Meningeal Hemangiopericytoma

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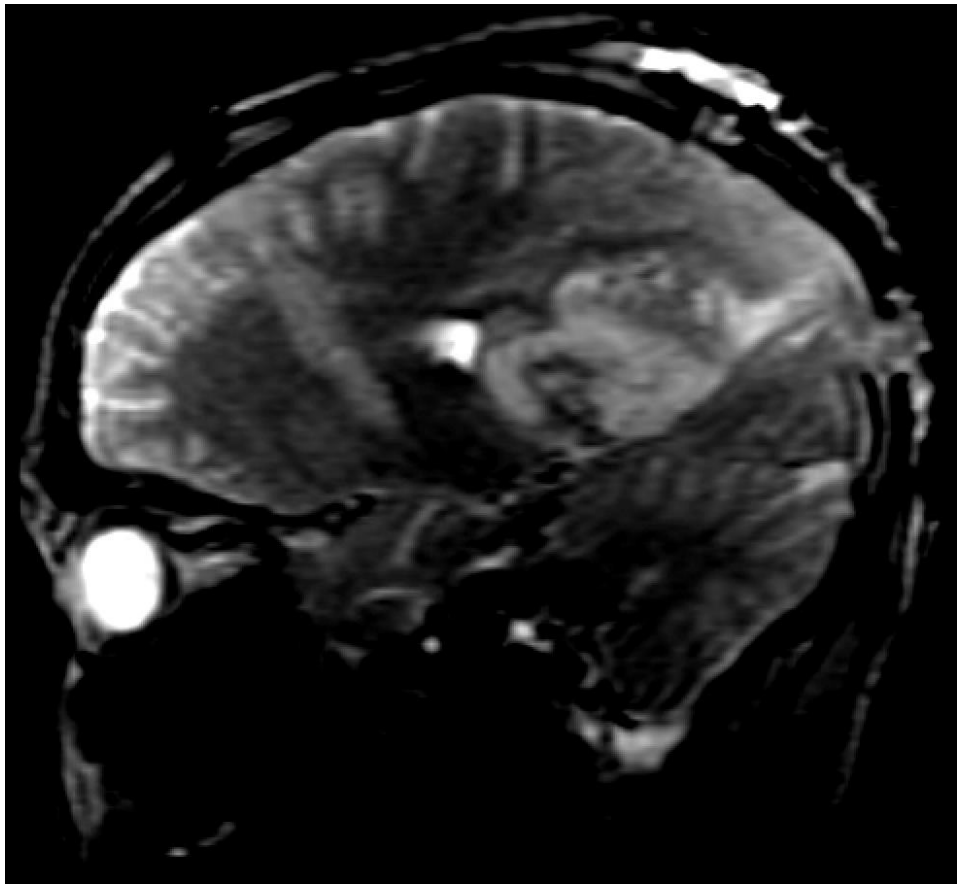
Case Presentation

- **HPI:** 19-year-old male noted “the worst headache of his life” associated with left visual field abnormalities
- **PMHx:** None
- **PSHx:** None
- **FHx:** No first-degree relatives with cancer
- **Soc Hx:** College student, non-smoker
- **ROS:** No other pertinent symptoms

Pre-Treatment Imaging

- MRI brain with contrast showed right parieto-occipital dural-based lesion that was enhancing and solid/cystic in nature with significant peri-tumoral edema

MRI brain at diagnosis: axial T1 post-contrast



Clinical Course

- Patient underwent craniotomy, and maximal safe resection of mass was attempted
- However, surgery was prematurely aborted due to significant intra-operative bleeding and edema requiring IV mannitol
- Pathology from surgery demonstrated <u>WHO grade II hemangiopericytoma</u>

Hemangiopericytoma (HPC)

- HPC: rare benign neoplasm derived from pericytes lining the endothelium of smaller vessels[1-2]
  - 1% of intracranial tumors
  - 2.5% of meningeal tumors
- Following WHO 2016 classification, now considered type of solitary fibrous tumor (SFT)[3]
  - SFT and meningeal HPC share a defining molecular characteristic: NAB2/STAT6 gene fusion[4]
- Meningeal HPC: dural-based, intracranial SFT

