SCaLPEL Erasmus+ 2022 / 2023 online session II

Department of Neurosurgery Clinical Hospital Centre Zagreb Medical School, University of Zagreb

Sergej Marasanov MD



Co-funded by the European Union





Brain Arteriovenous Malformations

radiosurgery

Natural history

- approx. 2-4 % annual risk of rupture
- risk higher with previous bleed
- can be associated to AVM size and presentation

• 10 % severe morbidity / mortality

Goal of AVM treatment

- resect or obliterate nidus prevent (re)bleed
- preserve neurological function
- treat associated seizures (when possible)

• as little damage as possible with treatment

Grading of AVMs

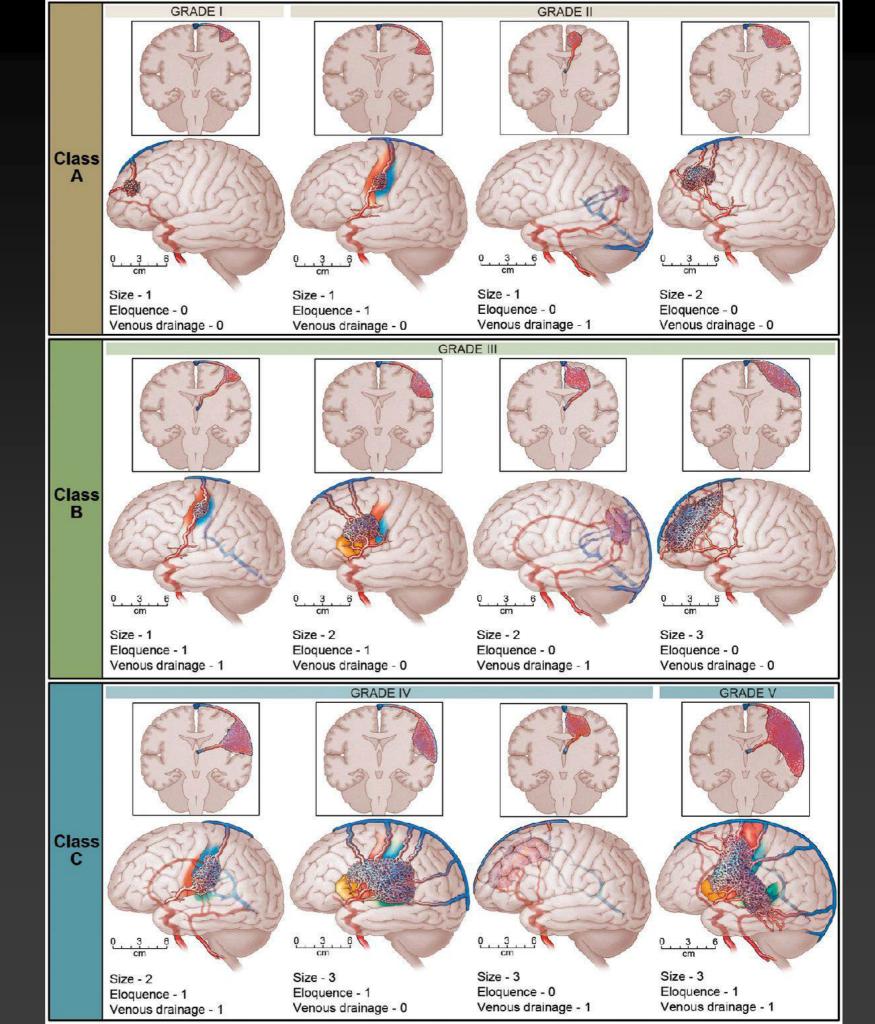
Spetzler - Martin Grading Scale

Characteristic	Number of points assigned
Size of AVM	
Small (<3 cm)	1 point
Medium (3–6 cm)	2 points
Large (>6 cm)	3 points
Location	
Noneloquent site	0 points
Eloquent site*	1 point
Pattern of venous drainage	
Superficial only	0 points
Deep component	1 point

*Sensorimotor, language, visual cortex, hypothalamus, thalamus, internal capsule, brain stem, cerebellar peduncles, or cerebellar nuclei.

Grading of AVMs

Spetzler - Ponce Grading Scale



Grading of **AVMs**

Supplemented SM **Grading Scale**

Lawton-Young **Grading Scale**

Spetzler-Martin g	adina
Sperzier-Indititi u	auniu

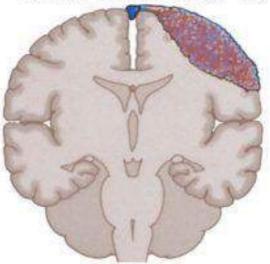
Size:	<3 cm = 1, 3-6 cm = 2, >6 cm = 3	s
Venous drainage:	superficial = 0, deep = 1	v
Eloquence:	no = 0, yes = 1	E

Lawton-Young grading

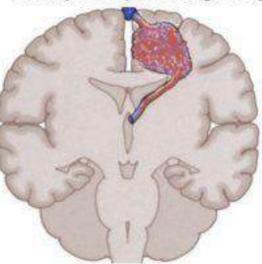
Age:	<20 y = 1, 20-40 y = 2, >40 y = 3	Α
Bleeding:	yes = 0, no = 1	в
Compactness:	compact = 0, diffuse = 1	c

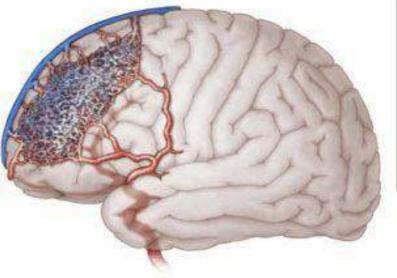
Supplemented Spetzler-Martin grade

Example 1: patient age 17 y



Example 2: patient age 43 y



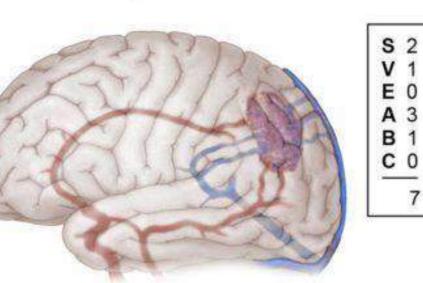


S 3 V 0 E 0 1 Α в 0 С

1

C 0

Total



Grading of AVMs

Virginia Radiosurgery AVM Grading Scale

	Points
Modified Pollock-Flickinger score Virginia Radiosurgery AVM scale	Score = (0.1)(volume, mL) + (0.02) (age, y) + (0.5)(location ^a)
Volume	
<2 mL	0
2-4 mL	1
>4 mL	2
Eloquent location	1
History of hemorrhage	1
Total	0-4 points

^aHemispheric/corpus callosum/cerebellar = 0; basal ganglia/thalamus/brainstem = 1.

Grading of AVMs

Radiosurgery based AVM Scale - RBAS (UPMC SRS)

	Characteristic	Coefficient
Volume Patient age Location ^b	frontal, temporal = 0 parietal, occipital, intraventricular, corpus callosum, cerebellar = 1 basal ganglia, thalamic, brainstem = 2	0.1 0.02 0.3

^a RBGS = (0.1) (volume) + (0.02) (patient age) + (0.3) (location).

^b When an AVM involves multiple sites, fractional values are used according to the number of sites (0.5 for two sites, 0.33 for three sites).

ruptured bAVM

ruptured bAVM



treatment

unruptured bAVM



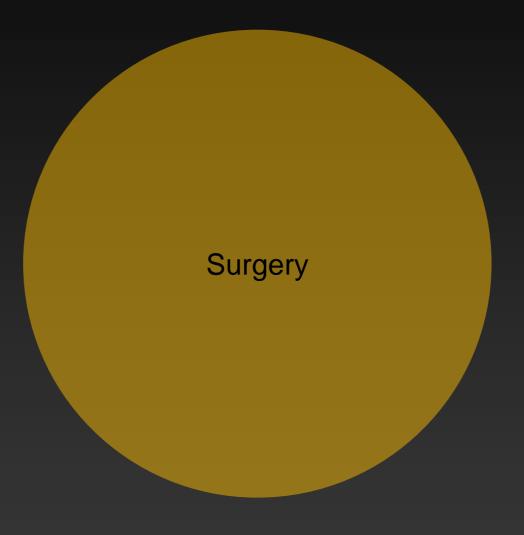


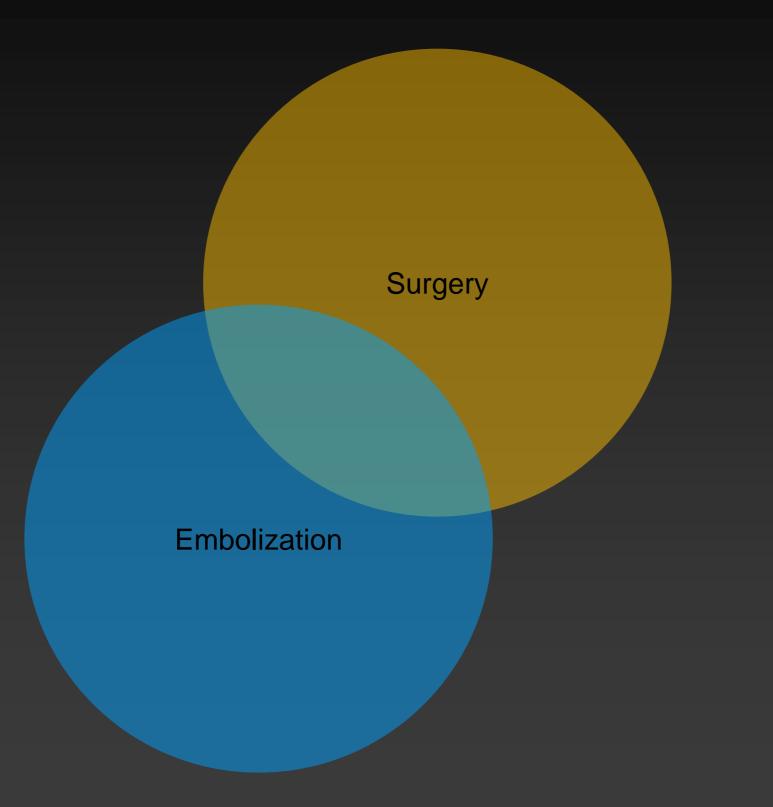
unruptured bAVM

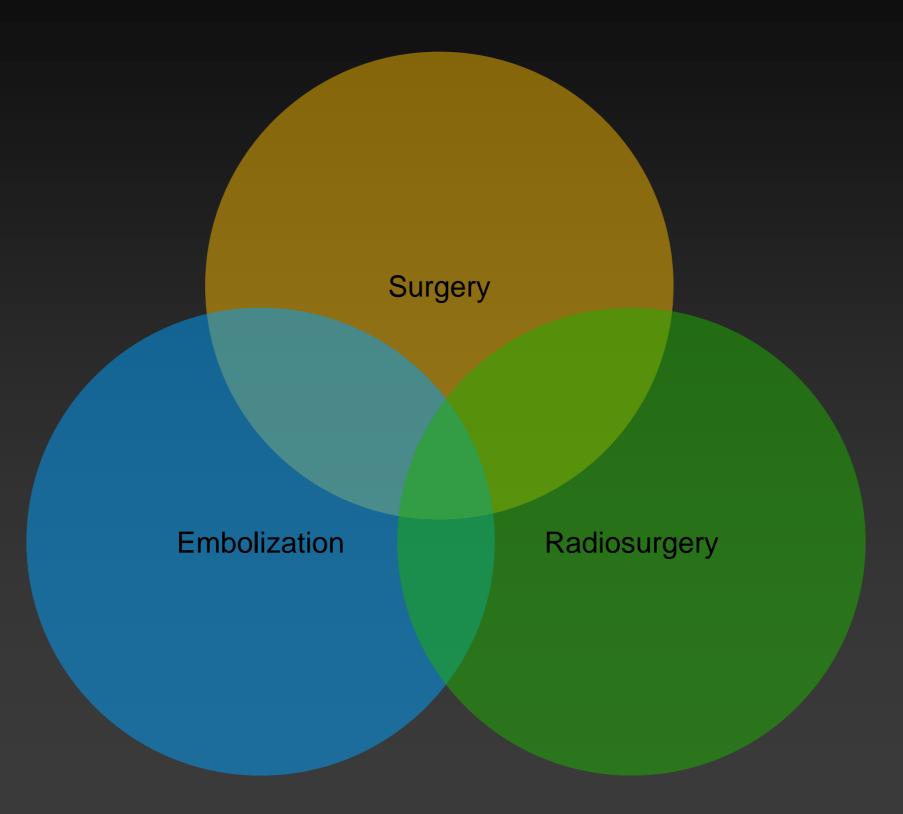


?? (ARUBA)

Conservative



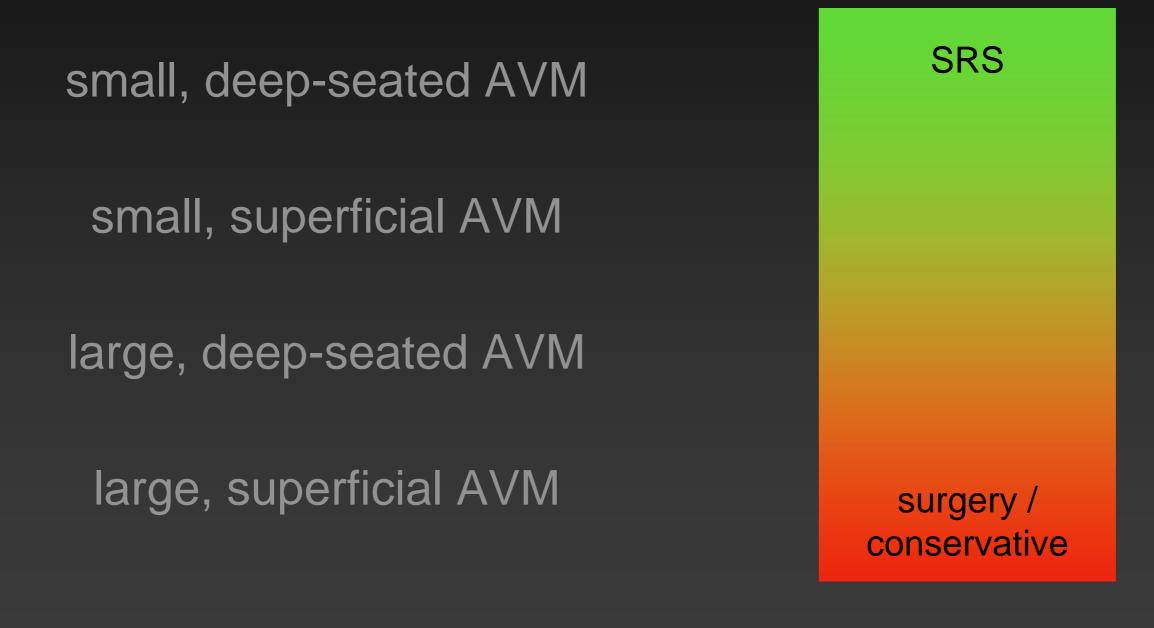






Radiosurgery for bAVMS

best candidates ?



