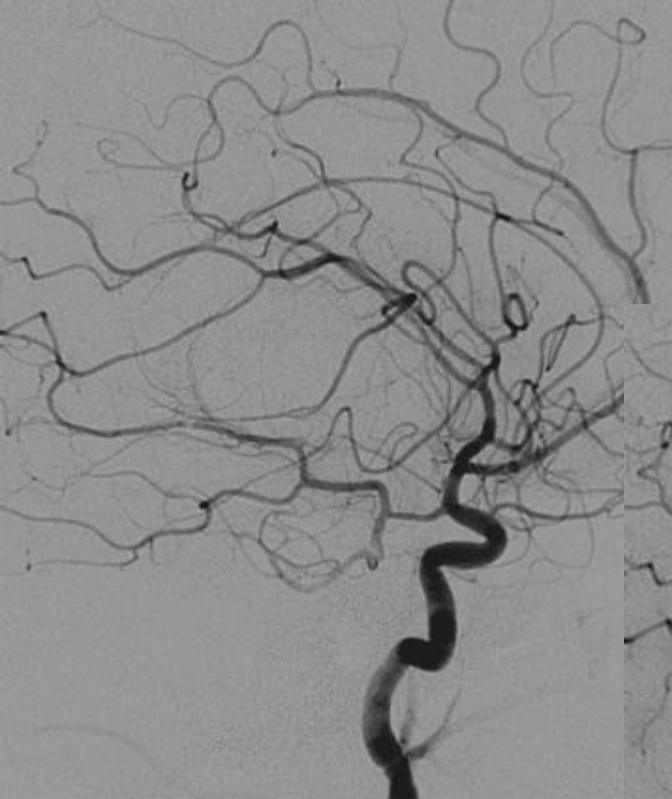






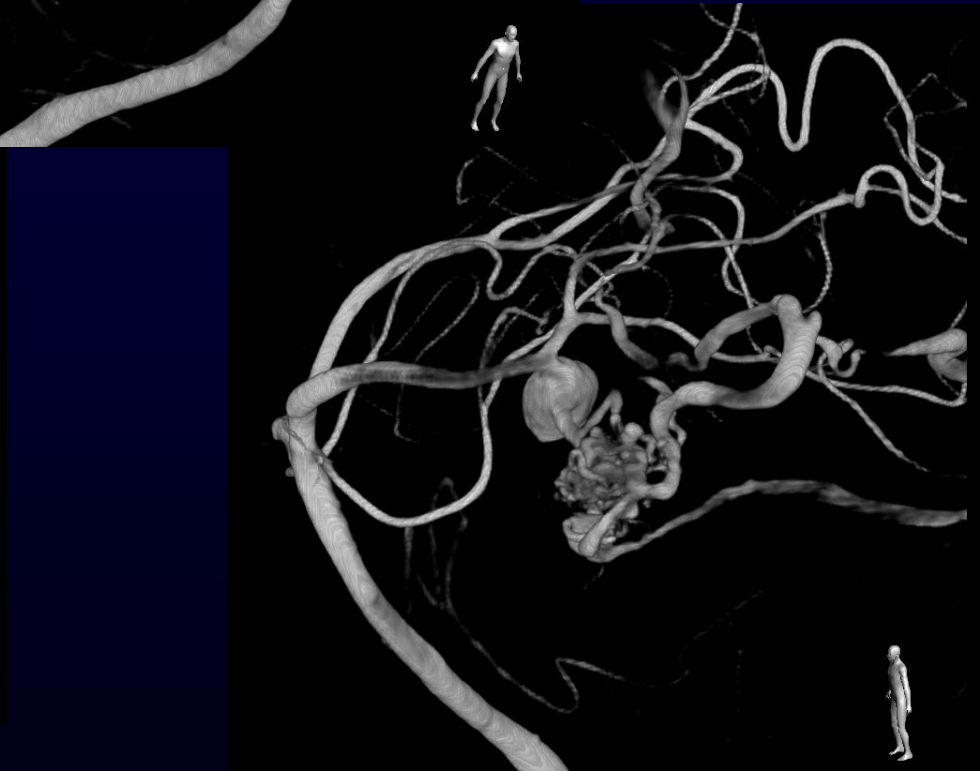
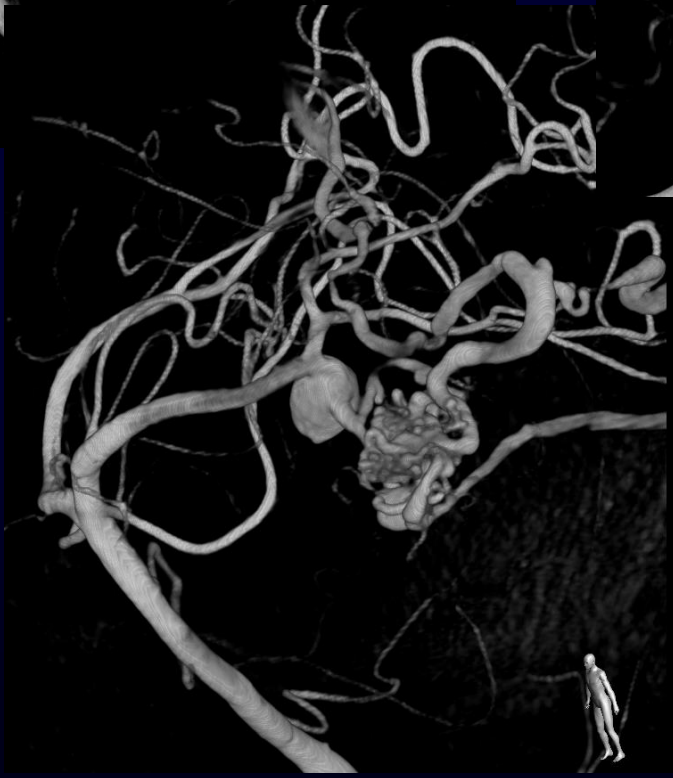
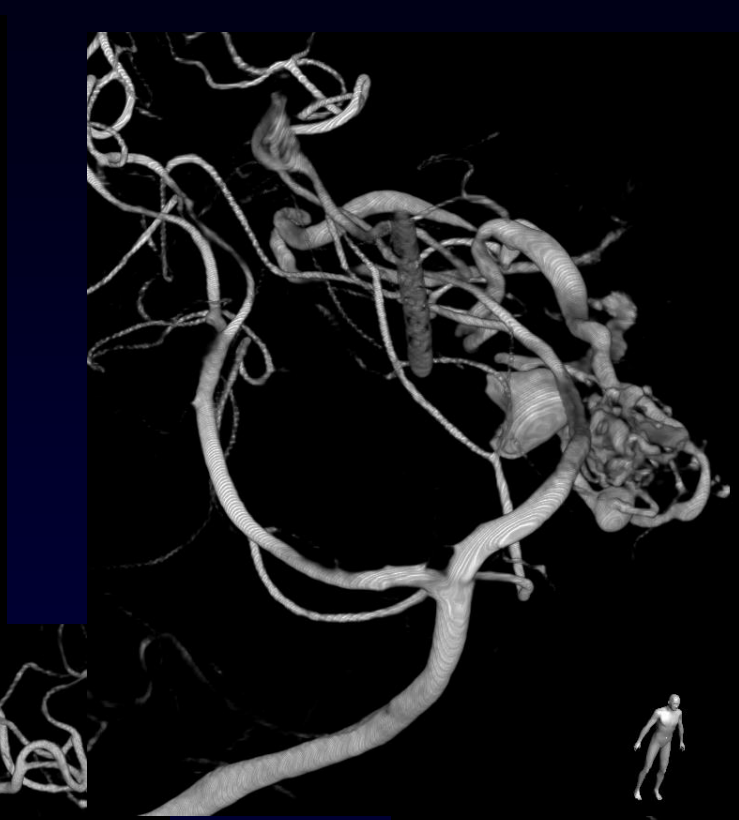
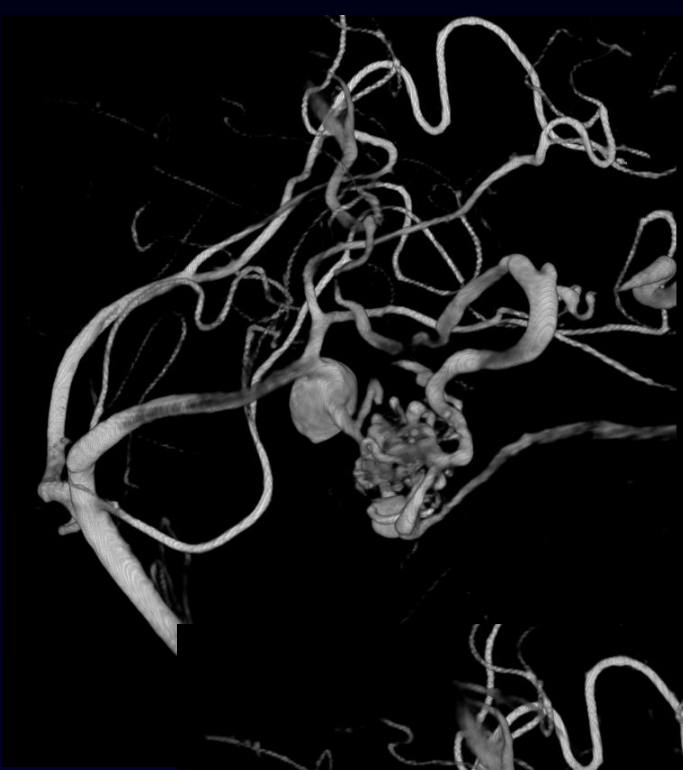






