# Hypofractionation in Benign Brain Lesions

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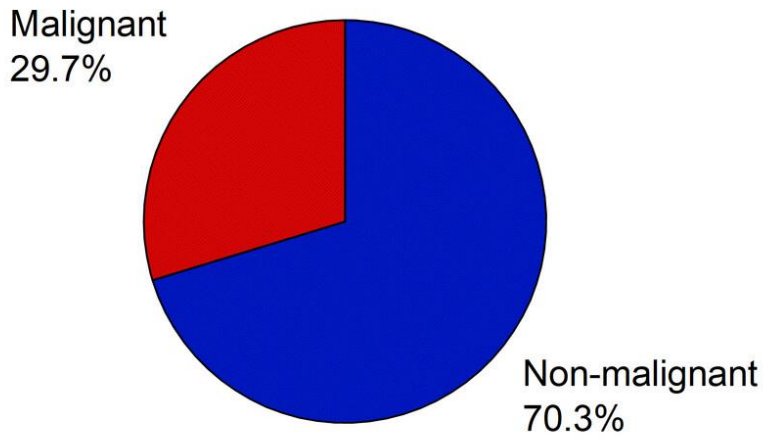
# Flow

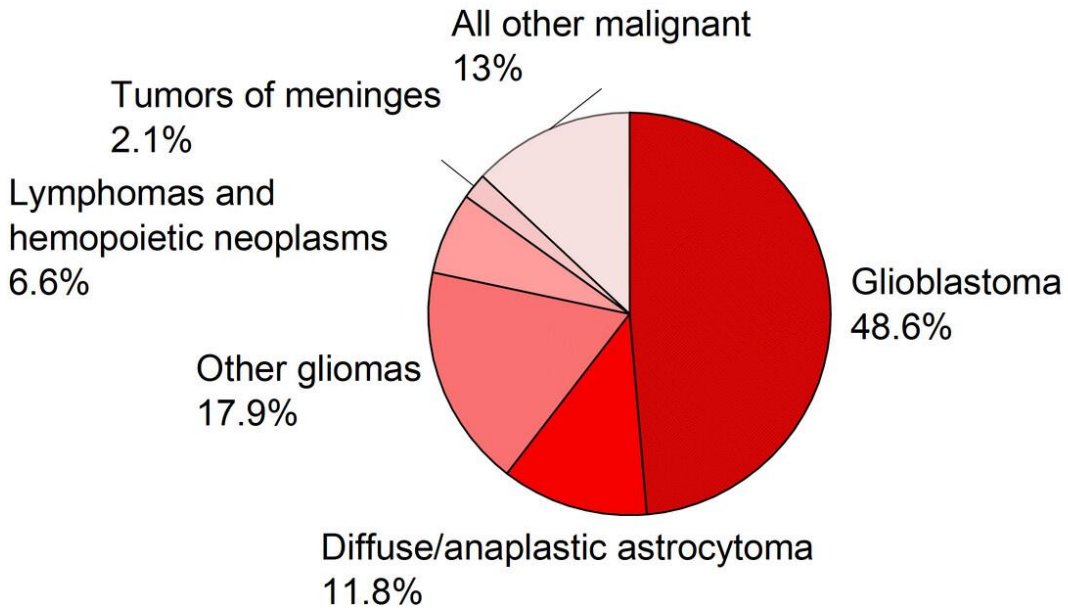
- Brief overview of benign CNS Tumours

- Individual Tumors in detail
  - Introduction
  - Case selection
  - Workup
  - Treatment Planning Considerations
  - Results and Toxicities