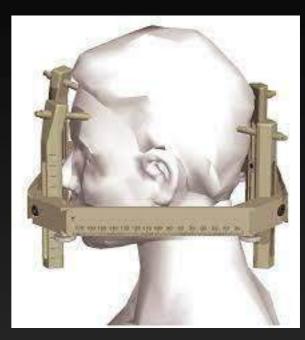
SRS technique

Positioning of stereotactic frame

- acquisition of images
- Digital Subtraction Angiography
- MR and MRA (TOF),
- CBCT-A

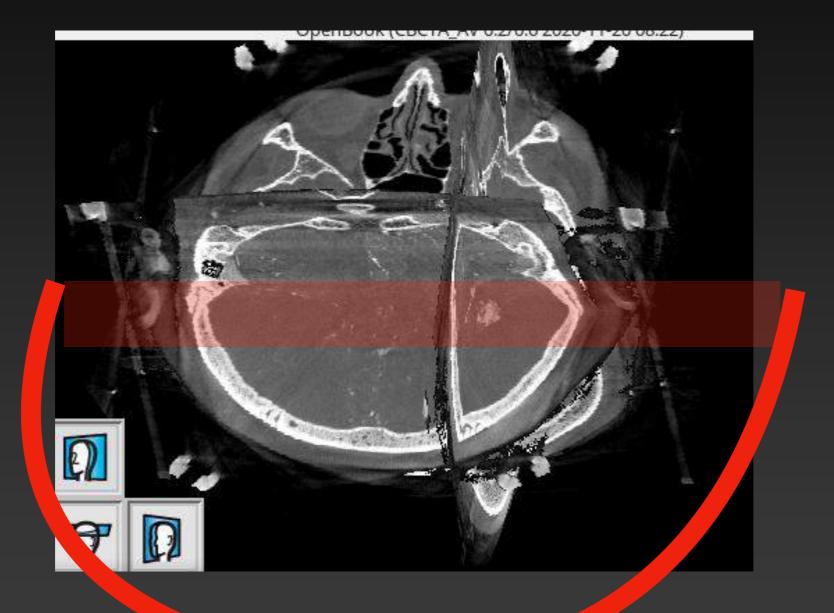
- Dosimetry planning
- Radiation delivery