44M found unresponsive



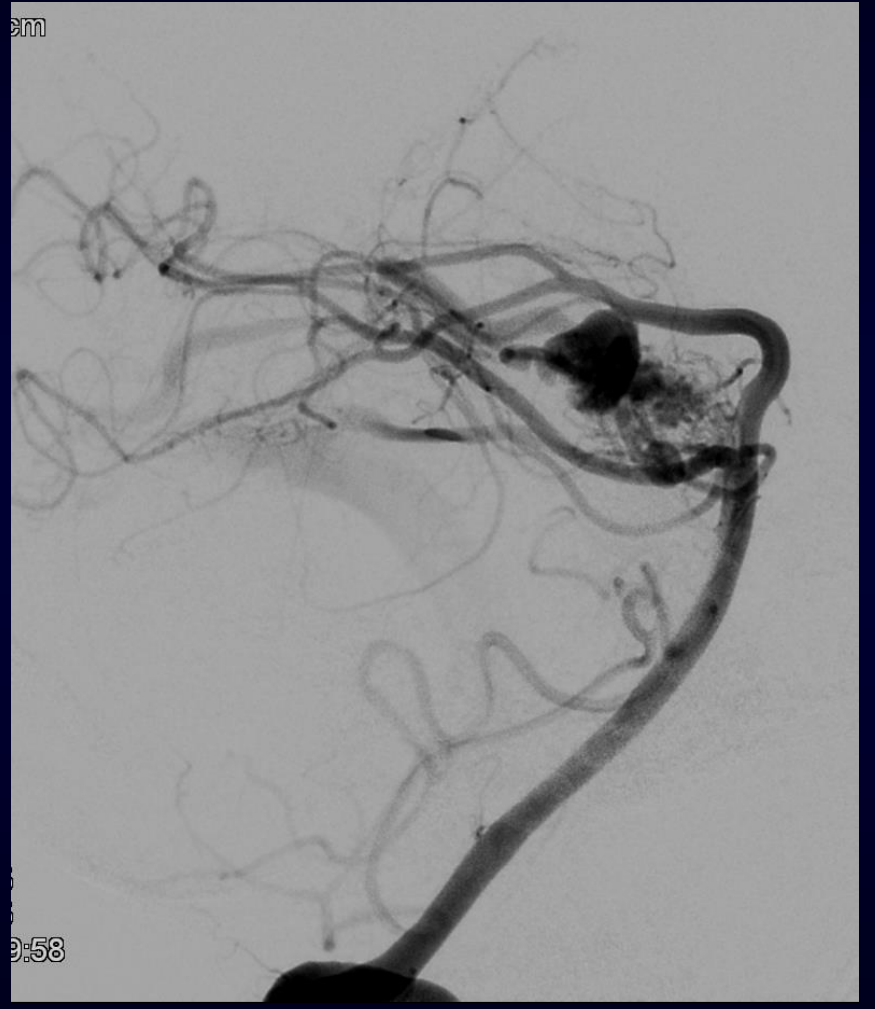


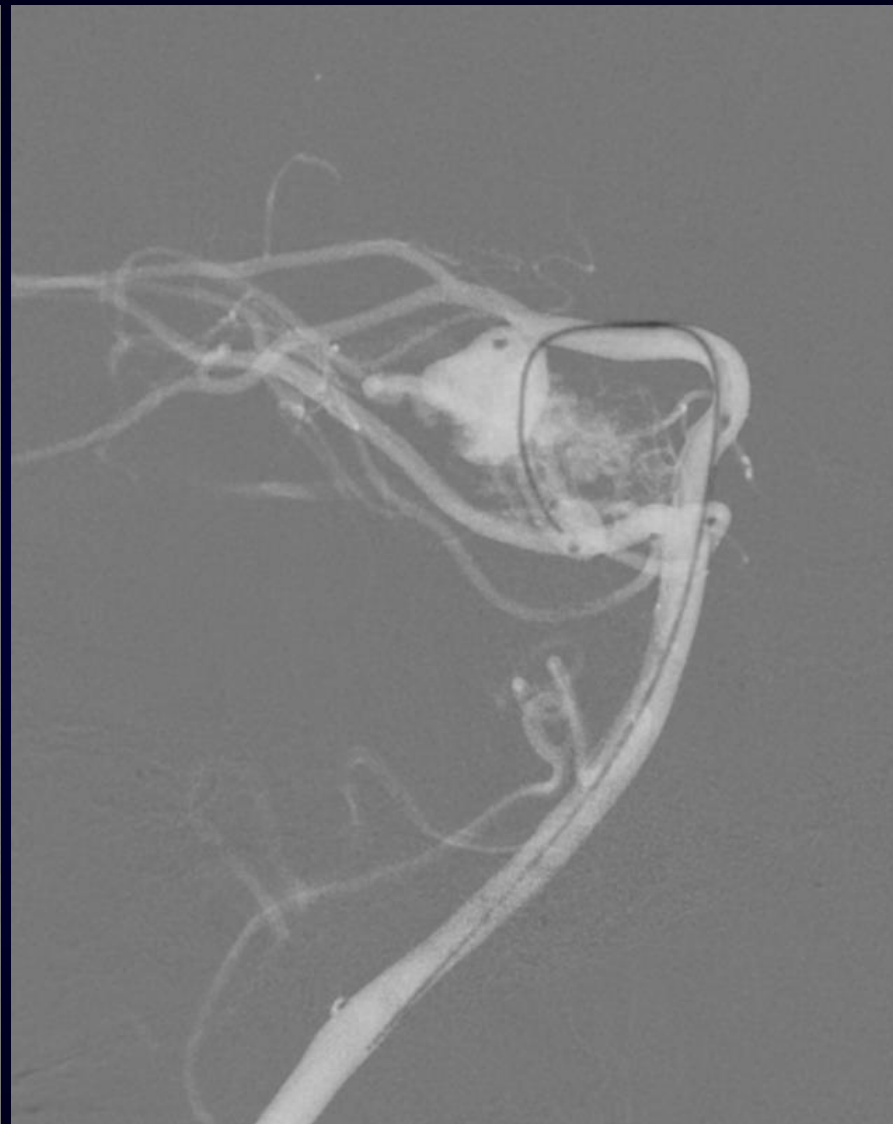
Rot -88°
Ang +0°
FD 25 cm



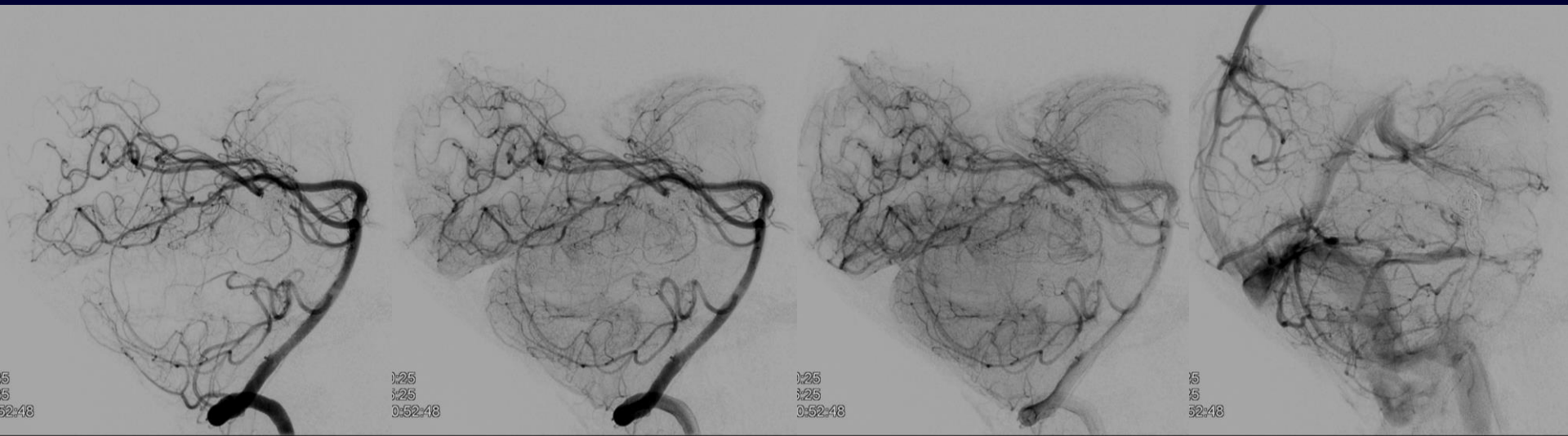
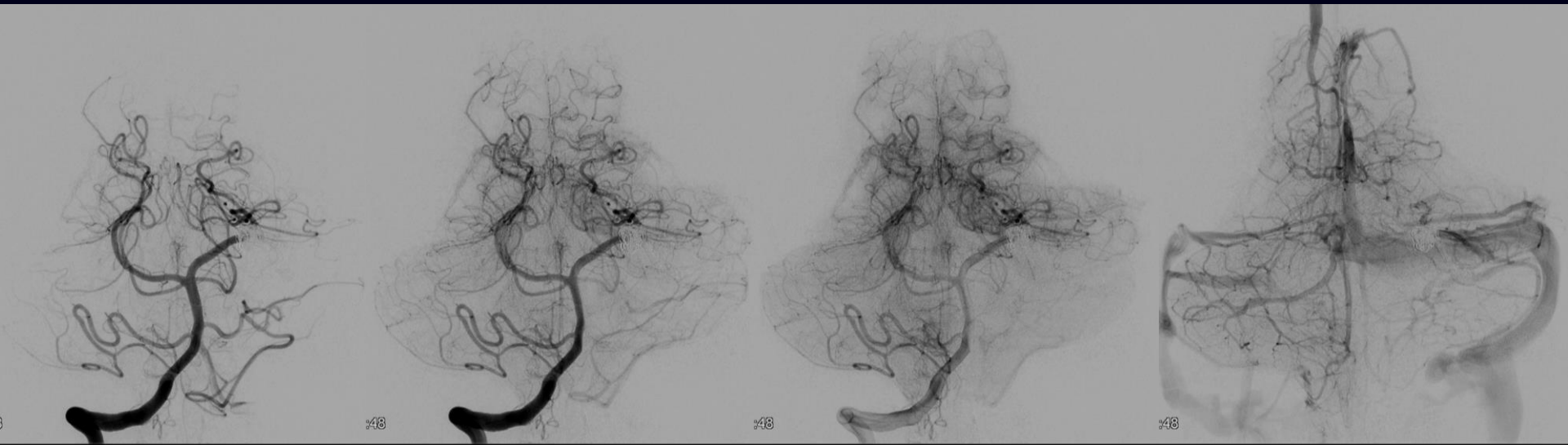
11:25
4:25
18:55:14











5
5
52:48

1:25
1:25
0:52:48

1:25
1:25
0:52:48

5
5
52:48

**48yo F know left frontal AVM
presenting after sudden onset of
severe headaches**



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Se:2
Im:17

[AH]

Study Date:4/5/2009
Study Time:6:00:19 PM
MRN:

[R]

[L]