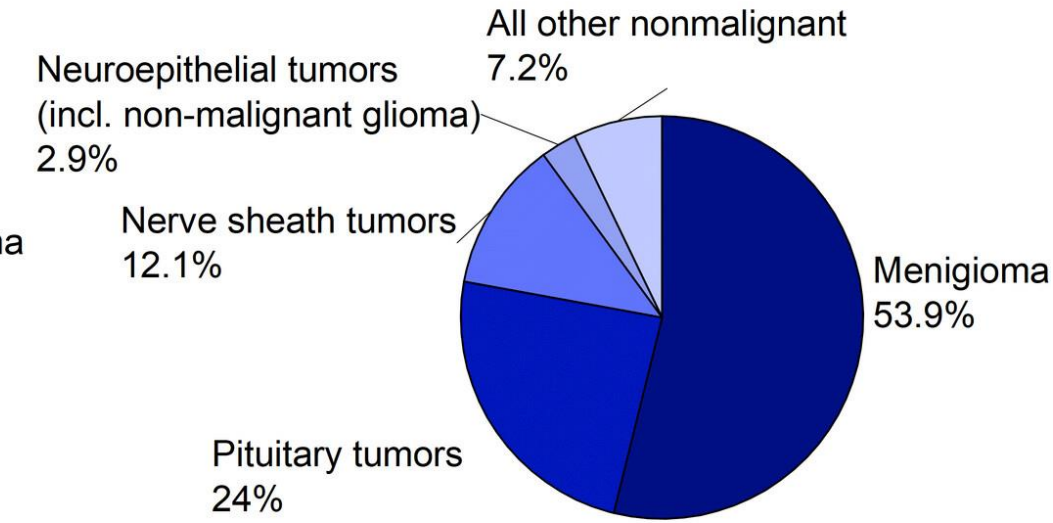
## All brain and other CNS




## Malignant

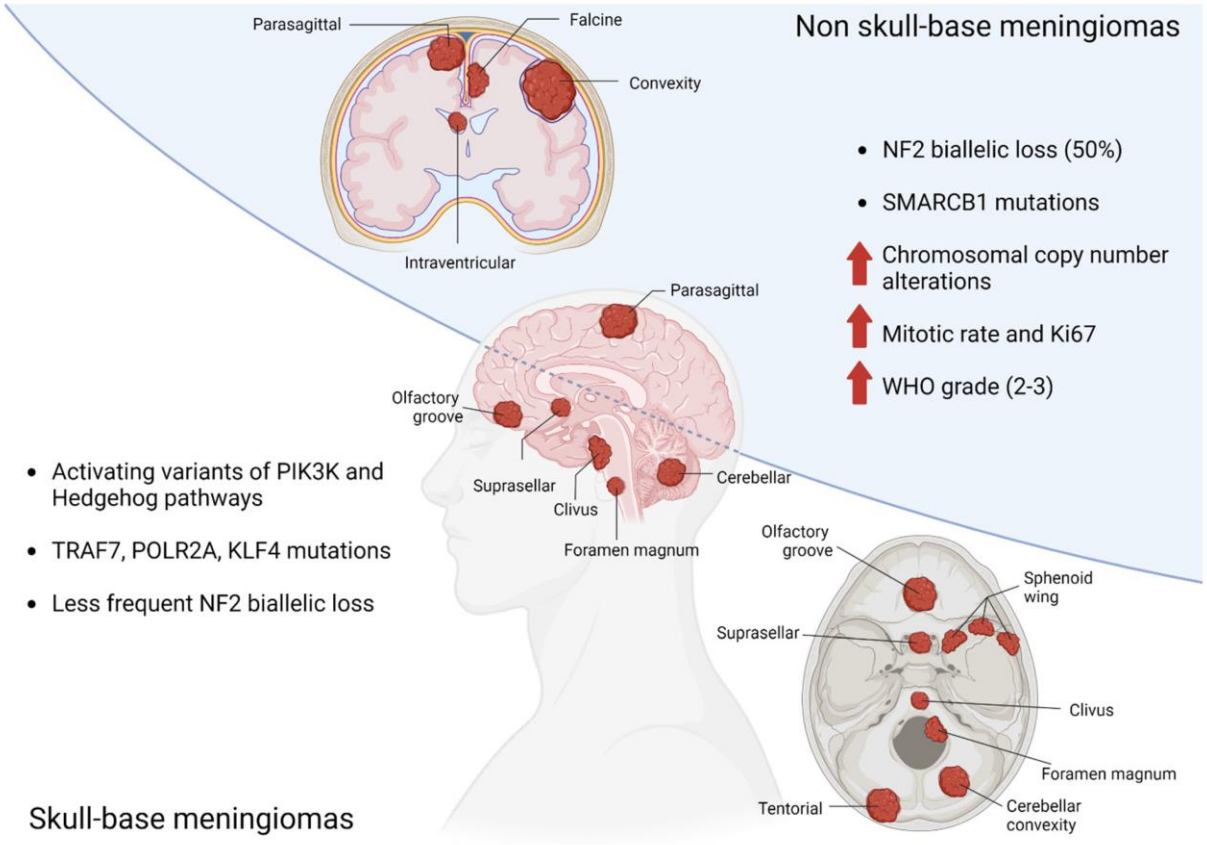



## Nonmalignant



# Meningioma

- Most frequent (20-35%)
- Higher association with seizure in convexity and parasagittal/para falcine locations and those with peritumoral edema.
- Treatment strategies: OBS/Sx/RT…Depending on tumor size, location, histology, and growth pattern over time.



# Meningioma

Imaging:

- CT: Well-circumscribed, extra-axial, intensely enhancing masses. 20–30%: Harbor calcifications, ~50% are associated with *hyperostosis or osteolysis* in the adjacent bone

- MRI: Iso or hypointense on T1W, and hyperintense on FLAIR sequences +/- edema. More than 90% of meningiomas display strong, homogenous contrast enhancement and approximately two-thirds demonstrate an adjacent dural thickening or "*dural tail.*"

