

Radiocirugía en Malformaciones Arteriovenosas Gigantes

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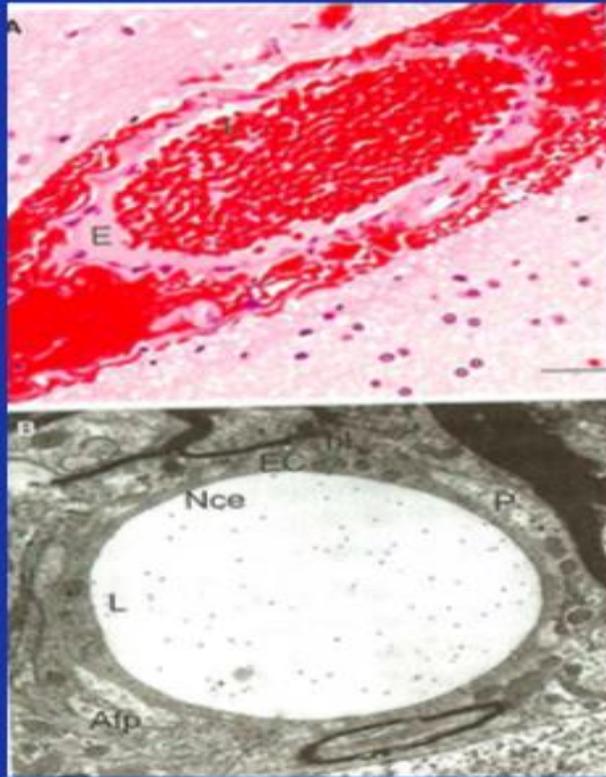
Incidencia MAV: 1,2 / 100.000 habitantes / año
Prevalencia: 18 / 100.000 habitantes

Autopsias: 613 MAV / cien mil habitantes / año

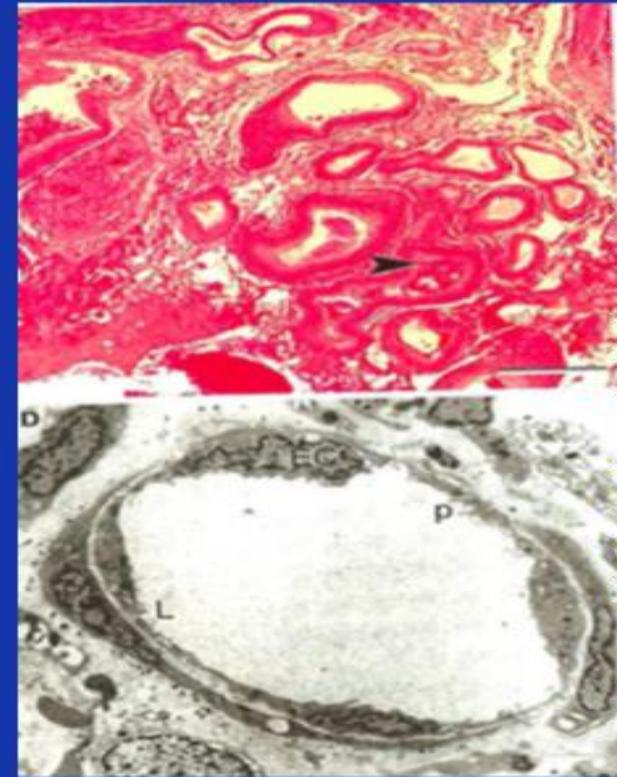
Mas de 65.000 tratamientos con RC hasta el año 2008

Incidencia **MAV grandes/gigantes:** 30% aprox. de las MAV

MAVs, histología: Vaso normal – Vaso malformativo



Vaso normal: Endotelio continuo



Conglomerado vascular en una MAV.
Vasos formados por una capa discontinua de células endoteliales

**Responses of Arteriovenous Malformations to Radiosurgery:
Ultrastructural changes**
Jian Tu, Marcus Stoodney, Michael Morgan, Kingsley Storer.

Neurosurgery 58: 749-758, 2005

La clasificación de *Spetzler-Martin* (5 grados)

- 1 punto
- 2 puntos
- 3 puntos

MAV < 3 cm de diámetro
MAV 3-6 cm de diámetro
MAV > 6 cm de diámetro

+1 punto
+1 punto

MAV localizada en áreas elocuentes de cerebro
MAV con drenaje venoso profundo

Está diseñada para predecir **resultados de CIRUGÍA**

TABLE 1: Grading systems for AVMs.