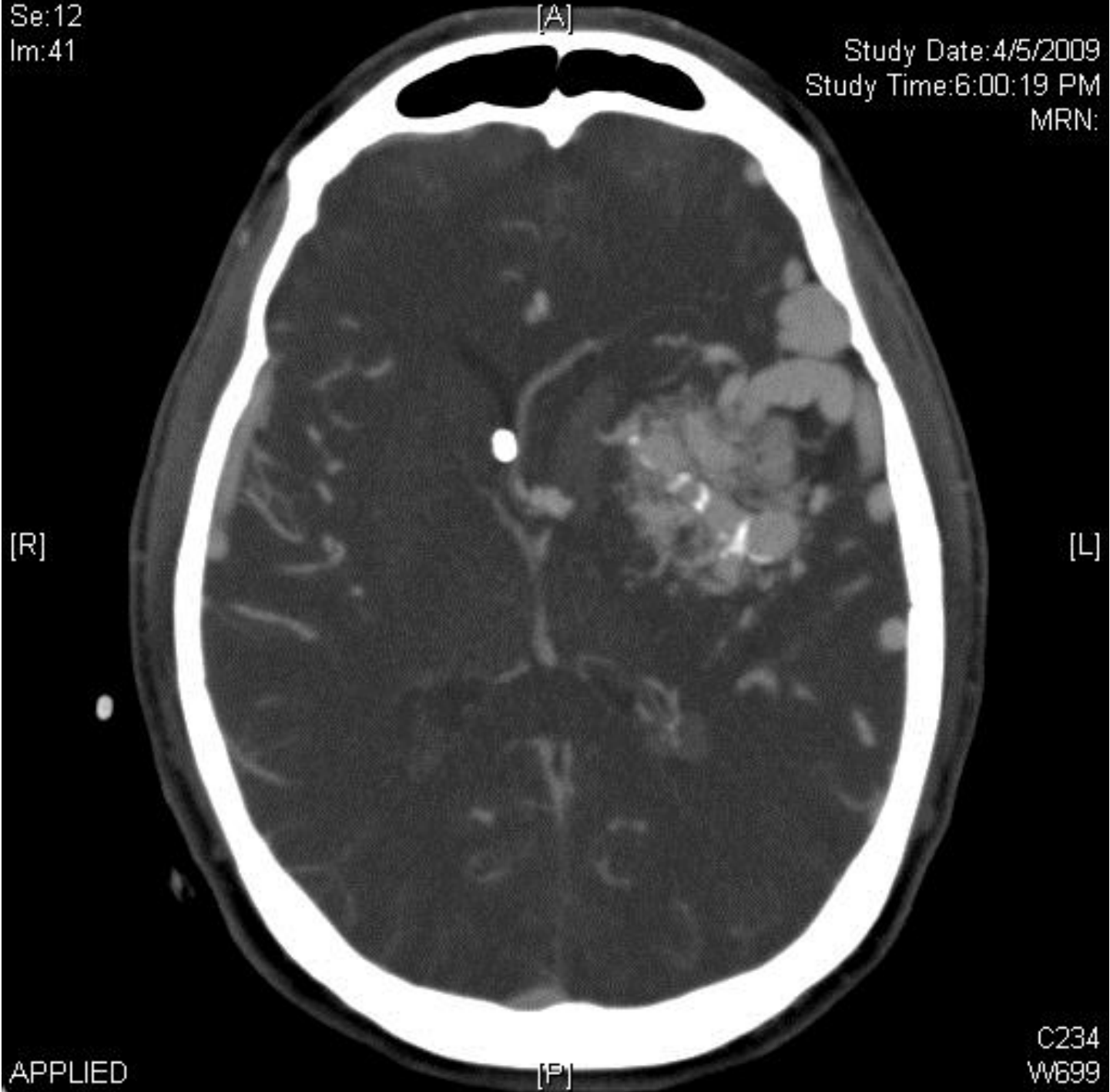


[PF]

C65
W155

Se:12
Im:41

Study Date:4/5/2009
Study Time:6:00:19 PM
MRN:



APPLIED

C234
W699

Se:11
Im:51

[H]

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MRN:

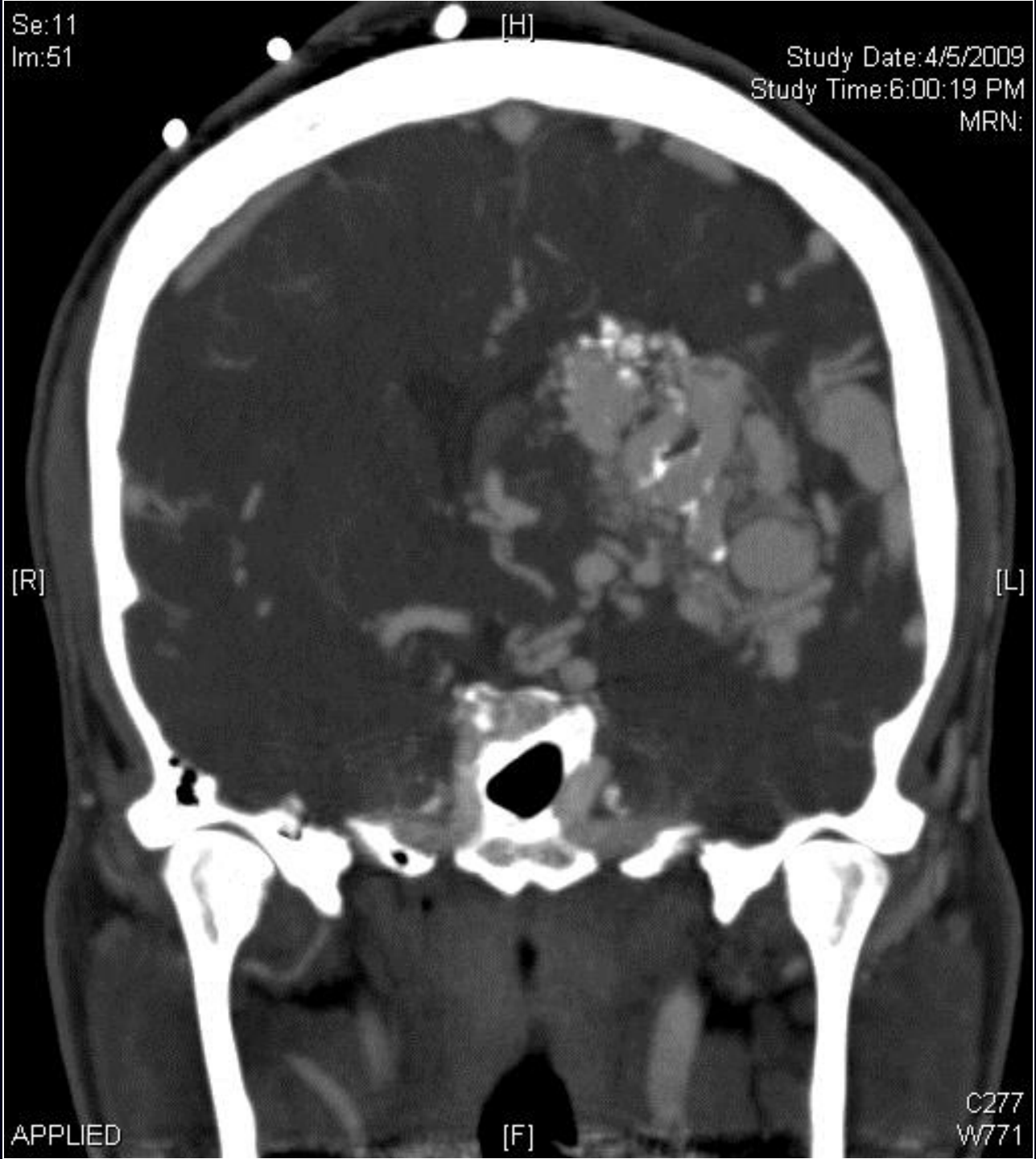
[R]