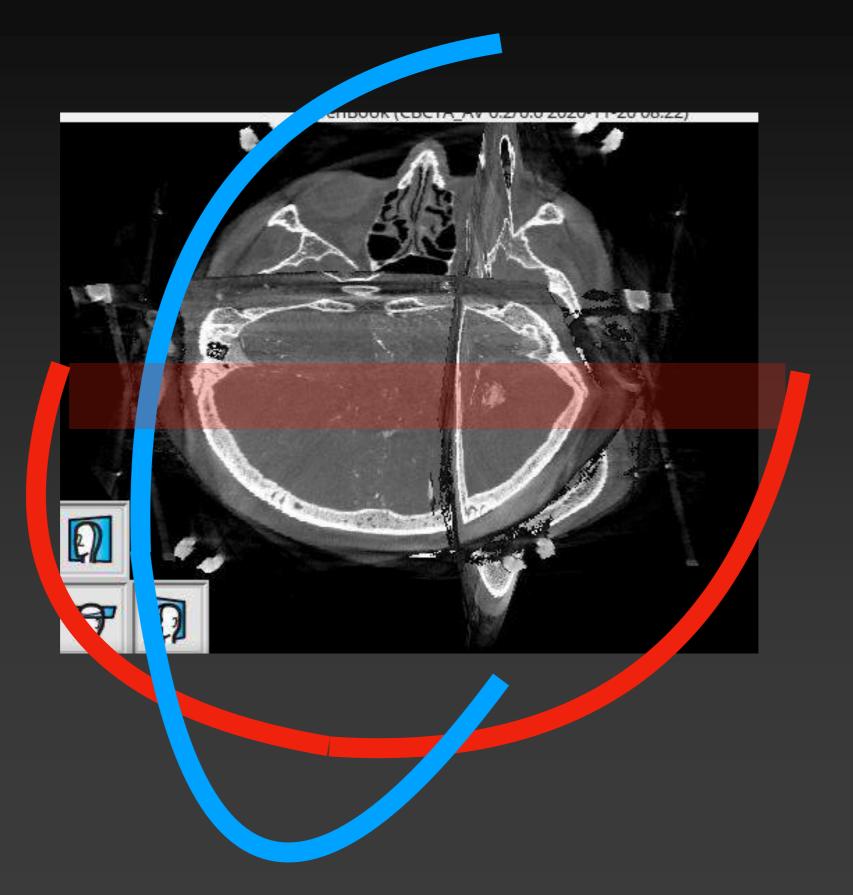


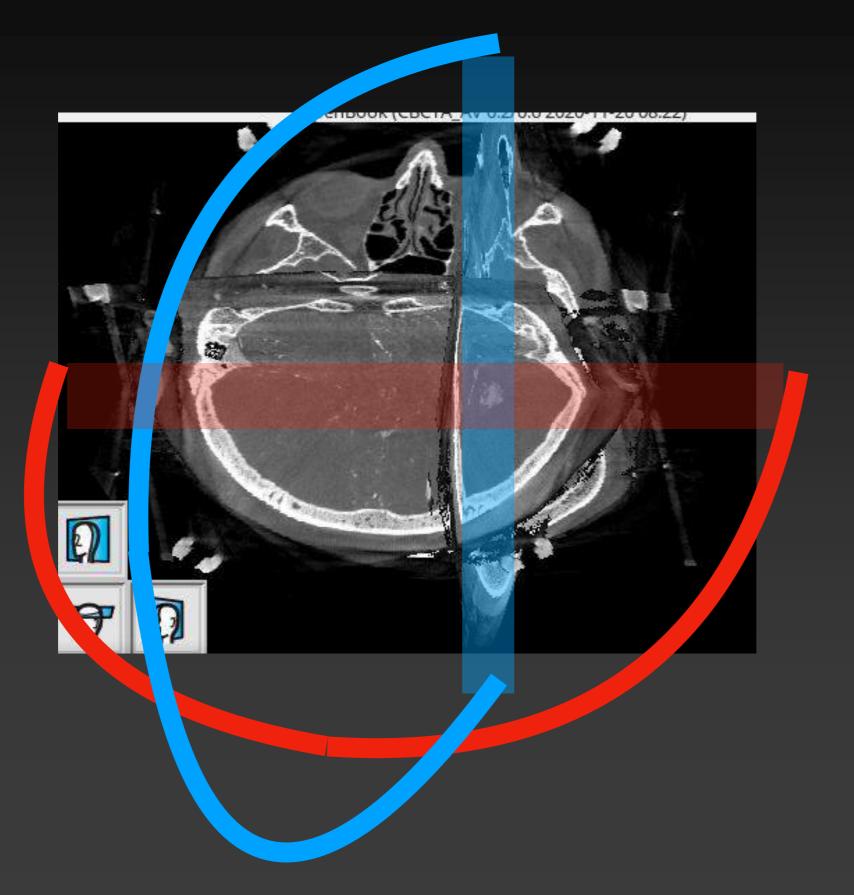


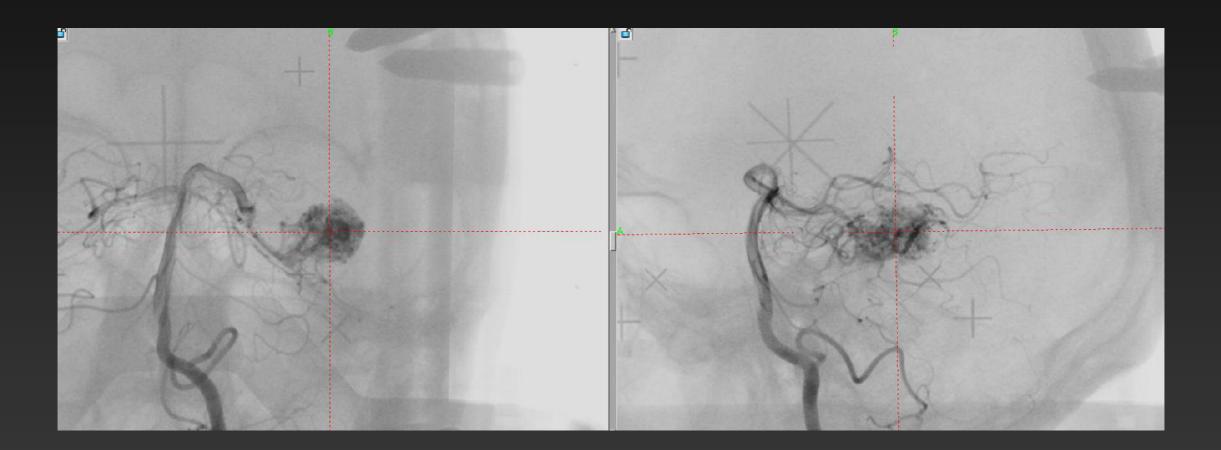


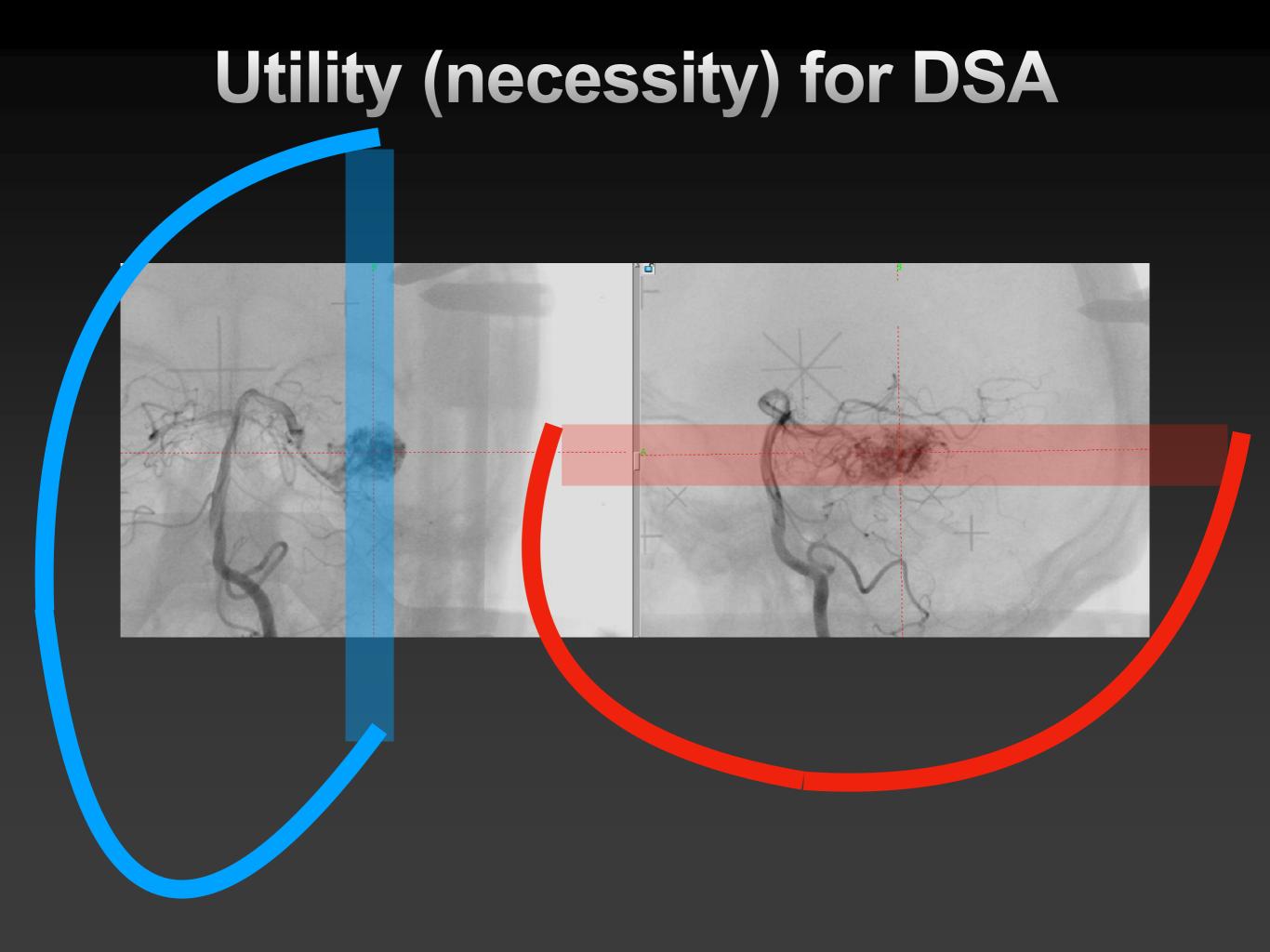


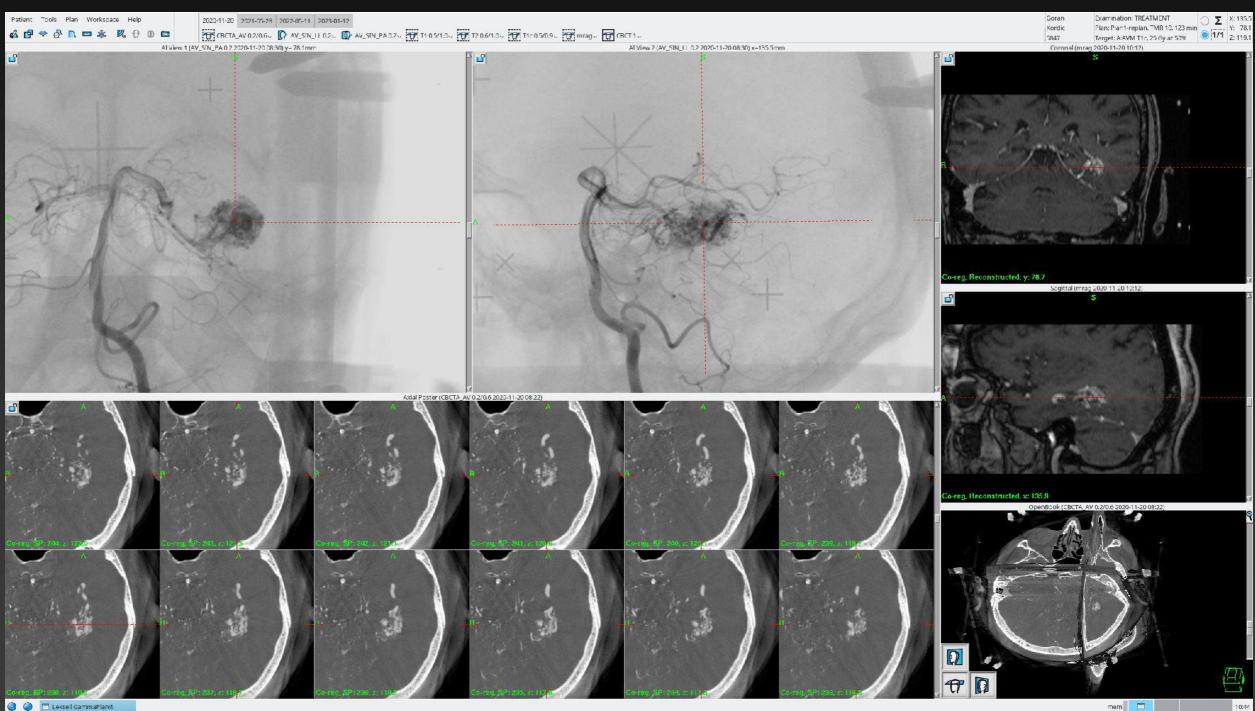






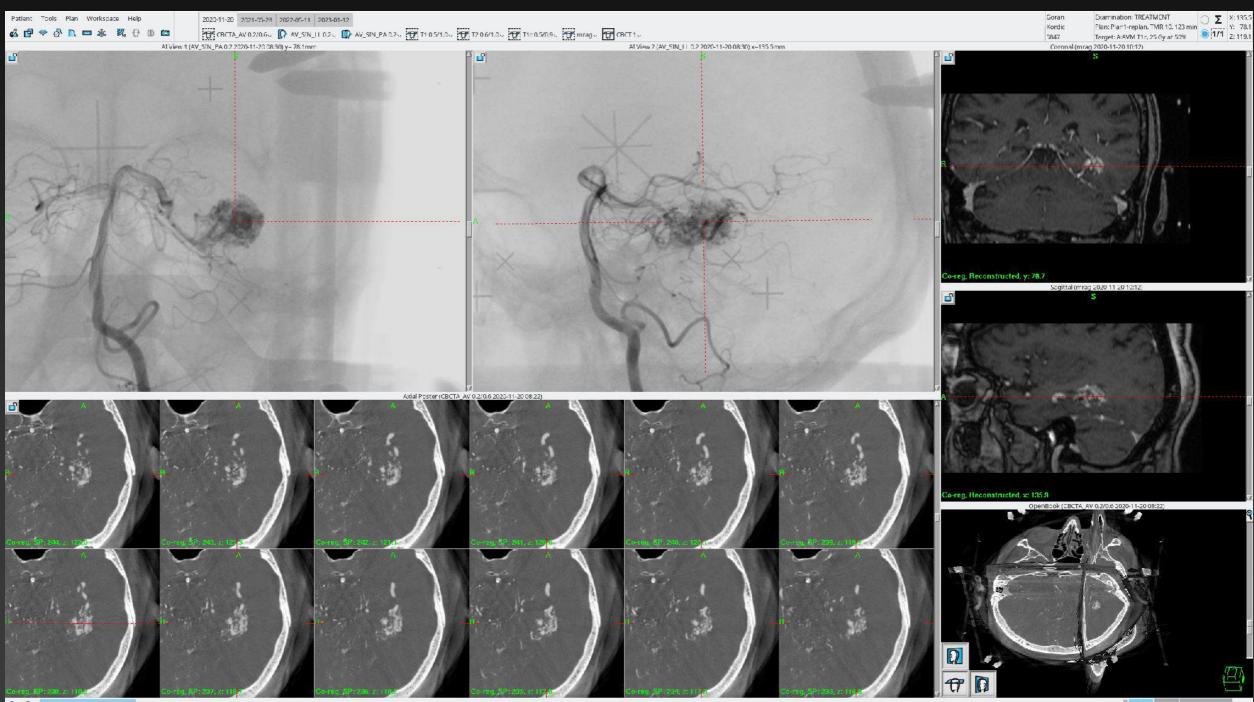






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Utility (necessity) for CBCT-A



Radiosurgery planning (dosimetry)

- factors we consider:
- volume
- location (eloquency, critical structures)
- prior hemorrhage, encephalomalacia
- prior embolisation
- radio surgical parameters (GI, conformity..)



- Obliteration rate
- Control of seizures (?)



- Obliteration rate
- time to obliteration 1-3 yrs (continues to rise up to 10 yrs)



- Obliteration rate
- time to obliteration 1-3 yrs (continues to rise up to 10 yrs)
- why ??



- Obliteration rate
- time to obliteration 1-3 yrs (continues to rise up to 10 yrs)
- why ??

• answer in radiobiology !!!

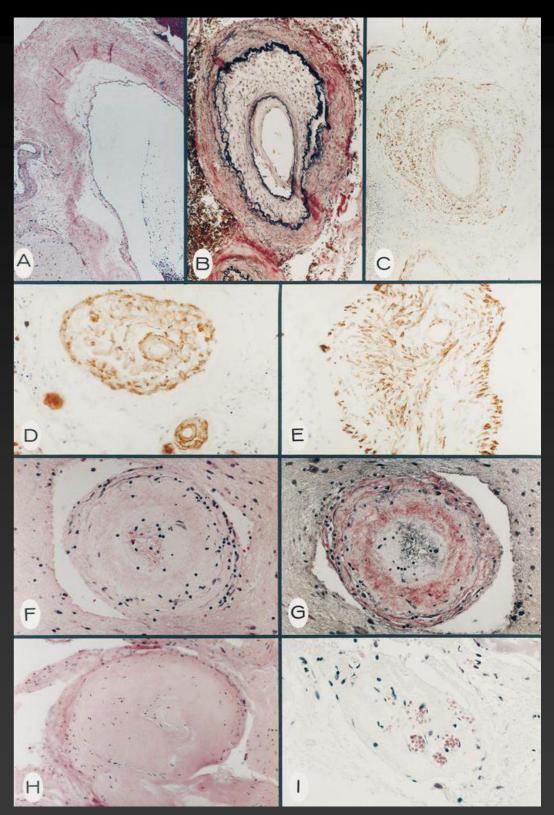
Radiobiology

- in radiobiology, two distinct tissue typer : early-responding (tumor, skin, mucosa, GI tract...) and late-responding tissues
- endothelial cells correspond to late-responding tissues
- more susceptible to single, high dose of radiation

Radiobiology

- effect of radiation is damage to endothelial cells of nidus
- followed by initiation of a chronic inflammatory process
- formation of granulation tissue, fibroblasts, new capillaries
- results in a radiation-induced vasculopathy, with progressive narrowing of vessels till thrombosis and occlusion

• takes time...



Histopathology of arteriovenous malformations after gamma knife radiosurgery

Bernard F. Schneider M.D., Ph.D., David A. Eberhard M.D., Ph.D., and Ladislau E. Steiner M.D., Ph.D.

Page Range: 352-357 Volume/Issue: Volume 87: Issue 3 DOI link: https://doi.org/10.3171/jns.1997.87.3.0352



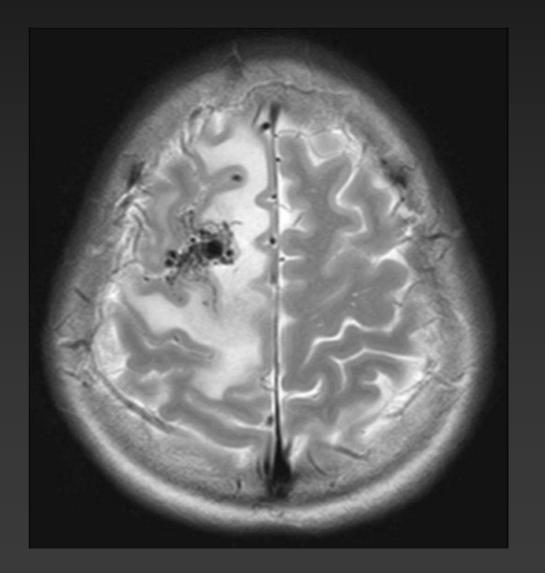
- Obliteration rate
- dependant on volume, marginal dose
- < 1 cc obliteration 88%
- 1-3 cc obliteration 78%
- > 3 cc obliteration 60%

• seizure control over 70%

Complications

- 3-5 % neurological complications
- 6-9 % temporary ARE
- 1-3 % permanent ARE

- risk for complications higher in larger volume, previous embolisation, eloquent regions
- th: steroids, hyperbaric O2, bevacizumab...



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

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

ARUBA

- intent to recruit 400 patients with ubAVMs
- follow for 5-10 yrs

• Prematurely halted after 33 months

 reported superior outcome for medical management over surgery (embo, microsurgery, radio surgery combined)

ARUBA

- substantial criticism !!
- bias in therapy
- short follow-up !!!

Treatment and outcomes of ARUBA-eligible patients with unruptured brain arteriovenous malformations at a single institution

W. CALEB RUTLEDGE, M.D.,¹ ADIB A. ABLA, M.D.,¹ JEFFREY NELSON, M.S.,² VAN V. HALBACH, M.D.,³ HELEN KIM, PH.D.,² AND MICHAEL T. LAWTON, M.D.^{1,2}

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Object. Management of unruptured arteriovenous malformations (AVMs) is controversial. In the first randomized trial of unruptured AVMs (A Randomized Trial of Unruptured Brain Arteriovenous Malformations [ARUBA]), medically managed patients had a significantly lower risk of death or stroke and had better outcomes. The University of California, San Francisco (UCSF) was one of the participating ARUBA sites. While 473 patients were screened for eligibility, only 4 patients were enrolled in ARUBA. The purpose of this study is to report the treatment and outcomes of all ARUBA-eligible patients at UCSF.

Methods. The authors compared the treatment and outcomes of ARUBA-eligible patients using prospectively collected data from the UCSF brain AVM registry. Similar to ARUBA, they compared the rate of stroke or death in observed and treated patients and used the modified Rankin Scale to grade outcomes.

Results. Of 74 patients, 61 received an intervention and 13 were observed. Most treated patients had resection with or without preoperative embolization (43 [70.5%] of 61 patients). One of the 13 observed patients died after AVM hemorrhage. Nine of the 61 treated patients had a stroke or died. There was no significant difference in the rate of stroke or death (HR 1.34, 95% CI 0.12–14.53, p = 0.81) or clinical impairment (Fisher's exact test, p > 0.99) between observed and treated patients.

Conclusions. The risk of stroke or death and degree of clinical impairment among treated patients was lower than reported in ARUBA. The authors found no significant difference in outcomes between observed and treated ARUBA-eligible patients at UCSF. Results in ARUBA-eligible patients managed outside that trial led to an entirely different conclusion about AVM intervention, due to the primary role of surgery, judicious surgical selection with established outcome predictors, and technical expertise developed at high-volume AVM centers. (http://thejns.org/doi/abs/10.3171/2014.7.FOCUS14242)

KEY WORDS • arteriovenous malformation • ARUBA • observation • microsurgical resection

Treatment and outcon with unruptured brain a single institution

W. CALEB RUTLEDGE, M.D.,¹ AD VAN V. HALBACH, M.D.,³ HELEN

¹Department of Neurological Surgery, Research, Department of Anesthesia (³Division of Neurointerventional Rad)

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KEY WORDS • arteriovenous microsurgical resection

Gamma Knife Radiosurgery for ARUBA-Eligible Patients with Unruptured Brain Arteriovenous Malformations

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ABSTRACT

Background: A randomized trial of unruptured brain arteriovenous malformations (ARUBA) reported superior outcomes in conservative management compared to interventional treatment. There were numerous limitations to the study. This study aimed to investigate the efficacy of gamma knife radiosurgery (GKS) for patients with brain arteriovenous malformations (AVMs) by comparing its outcomes to those of the ARUBA study. Methods: We retrospectively reviewed ARUBA-eligible patients treated with GKS from June 2002 to September 2017 and compared against those in the ARUBA study. AVM obliteration and hemorrhage rates, and clinical outcomes following GKS were also evaluated. Results: The ARUBA-eligible cohort comprised 264 patients. The Spetzler-Martin grade was Grade I to II in 52.7% and III to IV in 47.3% of the patients. The mean AVM nidus volume, marginal dose, and follow-up period were 4.8 cm3, 20.8 Gy, and 55.5 months, respectively. AVM obliteration was achieved in 62.1%. The annual hemorrhage rate after GKS was 3.4%. A stroke or death occurred in 14.0%. The overall stroke or death rate of the ARUBA-eligible cohort was significantly lower than that of the interventional arm of the ARUBA study (P < 0.001) and did not significantly differ from that of the medical arm in the ARUBA study (P=0.601). Conclusion: GKS was shown to achieve a favorable outcome with low procedure-related morbidity in majority of the ARUBA-eligible patients. The outcome after GKS in our patients was not inferior to that of medical care alone in the ARUBA study. It is suggested that GKS is rather superior to medical care considering the short follow-up duration of the ARUBA study.