HPC: Classic & Unique Features

- Imaging:
  - "Corkscrew" vascularization, extensive associated edema, and irregular/lobulated borders[5]
- Clinical features:
  - Prone to bleeding
    - Illustrated by patient in our case - intra-op bleeding
  - Predilection for:
    - Local recurrence, even for lower grade (I-II) tumors[6]
    - Distant metastases (DM rate as high as 65% at 15 years)[2]
      - Sites: lungs, bone, liver, subcutaneous tissue, pleura[7]
    - Late development of DMs (mean time to DM: 7.5 years)[7]

HPC: Clinical Features and DDx[8]

Feature	Meningeal HPC	Meningioma
Location	Supratentorial > infratentorial	Supratentorial > infratentorial
Incidence	<1% of intracranial tumors	15-20% of intracranial tumors
Age	4th decade of life	5th decade of life
Sex	Male > female	Female > male
Recurrence Risk	Very high/expected	Lower risk
Metastatic potential outside CNS?	Very high	Minimal
Enhancement on imaging?	Yes	Homogeneous
Calcification	Rarely	Commonly
Effect on adjacent bone	Bony erosion	Hyperostosis
Primary treatment	Surgery +/- adjuvant RT	Surgery +/- adjuvant RT
Bleeding risk?	High	Rare except for skull base

HPC: WHO Grading[9]

WHO Grade (2016)	Description	Prior WHO (2007) Name
I	Highly collagenous, relatively low cellularity, spindle cell lesion	Solitary fibrous tumor
II	More cellular, less collagenous tumor with plump cells and "staghorn" vasculature	Hemangiopericytoma
III	Five or more mitoses per 10 high-power fields	Anaplastic hemangiopericytoma

- By older WHO grading, grades II-III were classically regarded as HPCs (and stage I as SFT)

Back to our patient…

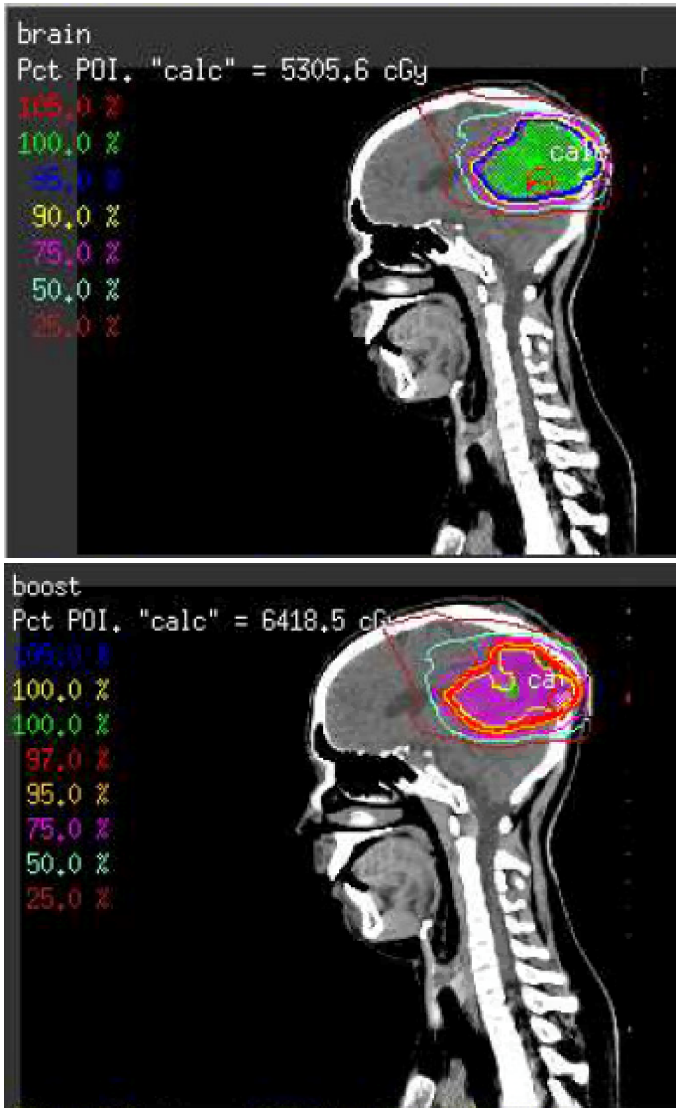
- Following initial attempt at surgery, a second effort was made at completing gross total resection (GTR). However, this was complicated by cerebral edema.
- The patient was subsequently seen for initial consultation in radiation oncology clinic in April 2012 following full staging work-up with CT C/A/P
- Recommendation was made for adjuvant radiotherapy with conventional fractionation