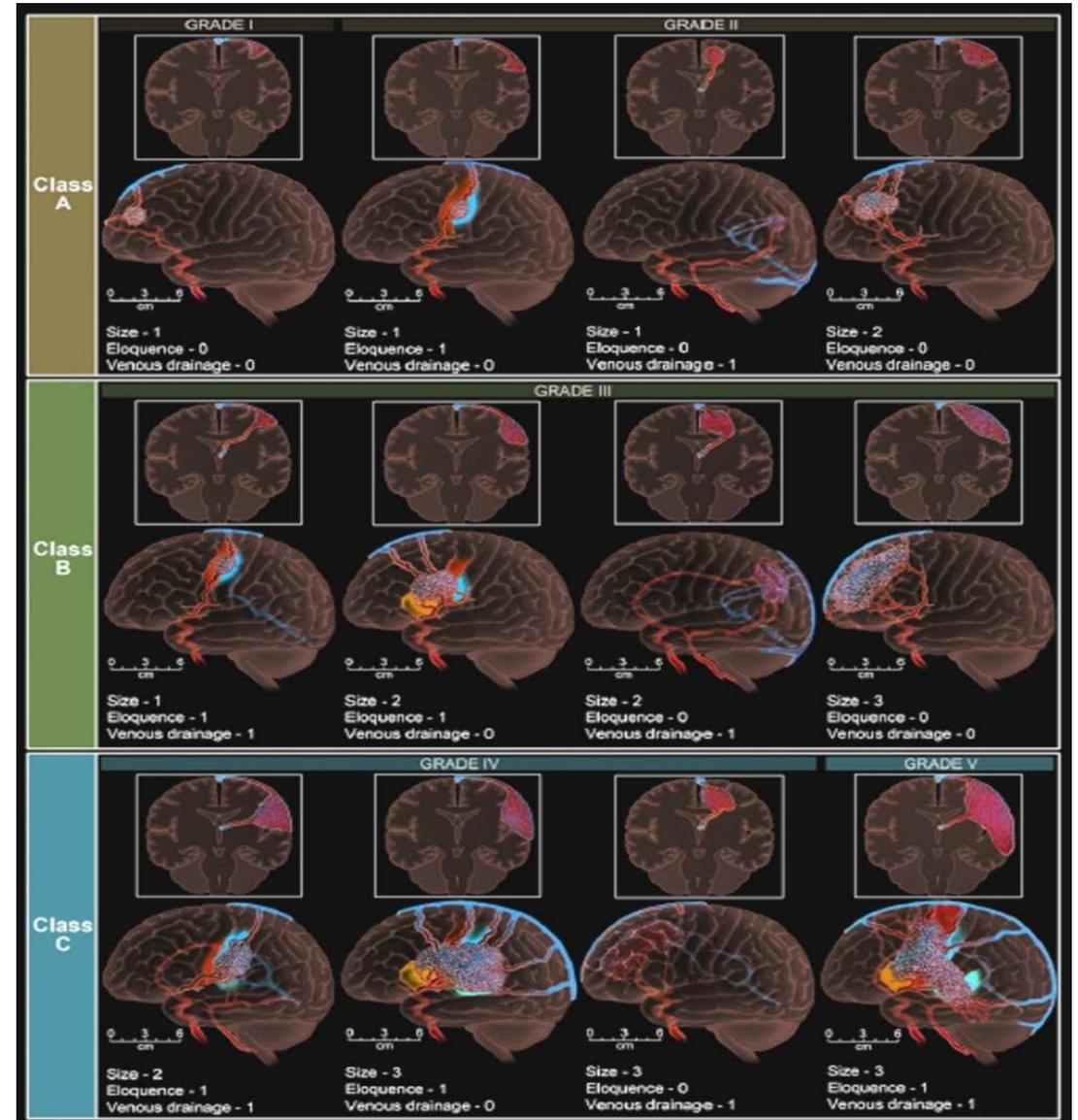
Spetzler-Martin grading system for AVMs [9]		Spetzler-Ponce grading system for AVMs [10]			Grading score proposed by Lawton [11]	
	Points	Class	Spetzler-Martin grade			Points
Size of nidus				Age (years)		
Small (<3 cm)	1	A	I, II	Surgical resection	<20	1
Medium (3-6 cm)	2	B	III	Multimodality treatment	20-40	2
Large (>6 cm)	3	C	IV, V	No treatment	>40	3
Location				Unruptured presentation		
Noneloquent site	0				No	0
Eloquent site	1				Yes	1
Pattern of venous drainage				Diffuse		
Superficial only	0				No	0
Deep	1				Yes	1

Equivalencia escalas Spetzler-Martin

vs.

Ponce -Spetzler

Se consideran MAV Grandes/Gigantes:
Grupos 3D,4 y 5



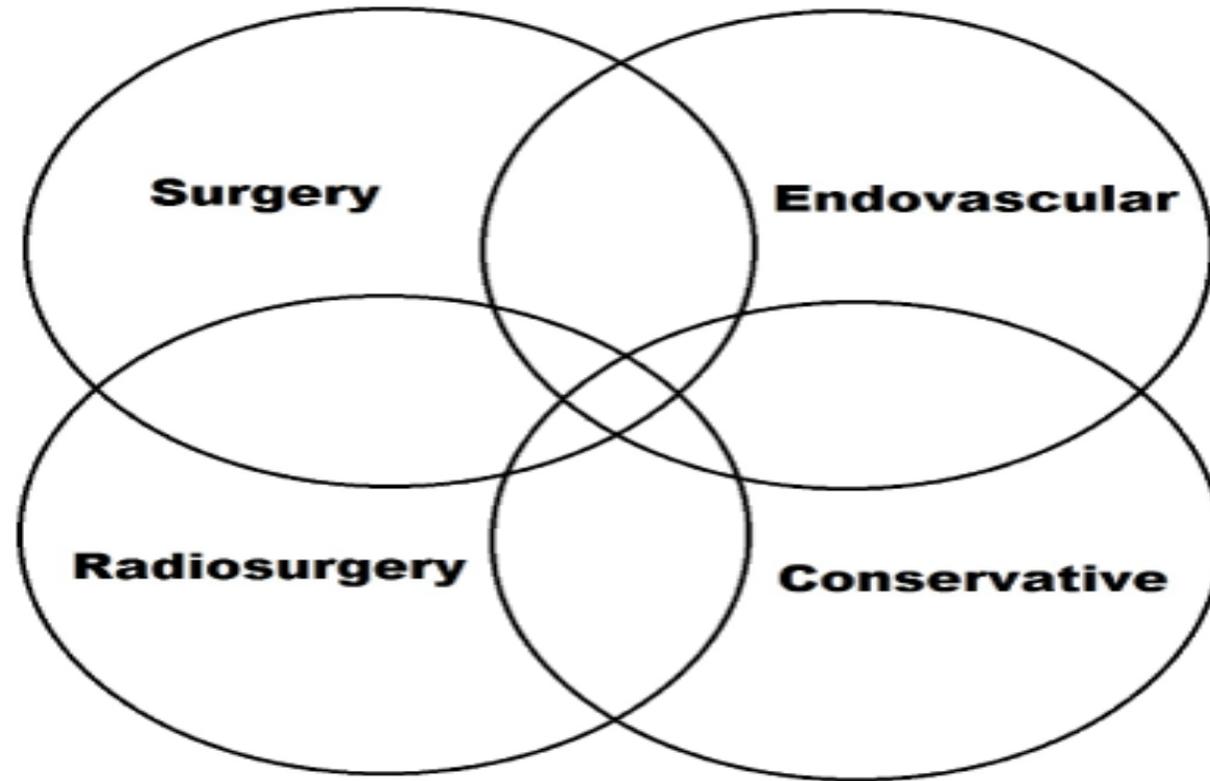
CONCEPTO: no definido unánimemente:

- Unos autores: MAV > 3 cm (14 cc en volumen) MAV >
- Otros autores: 10 cc, ó > 30 cc ó > 40

- **Según clasificación de Spetzler-Martin:**

- ❖ Grandes: MAV grado **IV** (> 3 cm)
- ❖ Gigantes: MAV grado **V** (> 6 cm)
- ❖ Clase **C** de la escala Ponce-Spetzler

OPCIONES



Cirugía en las MAV

- Papel bien establecido en las MAV grados I y II; de elección en las MAV I-II con sangrado reciente [riesgo triple de resangrado (6-8%) en el 1^{er} año]
- En las MAV Grado III ¿tratamiento multimodal?. Individualizar
- En los Grados IV-V : ¿mejora el tratamiento el resultado de la evolución natural?

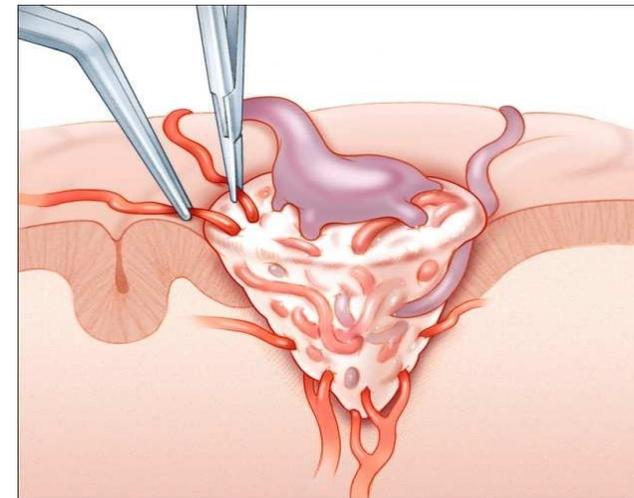
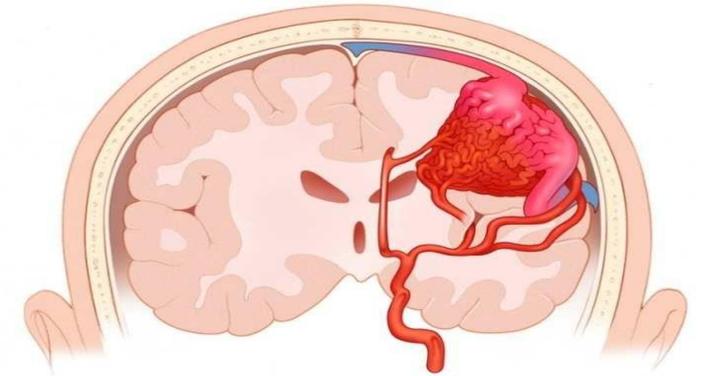


TABLE 1: Proposed 3-tier classification of cerebral AVMs with treatment paradigm

Class	Spetzler-Martin Grade	Management
A	I & II	resection
B	III	multimodality treatment
C	IV & V	no treatment*

* Exceptions for treatment of Class C AVMs include recurrent hemorrhages, progressive neurological deficits, steal-related symptoms, and AVM-related aneurysms.



Multidisciplinary Approach to Arteriovenous Malformations

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Abstract

The treatment of arteriovenous malformations (AVMs) depends on the efforts of a multidisciplinary team whose ultimate goal is to achieve better results when compared to the natural history of the pathology. The role of adjuvant treatment modalities such as radiosurgery and endovascular embolization is discussed. Treatment strategies and surgical results from a personal series of 344 patients operated in a 10-year period are reviewed. The Spetzler and Martin classification was modified to include subgroups IIIA (large size grade III AVMs) and IIIB (small grade III AVMs in eloquent areas) to assist the surgical resection criteria. The treatment strategy followed was surgery for grades I and II, embolization plus surgery for grade IIIA, radiosurgery for grade IIIB, and conservative for grades IV and V. According to the new proposed classification 45 (13%) patients were grade I, 96 (28%) were grade II, 44 (13%) grade IIIA, 97 (28%) grade IIIB, 45 (13%) grade IV, and 17 (5%) were grade V. As for surgical results 85.8% of the patients had a good outcome (no additional neurological deficit), 12.5% had a fair outcome (minor neurological deficit), 0.6% had a bad outcome (major neurological deficit), and 1.2% died. These figures indicate that the treatment of AVMs can achieve better results compared to the natural history if managed by a well trained group of specialists led by an experienced neurosurgeon.