Stereotactic Radiosurgery for Arteriovenous Malformations: The Effect of Treatment Period on Patient Outcomes

BACKGROUND: Stereotactic radiosurgery (SRS) has been performed on patients with cerebral arteriovenous malformations (AVMs) for over 40 years.

OBJECTIVE: To evaluate the impact of treatment period on obliteration, intracranial hemorrhage (ICH), and radiation-induced complications (RICs).

METHODS: Retrospective comparison of 381 AVM patients having SRS during a 20-year period (group 1, January 1990 through March 1997, n = 160; group 2, April 1997 through December 2009, n = 221). The median radiological and clinical follow-up after initial SRS was 77 months and 93 months, respectively.

RESULTS: Obliteration was 59.1% at 4 years and 85.1% at 8 years. Obliteration was more common in patients with hemispheric or cerebellar AVMs (P = .001), smaller prescription isodose volume (PIV) (P < .001), and group 1 patients (P < .001). The ICH rate was 7.7% at 4 years and 10.6% at 8 years. ICH was more common in older patients (P = .02), patients with deep AVM (P = .01), and larger PIV (P < .001). There was no difference in the ICH rate between the treatment groups (P = .18). The rate of permanent RICs was 4.4% at 4 years and 8.6% at 8 years. RICs were more common with larger PIVs (P < .001) and group 1 patients (P = .02). There was no difference in the number of patients having obliteration without new deficits between the 2 treatment periods (68.8% vs 73.3%, P = .33).

CONCLUSION: Advances in SRS procedures over the past 20 years have resulted in a lower risk of RIC, but fewer patients had AVM obliteration. Increasing the prescription dose for patients with medium- and large-volume AVMs by using current conformal dose-planning techniques may improve the obliteration rate while maintaining a low risk of RICs.

KEY WORDS: Arteriovenous malformation, Complications, Hemorrhage, Obliteration rate, Stereotactic radiosurgery

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Annual hemorrhage rate after SRS 1.3%

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ORIGINAL RESEARCH

Evaluation of the radiosurgical treatment of cerebral arteriovenous malformations: a retrospective singlecenter analysis of three decades

Dorian Hirschmann,¹ Philipp Goebl,¹ Frederic H Witte,¹ Brigitte Gatterbauer,¹ Wei-Te Wang,¹ Philippe Dodier ¹, Gerhard Bavinzski,¹ Adolf Ertl,¹ Wolfgang Marik,² Ammar Mallouhi,² Thomas Roetzer,³ Christian Dorfer,¹ Wilhelm Eisner,⁴ Andreas Gruber,⁵ Klaus Kitz,¹ Josa M Frischer ¹

J NeuroIntervent Surg 2020;12

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J NeuroIntervent Surg 2020;12

Overall annual hemorrhage rate after first GKRS: 1.3%

The Risk of Stroke or Clinical Impairment After Stereotactic Radiosurgery for ARUBA-Eligible Patients

Bruce E. Pollock, MD; Michael J. Link, MD; Robert D. Brown, MD

- Background and Purpose—The best management of patients with unruptured brain arteriovenous malformations (BAVM) is controversial. In this study, we analyzed the stroke rate and functional outcomes of patients having stereotactic radiosurgery (SRS) for unruptured BAVM using the same eligibility criteria and primary end points as the ARUBA trial. Methods—Retrospective observational study of 174 ARUBA-eligible patients having SRS from 1990 to 2005.
- *Results*—The median follow-up after SRS was 64 months. Fifteen patients (8.7%) had a hemorrhagic stroke at a median of 21 months after SRS. Six patients (3.5%) had a focal neurological deficit and 4 patients died (2.3%). The risk of stroke or death was 10.3% at 5 years and 11.5% at 10 years. Twelve additional patients (6.9%) had a focal neurological deficit from either radiation-related complications (n=7) or subsequent resection (n=5). The risk of patients' having clinical impairment (modified Rankin Score ≥2) was 8.4% at 5 years and 12.0% at 10 years. Increasing BAVM volume was associated with both stroke or death (hazard ratio=1.06; 95% confidence interval, 1.0–1.11; *P*=0.04) and clinical impairment (hazard ratio=1.06; 95% confidence interval, 1.01–1.09; *P*=0.01). The 10-year risk of stroke or death and clinical impairment for patients with BAVM ≤5.6 cm³ was 5% and 4%, respectively.
- Conclusions—The observed risk of stroke or death after SRS was approximately 2% per year for the first 5 years after SRS, declining to 0.2% annually for years 6 to 10. Patients with small volume BAVM may benefit from SRS compared with the natural history of unruptured BAVM over the planned follow-up interval of the ARUBA trial (5–10 years). (Stroke. 2013;44:437-441.)

Key Words: arteriovenous malformation ■ hemorrhage ■ stereotactic radiosurgery ■ stroke

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Key Words: arteriovenous malformation ■ hemorrhage ■ stereotactic radiosurgery ■ stroke

REVIEW: CEREBROVASCULAR

Stereotactic Radiosurgery for A Randomized Trial of Unruptured Brain Arteriovenous Malformations-Eligible Patients: A Meta-Analysis

Ilyas, Adeel MD^{*}; Chen, Ching-Jen MD[‡]; Abecassis, Isaac Josh MD[§]; Al-Saiegh, Fadi MD[‡]; Ironside, Natasha MBChB^{||}; Jabbour, Pascal M. MD[‡]; Tjoumakaris, Stavropoula MD[‡]; Gooch, M. Reid MD[‡]; Lee, Cheng-Chia MD, PhD[¶]; Sheehan, Jason P. MD, PhD^{||}; Ding, Dale MD[§]

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- study cohort included 8 studies comprising 1620 ARUBA-eligible patients who underwent SRS
- mean follow-up duration was 80 months
- rates of radiologic, symptomatic, and permanent radiationinduced changes were 45%, 11%, and 2%, respectively
- obliteration rate was 68% at last follow-up
- post-SRS hemorrhage and mortality rates were 8%, and 2%, respectively

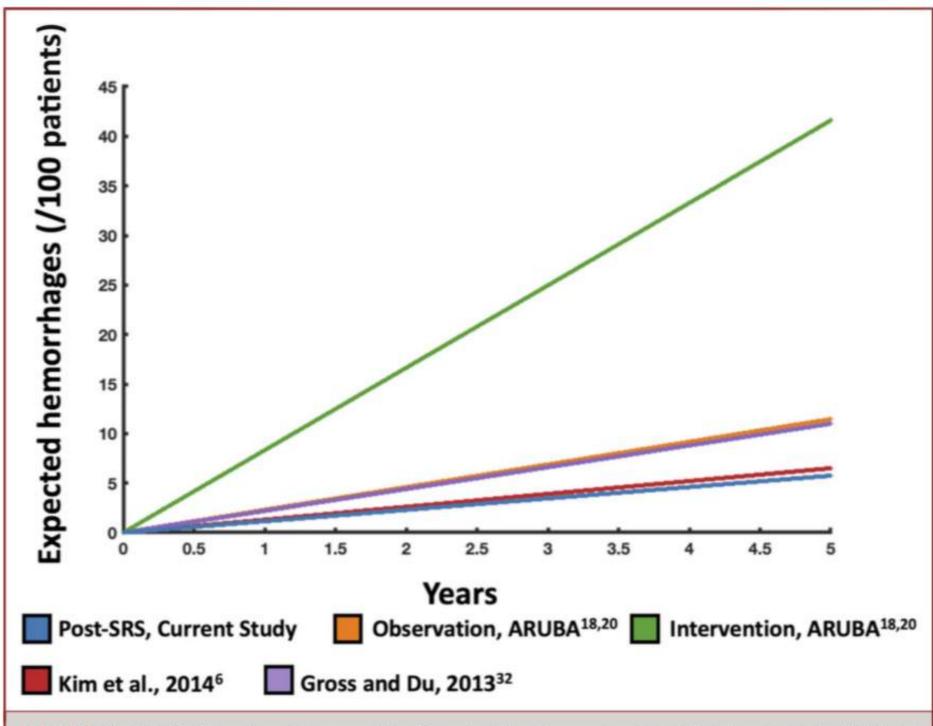


FIGURE 2. Graphical depiction of cumulative hemorrhage risk computed from the current meta-analysis and compared with ARUBA and 2 arteriovenous malformation natural history studies. ARUBA, A Randomized Trial of Unruptured Brain Arteriovenous Malformations; SRS, stereotactic radiosurgery.

REVIEW: CEREBROVASCULAR

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Author Information 📀

Neurosurgery 91(5):p 684-692, November 2022. | DOI: 10.1227/neu.000000000002115

- lower Spetzler-Martin grade (odds ratios [OR] = 0.84 [0.74-0.95], P = .005),
- lower radiosurgery-based AVM score (OR = 0.75 [0.64-0.95], P = .011),
- lower Virginia Radiosurgery AVM Scale (OR = 0.86 [0.78-0.95], P = .003), and
- higher margin dose (OR = 1.13 [1.02-1.25], P = .025)
- were associated with obliteration

REVIEW: CEREBROVASCULAR

Stereotactic Radiosurgery for A Randomized Trial of Unruptured Brain Arteriovenous Malformations-Eligible Patients: A Meta-Analysis

Ilyas, Adeel MD^{*}; Chen, Ching-Jen MD[‡]; Abecassis, Isaac Josh MD[§]; Al-Saiegh, Fadi MD[‡]; Ironside, Natasha MBChB^{||}; Jabbour, Pascal M. MD[‡]; Tjoumakaris, Stavropoula MD[‡]; Gooch, M. Reid MD[‡]; Lee, Cheng-Chia MD, PhD[¶]; Sheehan, Jason P. MD, PhD^{||}; Ding, Dale MD[§]

Author Information 🛞

Neurosurgery 91(5):p 684-692, November 2022. | DOI: 10.1227/neu.000000000002115

CONCLUSION:

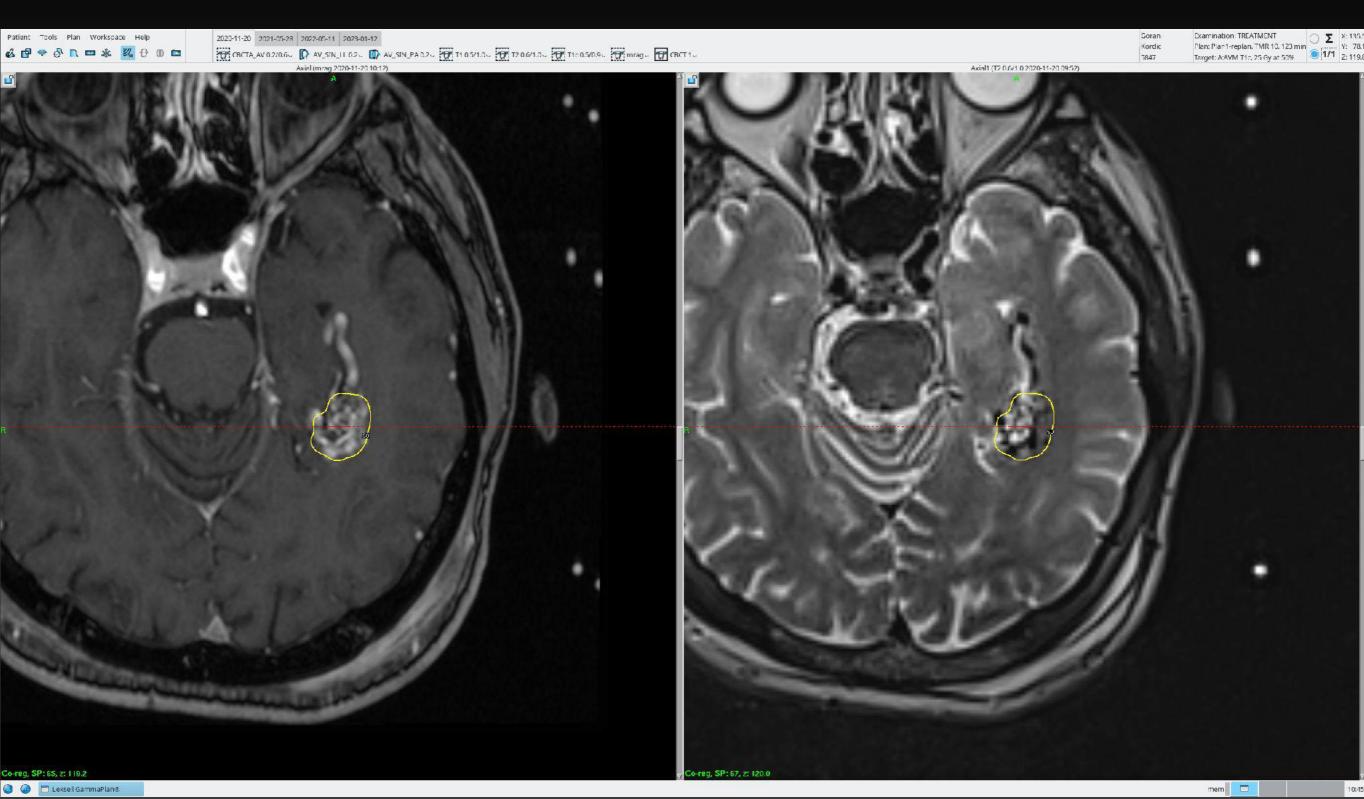
SRS carries a favorable risk to benefit profile for appropriately selected ARUBA-eligible patients, particularly those with smaller volume AVMs. Our findings suggest that the results of ARUBA do not reflect the real-world safety and efficacy of SRS for unruptured AVMs.