[L]

APPLIED

[F]

C277
W771



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Study Time: 8:58:51 AM
MRN:



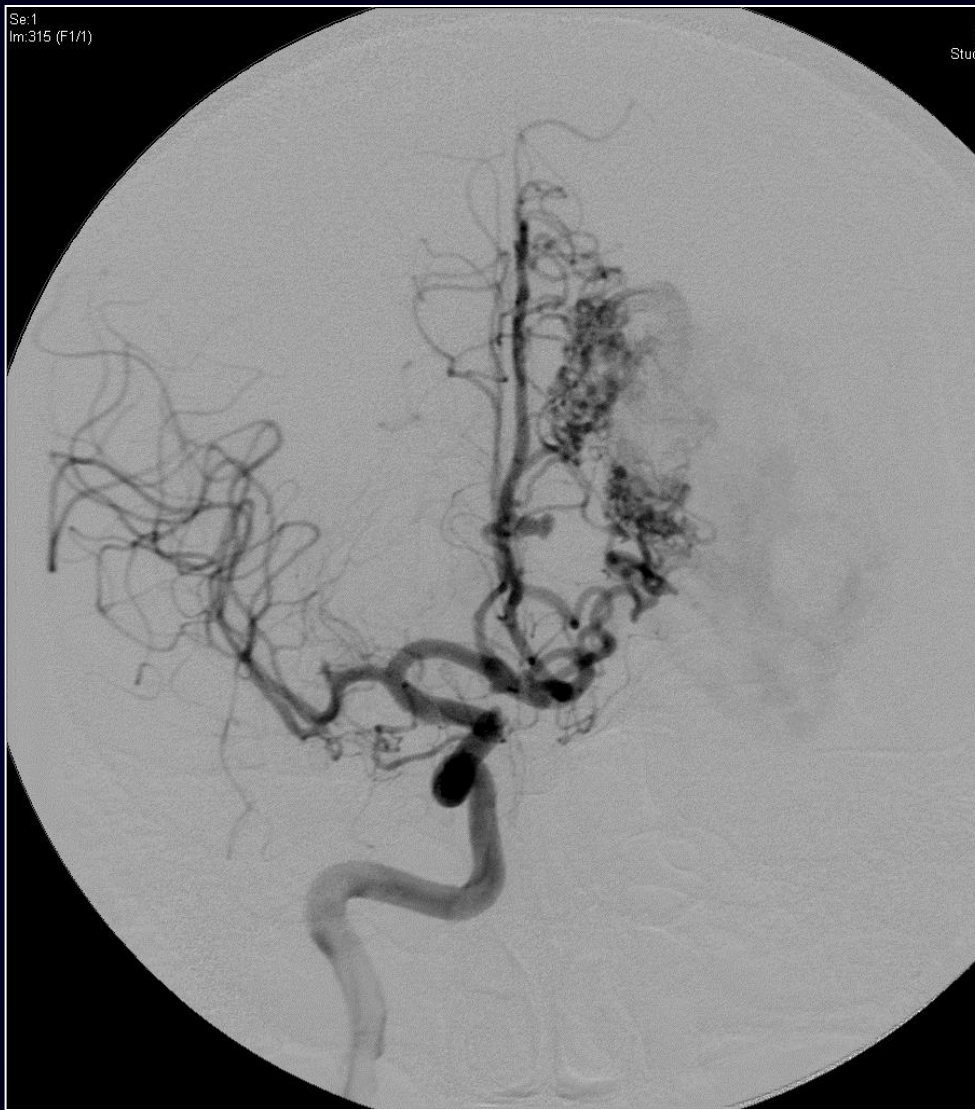
C571
W988

Study Date: 4/6/2009
Study Time: 8:58:51 AM
MRN:



C571
W988

Se:1
Im:315 (F1/1)



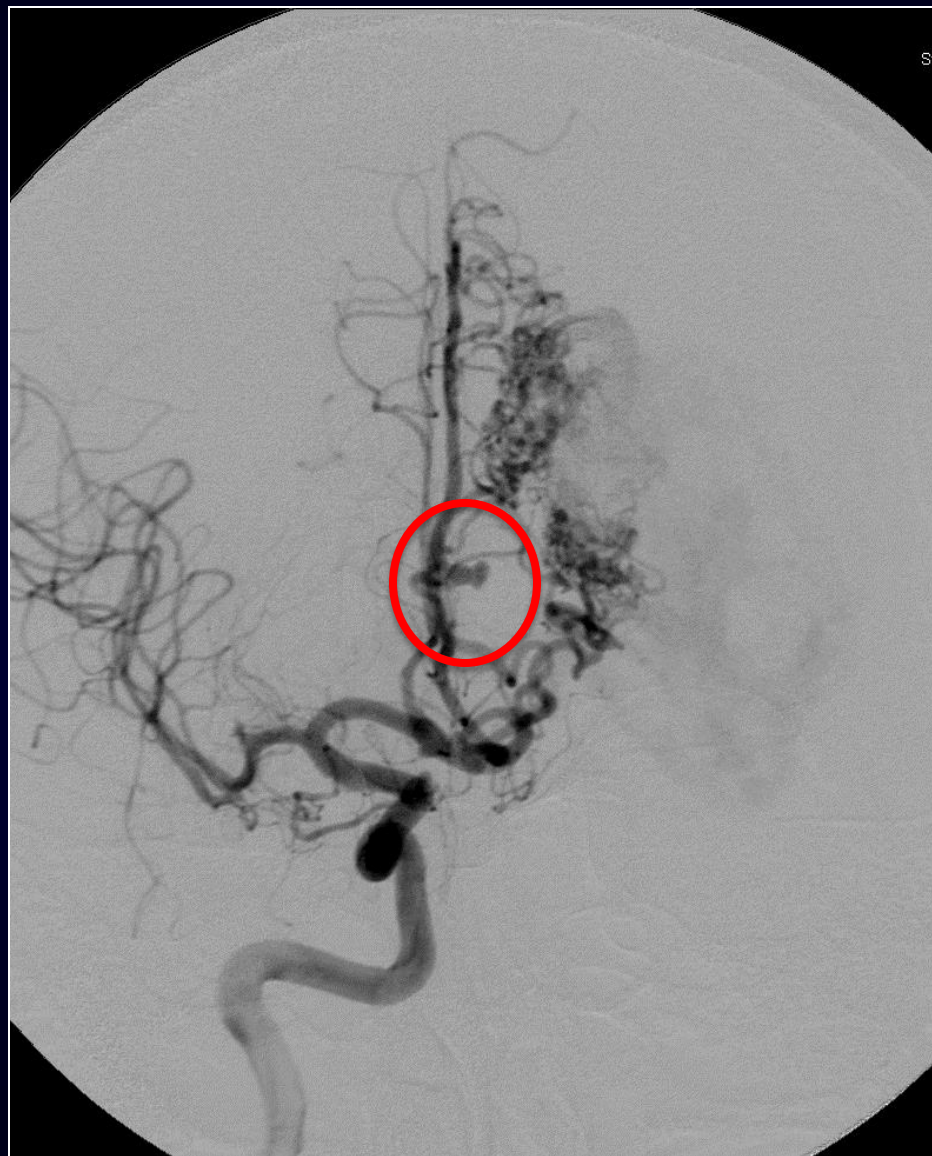
Stu



Study Date: 4/9/2009
Study Time: 12:34:53 PM
MRN:

C561
W1031

PRE EMBO

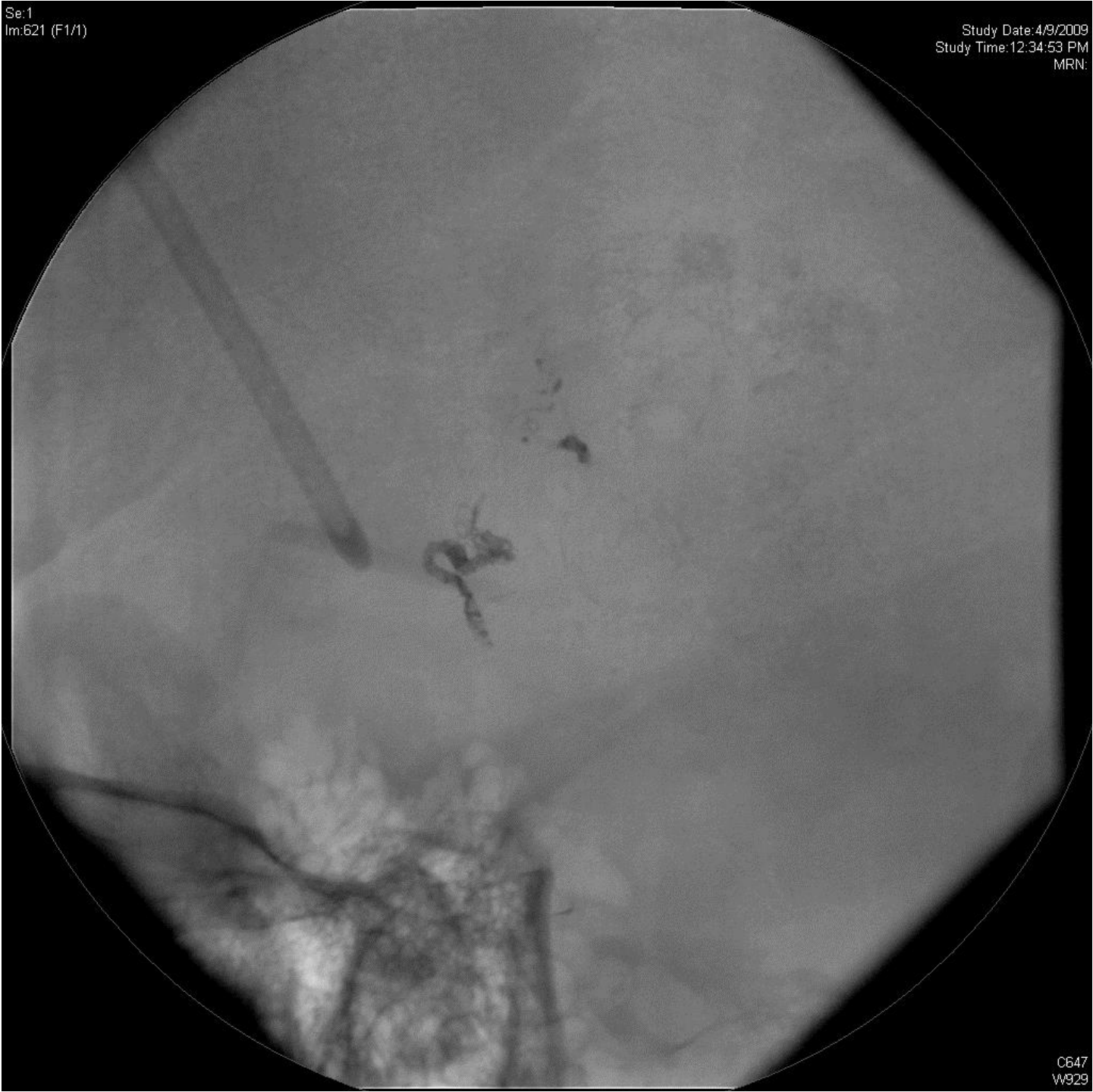


POST EMBO



Se:1
Im:621 (F1/1)

Study Date: 4/9/2009
Study Time: 12:34:53 PM
MRN:



C647
W929

Se:2
Im:14

[AH]

Study Date:4/10/2009
Study Time:2:12:37 AM
MRN:

[R]

[L]

