Causes of Intracranial Aneurysms

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Disclosures

Consultant:

- Ablynx
- Amnis Therapeutics
- Anaconda
- Cerenovus – Neuravi Ltd
- Medtronic - Covidien
- Rapid Medical

Purpose

1. Discuss mechanisms for IC aneurysm formation and rupture

2. Provide a perspective on the IC aneurysm disease and possible treatment options

What is an intracranial aneurysm?

- A manifestation of different underlying disease processes…something causes the aneurysm to appear

- The nomenclature that we use *may* relate to such process but is often only morphological and descriptive…basically it´s a mess

Appearance

- Saccular – berry
- Serpentine
- Fusiform
- Blood-blister
- Dysplastic

Size

- Small
- Large
- Giant

Underlying, known causative disease/mechanism

- Mycotic
  - Streptococcus
  - Staphylococcus
  - Fungi
- Oncotic
  - Myxoma
  - Choriocarcinoma
- Drug abuse
  - Amphetamine
  - Cocaine

Underlying, known genetic problem

- Familial
- Polycystic kidney disaese
- Ehler-Danlos diesease type IV
- Fibromuscular dysplasia

Underlying, presumed mechanism

- Dissecting
- Pseudo
- False
- Flow-related

So, consequently…

- Nomenclature is inconsistent
- There are of course combinations; a familial aneurysm may be large and saccular

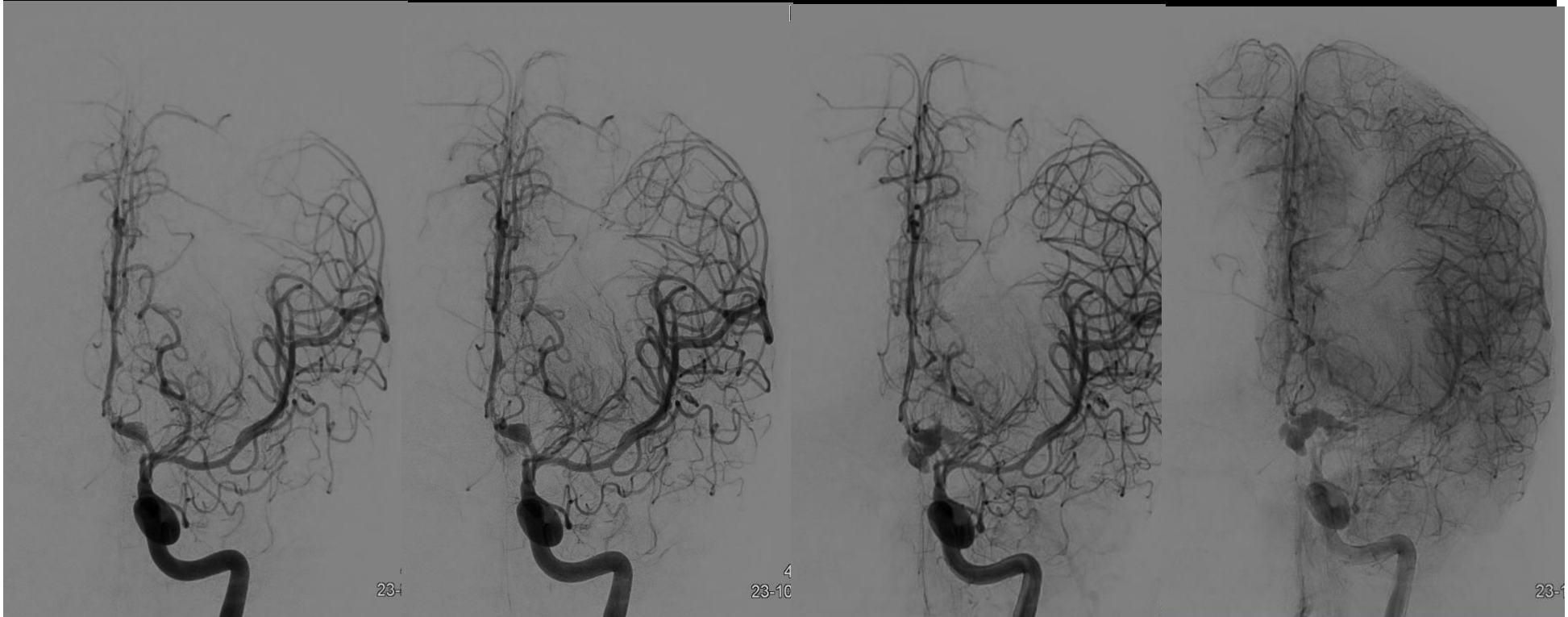
Important

- The various intracranial aneurysmal diseases have *different natural history* and warrant *individualized and optimized treatment strategies*

- And, we don´t really know where the disease process starts and ends - *“Aneurysmal vasculopathy”*

Case: 30 yo male

- Cardiac surgery x2 - artificial valve – lifelong Coumadin
- 4 weeks relapsing fever - found with seizure – intubated
- GCS 3, H&H 4, WFNS 5, Fisher 4 – EVD
- Strange looking AcomA aneurysm - not typically mycotic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DAP
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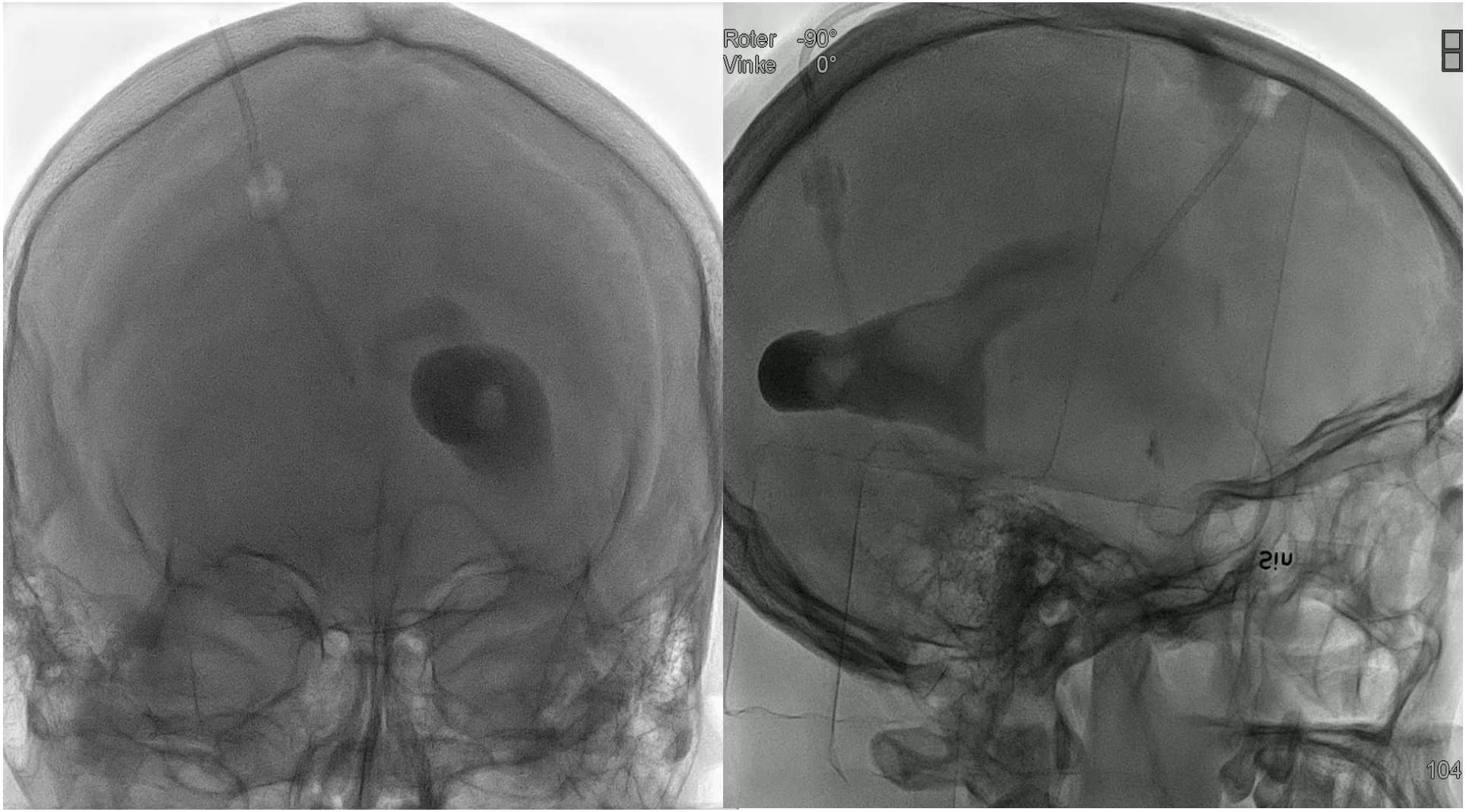
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104

Why?

- This was probably *not* a saccular/berry aneurysm
  - Mycotic - probably
  - Collagen disease?
  - Something else?

It was a different disease process!

So, intracranial aneurysms…

- Are not one entity
- Need different treatment approaches
- The way we describe them is inconsistent
- Some are VERY difficult and risky to treat…

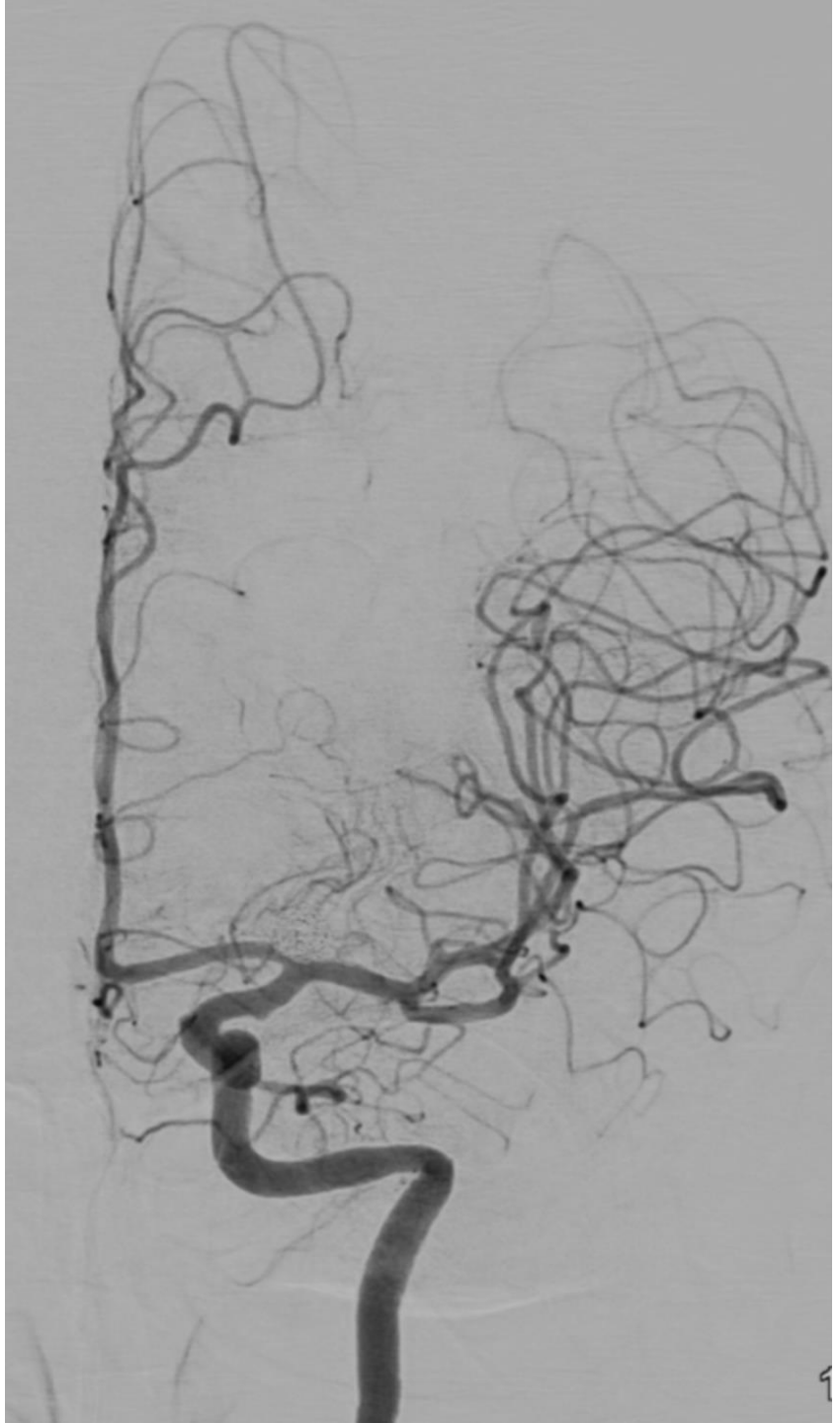
…***regardless*** of chosen technique

EV treatment strategies:

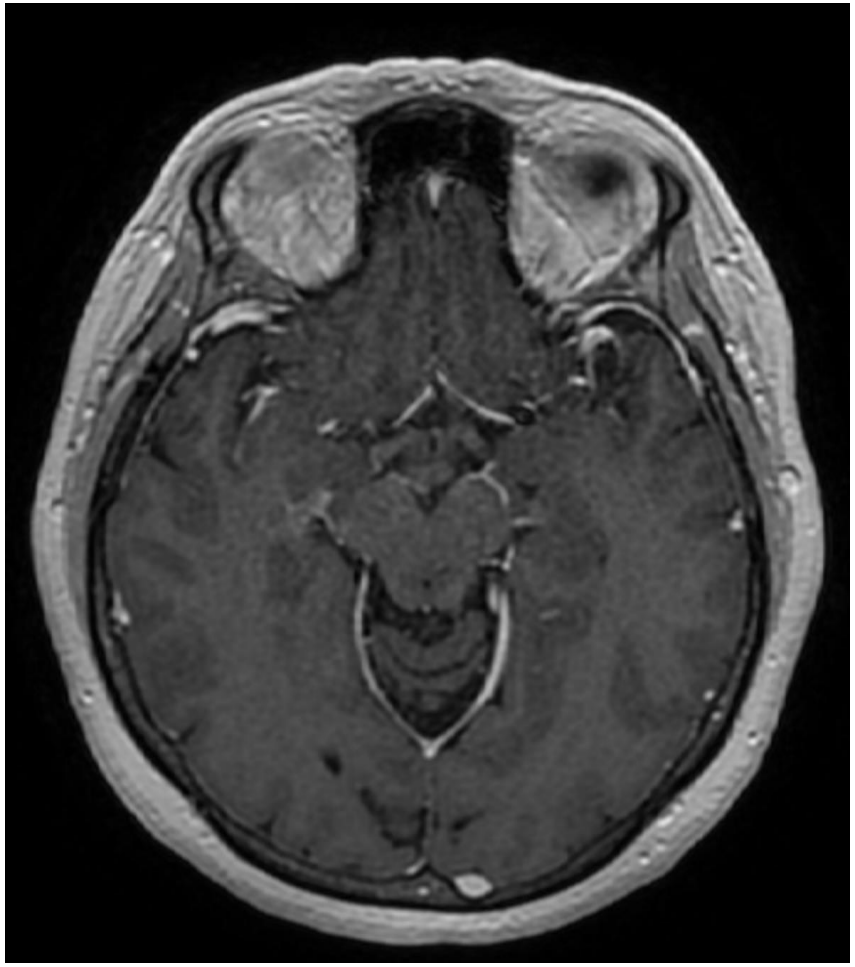
1. Plain coiling
2. Balloon assisted coiling
3. Stent assisted coiling
4. Neck-bridging devices
5. Flow diverters
   - Intrasaccular
   - Extrasaccular