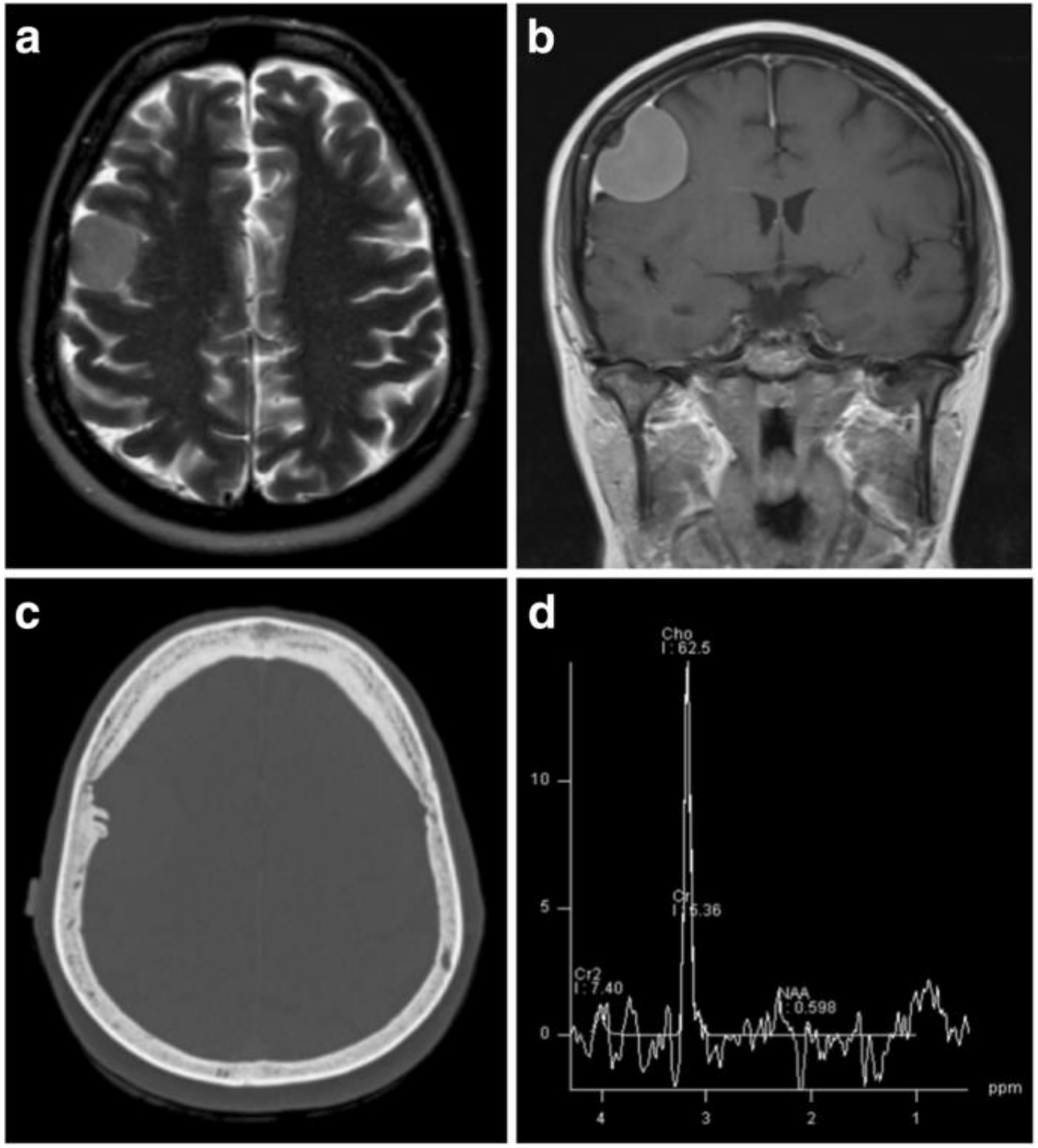


**Table 5.2** Simpson grade of resection and recurrence risk[a]

| Grade | Extent of tumor resection | Recurrence rate (%) |
|---|---|---|
| I | Macroscopic complete resection of tumor, dural attachments, and abnormal bone | 9 |
| II | Macroscopic complete resection of tumor, coagulation of dural attachments | 19 |
| III | Macroscopic complete resection of tumor, without resection, or coagulation of dural attachments or extradural disease | 29 |
| IV | Subtotal resection of tumor | 44 |
| V | Decompression or biopsy only | N/A |

- Role of RT/SRT
  - Residual or recurrent benign meningiomas following Surgical resection,
  - Unresectable tumors or not amenable to surgery

# Treatment Planning Considerations

- **Position**
- **Immobilization**
  - GaK: Head frame in conjunction with a metal collimator helmet.
  - Linac based: Various, including rigid frame with external skull fixation, noninvasive modified GTC frame (noninvasive fixation by use of a dental plate), or a three-point thermoplastic mask with a modified stereotactic frame .

- **CT**: **Diagnostic imaging**: Co-registration of planning CT with contrast-enhanced MRI.

- **MRI sequences:**

  T1W, pre-contrast T2-weighted and FLAIR, and multi-planar (axial, sagittal, and coronal) post-contrast T1-weighted images.

  High-resolution series, such as MP-RAGE, should be obtained for contrast-enhancing targets.

  Cranial nerves may be more readily visualized on a CISS or 3D FIESTA series as needed.

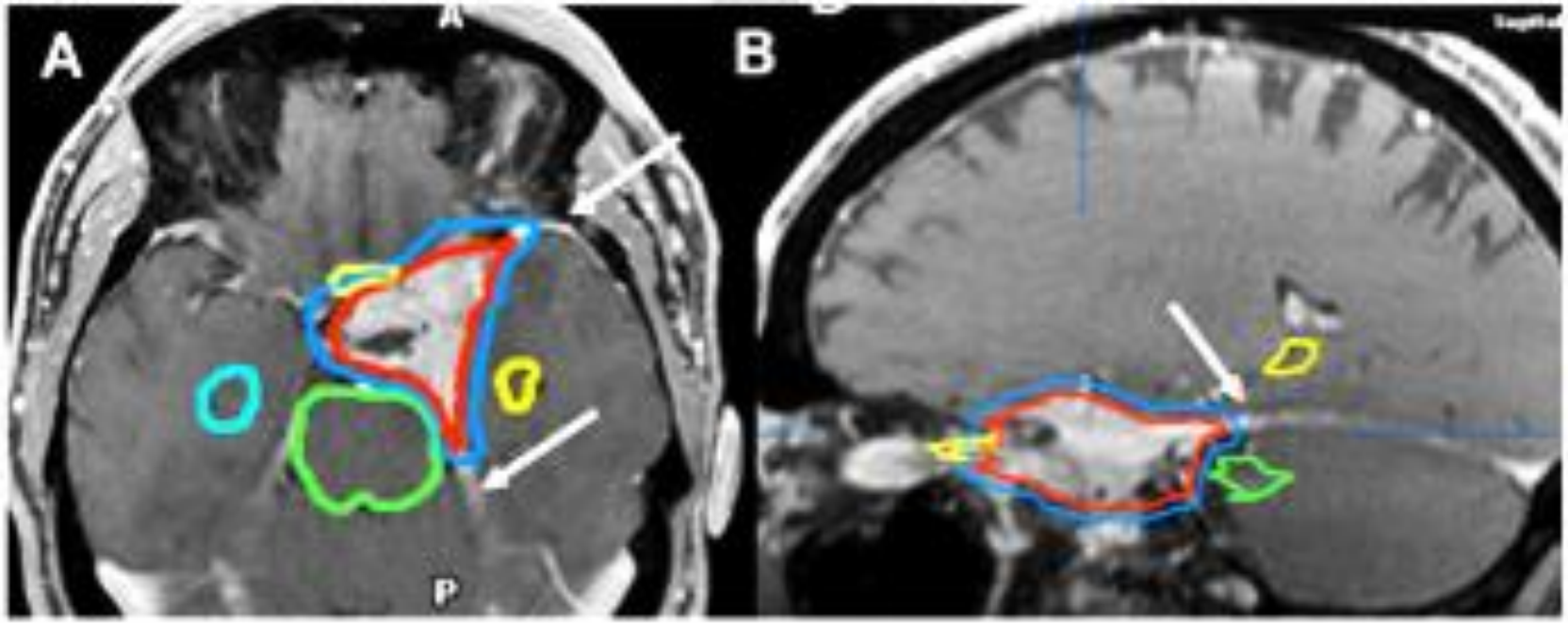
# Patient Selection:

- Factors influencing treatment recommendations
  - age, comorbidities, cranial nerve deficits, tumor size, presenting symptoms, competing symptoms (i.e., contralateral hearing or vision loss), and proximity to OARs.
- For single-fraction SRS, targets should generally be:
  - – <3 cm.
  - – Not directly abutting critical OARs.
  - – >3–5 mm from the optic apparatus (optic chiasm, optic nerves) to achieve
  - adequate dose falloff between the prescription dose and OAR tolerance (<8– 10 Gy for single-fraction SRS).