Target Volumes (Conventional Fractionation)

- Gross tumor volume (GTV)
  - Tumor bed with any residual nodular enhancement noted on post-op T1 post-contrast MRI
- Clinical target volume (CTV)
  - GTV + areas at risk for microscopic spread. Often incorporates a 1-2 cm margin (e.g. dura) while respecting anatomic boundaries.
- Planning target volume (PTV)
  - 3-5 mm depending on institutional practice, IGRT

Treatment

- May 2012 – July 2012: Patient received adjuvant radiotherapy with 50.4 Gy in 28 fractions with IMRT to the post-op tumor bed and gross residual disease
- Boost to gross disease: 10.8 Gy in 6 fractions
- Cumulative dose: 61.2 Gy in 34 fractions



Treatment Paradigm for HPC: GTR

- For all SFTs, 1st step: upfront surgical resection[10]
- First step for all HPC cases: Gross total resection (figure: Simpson grading)[11]
  - Based on high vascularity, even with pre-op embolization, estimated GTR rate about 33-66%[12]
  - Extent of resection associated with recurrence-free survival[13]

SIMPSON GRADE	DEGREE OF RESECTION
I	Macroscopic complete removal with excision of dural attachment & abnormal bone
II	Macroscopically complete with endothermy coagulation of dural attachment
III	Macroscopically complete without resection or coagulation of dural attachment or of its extradural extensions
IV	Partial removal leaving tumor in situ
V	Simple decompression ± biopsy

Treatment Paradigm for HPC: Adjuvant RT

- No existing randomized data; limited retrospective/population-based analyses only
- However, adjuvant radiotherapy following GTR has a well-established role due to notoriously high risk for locoregional recurrence
- Adjuvant RT improves:
  - Local control
    - Study by Rutkowski et al. (n=35) found that adjuvant RT increased time to recurrence from 3.9 years to 6.6 years, independent of extent of resection[14]
  - Overall survival (see Table on next slide*)[12-20]

*Table extrapolated from Bernard V, Ghia AJ. "Hemangiopericytoma." In: Chang, E. L. et al. (eds) *Adult CNS Radiation Oncology* 1st edn (Springer, 2018), pp 307-315.

Study Year	# of Patients	Median FU (mo, range)	Median tumor volume (cm^3)	Median marginal dose or mean dose (Gy, range)	New lesions (% of patients)	Extra-cranial metastasis (%)	Median OS	Summary of Study Findings
Rutkowski et al., 2010	277	78	5.36	N/A	43	27	156	OS benefit demonstrated with gross total resection (GTR)
Rutkowski et al., 2012	35	2-408	4.4	N/A	46	20	194.4	Trend towards statistical significance for improved recurrence-free survival with post-op radiation
Ghia et al., 2013	88	N/A	N/A	N/A	N/A	N/A	111	Both GTR and post-op radiation associated with improved OS
Ghia et al., 2013	63	N/A	N/A	60 (35-66.4)	51	N/A	154	Post-op radiation associated with better local control, especially at doses > 60 Gy
Sonabend et al., 2014	227	34	5	N/A	N/A	N/A	N/A	Statistically significant improvement in OS with GTR and radiation vs GTR alone
Chen et al, 2015	38	61 (15-133)	4.6	N/A	66	13	N/A	GTR with adjuvant radiation associated with improved OS and recurrence-free survival
Cohen-Inbar et al., 2016	90	59 (6-183)	4.9	14 (12-16)	55	24.4	N/A	Margin dose >16 Gy associated with better local control
Kim et al., 2017	18	71.8 (3.3-153.3)	1.2	20 (13-30)	80	38.9	225.7	GK SRS may be used repeatedly for intracranial recurrence or progression

Adjuvant RT: Modality & Dose

- Adjuvant RT following maximal safe resection may be administered using IMRT or SRS (if candidate)
- Dose escalation is important!
  - For IMRT: Improved local control with >60 Gy versus 50 Gy[13,16]
  - For SRS: While recommendations for marginal dose range from 14-22 Gy, ≥16-17 Gy advised[19]
    - Kim et al. (2010, n=17) found improved local control with marginal doses ≥17 Gy without significantly worse radionecrosis or peritumoral edema[21]
  - Regardless of modality: push dose when feasible

What about protons?!