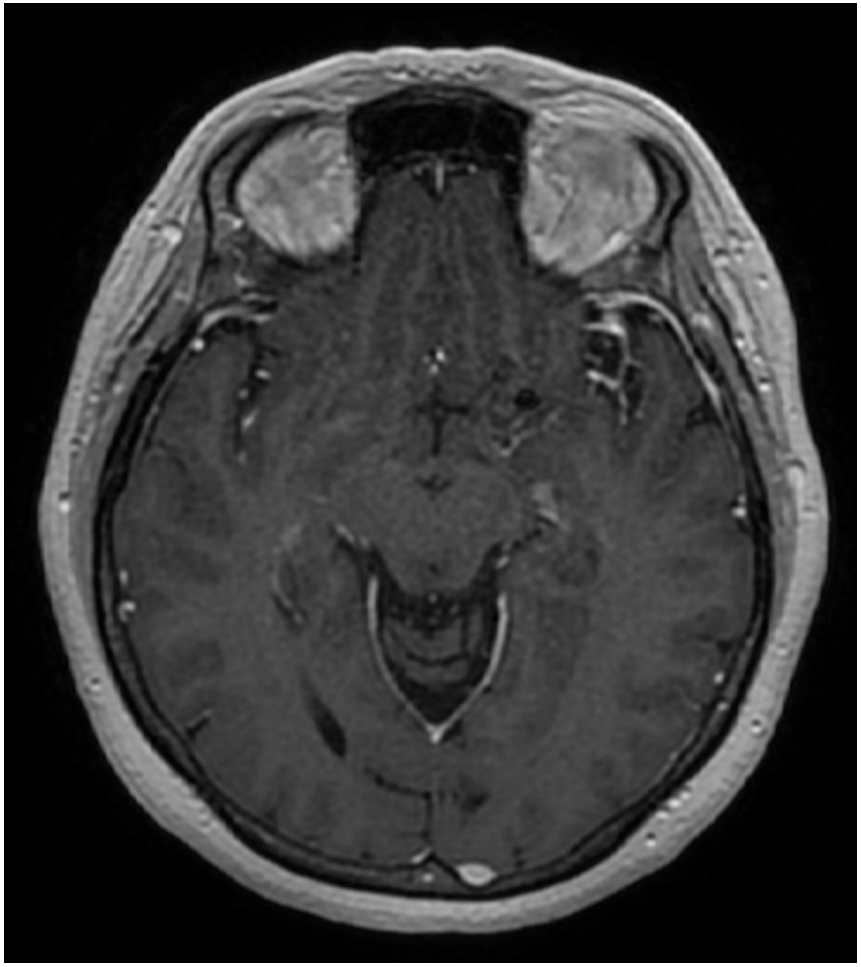


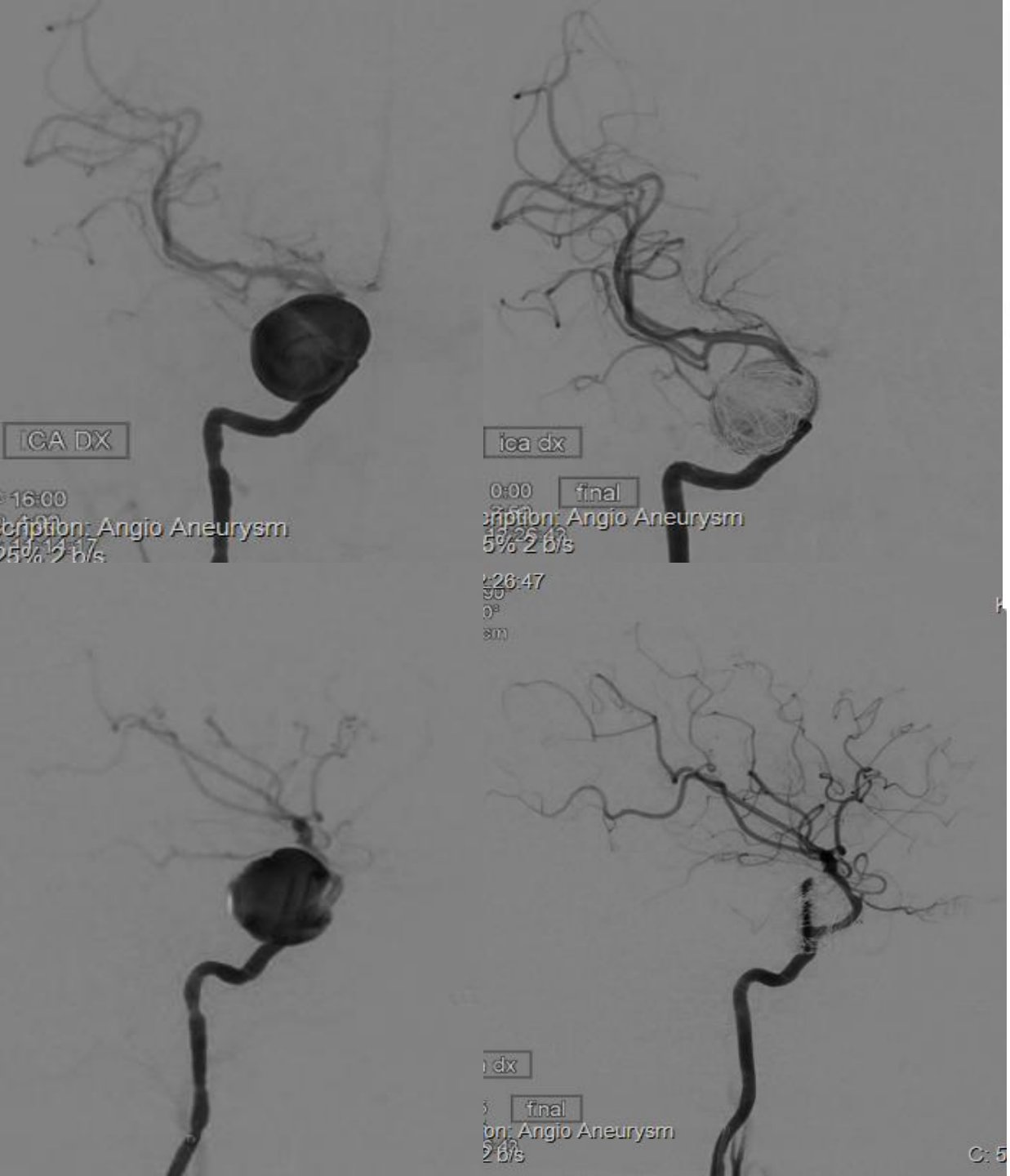
12 months DSA

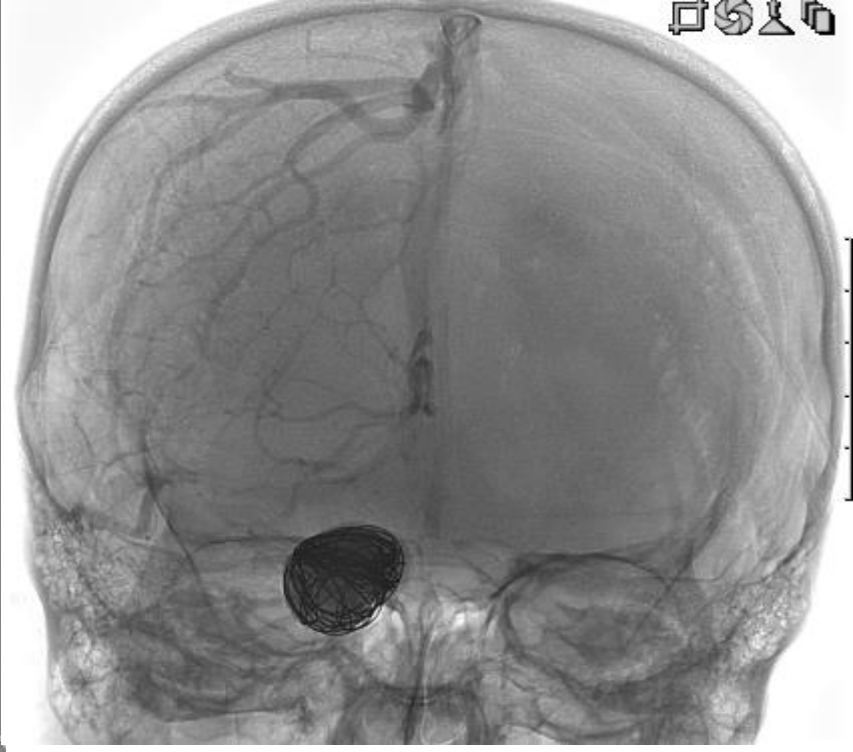


3 years MR/MRA

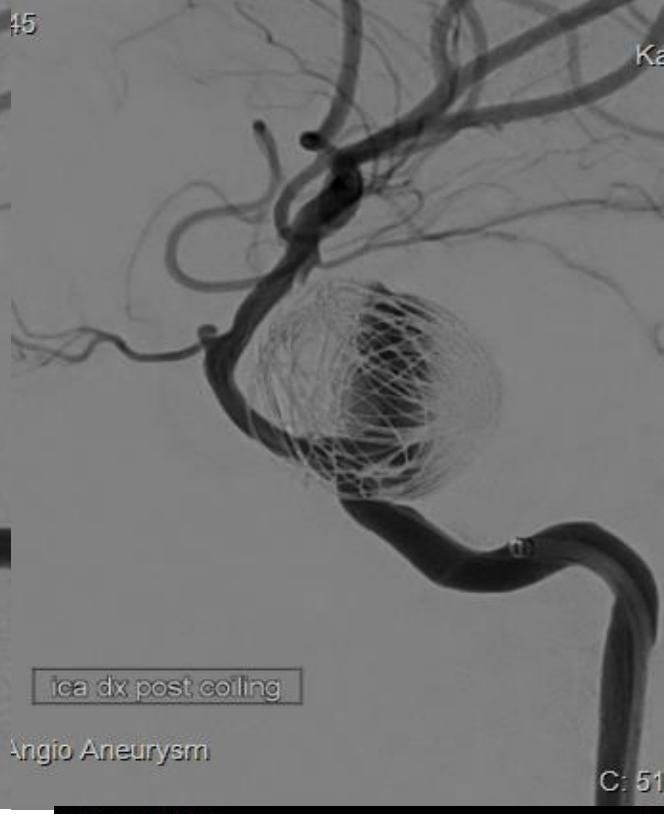








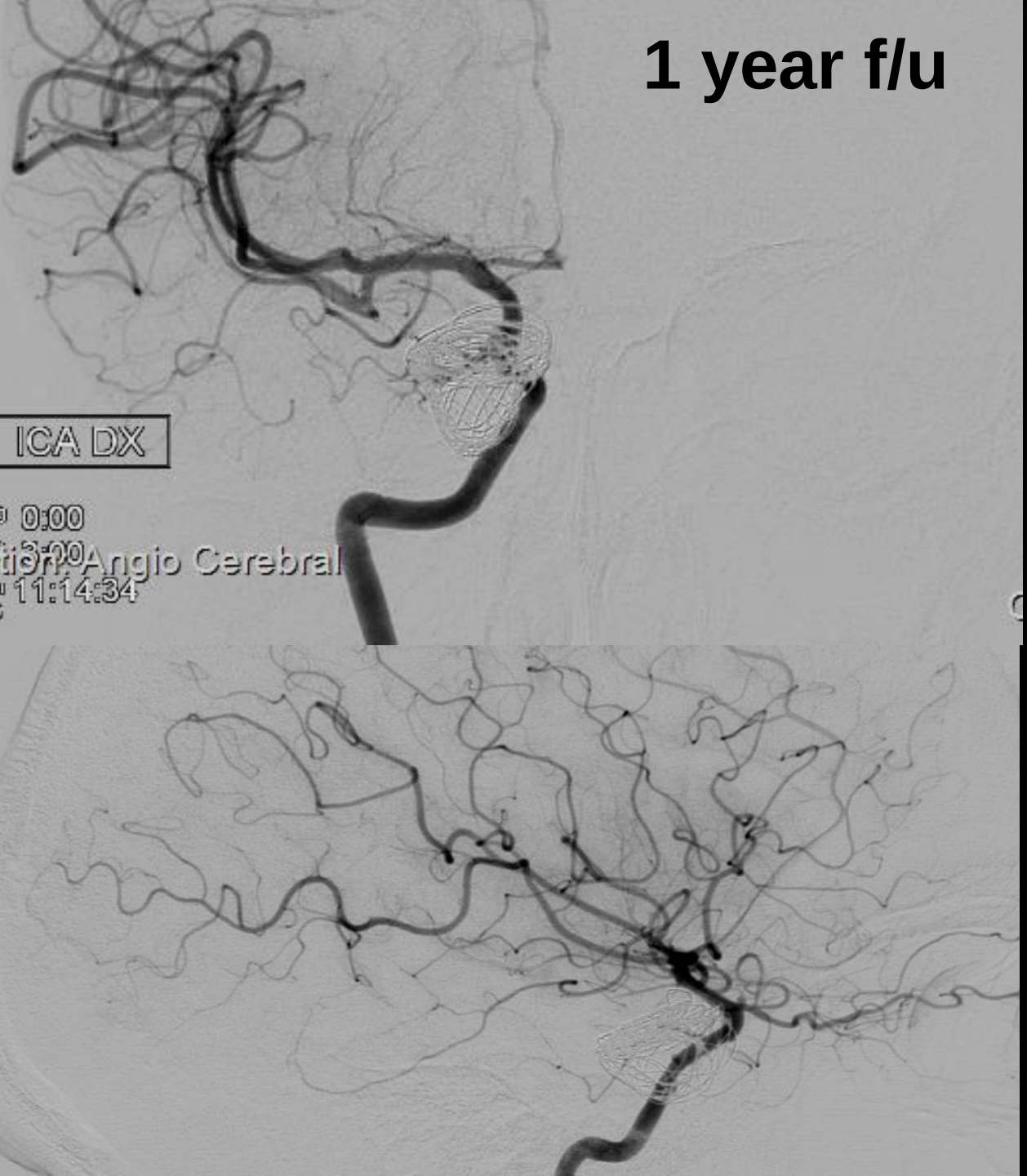
Immediate stagnation

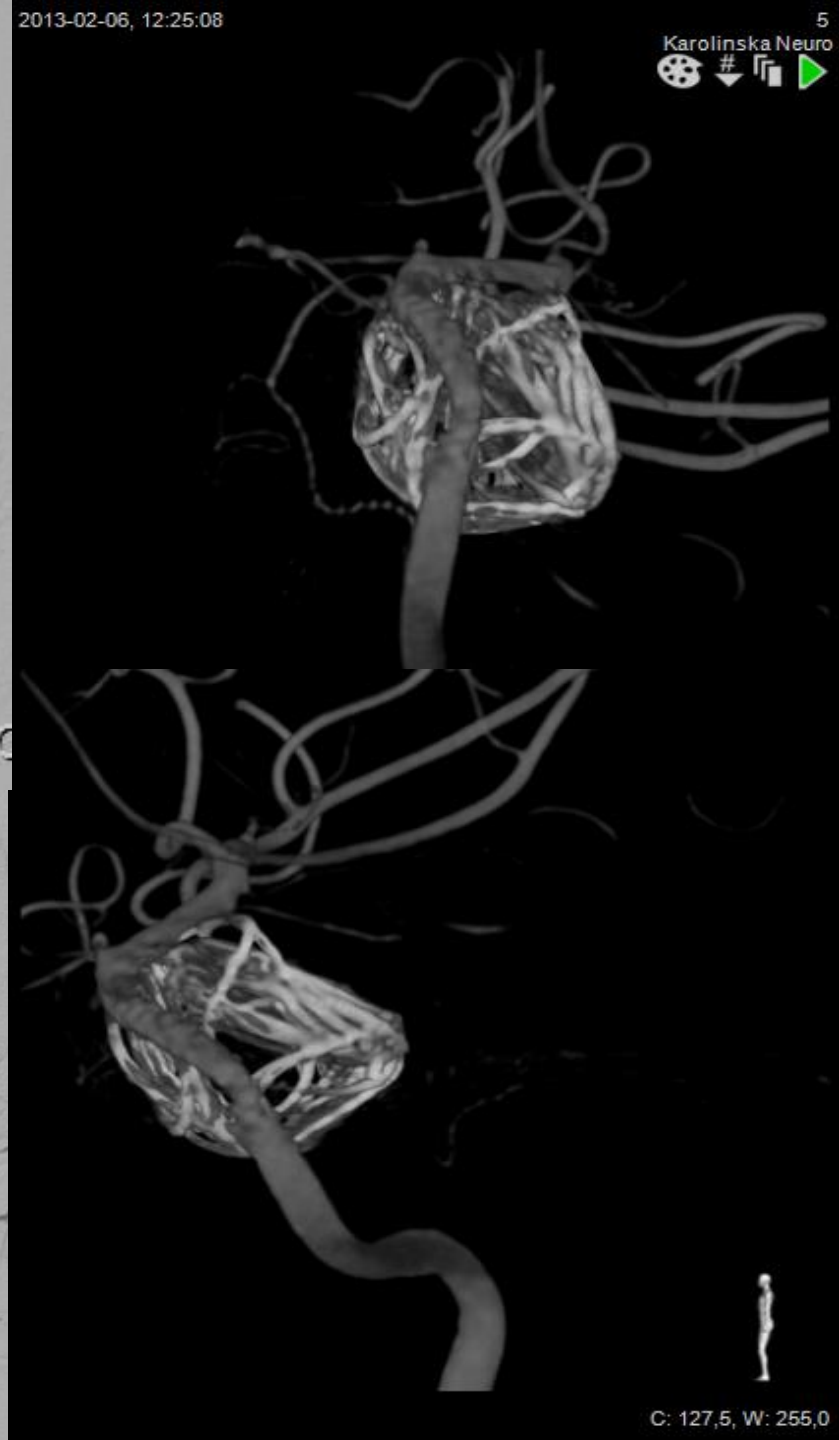


Working projection - measurements

After FD and coils

3D after treatment


1 year f/u
ICA DX
0:00
Angio Cerebral
11:14:34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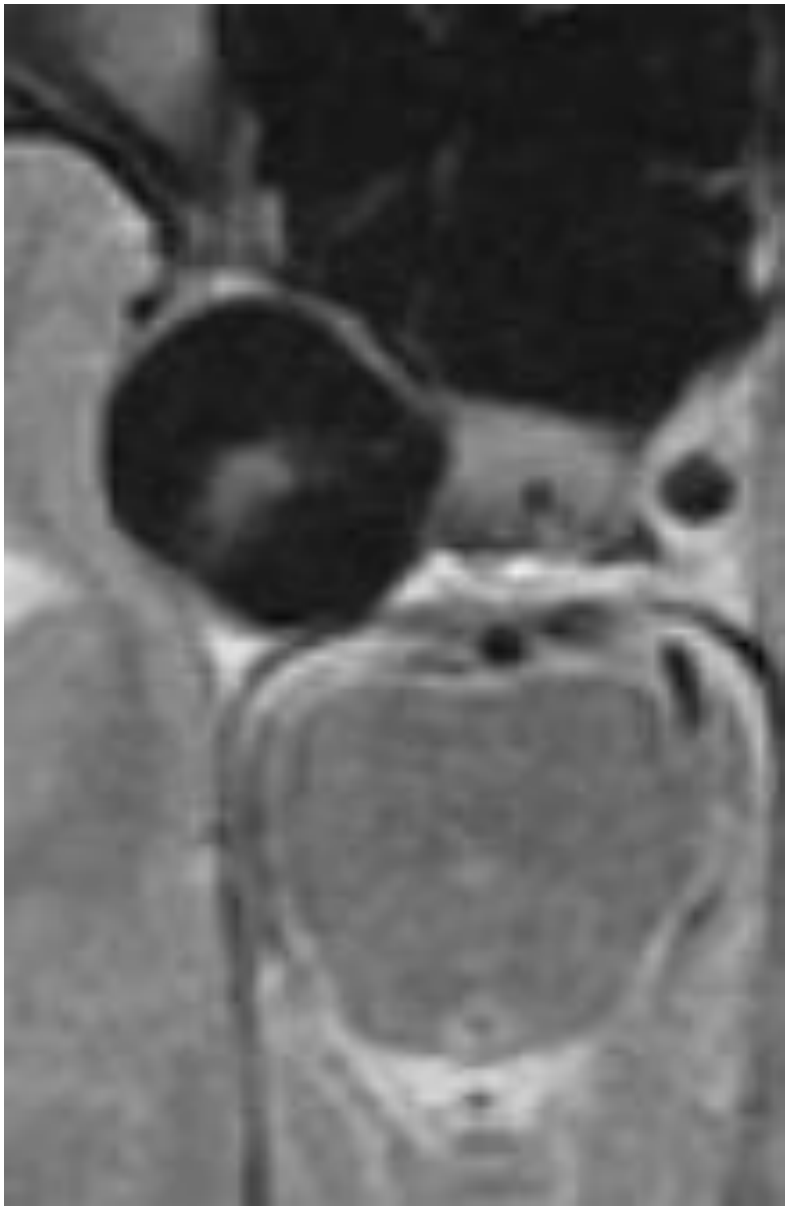
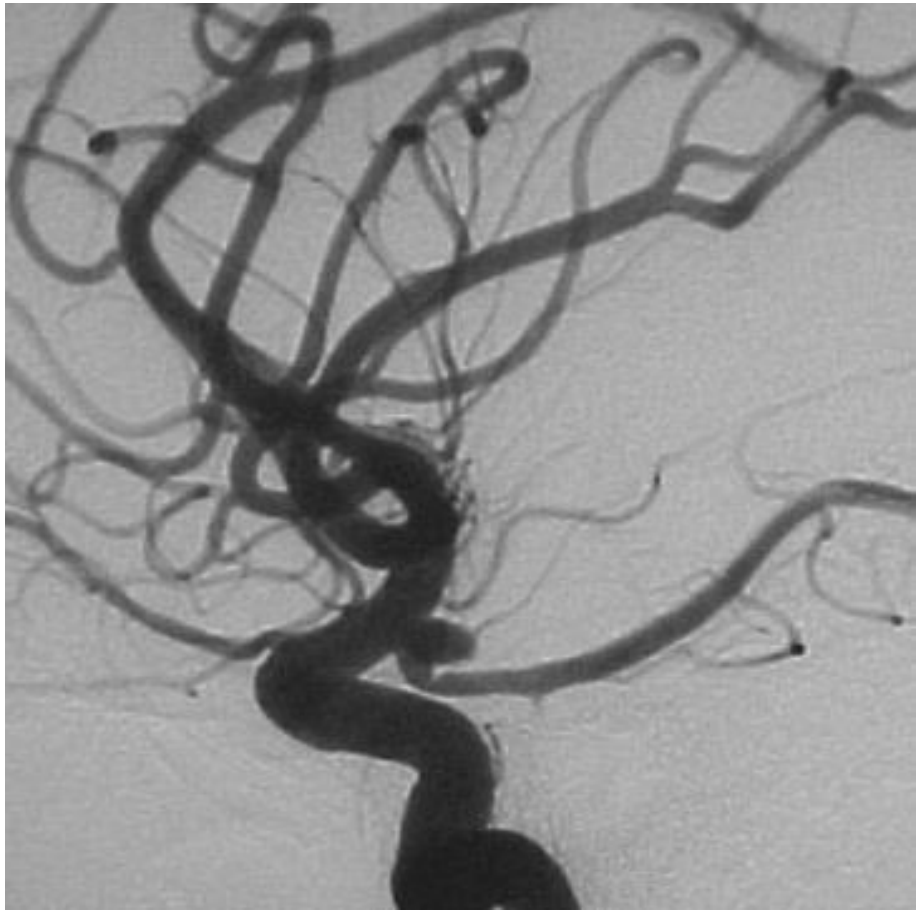
Karolinska Neuro
C: 127,5, W: 255,0