- GTV:
  - Enhancing lesion on T1W Contrast MRI.. NO edema (T2W)
  - For postoperative cases, the GTV is defined as the resection bed plus any residual nodular enhancement.

- CTV:
  - For benign meningiomas, GTV = CTV.
  - May consider 0.5–1.0 cm margin for Dural tail or uncertainty on T1C

- PTV
  - CTV plus 0–5 mm uniform expansion.
  - Generally CTV plus 3–5 mm uniform expansion for standard thermoplastic mask or CTV plus 0–2 mm uniform expansion for a stereotactic frame.




According to RTOG 0539 and EORTC 1308 trials, ***only*** clearly thickened dural tail should be considered as target and included in the GTV; in contrast, linearly enhanced dura and non-enhancing but thickened dura trailing off the tumor would ***not*** be included in the GTV.

## 5.5 Commonly Used Dose/Fractionation Schemes (Table 5.4)

**Table 5.4** Commonly used dose/fractionation schemes

| Commonly used dose/fractionation schemes | | | |
|---|---|---|---|
| | Patient selection considerations | Dose/fractionation | Criteria for SRS |
| SRS | – More than 3–5 mm from optic apparatus<br>– Optic nerve sheath and tuberculum sellae meningiomas are generally a contraindication to SRS (therapeutic doses exceed OAR tolerance) | WHO grade I: 12–15 Gy × 1 fx<br>WHO grade II–III: 16–20 Gy × 1 fx | • Lesion <3 cm<br>• Not directly abutting critical OARs<br>• >3–5 mm from the optic apparatus |
| FSRT | Larger tumor and/or <2–3 mm from optic apparatus or other critical OAR | WHO grade I: 5–6 Gy × 5 fx [9], 2.5 Gy × 15 fx [10] | |

Significant predictors of pro- gression included >1 prior surgery, prior RT, and tumor marginal dose <13 Gy. (Sheehan JP et al. J Neurosurg. 2014;120: 1268–77.)

# Follow-Up

- Yearly imaging (ideally MRI, CT with contrast if non-tolerant, or MRI contraindicated) for 4–5 years, then every 2 years.
- For cavernous sinus or base of skull locations, monitor for hypopituitarism with regular serum analyses annually or as needed.
- Recommend endocrinologist for long-term management and monitoring of endocrine dysfunction.

**Table 5.6** Relevant literature

| Study | Patients (*n*) | Median follow-up (months) | Median tumor vol ($cm^3$) | Modality, dose, fractionation | LC (%) |
|---|---|---|---|---|---|
| Torres, 2003 [18] | 77 | 40.6 | 12.7 | Linac, 15.6 Gy × 1 fx | – 92% 5 years |
| DiBiase, 2004 [19] | 162 | 54 | 4.5 | GaK, 14 Gy × 1 fx | – 86% 5 years |
| Kreil, 2005 [20] | 200 | 95 | 6.5 | GaK, 12 Gy × 1 fx | – 98.5% 5 years<br>– 97% 10 years |
| Kollova, 2007 [21] | 368 | 60 | 4.4 | GaK, 12.5 Gy × 1 fx | – 98% 5 years |
| Feigl, 2007 [22] | 214 | 24 (mean) | 6.5 (mean) | GaK, mean 13.6 Gy × 1 fx | – 86% 4 years |
| Kondziolka, 2008 [17] | 972 | 48 (mean) | 7.4 | GaK, mean 14 Gy × 1 fx | – 87% 10 years |
| Gorman, 2008 [10] | 38 | 47 | 8.3 | Linac, 2.5 Gy × 15 fx | 100% |
| Mahadevan, 2011 [23] | 16 | 22 | 10.5 | CyK, mean 5.62 Gy × 5 fx | 100% |
| Han, 2014 [9] | – SRS, 55<br>– FSRT, 22<br>– Conventional fx, 143 | 32 | 2.8<br>4.8<br>11.1 | Linac, 12.5 Gy × 1 fx (SRS), 5 Gy × 5 fx (FSRT), 1.8 Gy × 28 fx (conventional fx) | – SRS 91%<br>– FSRT 94%<br>– Conventional fx 95% |
| Smith, 2014 [24] | 28 | 32.6 | 14.7 | CK, 4.5–6 Gy × 5 fx | 100% |
| Navarria, 2015 [25] | 26 | 24.5 | 13 | Linac, 5 Gy × 5 fx | 100% |
| Conti, 2015 [26] | 25 | 17 (mean) | 4.95 | CyK, median 4.6 Gy × 5 fx | 100% |