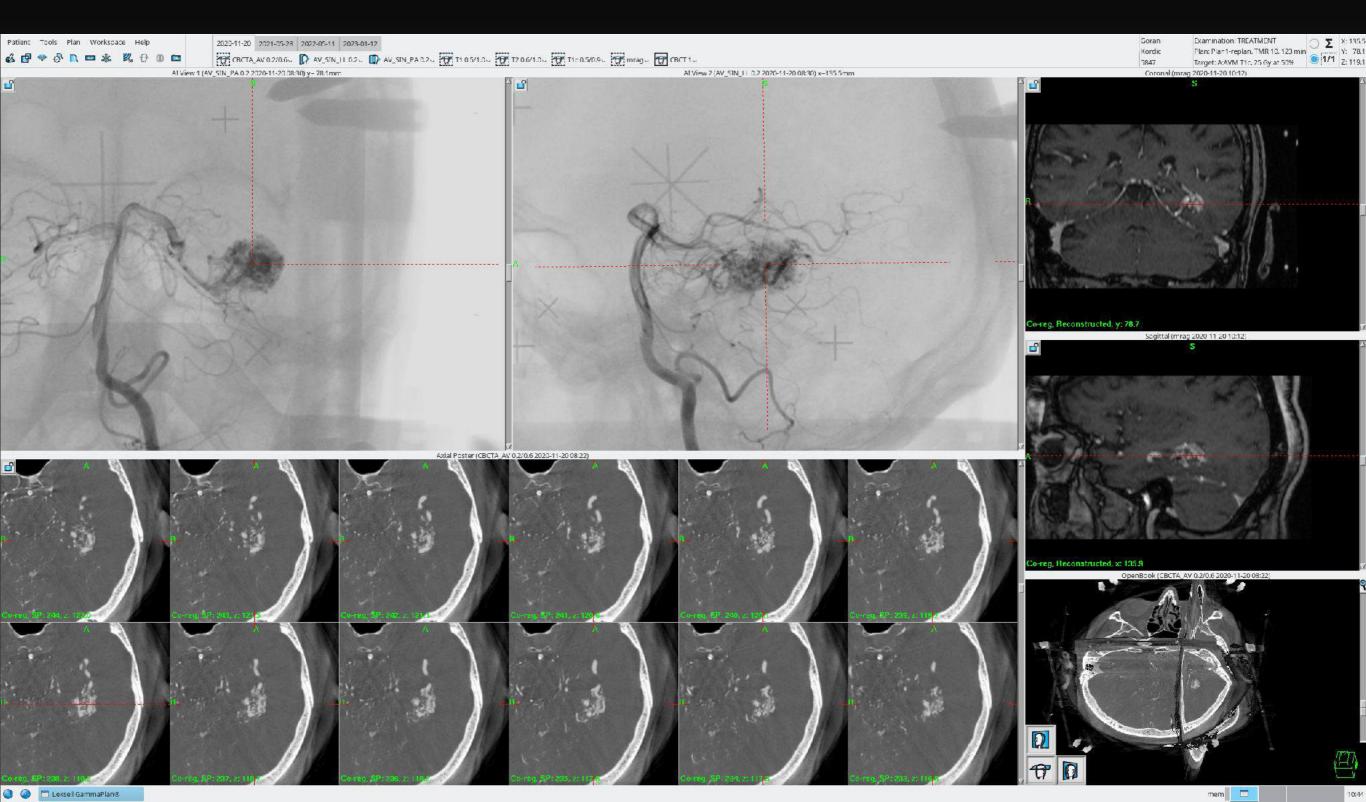




- 44 y.o. male
- Medical history mild retardation, epilepsy for many years
- development of instability in gait
- CT-A, MR-A signs of bAVM
- admitted to Neurology for DSA evaluation

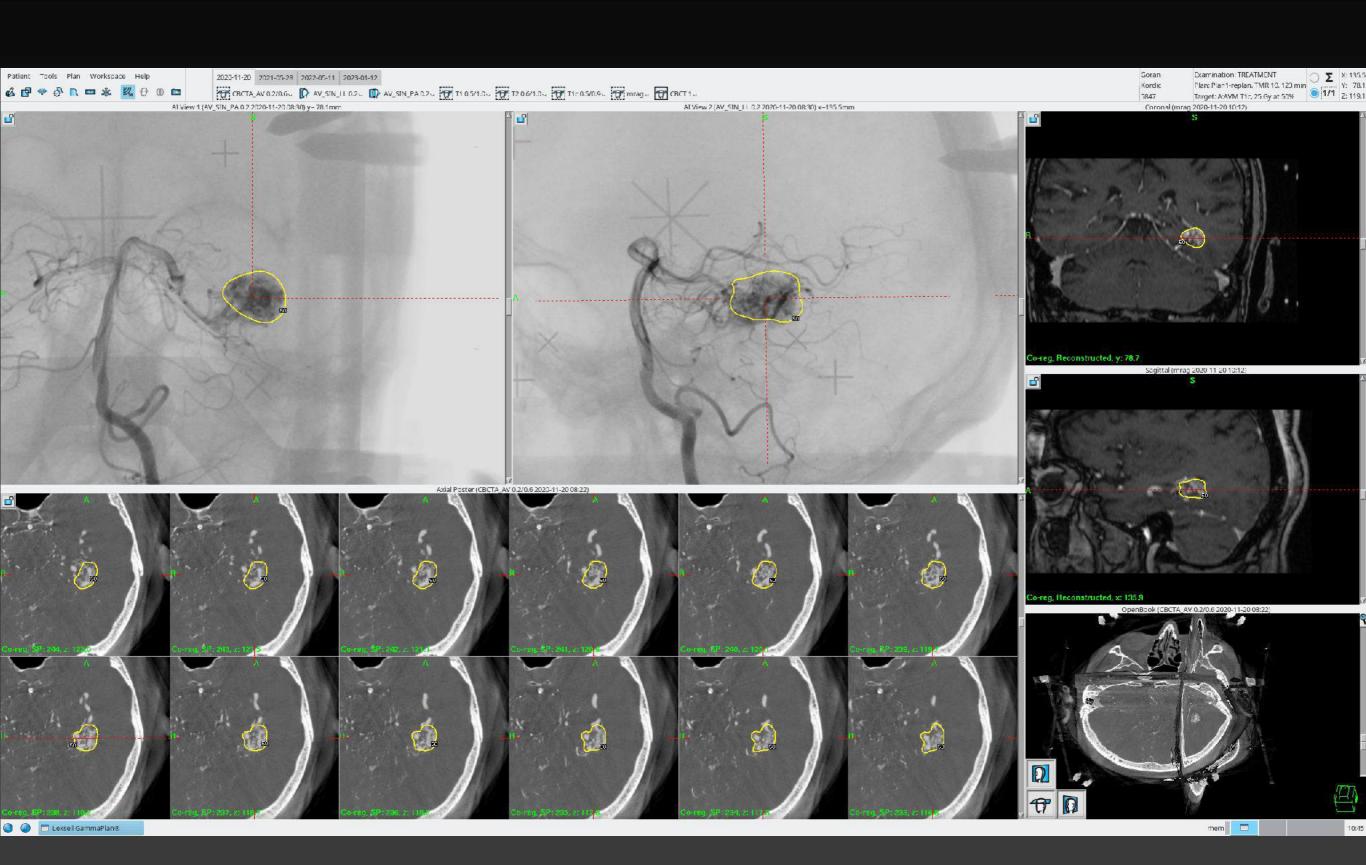


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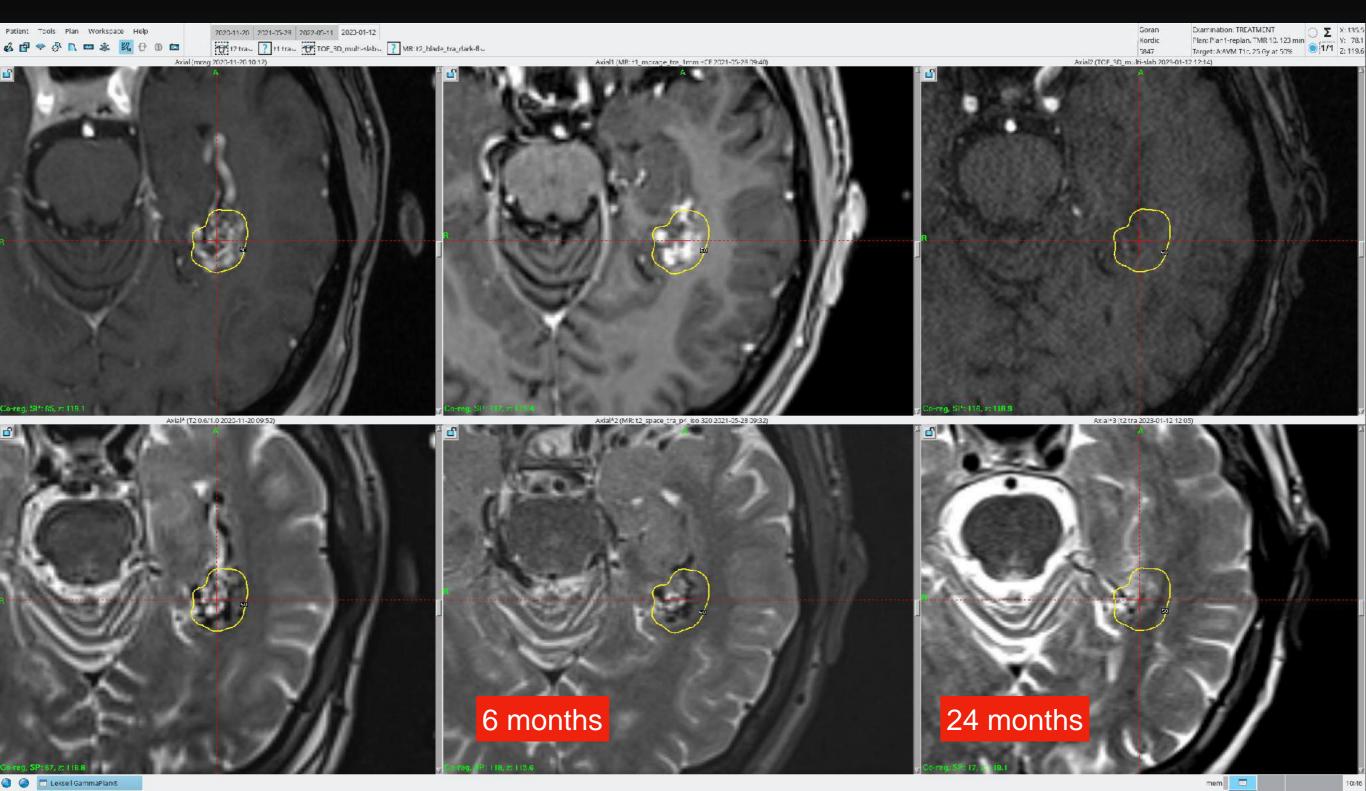
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Nidus volume : 1,571 ccm