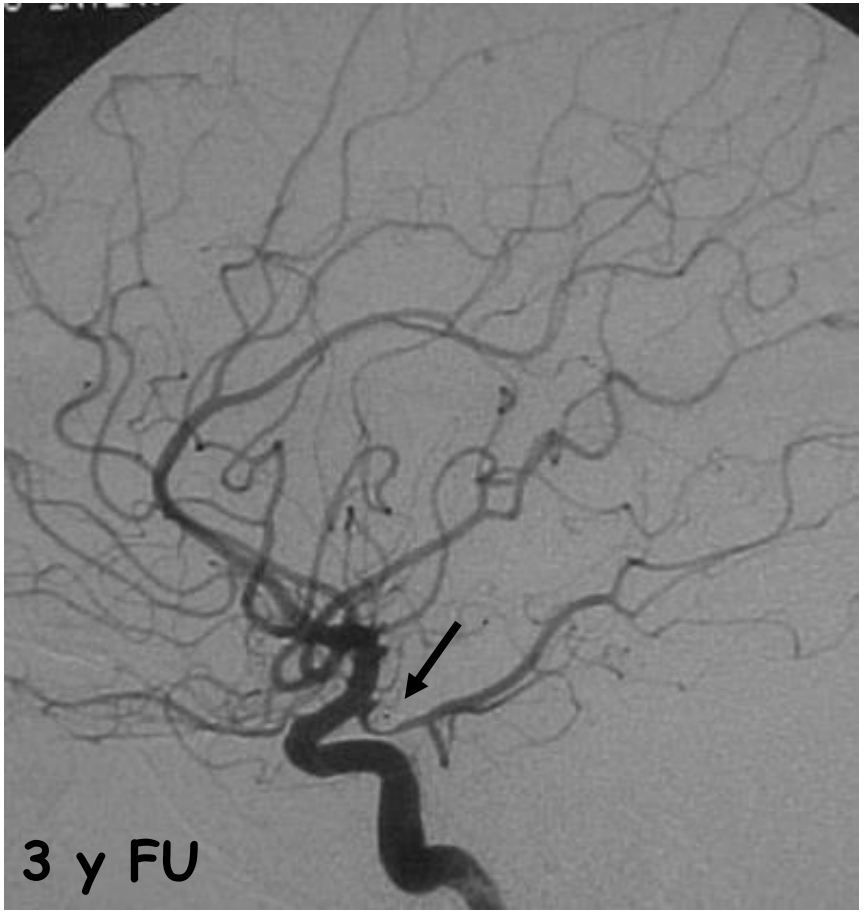
Before



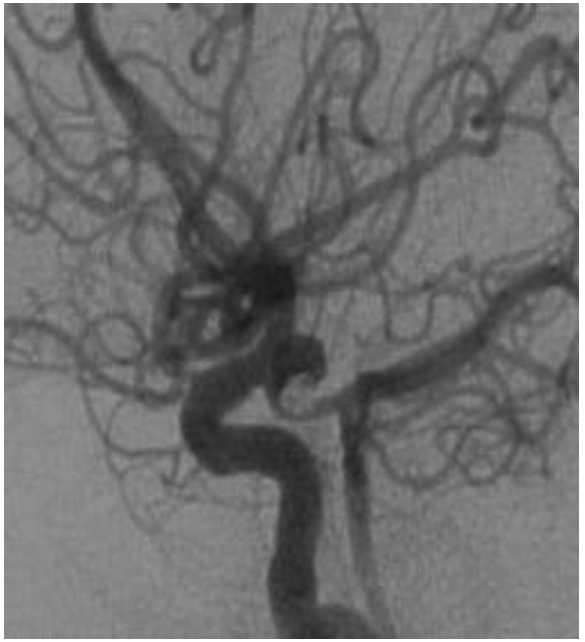
1 year f/u

23-year-old girl had SAH due to left Pcom-AA that was coiled

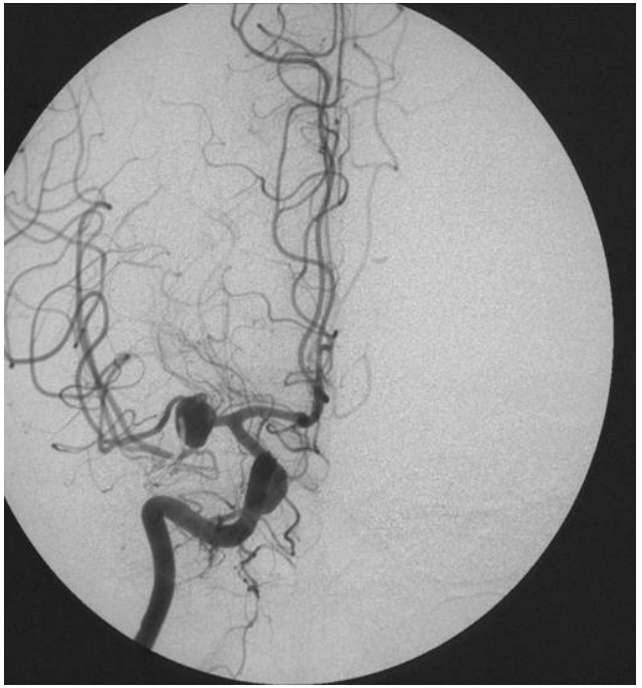


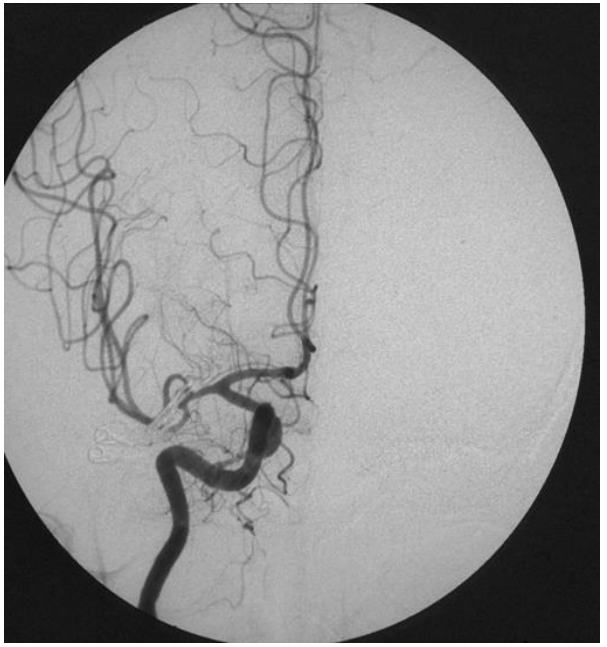
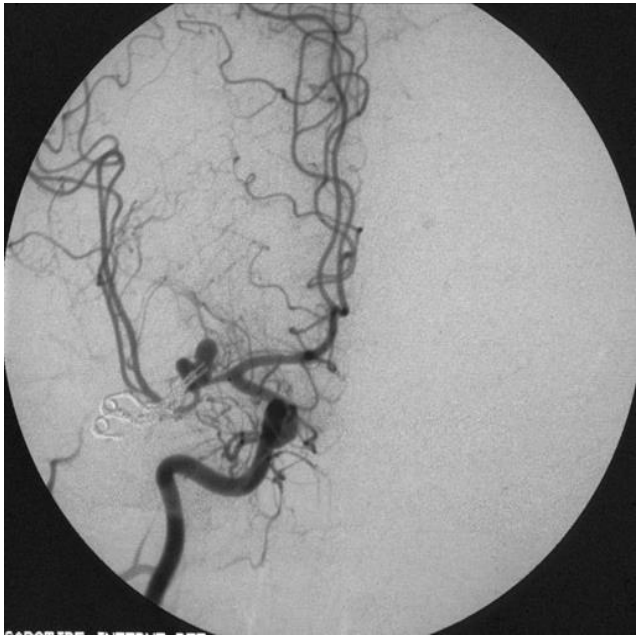


5 years later : new SAH







Saccular/berry intracranial aneurysms

- Non-congenital pathological dilatations of intracranial arteries
- May rupture due to an abnormally weak vessel wall
- Impossible to define where the disease process starts in the affected segment

Risk factors for aneurysm formation

- Smoking
- Excessive alcohol
- Uncontrolled hypertension
- Female gender
- ADPKD
- + family history

Risk factors for aneurysm rupture

- Smoking
- High shear stress
- Morphology: size, shape and location
- Presence of other, ruptured aneurysms

Probable cause: genetics

- Genetic predisposition - not possible to find association to specific gene – formation/rupture

- Familial form with higher prevalence (10%)
- Screening: ≥ 2 first degree relatives with known aneurysms

- Still, modifiable risk factors play a greater role for *rupture*

Probable cause: arterial wall weakening and hemodynamic stress

- To form aneurysms, there has to be a *vessel wall abnormality*, which can be genetic but is mostly acquired, and the aneurysm is formed by a *combination of weakening of the arterial wall and hemodynamic stress*

- All situations that affect any of these two are potential risk factors

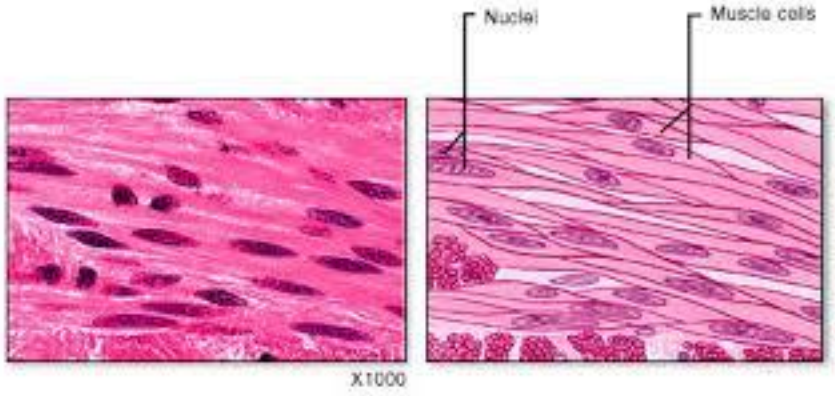
Why do some aneurysms rupture?