# Pituitary Adenoma

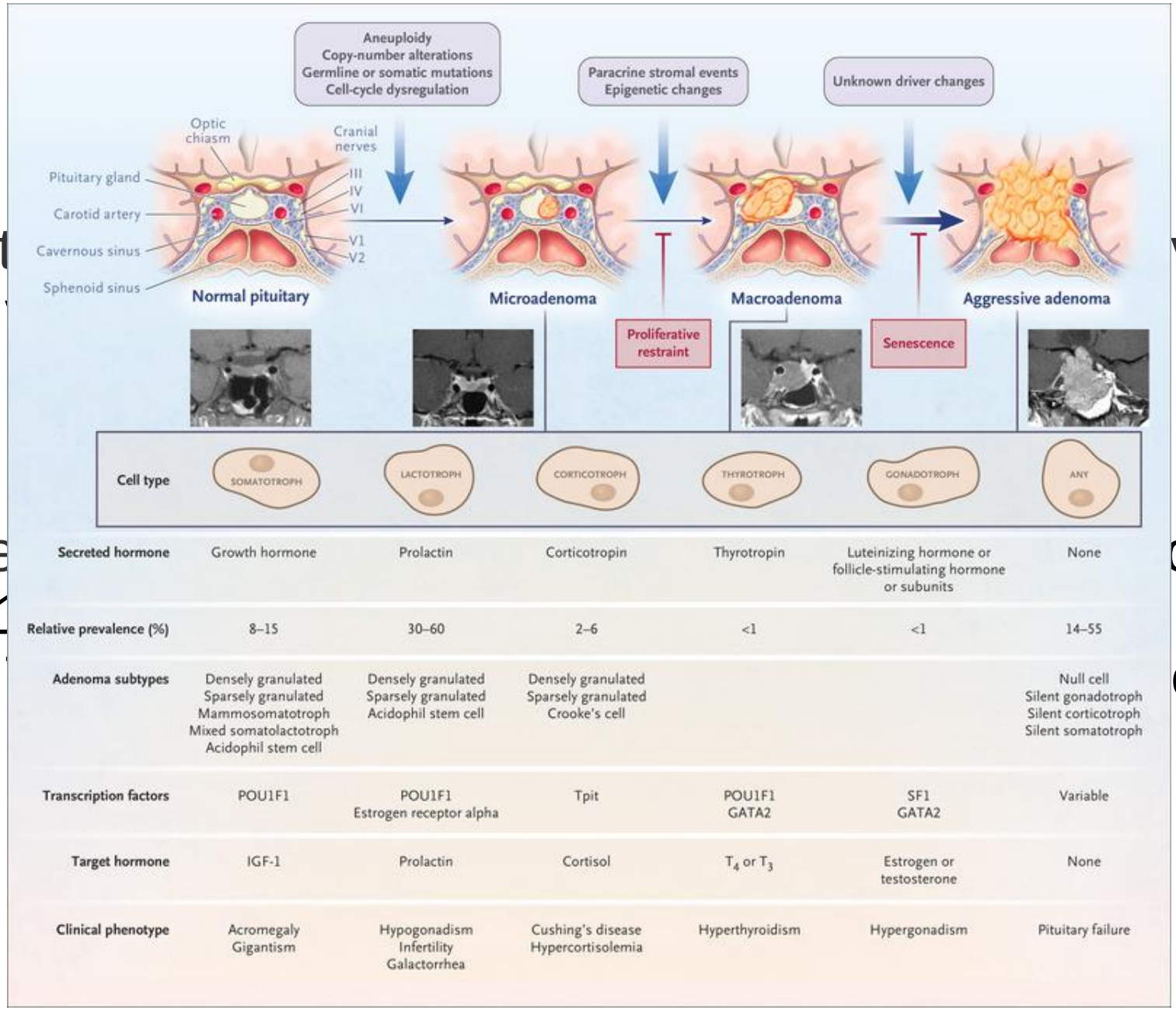
- Secretory: 70% ( 60% Prolactinoma, 20% GH Secreting.. ACTH &TSH secreting)
- Non-secretory: 30%

- Secretory tumors are often diagnosed early by the clinical symptoms. Often they are small on imaging compared with non-secreting tumours which often compress the optic apparatus at diagnoses with visual field loss being the patient's presenting symptom.

- Also, large non-secreting pituitary adenoma can cause hypopituitarism by compressing a significant amount of the normal glands.

- Both mass effect and radiation damage to the pituitary infundibulum can cause an elevation in prolactin due to loss of hypothalamic inhibition ("stalk effect")

- **Work-up:**
  - A complet valuation, including
  - Pituitary e olactin, Basal GH, IGF-1 suppression, TSH, T3, one levels.)