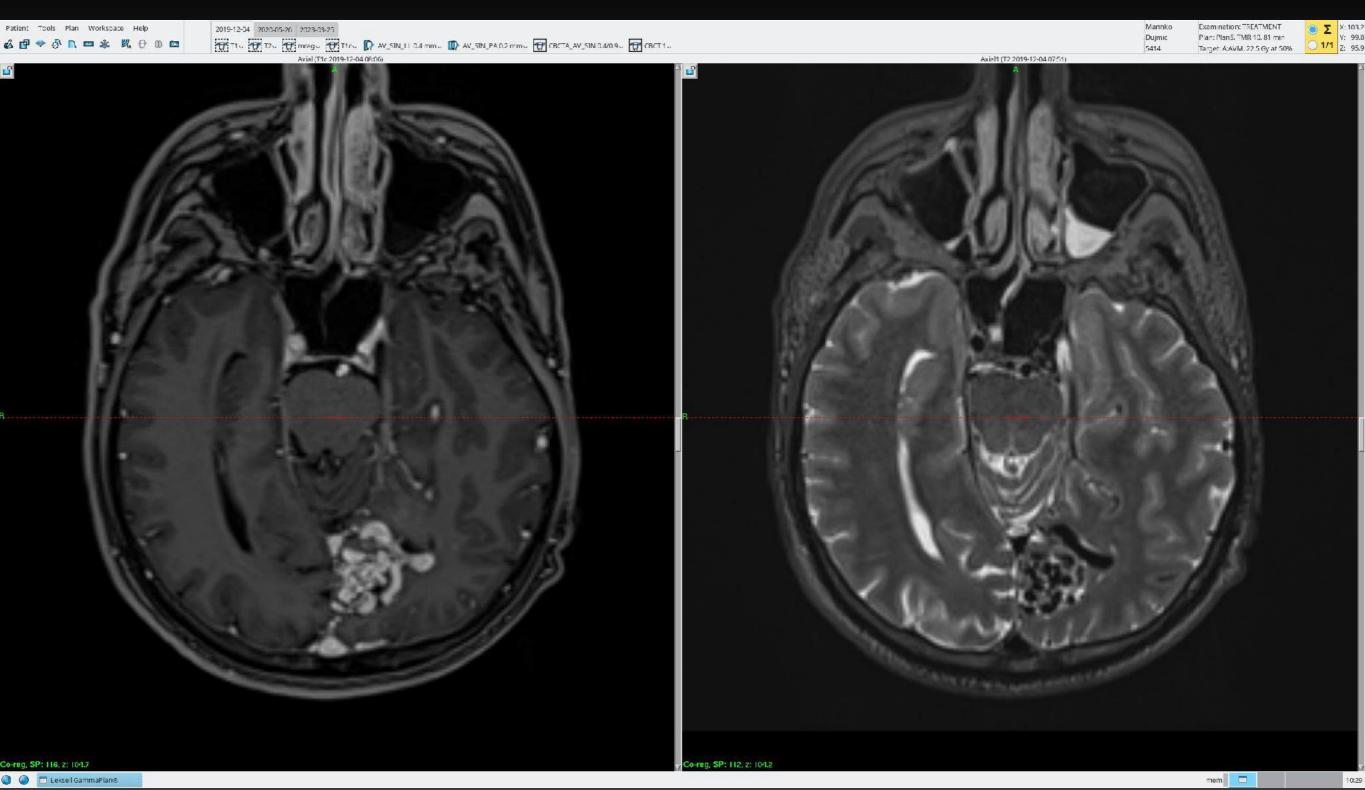
PD 25 Gy / 50% isodose

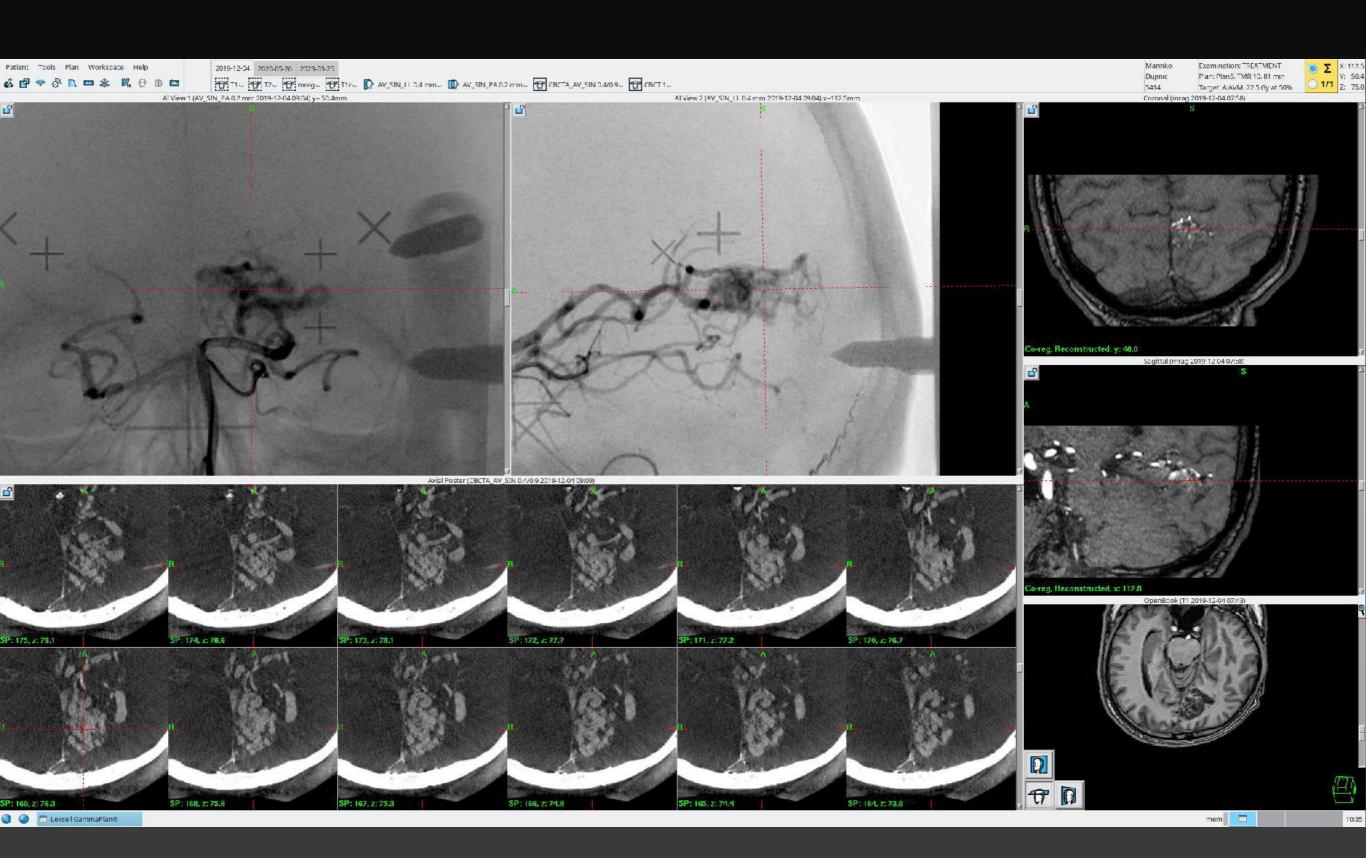


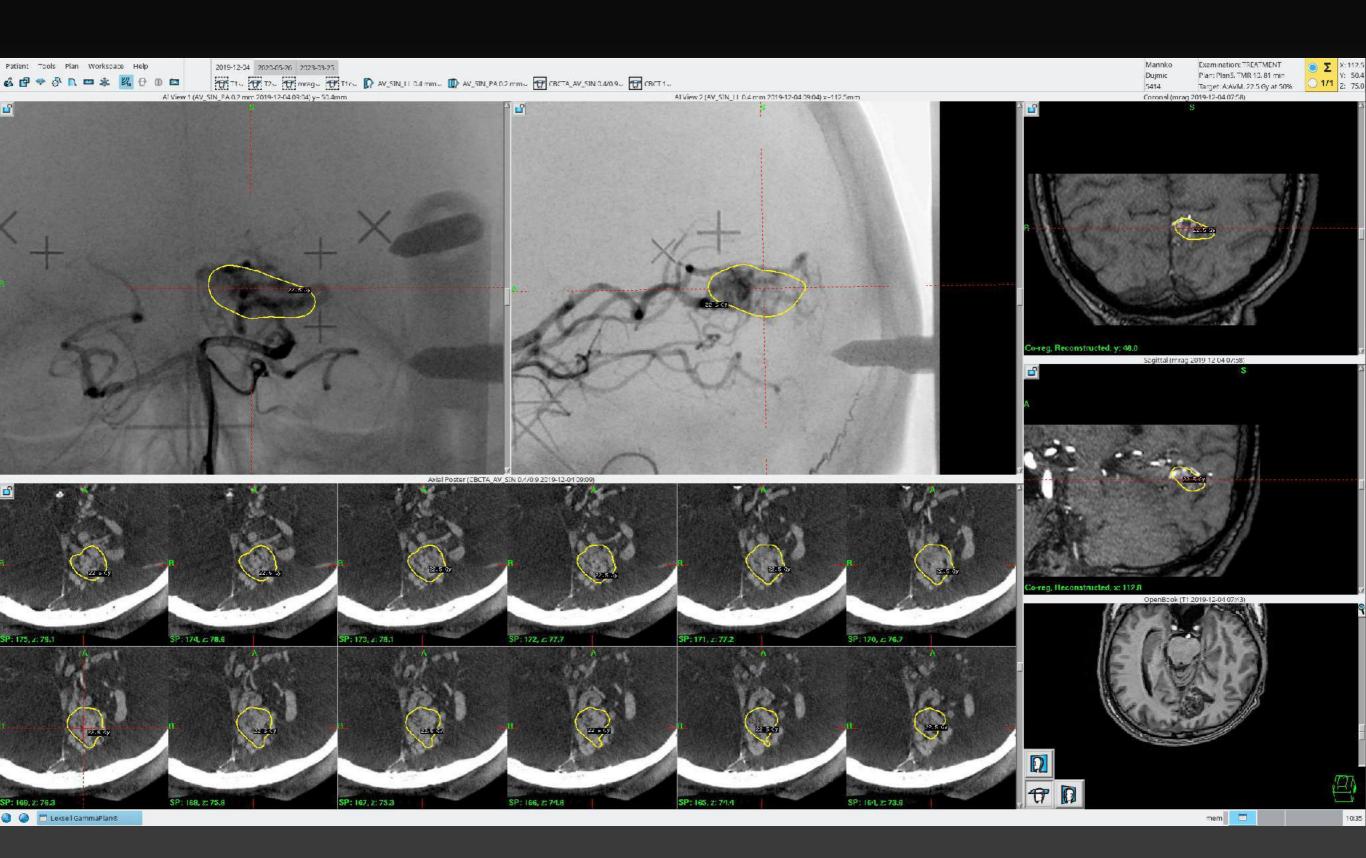




- 54 y.o. male
- Medical history chronic gastritis, depression
- development of new-onset headaches
- CT-A, MR-A unraptured bAVM occipital
- admitted to Neurology for DSA evaluation