- Formation and rupture are separate processes
- Basically, when hemodynamic forces exceed vessel wall strength – the aneurysm ruptures
- Vessel wall balance between degradation and repair

Prevention of rupture

- *Smooth muscle cells* in particular may repair and strengthen the aneurysmal wall
- *Loss* of such mural cells + degradation of functioning *endothelium* with *thrombus* formation may cause rupture
- *Oxidative stress, inflammation* and *aberrant flow conditions* in the aneurysm lumen, geometry, may be the cause for this – compare Flow diverters!

Aneurysm rupture



<u>Caused by:</u>
Oxidative stress
Inflammation
Aberrant flow conditions

<u>Mechanism:</u>
Loss of smooth muscle cells
Endothelial degradation
Thrombus formation

Arterial aneurysms rupture

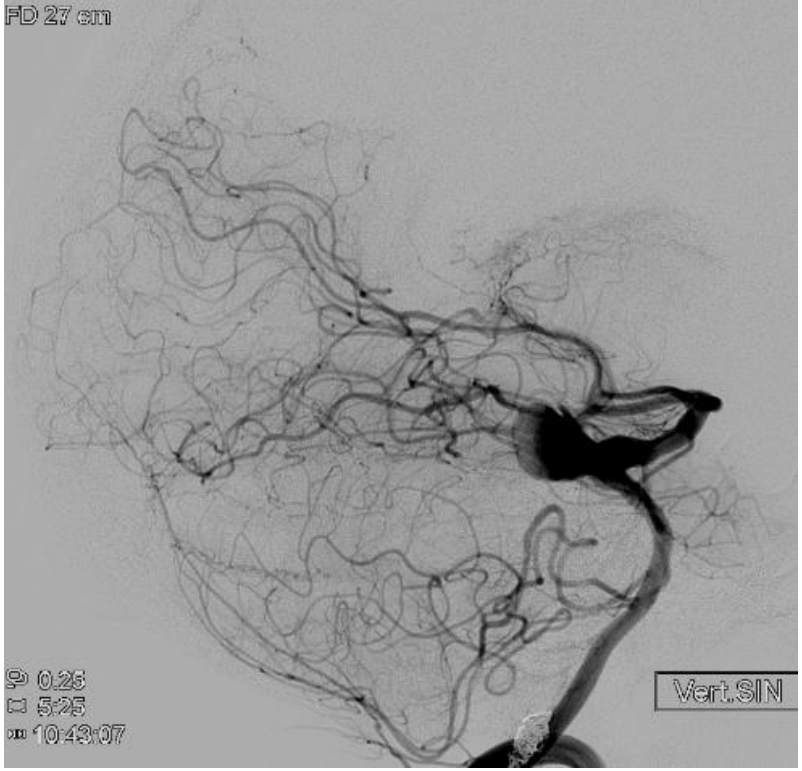
When we treat

- Change the hemodynamics

- Arterial wall disease process may
  1. *Diminish and heal*
  2. *Remain stable*
  3. *Progress and worsen*
     - Coiling or clipping – regrowth and risk for rupture
     - Flow diverter – risk for rupture

- Implications for follow-up – when can we stop the examinations? Never?

- And perhaps we can *trigger a bad evolution*?


FD 27 cm
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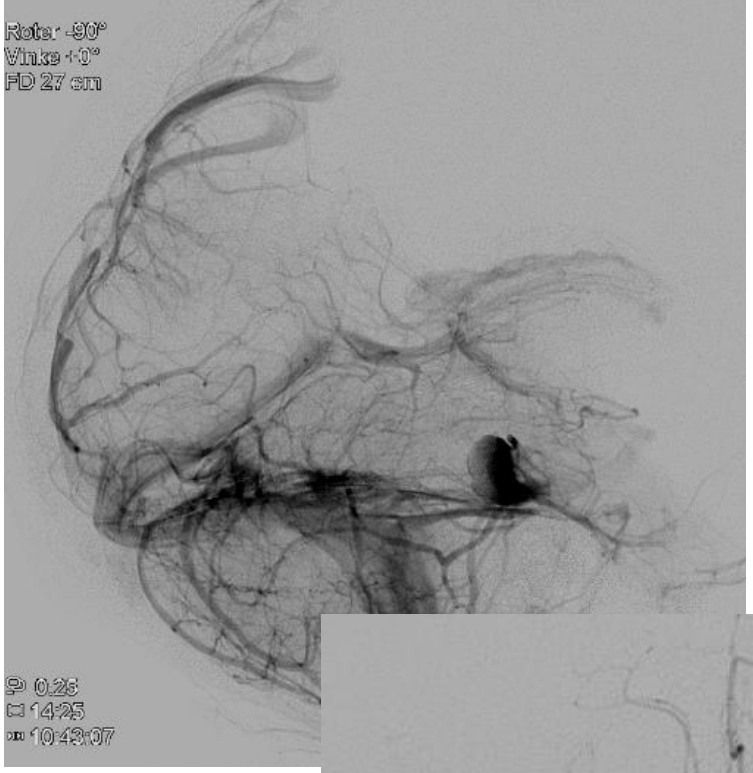
Vert.SIN


Rota: -90°
Winke +0°
FD 27 cm
0.25
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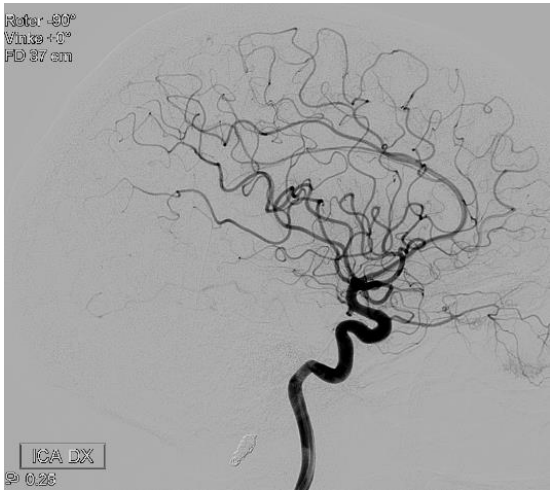
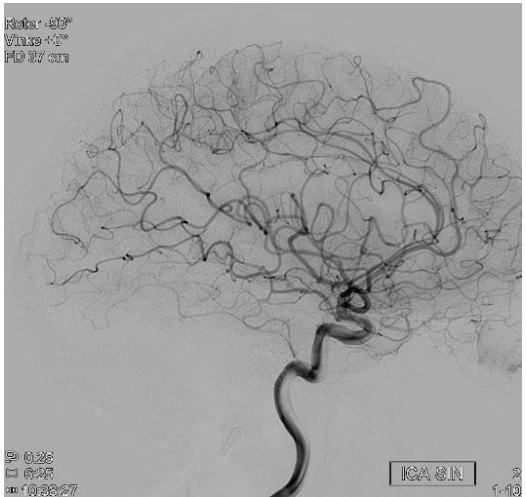
10:43:07


Rota: -90°
Winke +0°
FD 37 cm
ICA DX
0.25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Winke +0°
FD 37 cm
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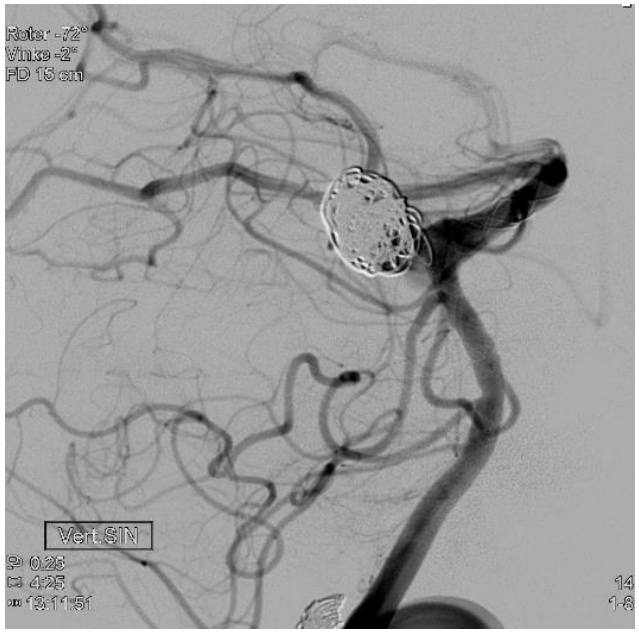
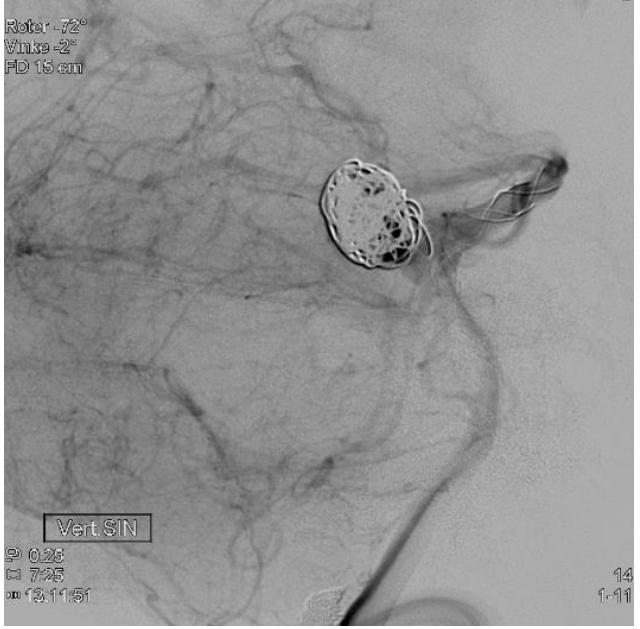
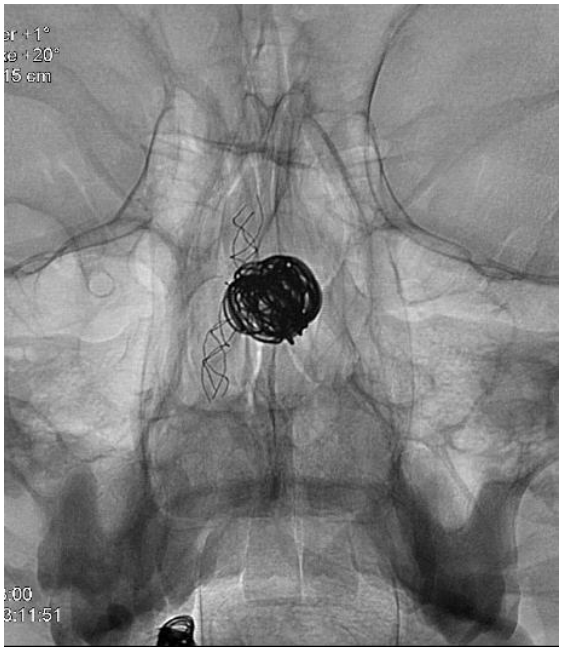
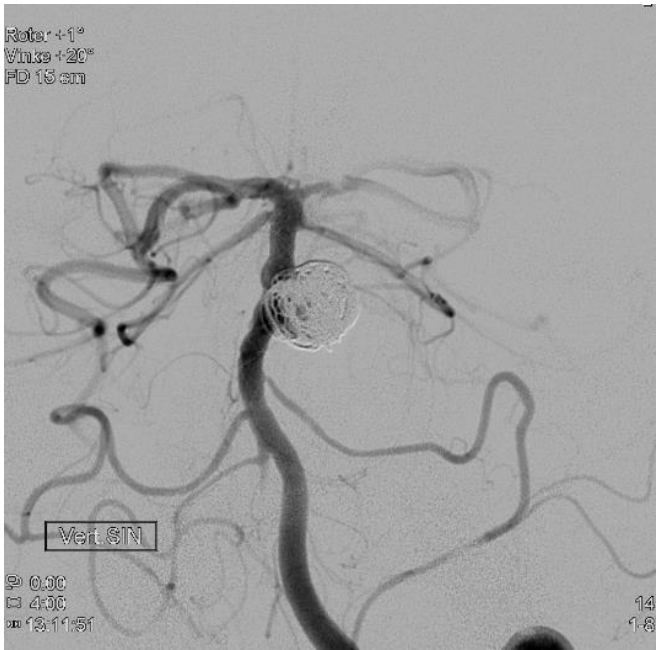
6:25
ICA SIN