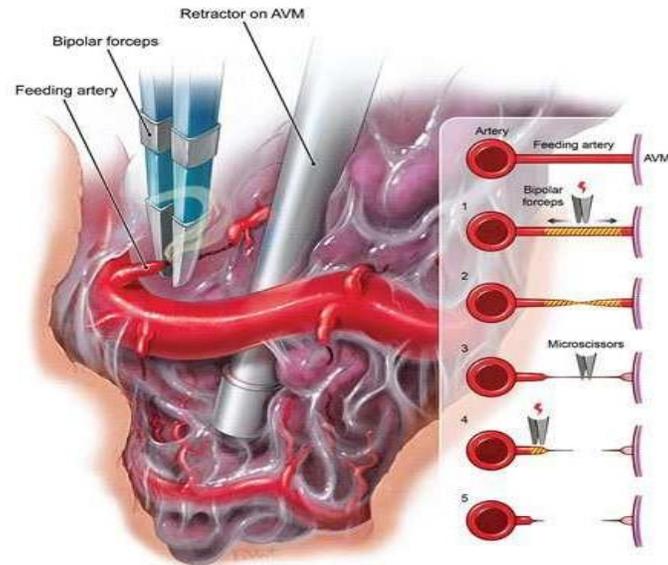
Editorial

Spetzler–Martin Grades IV and V arteriovenous malformations

ROBERTO C. HEROS, M.D.

Department of Neurological Surgery, University of Miami School of Medicine, Miami, Florida

J Neurosurg 98:1–2, 2003



This timely and excellent paper by Han, et al., essentially makes three important points that I will discuss separately. The first point is that treatment of Spetzler–Martin Grades IV and V arteriovenous malformations (AVMs) is associated with very significant risks of morbidity and mortality and, therefore, we must be extremely conservative and selective in recommending treatment to patients harbouring these lesions. The second point made by the article is that partial treatment of Grades IV and V AVMs is likely to alter the natural history of the lesion negatively and to lead to a higher rate of bleeding than no treatment at all. I also agree strongly with this point, although the case is a bit more difficult to make than the first issue.

The third point made by the authors is one with which I would like to agree, but supporting evidence is relatively weak.

RESPONSE: We agree completely with Dr. Hero's comments. He emphasizes the points that we wanted to stress in our paper with greater eloquence than we were able to muster. We also agree that the evidence concerning whether smaller AVMs hemorrhage more frequently than larger lesions is slim. Unfortunately, papers on the natural history of these lesions do not provide uniform data on this point. We appreciate Dr. Heros' kind comments and look forward to further debate on the critical question of decision making regarding these formidable lesions.

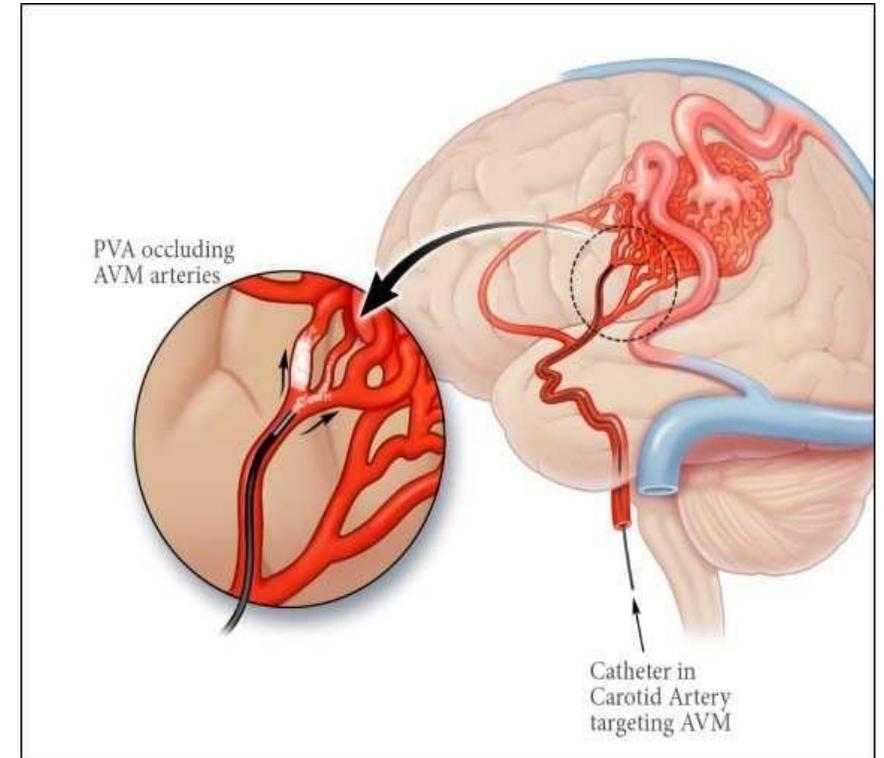
ROBERT F. SPETZLER, M.D. Barrow Neurological Institute Phoenix, Arizona