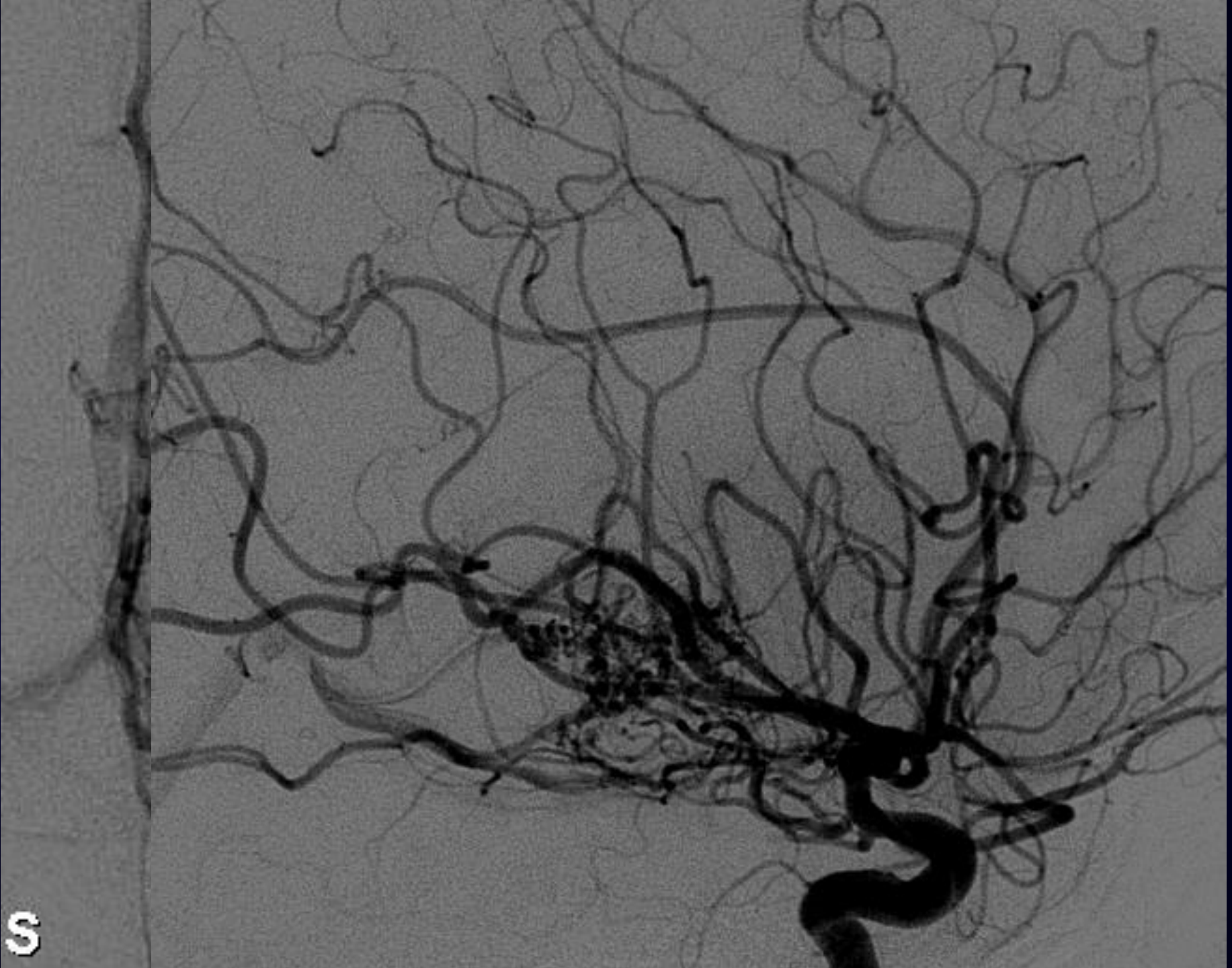


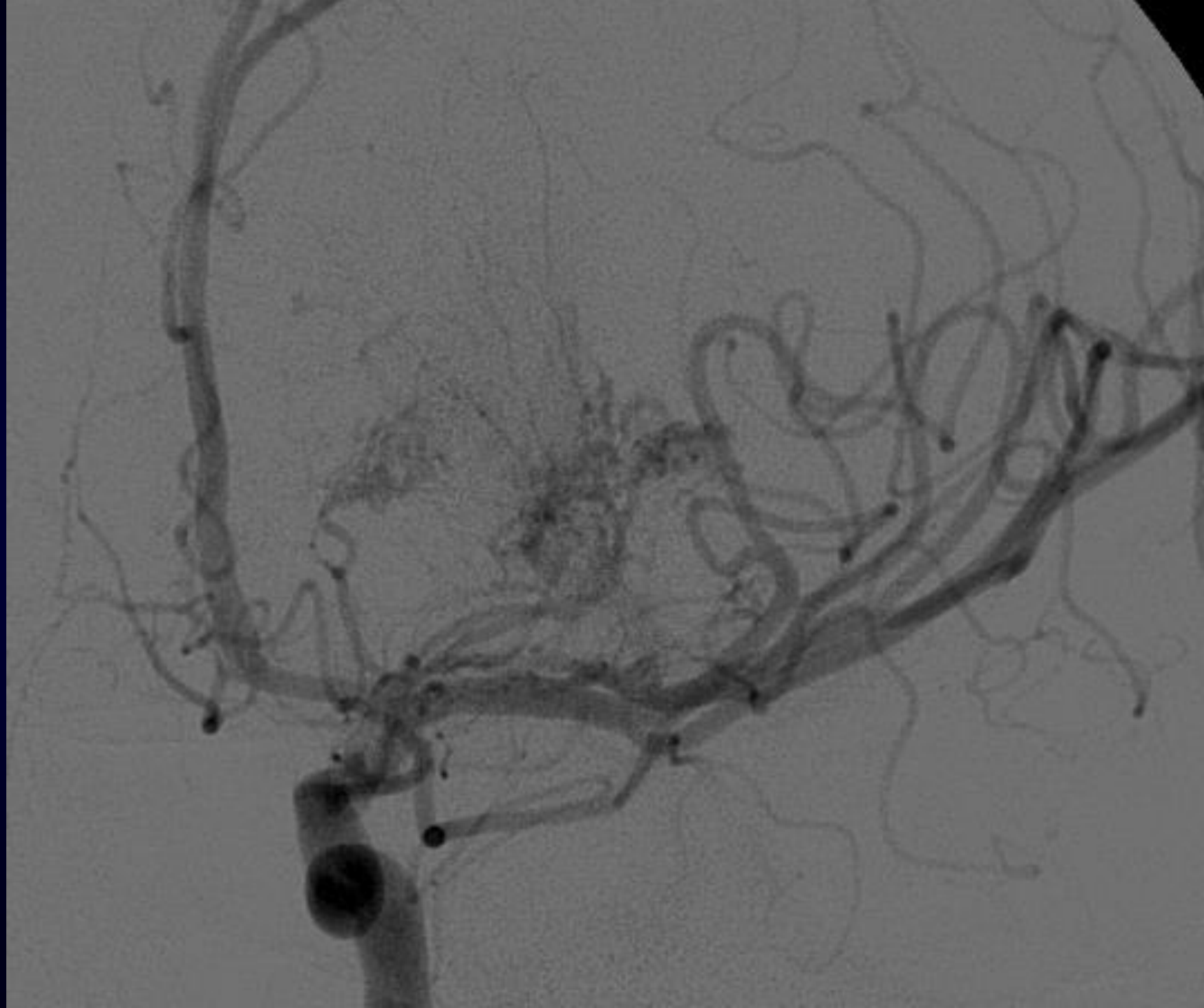
[PF]