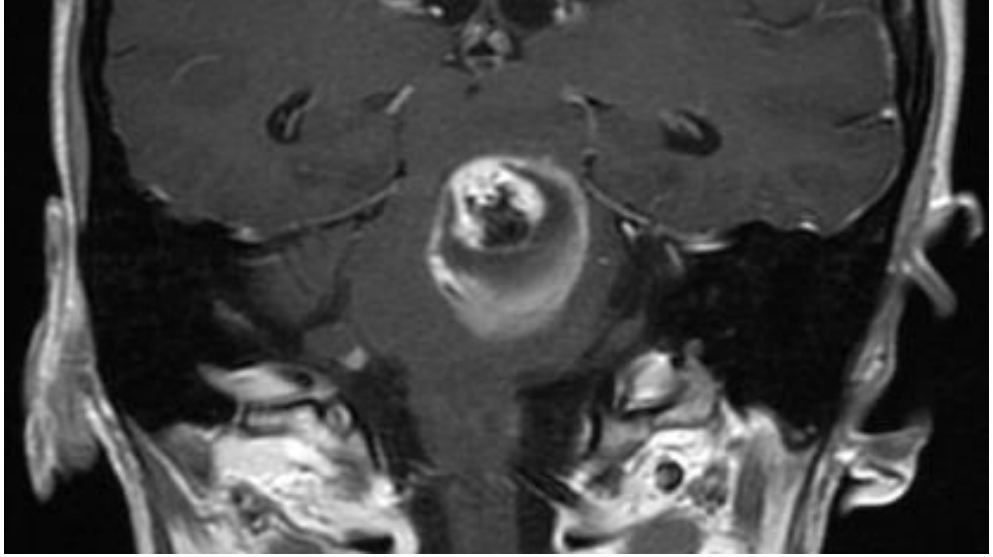


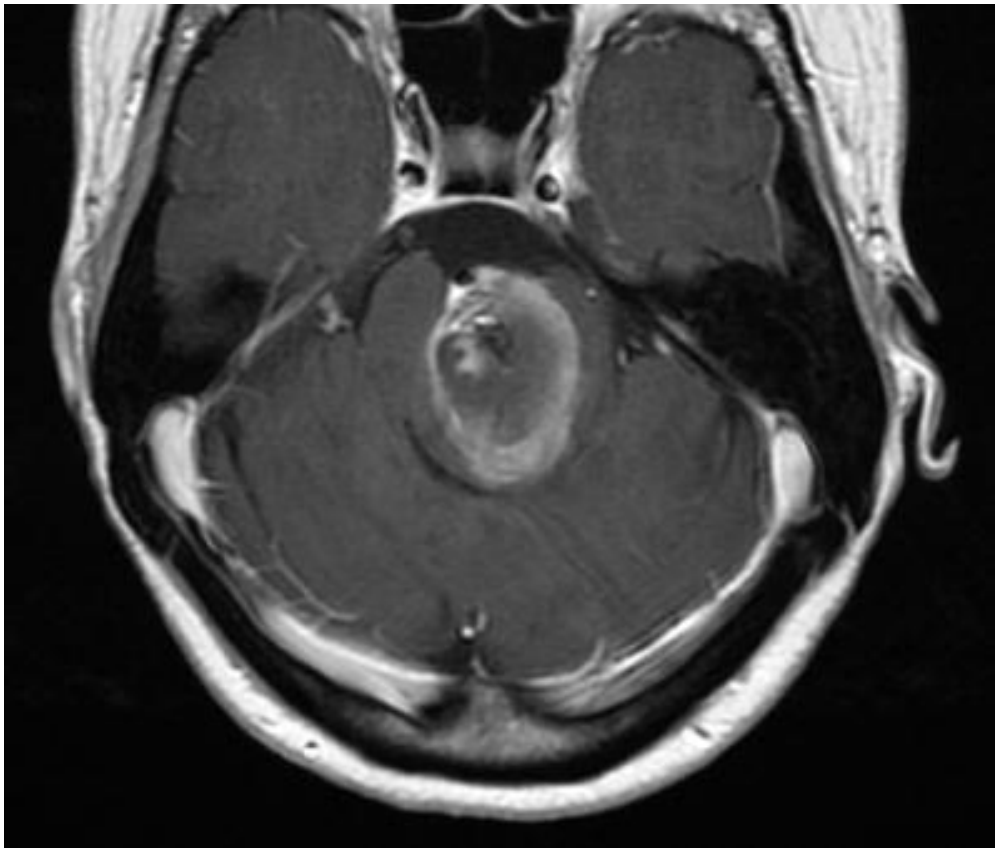


After stent and coil

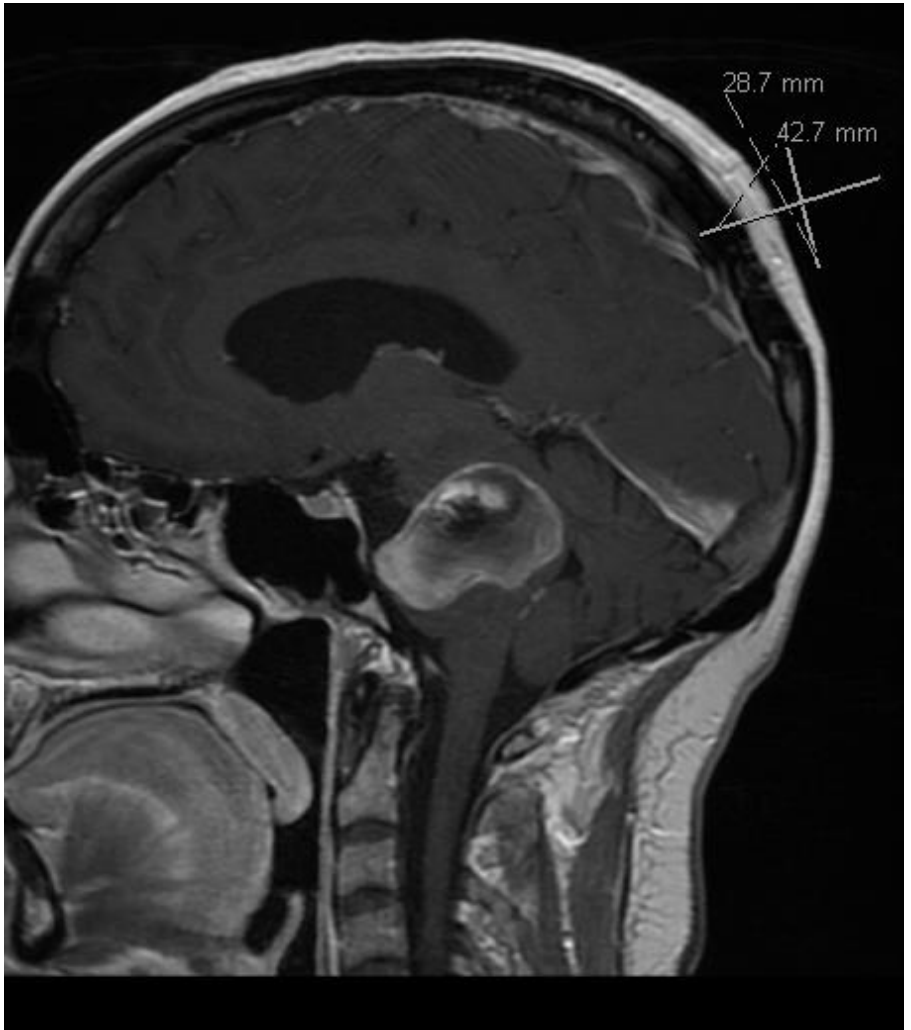


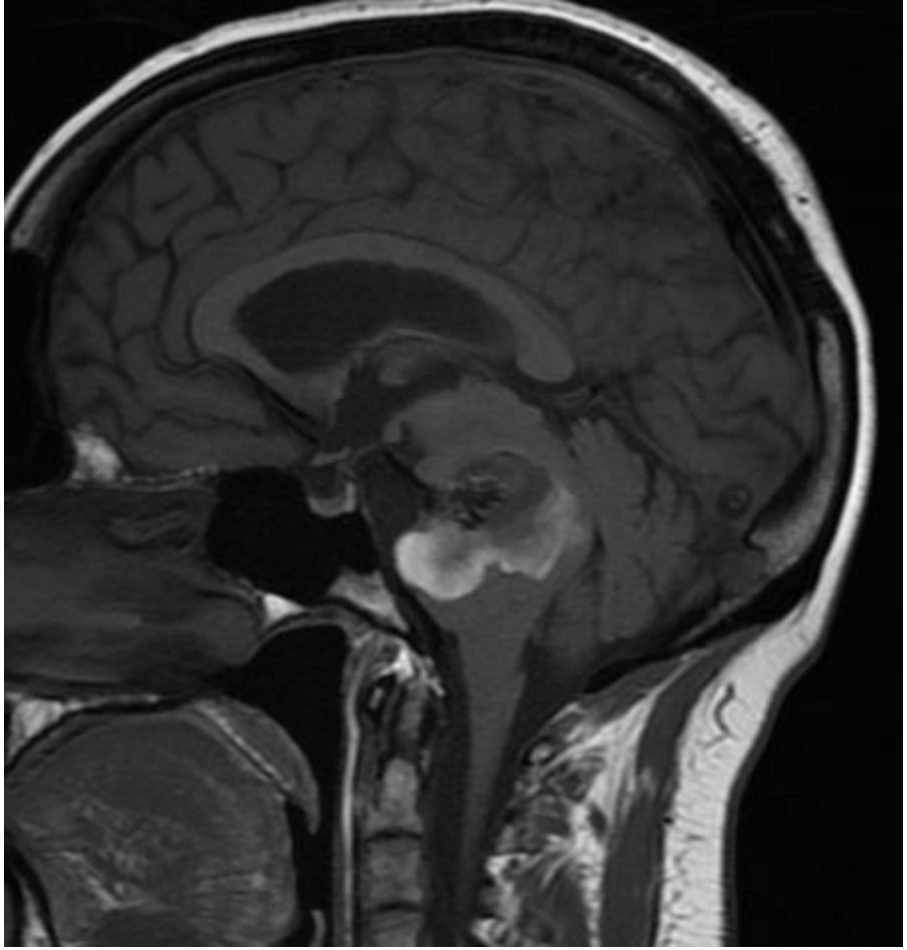


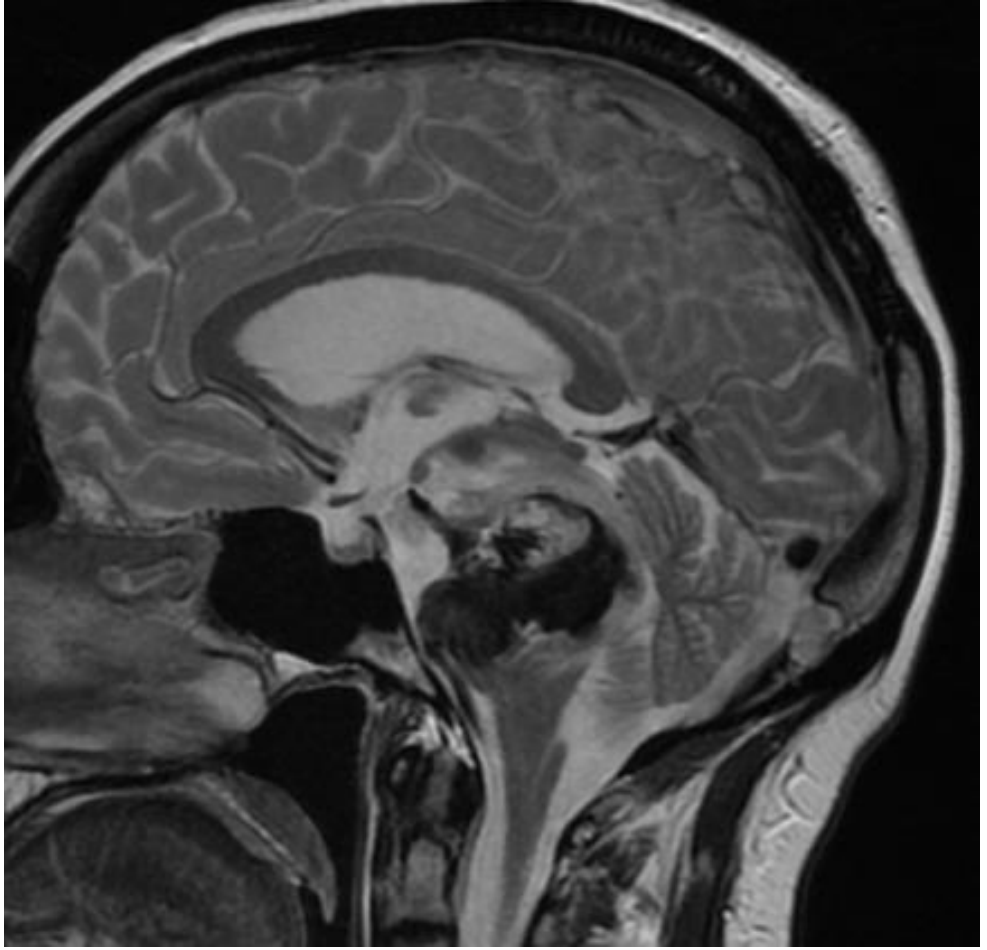


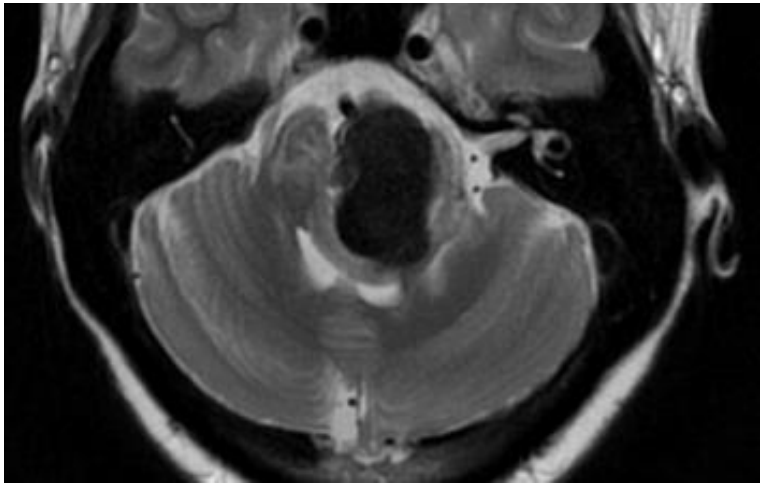


Kept growing in spite of VA sacrifice 2 stents and coil, FD









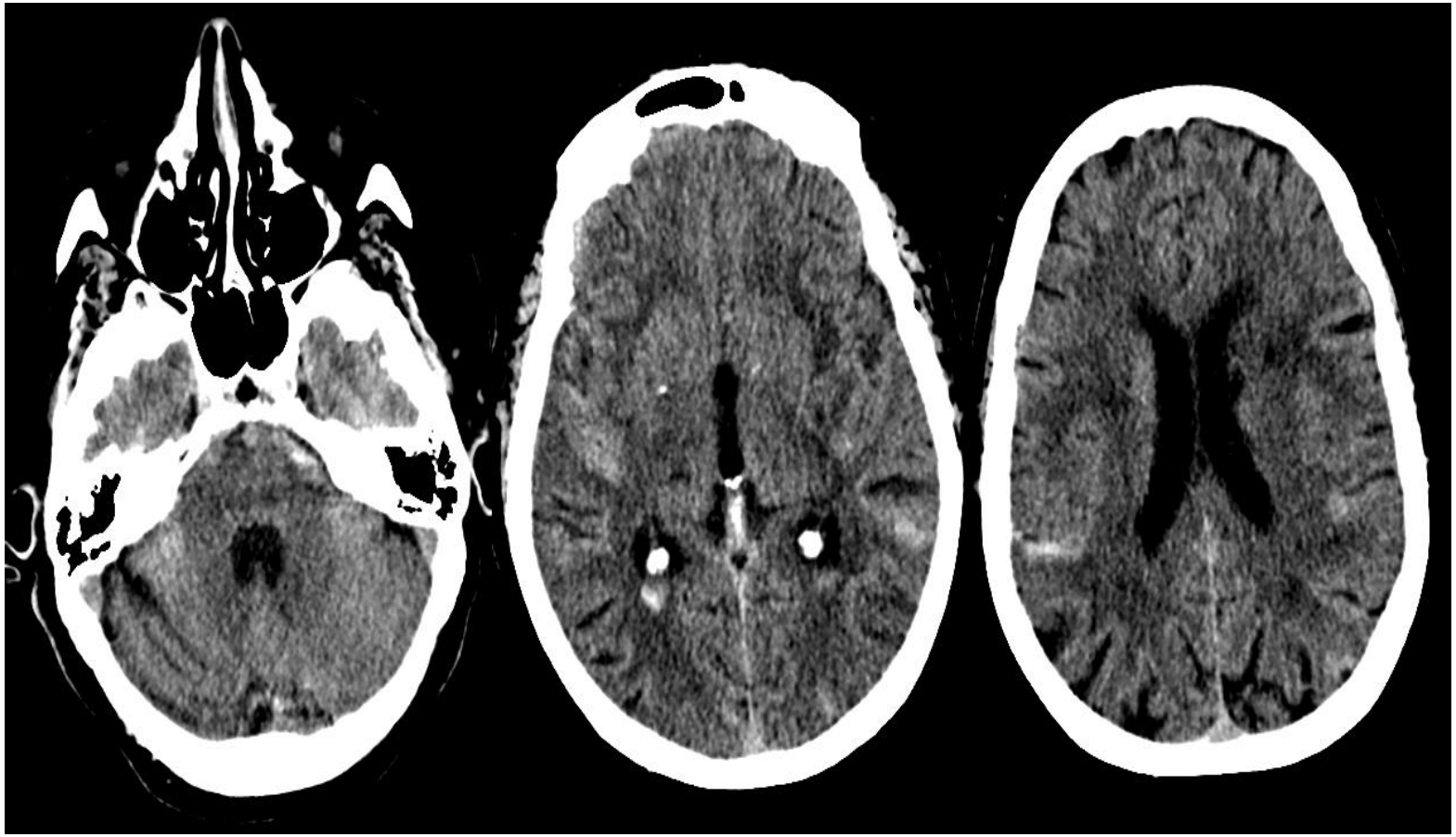
Another case – 65yo male

- BA-tip/P1 aneurysm - SAH – from vasa vasorum?
- Plain coiling → growing
- Stent and coil → growing
- Flow-diverter and sacrifice of one VA and PComA → growing
- Planned another FD → found dead from brain stem compression

Future