EMBOLIZACIÓN

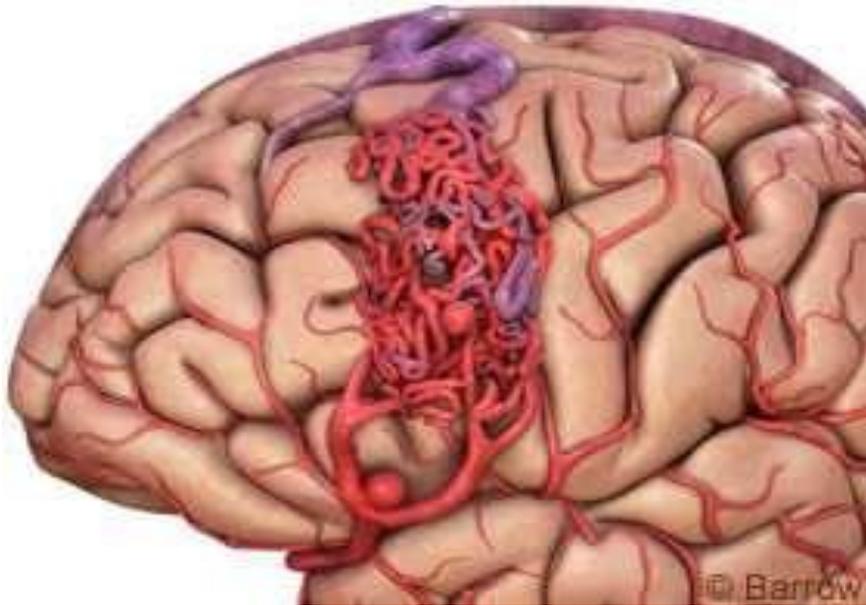
Criterios de Embolización:

- Reducir volumen real
- Reducción de flujo
- Discusión previa con neurocirujano
- Se puede aplicar también después de la radiocirugía--> ¿acelera obliteración?
- Previo a la intervención quirúrgica

La decisión terapéutica tiene que ser conjunta.



EMBOLIZACIÓN



Flow reduction without AVM volume reduction provides no benefit before radiosurgery and, in fact, may make it more difficult to provide a conformal dose plan at the time of radiosurgery. As noted by the authors, “a major difficulty was the irradiation of large AVMs when partial embolization had divided the AVM into multiple compartments.”

BRUCE E. POLLOCK, M.D. L. DADE LUNSFORD, MD. DOUGLAS
KONDZIOLKA, M.D. JOHN C. FLICKINGER, M.D. University of Pittsburgh Medical
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Radiocirugía

- Más de 100.000 pacientes tratados en todo el mundo, desde 1970
- Alta eficacia en MAV grado I-II-III y hasta 3 cm. de diámetro
- Tiempo medio de oclusión aproximado 3 años
- Mínima morbilidad
- Mínima mortalidad
- Se puede aplicar en cualquier localización: áreas elocuentes
- ¿ Se puede utilizar con éxito en MAV grandes/gigantes?

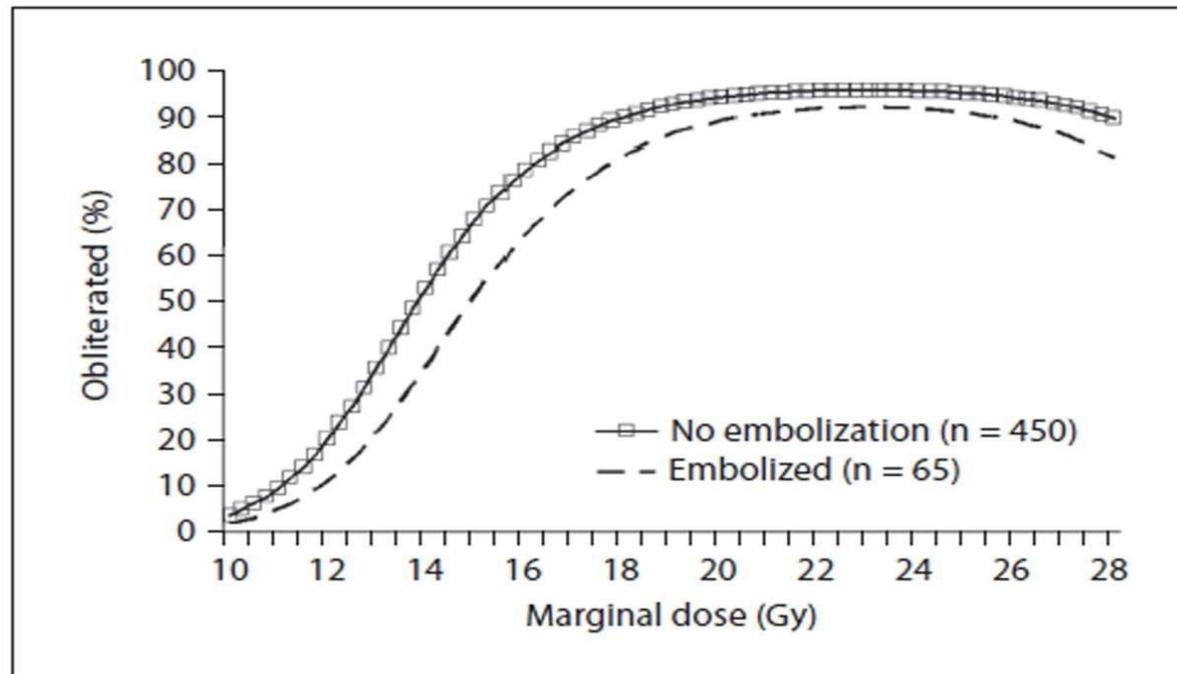
Radiobiología en MAV

- La irradiación produce dos efectos importantes, y quizá contrapuestos, **proliferación y destrucción**.
- En MAV la irradiación produce un **proceso de proliferación** de las células de la adventicia y del endotelio (endarteritis obliterante).
- Se ha demostrado que la irradiación produce una respuesta tardía en las células endoteliales, con un cociente α/β bajo, a partir de los 10 Gy.
- La pregunta que se plantea es:

mayor dosis = mayor respuesta

Curva dosis-respuesta en Radiocirugia - MAV cerebrales

Fig. 2. Dose response curves for AVM obliteration according to prescription dose and history of prior embolization from 515 patients with >5 years of follow-up. Logistic model, $\alpha/\beta = -45.9$; maximum obliteration at 23 Gy; 95.7% with no embolization, 91.8% with prior embolization.