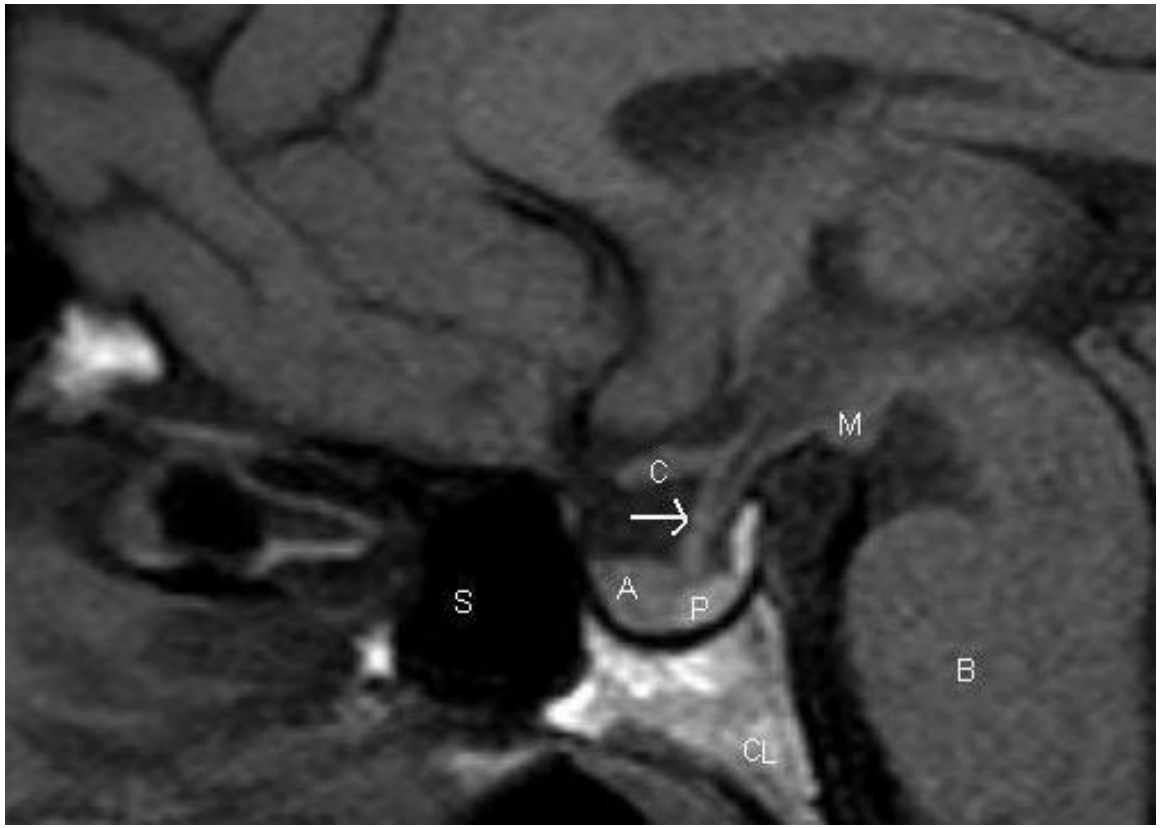



| | | | | | | |
|---|---|---|---|---|---|---|
| **Secreted hormone** | Growth hormone | Prolactin | Corticotropin | Thyrotropin | Luteinizing hormone or follicle-stimulating hormone or subunits | None |
| **Relative prevalence (%)** | 8–15 | 30–60 | 2–6 | <1 | <1 | 14–55 |
| **Adenoma subtypes** | Densely granulated<br>Sparsely granulated<br>Mammosomatotroph<br>Mixed somatolactotroph<br>Acidophil stem cell | Densely granulated<br>Sparsely granulated<br>Acidophil stem cell | Densely granulated<br>Sparsely granulated<br>Crooke's cell | | | Null cell<br>Silent gonadotroph<br>Silent corticotroph<br>Silent somatotroph |
| **Transcription factors** | POU1F1 | POU1F1<br>Estrogen receptor alpha | Tpit | POU1F1<br>GATA2 | SF1<br>GATA2 | Variable |
| **Target hormone** | IGF-1 | Prolactin | Cortisol | $T_4$ or $T_3$ | Estrogen or testosterone | None |
| **Clinical phenotype** | Acromegaly<br>Gigantism | Hypogonadism<br>Infertility<br>Galactorrhea | Cushing's disease<br>Hypercortisolemia | Hyperthyroidism | Hypergonadism | Pituitary failure |

# Imaging

- CT:
  - Pituitary microadenomas are hypodense and less contrast enhancing than normal pituitary gland.