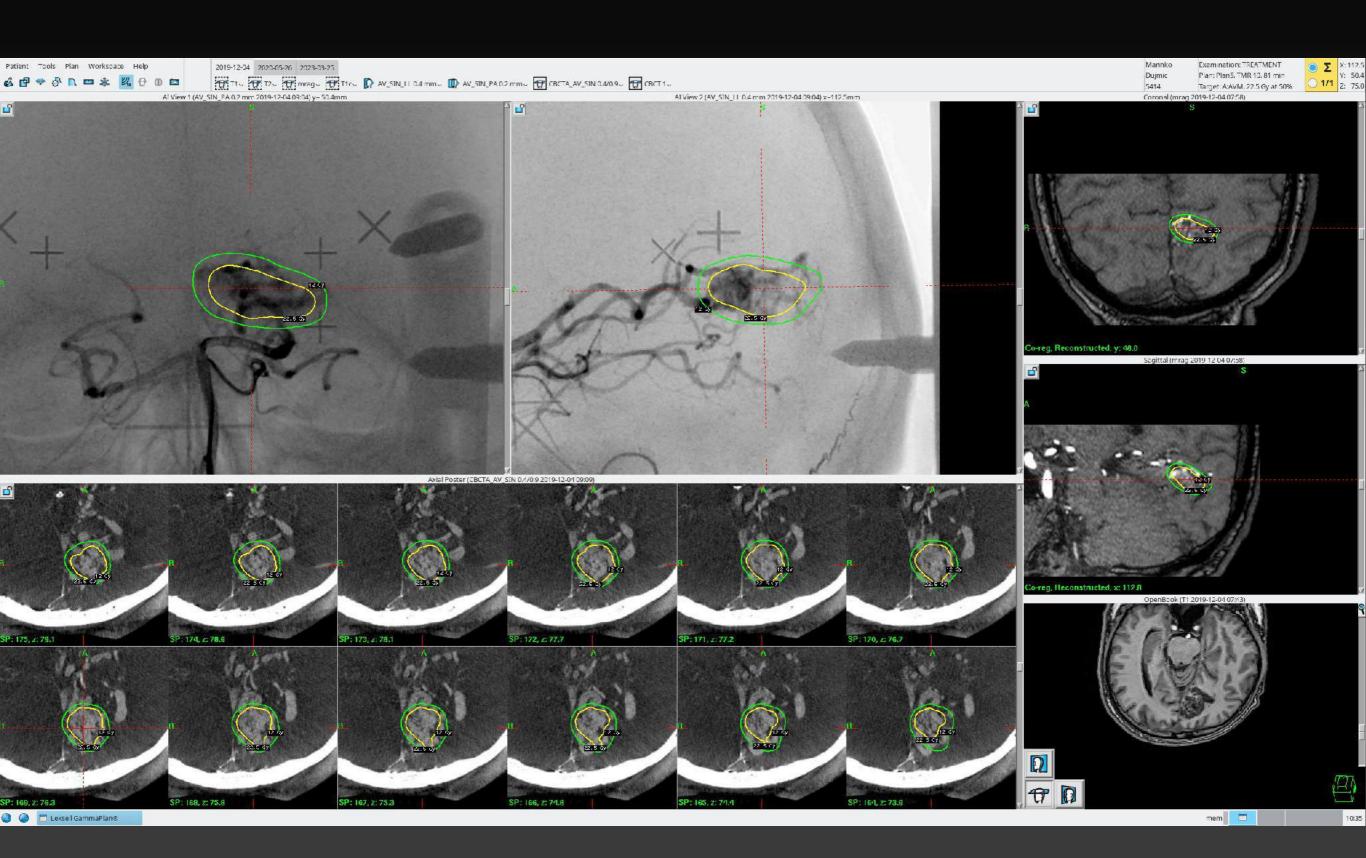


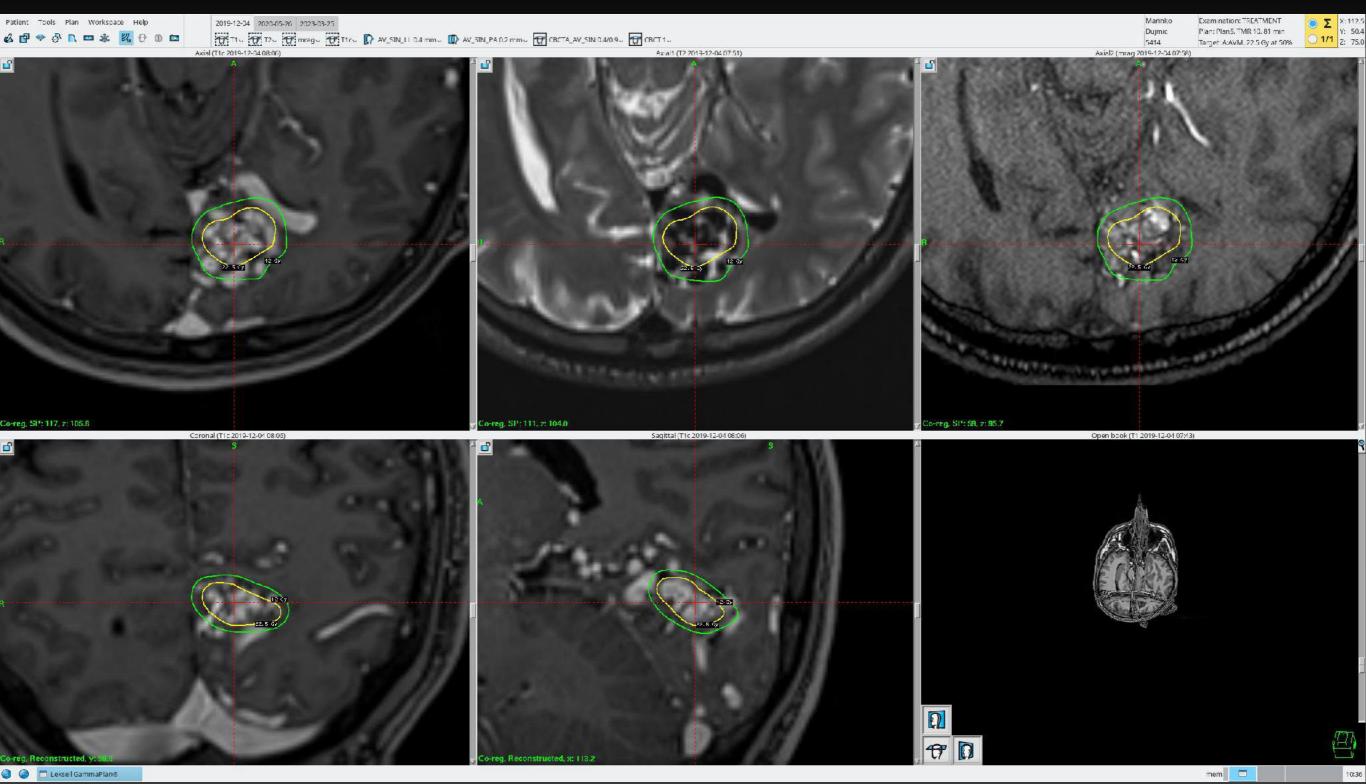


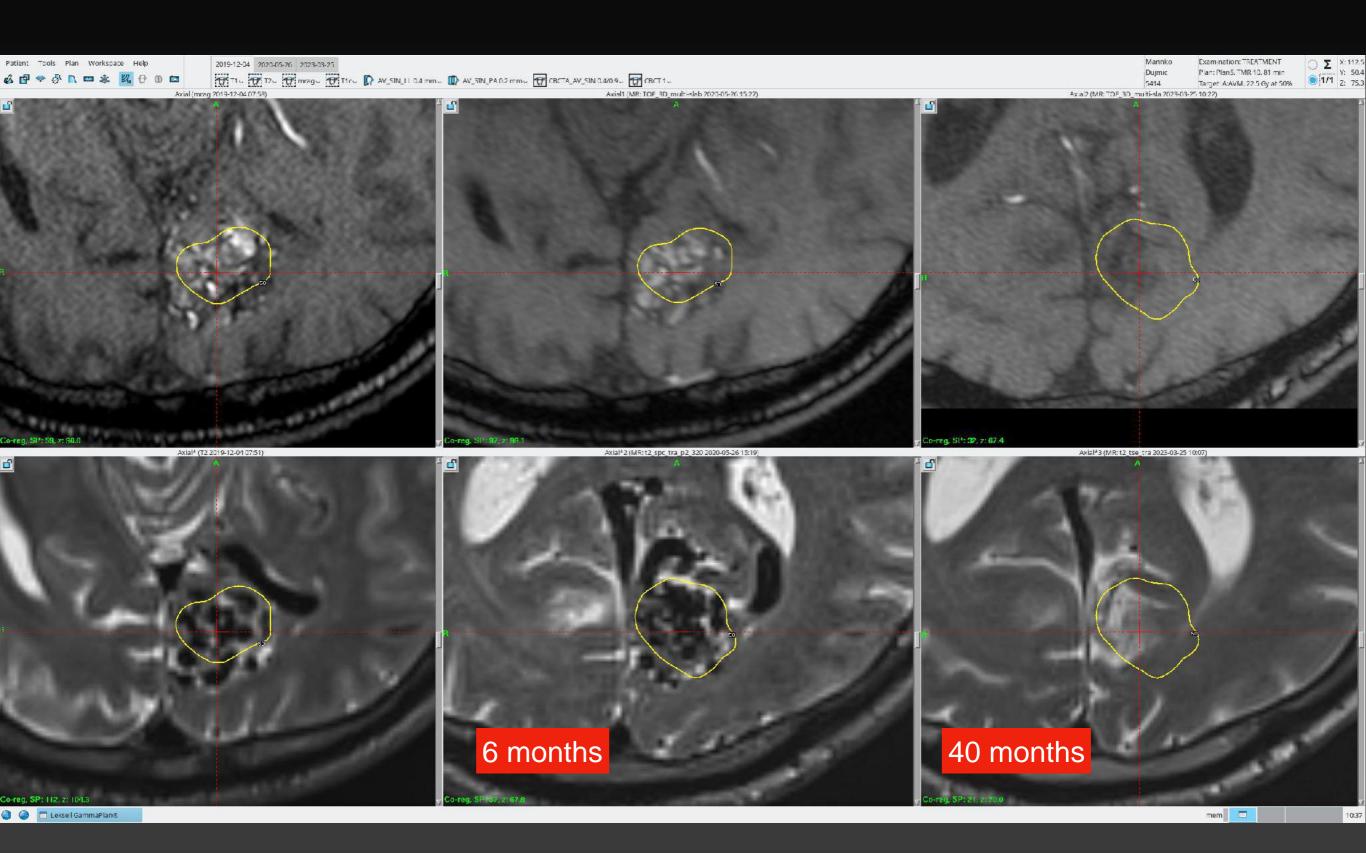


Nidus volume : 1,616 ccm

PD 22.5 Gy / 50% isodose









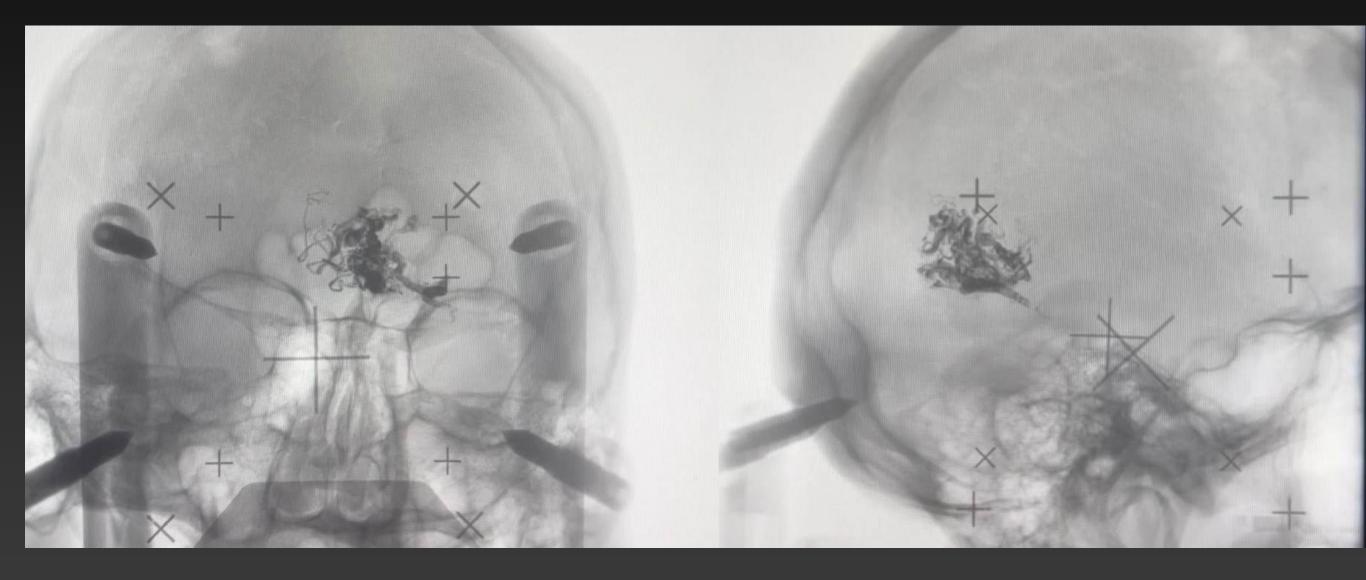
Case 3

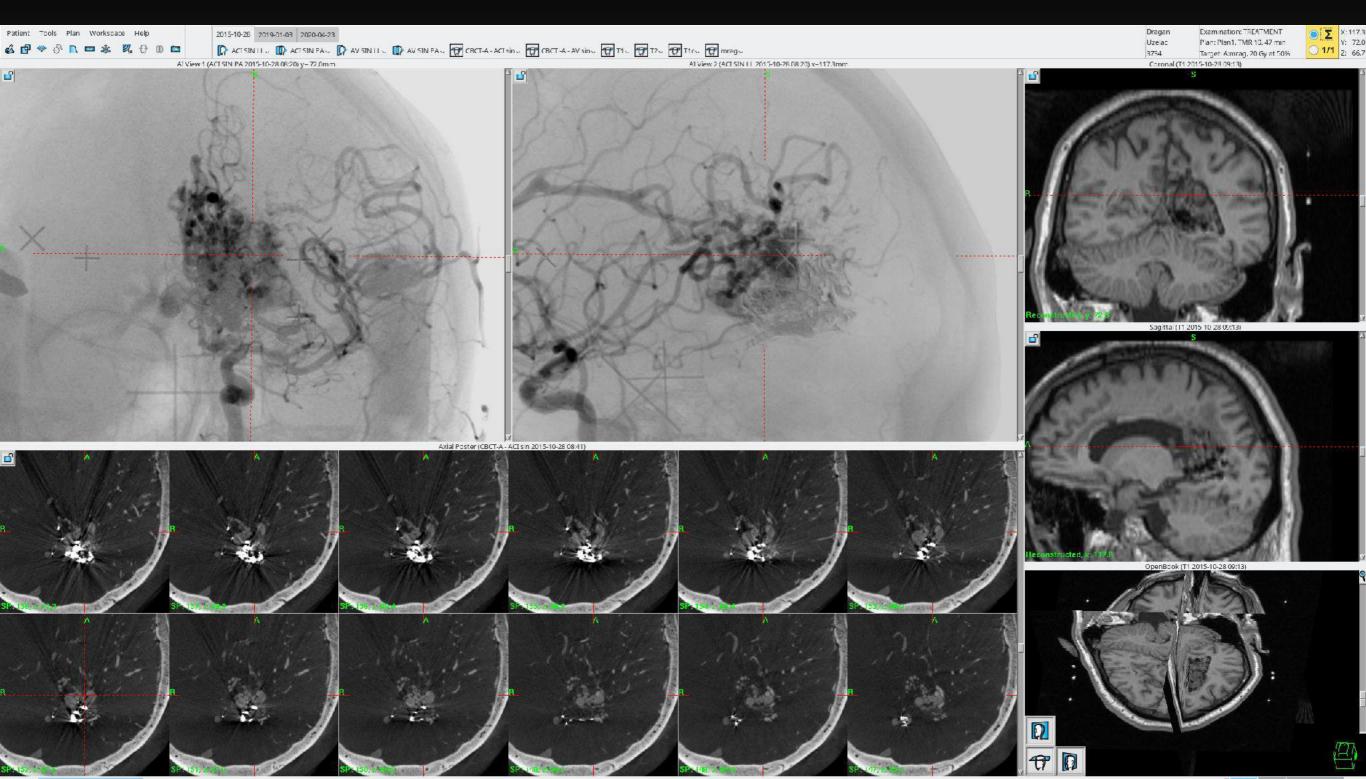


- 50 y.o. male
- Medical history IC hematoma, with hematocephalus 9 months previously
- CT-A, MR-A bleeding from ruptured bAVM occipital
- status right sided hemiparesis

- admitted to Neurology for DSA evaluation and embolisation
- partially embolised with Onyx

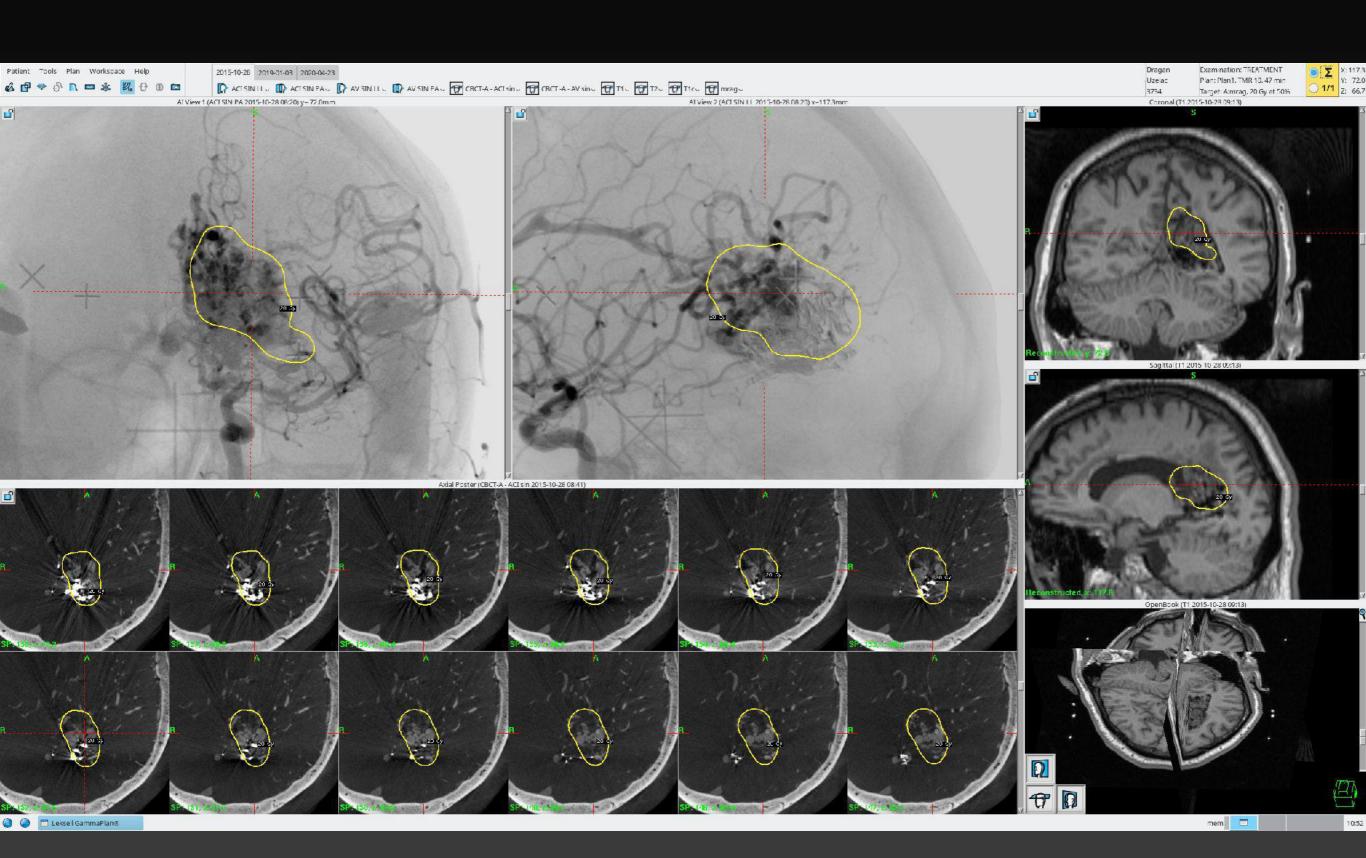
referred to radiosurgery for residual nidus