Flickinger JC, 2002

Cambios Histológicos

- Tras la RCE en las MAV los cambios más frecuentes de los vasos de pequeño y mediano calibre ocurren en la **íntima**; esto se manifiesta por **edema** y **vacuolización** de las células endoteliales.
- La expansión progresiva de la íntima, incluyendo la proliferación de las células del músculo liso y **engrosamiento** de capas **media** y **adventicia**, causan un **estrechamiento** concéntrico de la luz del vaso.

Radiosurgery in AVM I.

pathological changes in nidus vessels

Endothelial cell damage

platelet aggregation, fibrin microthrombi

migration/proliferation of myofibroblasts, pericytes

a

Radiosurgery in AVM II.

acellular hyalinised vessels

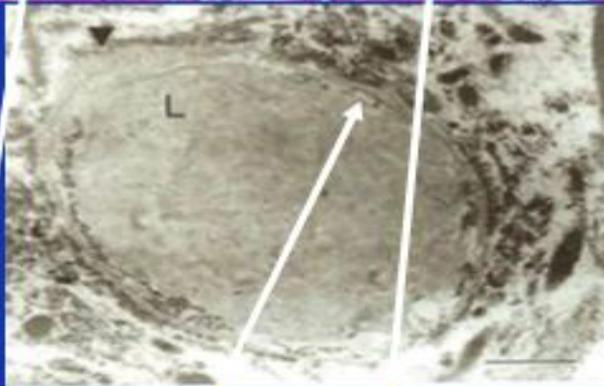
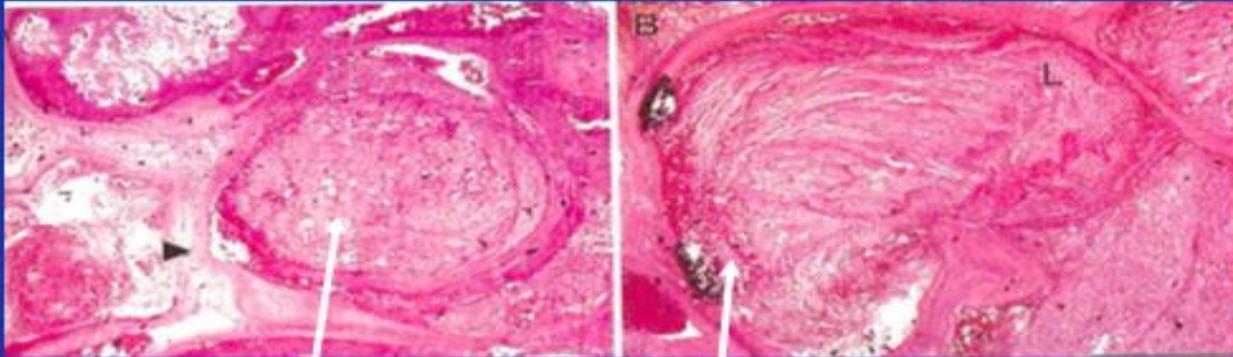
progressive occlusion of vessels' lumina

transformation of myofibroblasts into resting cells

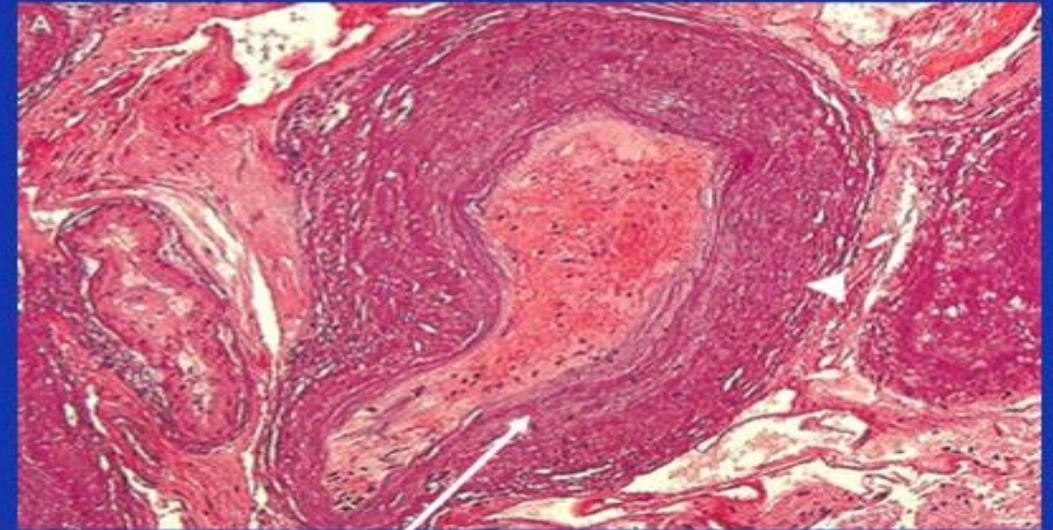
b

Fig. 6. Summary of pathological changes evoked by radiosurgery on AVM vessels.

Cambios en las MAVs post Rc



Oclusión por trombps y degeneración hialina de las paredes a los 48 m. de la Rc.