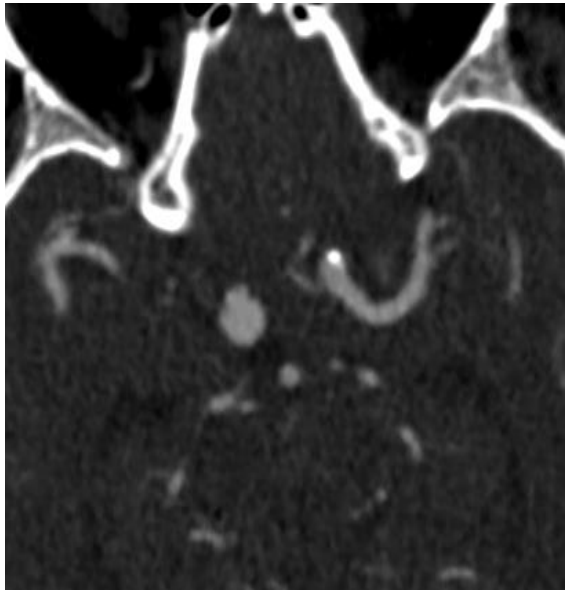
- Better understand the different disease processes
- Detection of rupture-prone aneurysms more accurately?
  - MR – vessel wall imaging?
  - New methods?
- Medication that stops or stabilize the disease process and pushes the balance towards repair?

Courtesy D Mandell TWH Toronto

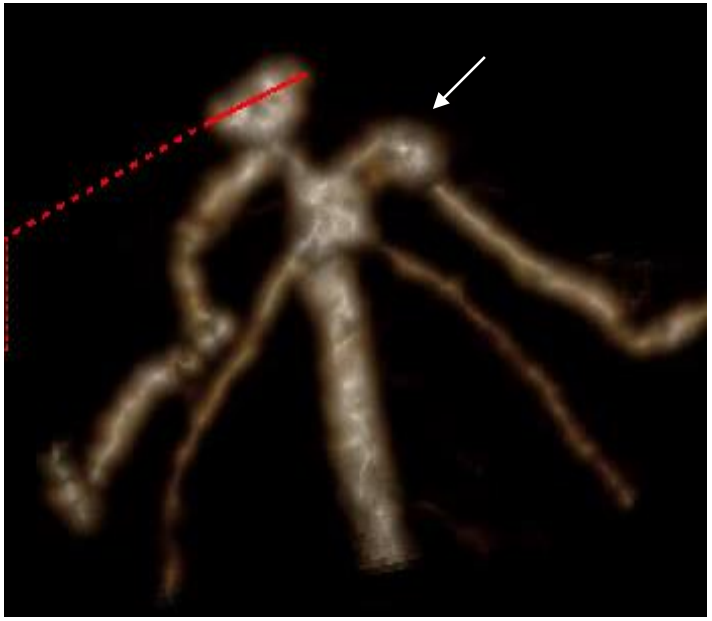


F 76 with thunderclap
headache

Rt para opth An
7 mm

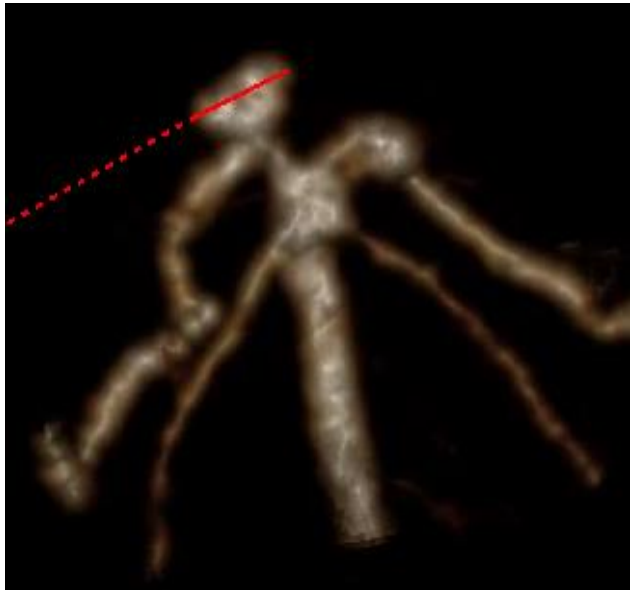


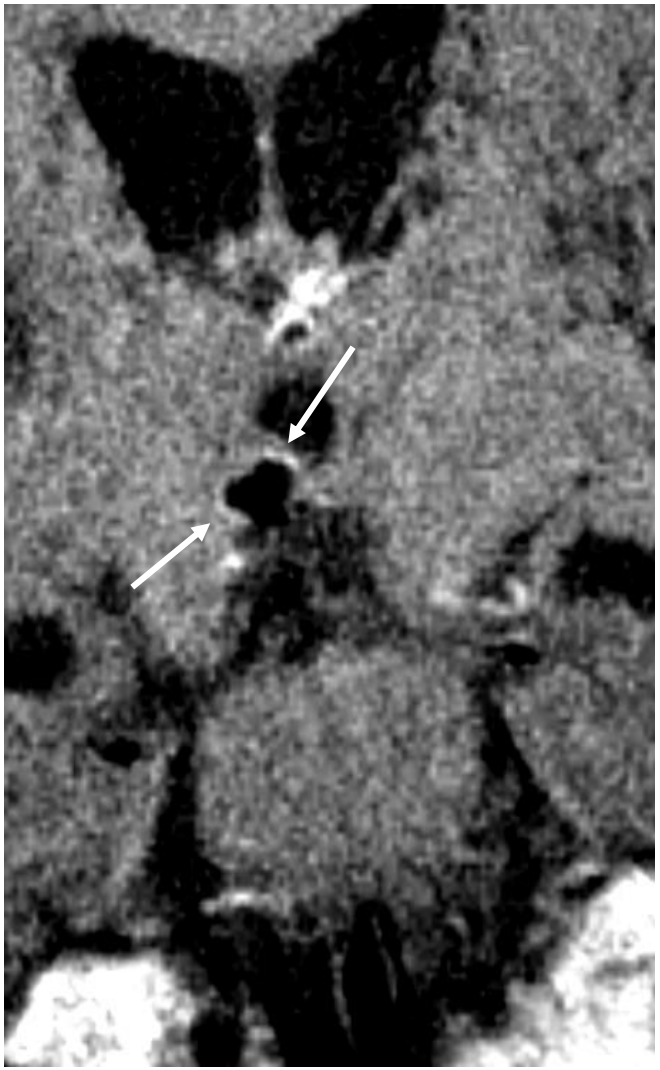
Rt P1-P2
An
5 mm



Lt P1 fusiform
ectasia

Rt P1-P2 Aneurysm demonstrates enhancement





T1 gado

Proven to be the aneurysm that bled!