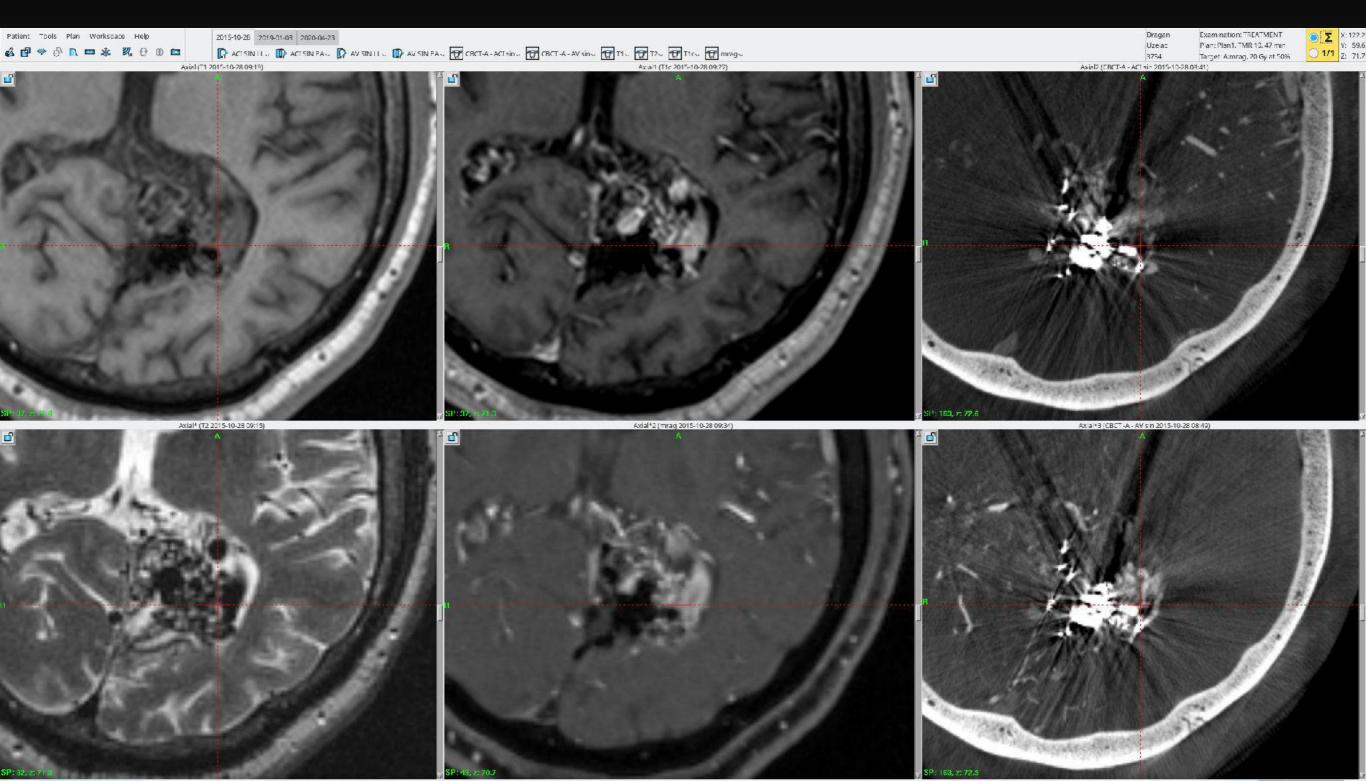
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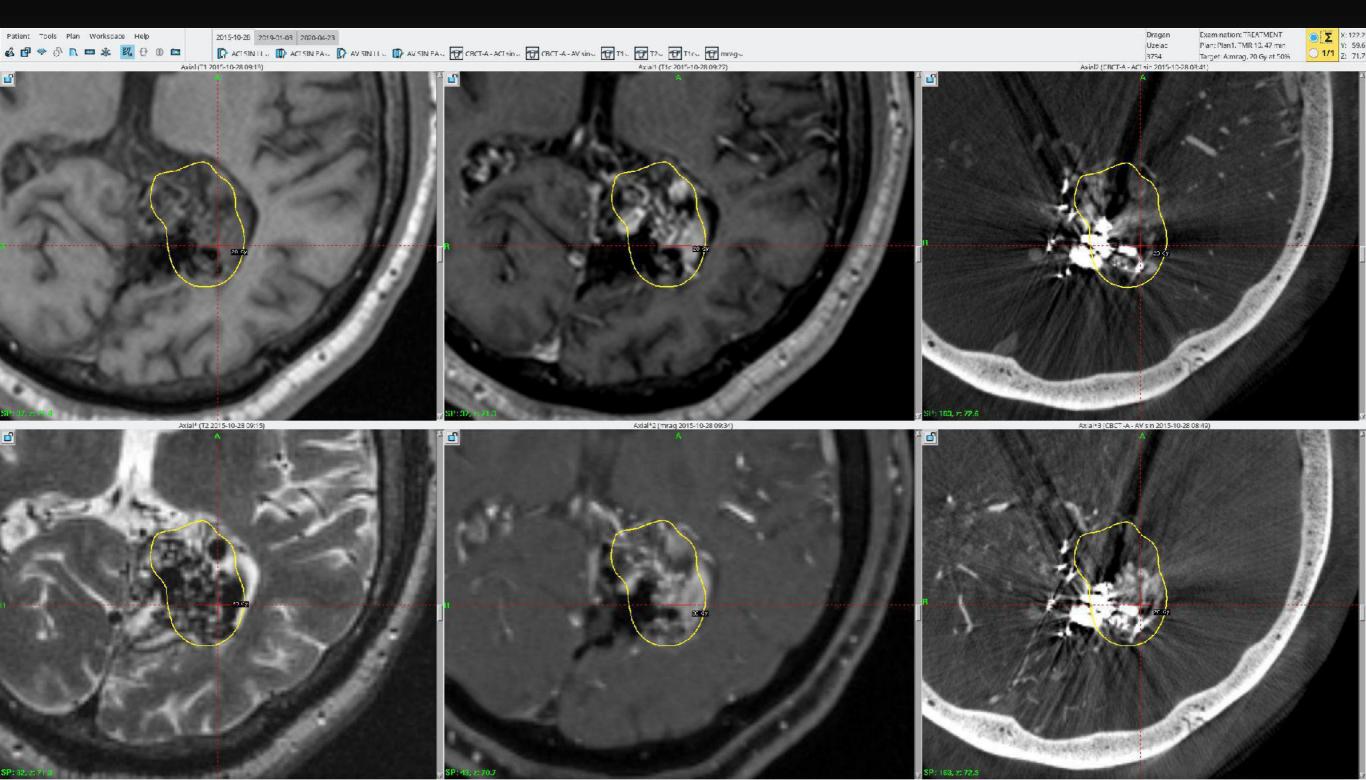
Nidus volume : 8,81 ccm

PD 20 Gy / 50% isodose



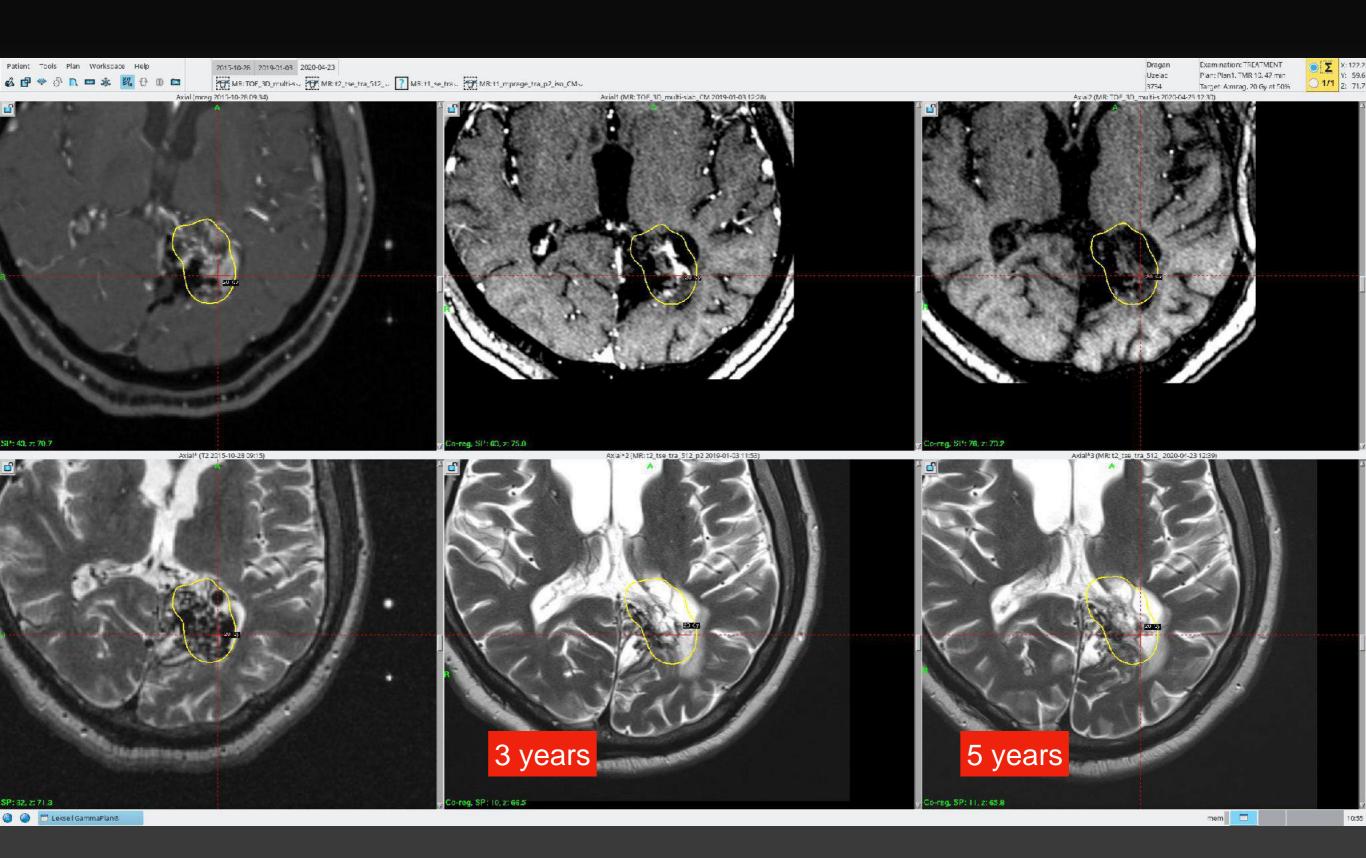
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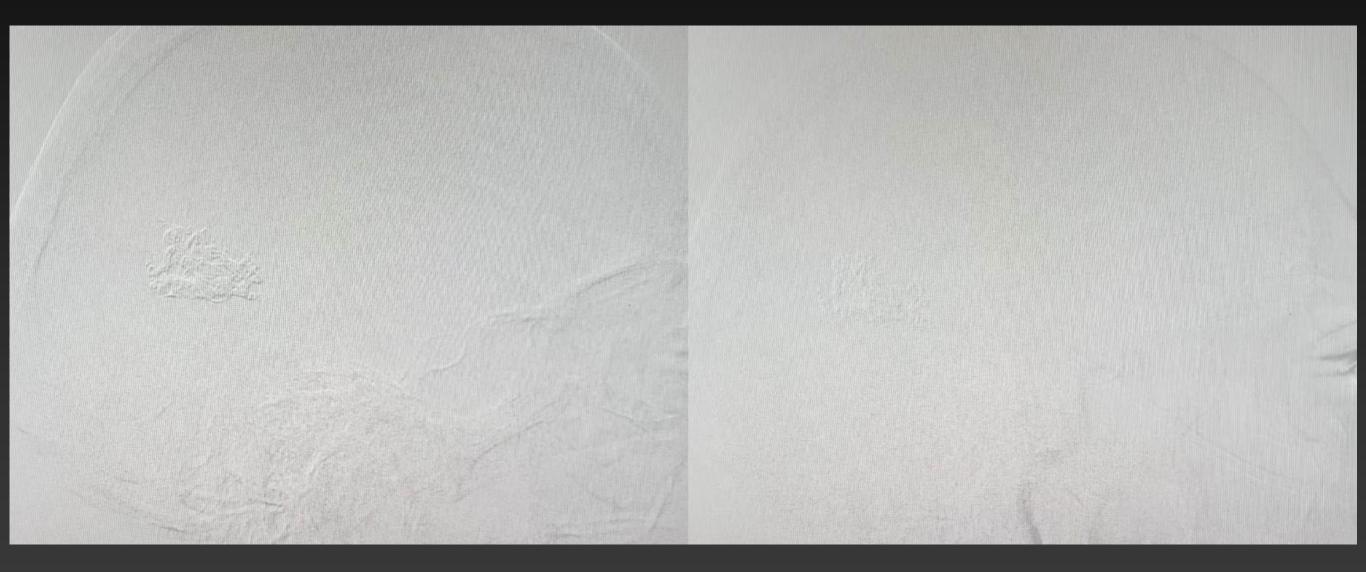
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DSA verification of complete obliteration, 5 yrs after GKRS

Conclusion

- Radiosurgery is a safe, efficient treatment method for bAVMs
- indications should be based on an interdisciplinary agreement
- factors correlating with higher occlusion
- size (volume)
- eloquence / critical structures
- (bleeding status, age)