Neoproliferación de las células musculares lisas a los 33m. de la Rc. Engrosamiento de la capa media y estenosis de la luz vascular

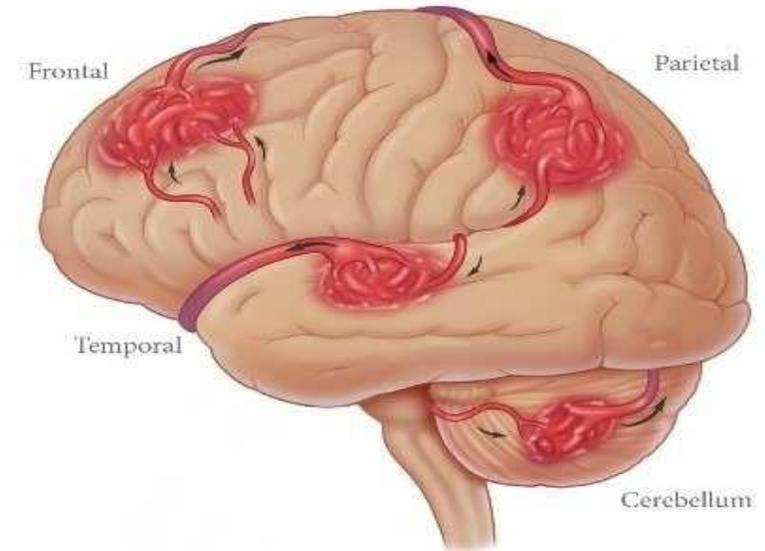
Responses of Arteriovenous Malformations to Radiosurgery: Ultrastructural changes

Jian Tu, Marcus Stoodney, Michael Morgan, Kingsley Storer.

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Los tres factores más importantes que determinan la obliteración de una MAV son:

- Dosis
- Volumen
- Órganos de riesgo



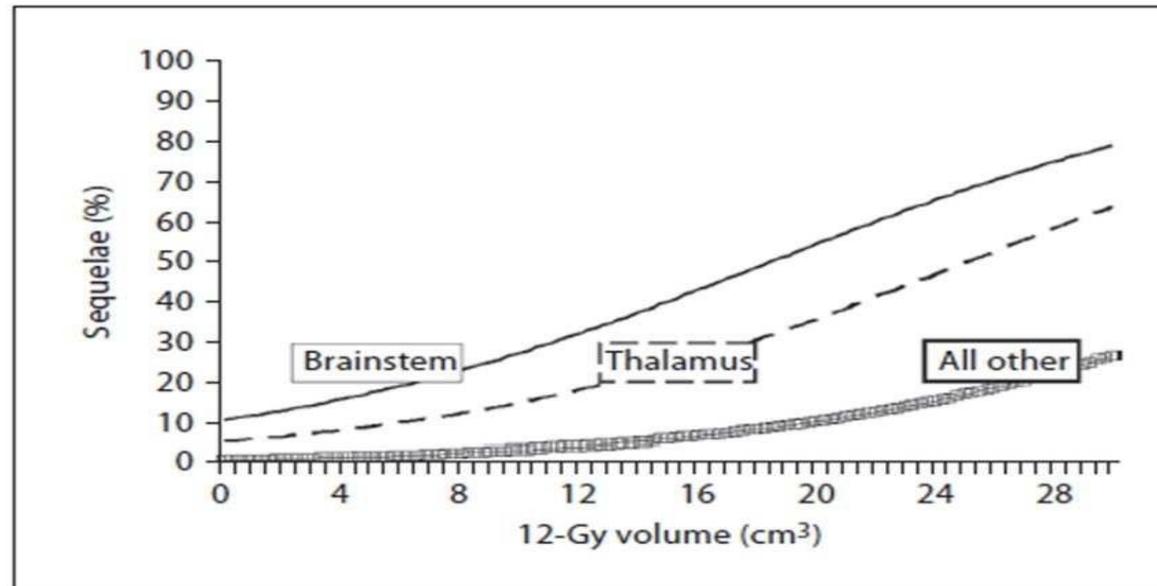
Problemas que el tamaño grande del nido plantea para la Radiocirugía

1º) para la dosis de prescripción

2º) ↑volumen implica ↑riesgo toxicidad a cerebro sano

3º) mayor cercanía a áreas elocuentes y órganos de riesgo

Fig. 1. Risk prediction curves correlating the probability of developing persistent symptomatic postradiosurgery sequelae for 815 AVM patients according to the volume of tissue receiving 12 Gy or more and location (brainstem, thalamus or other).



- La radiocirugía convencional en dosis única no es suficiente en el tratamiento de las MAV grandes/gigantes
- Las tácticas alternativas que se plantean para el cierre de MAV gigantes:
 - Radiocirugía en dos fases: Tratamiento secuencial
 - Fraccionamiento de volúmenes: “staged-volume RS”
 - Fraccionamiento de dosis: hipofraccionamiento

Mujer, 38 años
2400 cGy/ 3 Fr

ACURAY
CyberKnife
MultiPlan

Fuse Contour Align Plan Visualize
Setup Isocentric Conformal Sequential Evaluate Finetune

Utilities Settings Help

Dose Calculation
Algorithm: Ray-Tracing
Resolution: High
Uncertainty %: 0
Calculate
Prescription
Prescription
Reference Point
 Use max dose point
Dose (cGy): 2823.53
Point: Go to >>
-17.77, -38.67, -42.75
Set to Cross-hair Point
Save Plan
Save Plan
Standard Display

Patient: AINHONA MURELAC 12EV071
Plan: MAV_24G85p3f 06 Jun 2012, 09:31:
Rx: 85%, 2400.00 cGy