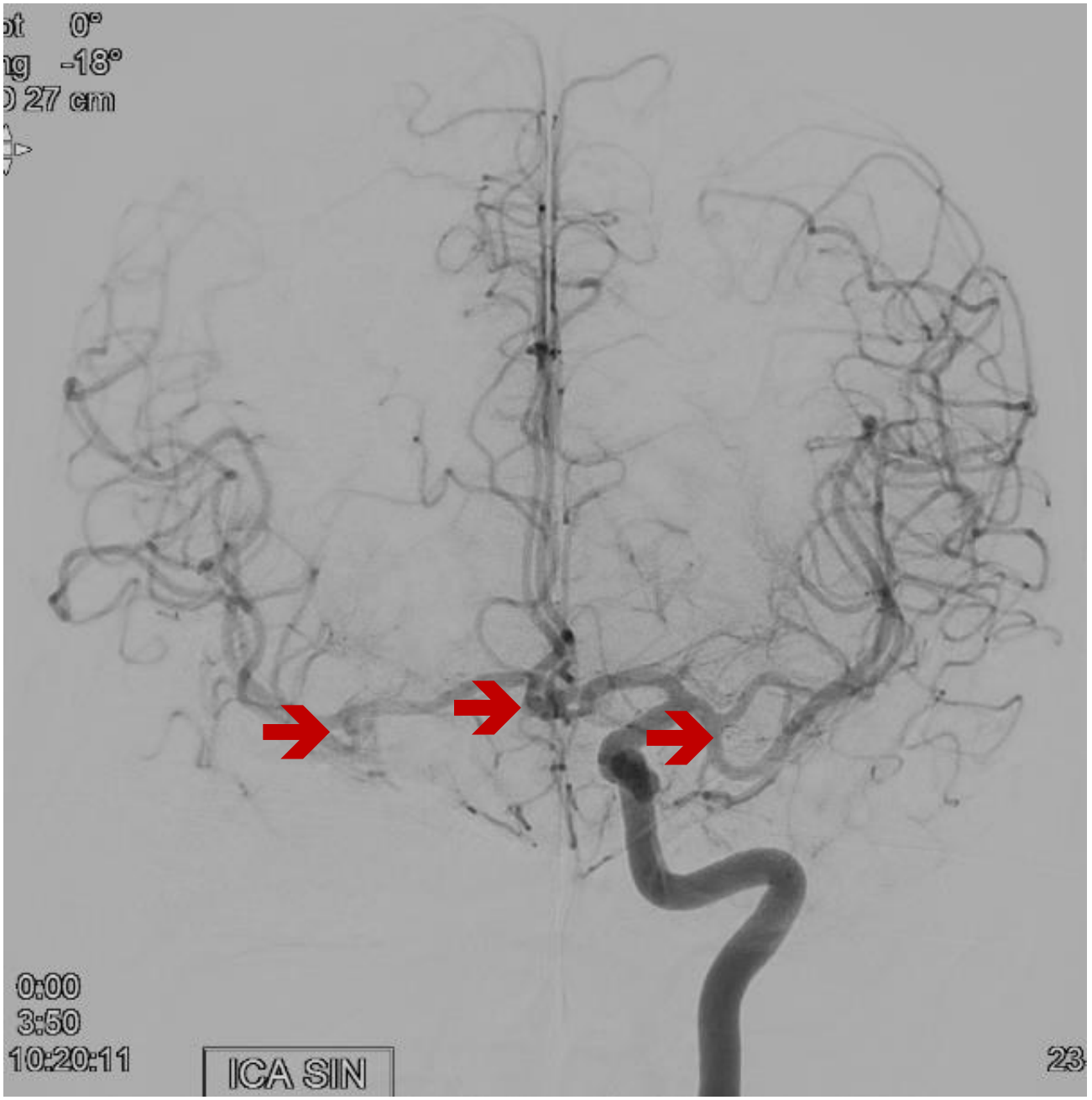
60 yo female

SAH IH and R

Previously coiled L MCA

AComA-aneurysm

R MCA-aneurysm




+46°
+35°
15 cm
0:00
3:00
10:33:12
ICA SIN


+30°
+6°
15 cm
0:35:27
ICA SIN


Huvudända
Serie nr: 5006
Volymtyp: 3DRA
Seriedatum: 2019/05/16
Serietid: 10:25:50
Kubstorlek: 90.54 mm
MCA A DX


Rot: -172°
Vinkel: +32°
Huvudända
Serie nr: 5006
Volymtyp: 3DRA
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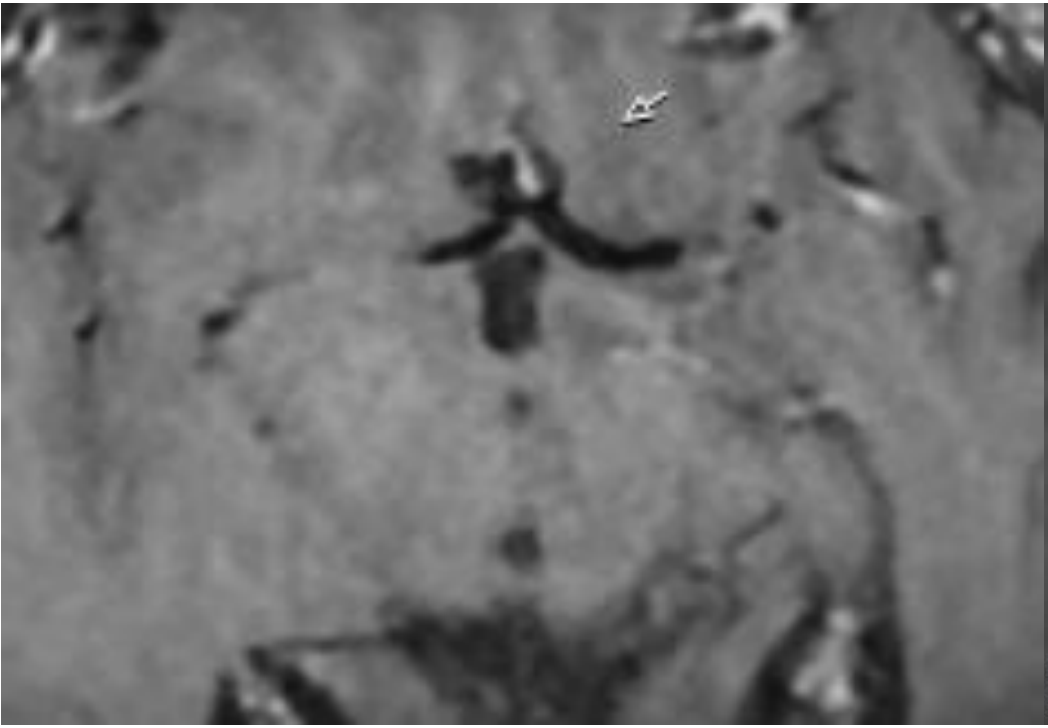

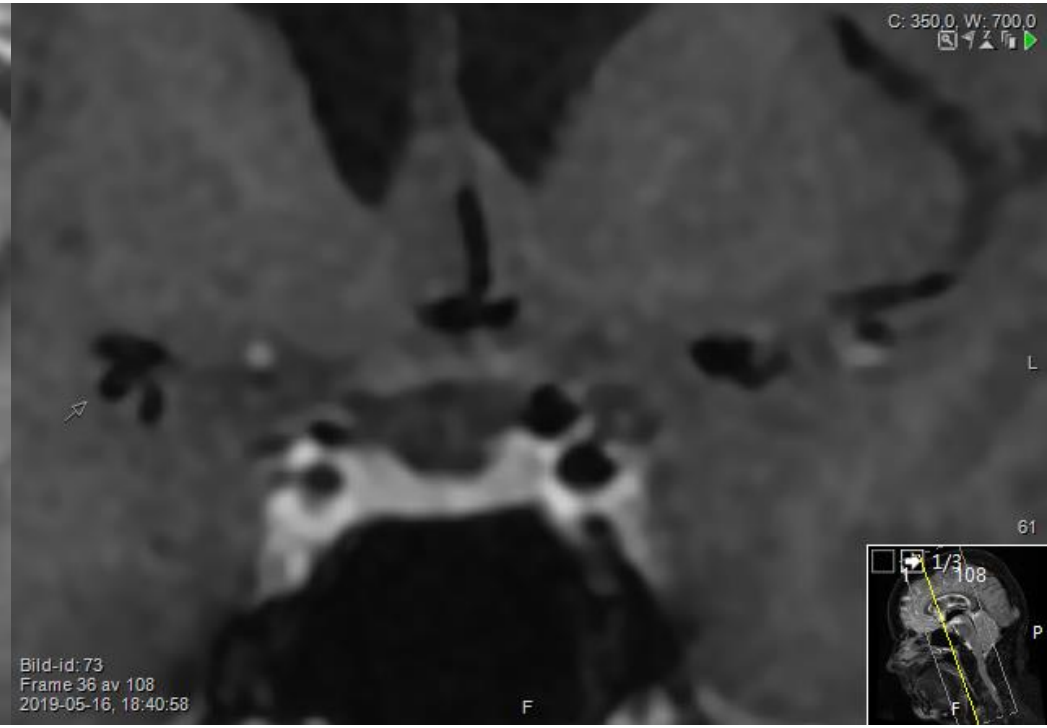
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L
61
1/3
108
P
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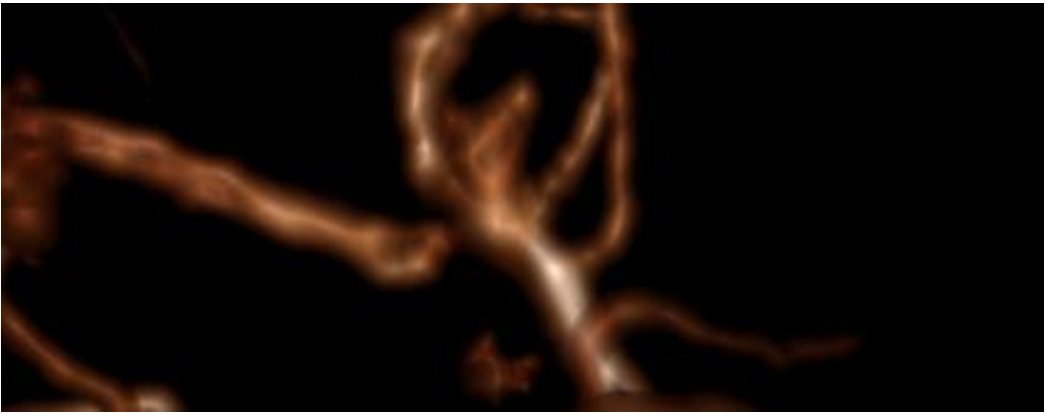
Bild-id:73
Frame 36 av 108
2019-05-16, 18:40:58
F



"Aneurysmal Wall Enhancement and Peri-aneurysmal edema after coiling of Unruptured Aneurysms"

- 132 unruptured aneurysms in 124 patients underwent endovascular treatment
- 85 (64.4%) aneurysms had wall enhancement
- 9 (6.8%) aneurysms had peri-aneurysmal brain edema

Su et al. Neuroradiology, 2014; 56: 487-495

Take home

- Aneurysms are *different* and warrant different *treatment strategies*
- Saccular aneurysms are *formed* by a *combination* of arterial wall weakening and hemodynamic stress
- *Balance* between protective/degenerative mechanisms and hemodynamic forces determine the risk of *rupture*

Take home

- *Oxidative stress, inflammation, aberrant luminal flow with thrombus formation* may cause loss of protective smooth muscle cells and endothelial degradation leading to a rupture

- The disease process may stop, stabilize or progress – implications for treatment and follow-up

References

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Thank you!!!