- Proton therapy is an emerging area of study
- Ongoing phase II feasibility study by PTCOG (NCT01117844): Proton Radiation for Meningiomas and Hemangiopericytomas[22]
  - Eligibility: Age 18 or older with WHO grade I-III meningiomas and hemangiopericytomas
  - "Standard dose" (non-dose escalation study)
  - Primary objectives: feasibility and safety
  - Secondary objectives: side effects, QOL, late complications, dose distribution/DVH, and local control/survival outcomes

Our Patient: Toxicity

- Our patient completed his prescribed course of treatment and tolerated it well overall with mild fatigue and alopecia

<u>Anticipated side effects (conventional fx):</u>

- Acute: fatigue, dermatitis, alopecia, headache, n/v
- Late: Location-dependent
  - Neurocognitive/audiovisual deficits
  - Hypopituitarism if treating close to sella turcica with doses exceeding 50 Gy

Our Patient: Surveillance

- Completed adjuvant RT in July 2012
- Underwent surveillance (clinical exam/imaging)

<u>Surveillance Recommendations:</u>

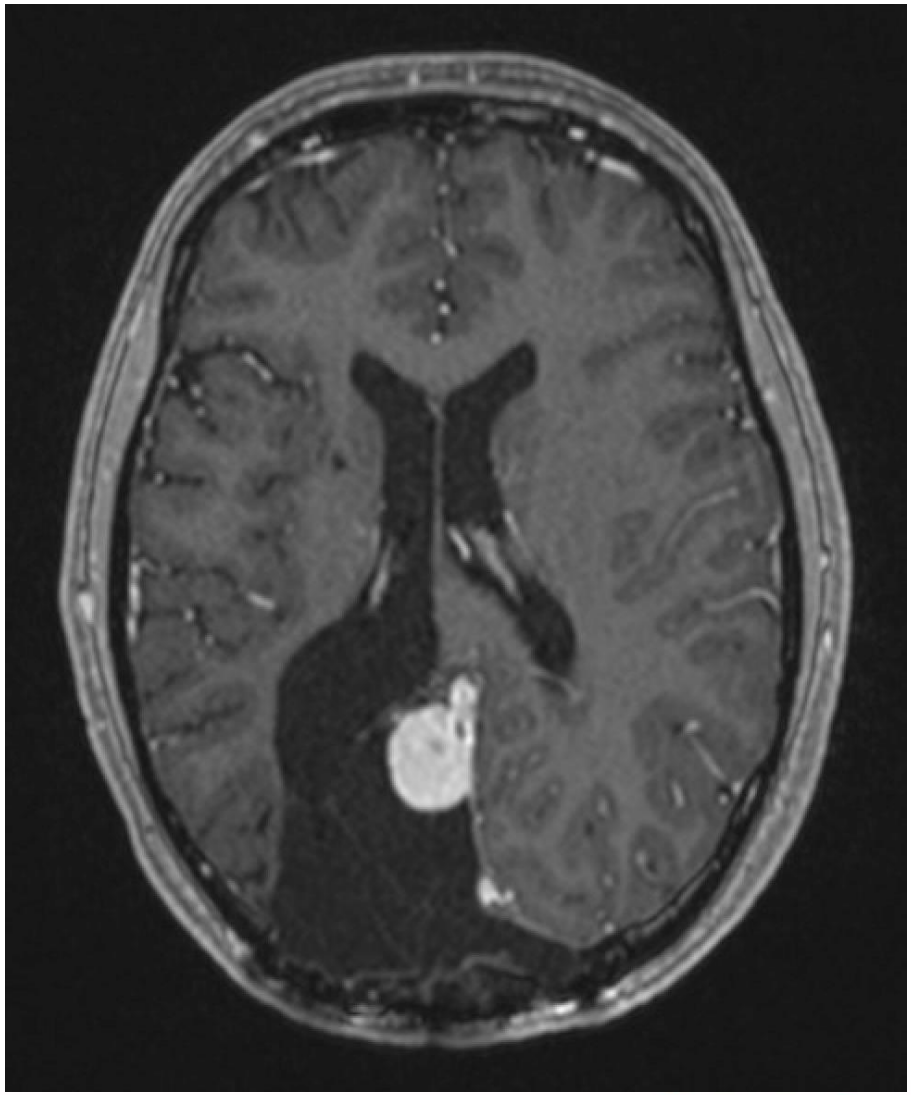
- MRI brain with contrast at 3 months and 6 months following completion of RT, then every 6 months
- Patients undergo lifetime surveillance (at least up to 20 years) due to risk of late recurrence
- Based on index of suspicion, consider imaging of common sites of DM (lungs, liver) with CT C/A/P