C56
W181

**26 year old with sudden onset of
headache and right hemiplegia**

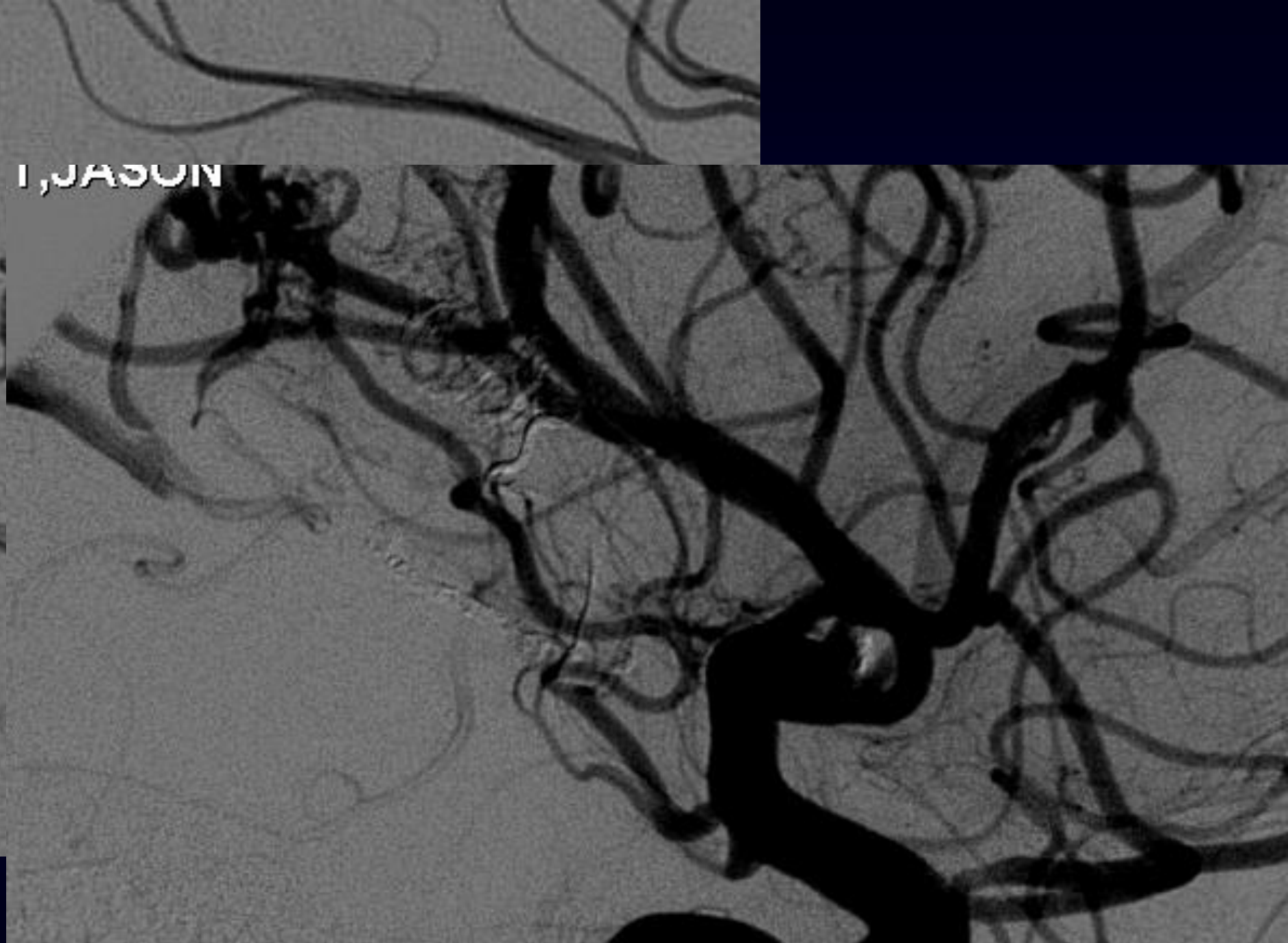








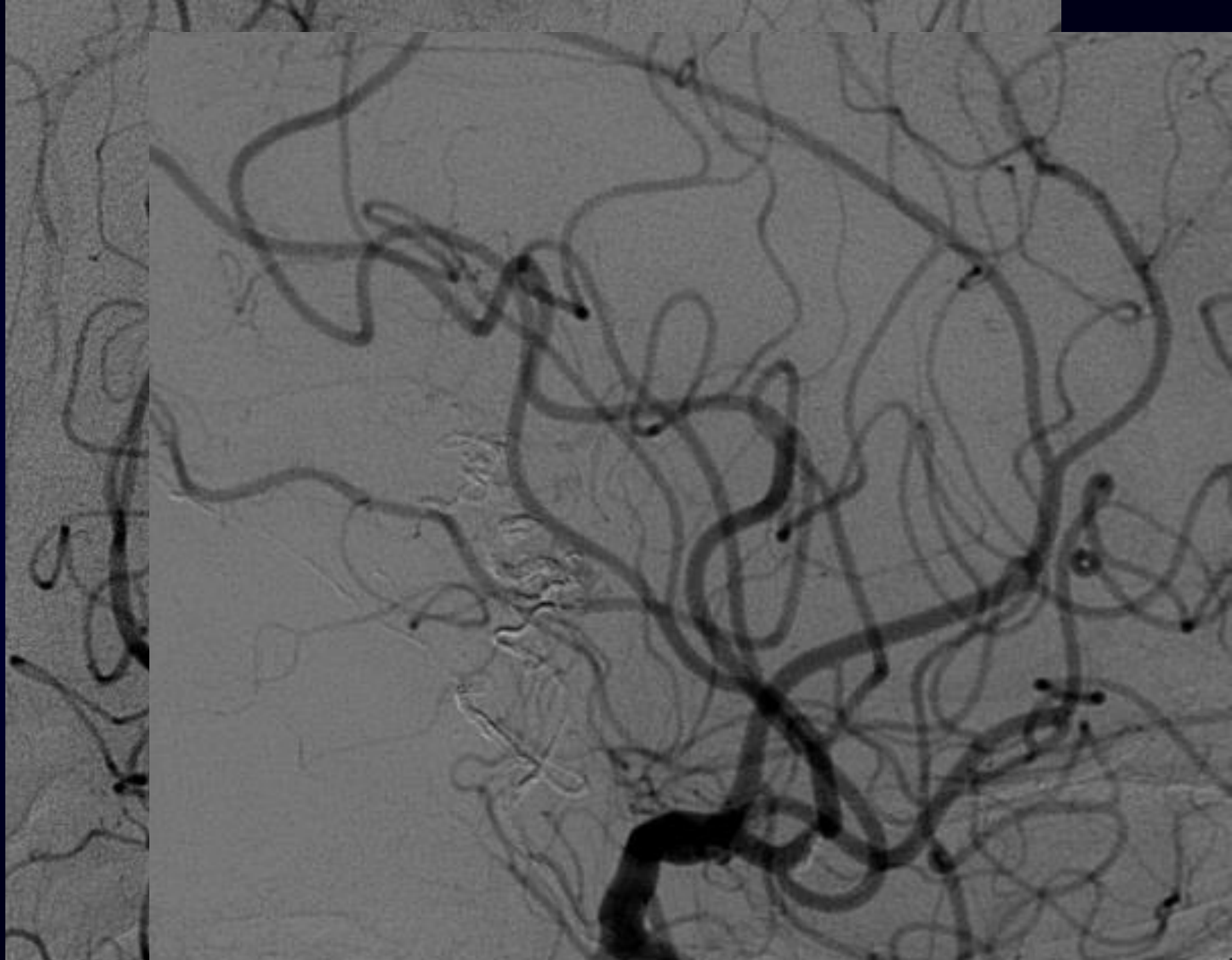
I, JASON



DN

ACQUA AR IN







AVM Embolization Post-ARUBA

- Not much has changed...
- Exclude risk factors
- Downsize the AVM in preparation for Surgery for surgically accessible lesions
- Downsize the AVM in preparation for Radiation for deep lesions
- Embolization with intent to cure as sole modality is not a common practice in the USA



Thank you!!!



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