A A=0 B=3
B A=0 B=3
B A=0 B=3
B A=0 B=3

Ray High (C) 2400 2700 2100 1800 1500 1200 900

50 mm 1728 7996 252 149 240

X:252 Y:240 Z:149 Value:1040

ACCURAY®
CyberKnife®
 MultiPlan™

Fuse Contour Align Plan Visualize Utilities Settings Help

Setup Isocentric Conformal Sequential Evaluate Finetune

Dose Calculation
 Algorithm: Ray-Tracing
 Resolution: High
 Uncertainty %: 0
 Calculate

Prescription
 Prescription

Reference Point
 Use max dose point
 Dose (cGy): 3037.97
 Point: Go to >>
 12.99, -66.59, 25.25
 Set to Cross-hair Point

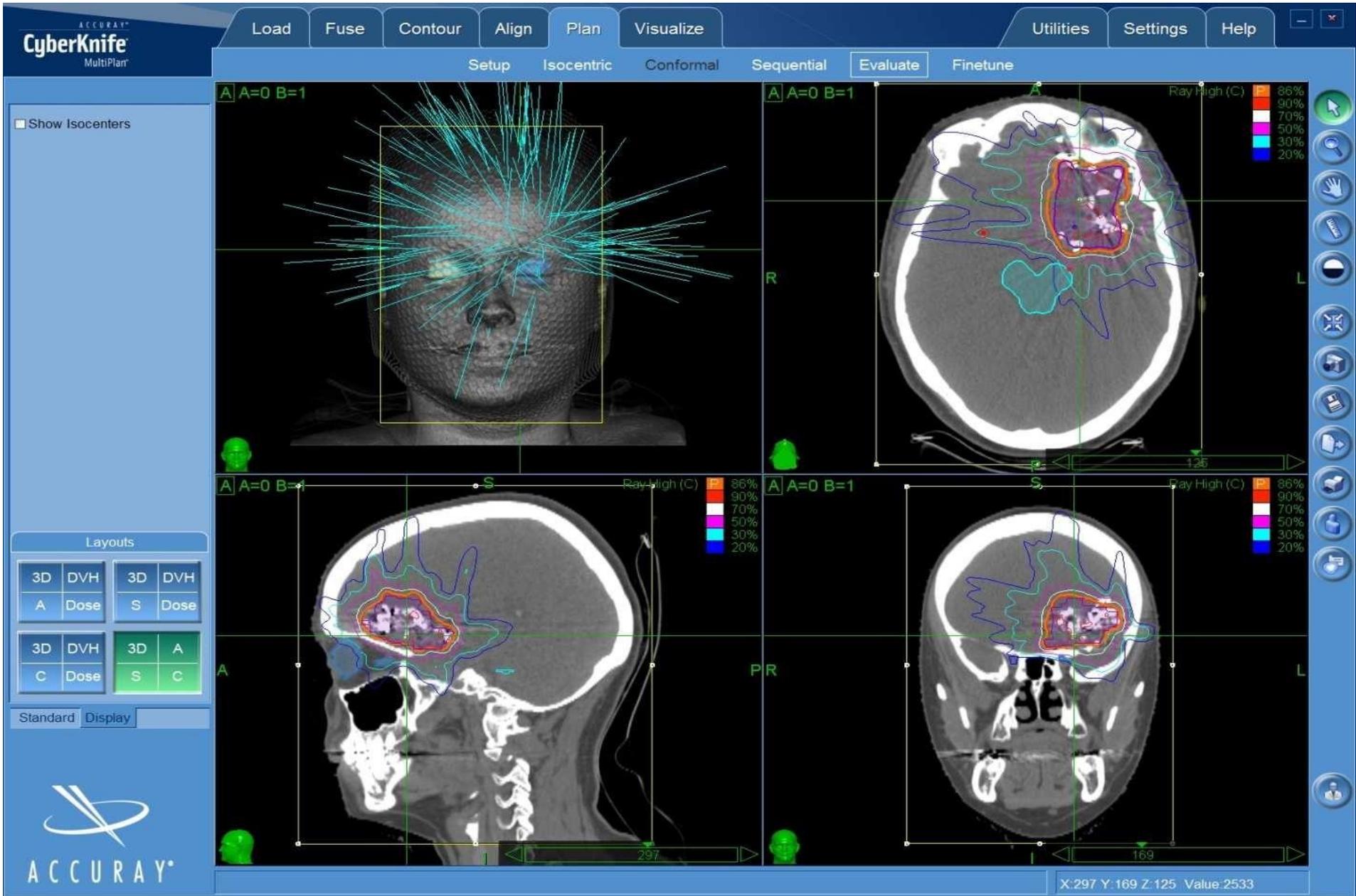
Save Plan
 Save Plan

Standard Display

ACCURAY®

X:276 Y:162 Z:147 Value:1062

Mujer, 14 años
2400 cGy/3 Fr



Mujer, 37 años,
3000 cGy/ 5 Fr

Conclusiones

En el tratamiento de las Malformaciones arteriovenosas gigantes el tratamiento debe ser multidisciplinario con la participación de Neurocirujanos, Radio Oncólogos y Neurorradiólogos intervencionistas.

Deben tomarse en cuenta las ventajas y posibles complicaciones en los tratamientos que sigan posterior a la primer intervención.

Definitivamente la Radiocirugia tiene un papel esencial en el tratamiento de malformaciones gigantes

La radiocirugía fraccionada por volúmenes y el hipofraccionamiento posiblemente nos ayudaran en afrontar definitivamente las malformaciones gigantes



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