Treatment Response/Tumor Kinetics

- For SFTs, tumor response following RT reflects the kinetics associated with tumor growth[23]
- While HPCs may respond more quickly than other SFTs, tumor response time exhibits a wide range of variability
  - Some intracranial HPCs may take as long as 2 years to demonstrate even a partial response[24]

Our Patient: Response

- July 2012-May 2020: No evidence of recurrence
- May 2020: Surveillance MRI brain demonstrated radiographic progression of enhancing nodule at the anteromedial aspect of the resection cavity, now measuring about 2 cm in widest diameter.



HPC: Salvage Treatment

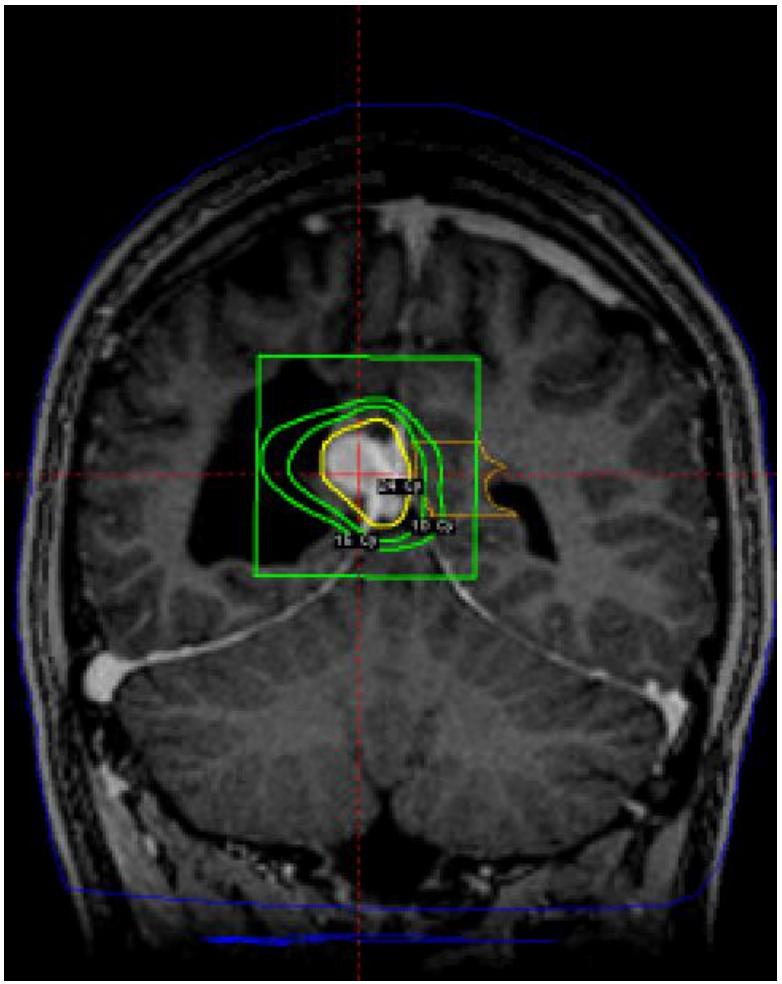
- Options:
  - Repeat surgical resection
  - Salvage radiotherapy
- Considerations:
  - Neurologic functioning
  - Extracranial disease status
  - Timing of prior radiotherapy
  - Intracranial tumor volume

HPC: Salvage Treatment

- Most studied treatment option for salvage reirradiation is SRS
- Limited existing data in reirradiation setting
  - Olson et al. (2010): Repeat SRS (n=13)[25]
    - Mean Rx dose: 17 Gy; maximum dose: 40.3 Gy
    - Found SRS to be safe and effective for treating new or recurrent HPCs over long follow-up period
  - Kim et al. (2017):[20]
    - Mean marginal dose 20 Gy (range: 13-30 Gy)
    - Used GK SRS – found it may safely be used repeatedly for recurrence

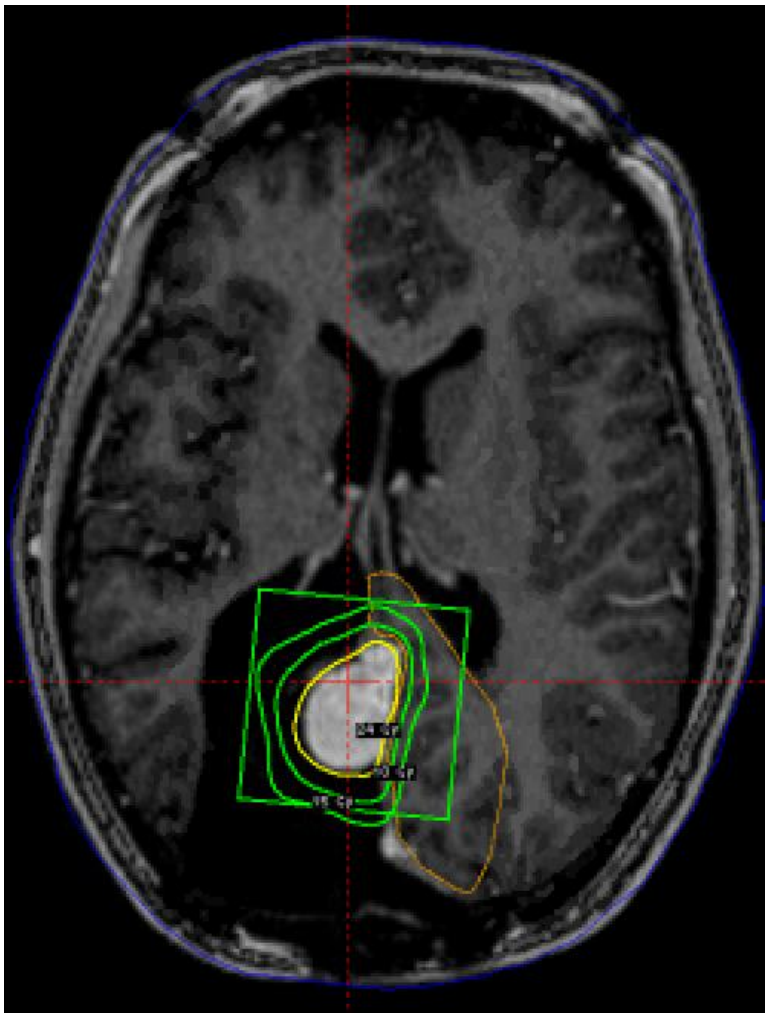
Our Patient: Salvage Treatment

- Patient decided against surgery
- Our patient received salvage reirradiation with Gamma Knife (GK) SRS
- 24 Gy prescribed to the 50% isodose line was delivered to the right parieto-occipital/parafalcine mass



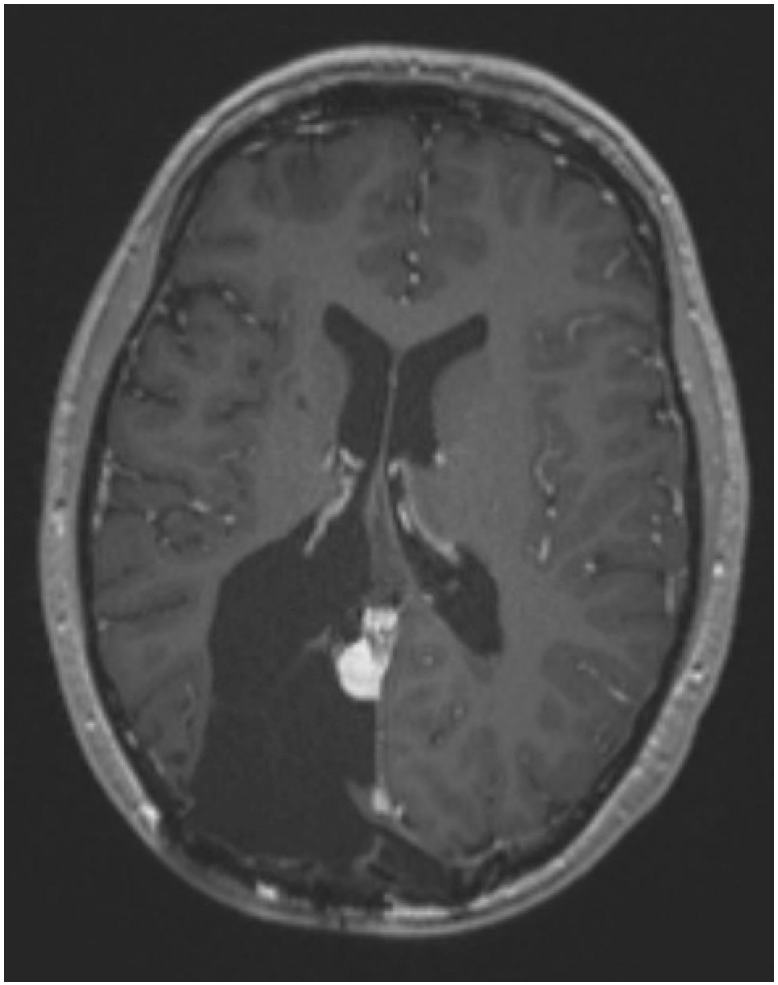
Our Patient: Treatment Technique

- 33 shots were placed
- Elegant solution:
  - Preferential dose spill into surgical cavity to preserve adjacent normal tissue (delineated in orange)
  - Allowed for ability to push prescription dose to 24 Gy to maximize local control
    - Especially important in salvage setting



Our Patient: Follow-Up

- Most recent follow-up: March 2021
- Patient doing well without clinical or radiographic evidence of progression
- Most recent MRI brain with contrast shown on the right



Summary

- HPCs are highly vascular and carry significant bleeding risk, making GTR challenging and further increasing importance of adjuvant radiotherapy
- They are likely to recur as well as spread distantly & up to many years following initial therapy
- When feasible, escalating RT dose improves outcomes
- SRS is an excellent salvage option

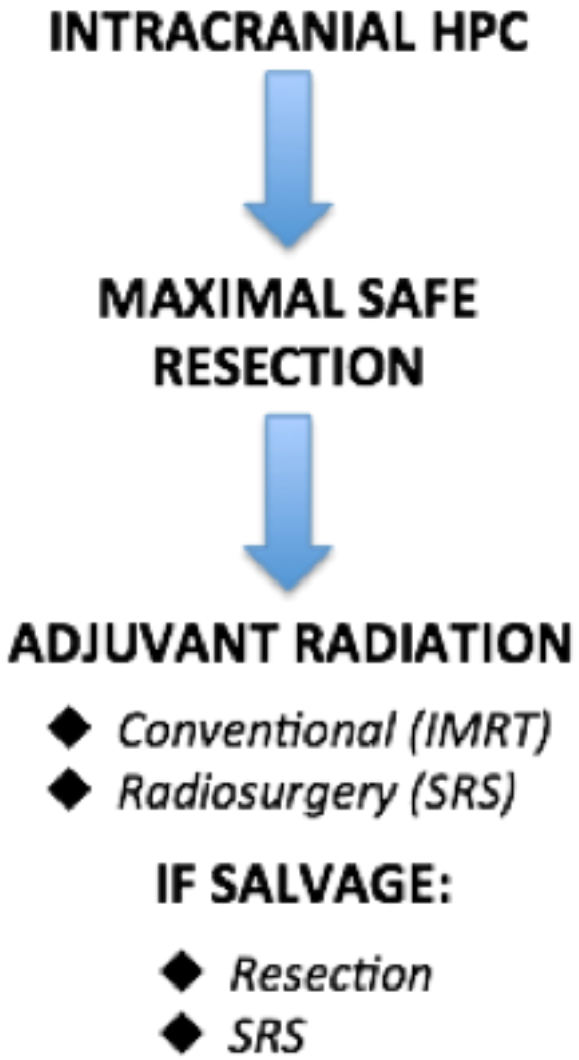


*Figure extrapolated from: Bajaj A, Saeed H. Solitary fibrous tumors/hemangiopericytoma. *Sarcomas and Skin Cancers: A Practical Guide on Radiation Treatment Techniques*. Publisher: Springer; Editors: Edward Kim MD, Upendra Parvathaneni MBBS, Meng Welliver, MD. In process.

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