- MRI:
  - hypointense to normal pituitary on T1W images, while they can be iso-, hypo-, or hyperintense to normal pituitary on T2W images
  - There may be hyperintensity on T1W images in the setting of cystic lesions/ intralesional hemorrhage.
  - In contrast to meningiomas, pituitary adenomas demonstrate partial, incomplete, or heterogenous contrast enhancement.
  - The closest distance between the tumour and optic chiasm and optic nerves should be determined, particularly when a suprasellar extension is present.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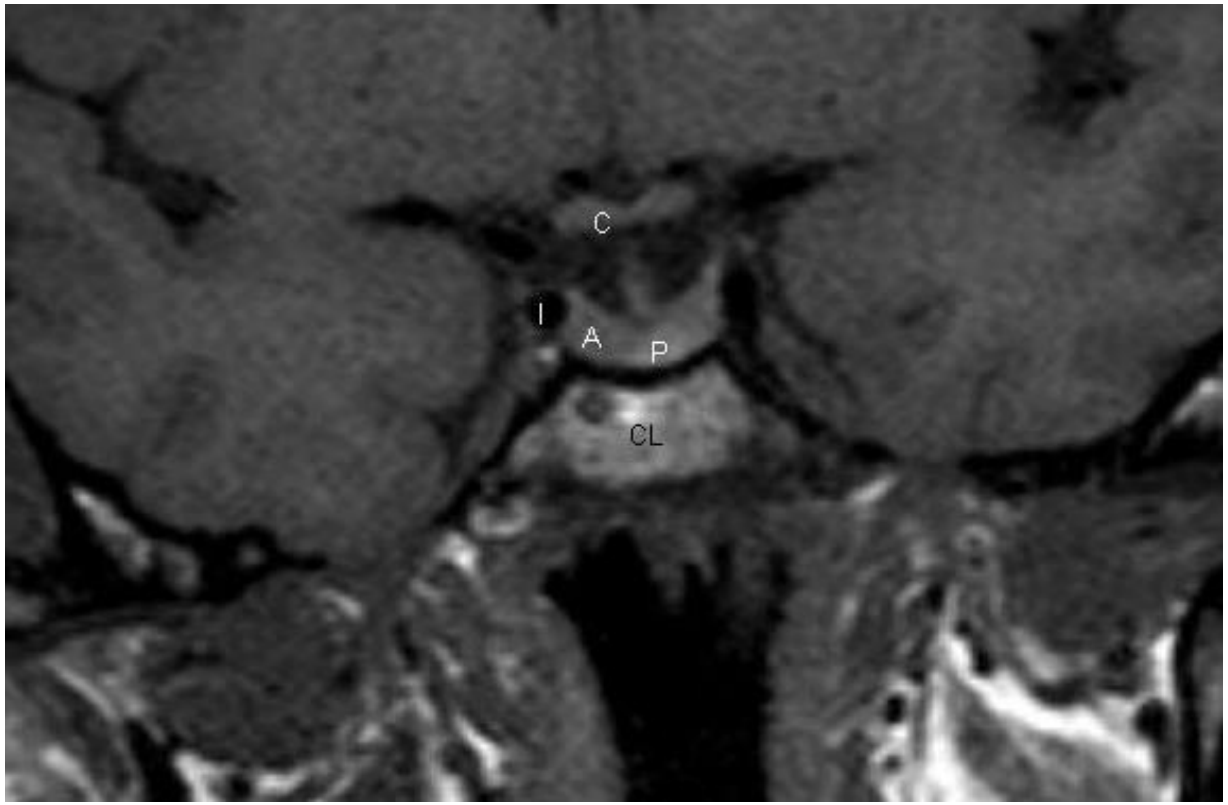
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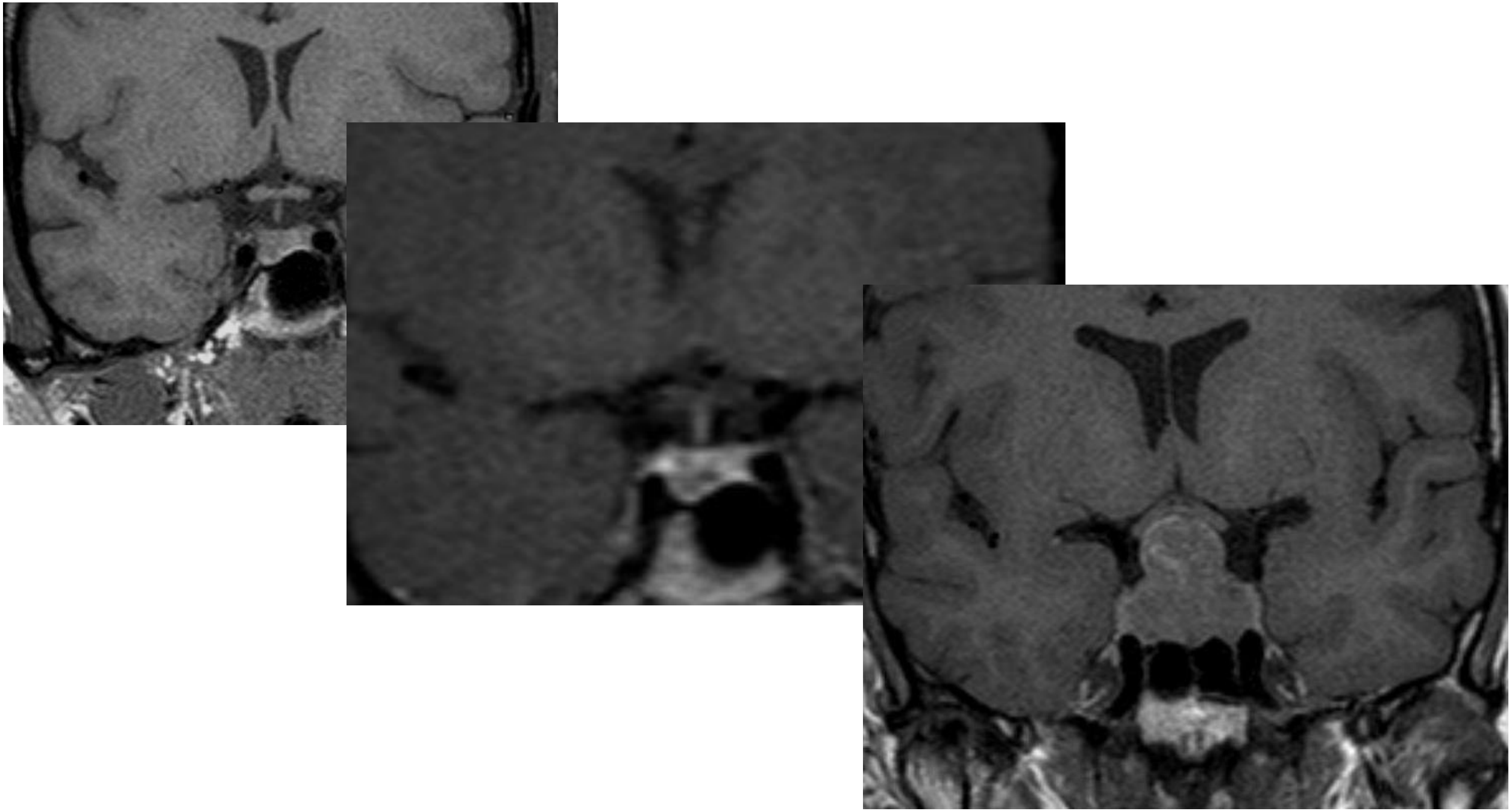
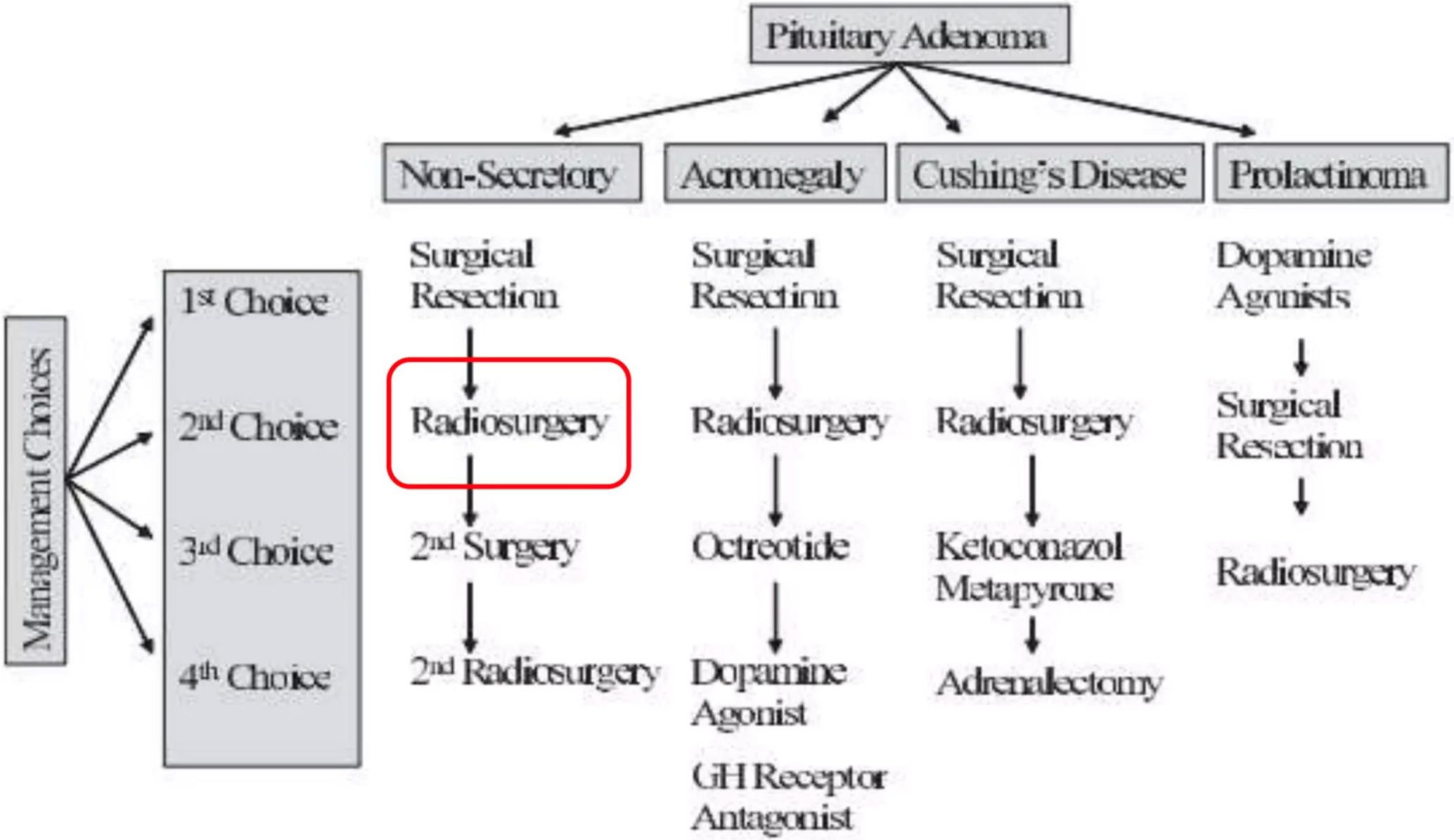
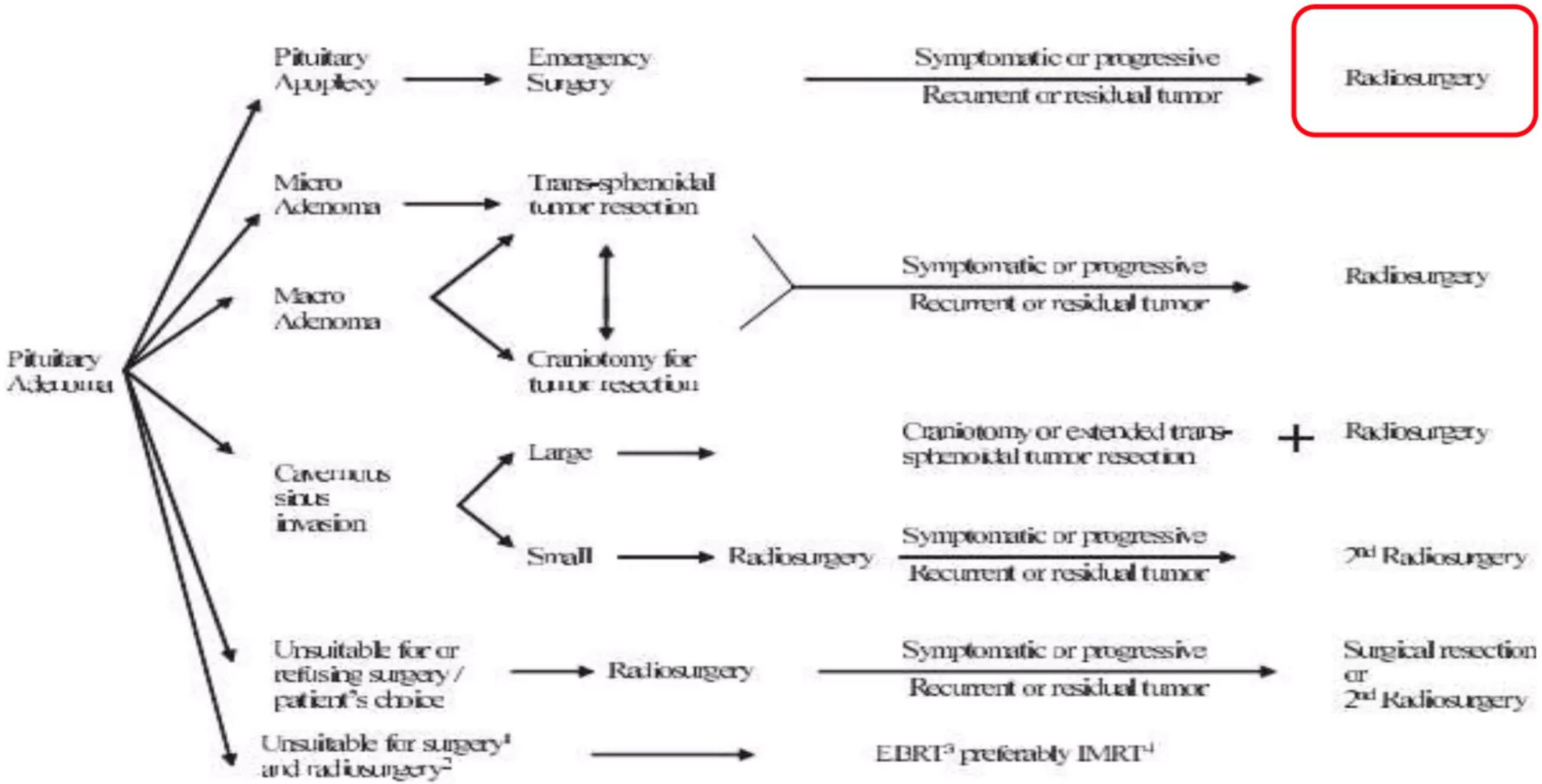



Pituitary Adenoma
Non-Secretory
Acromegaly
Cushing's Disease
Prolactinoma
Management Choices
1st Choice
2nd Choice
3rd Choice
4th Choice
Surgical Resection
Radiosurgery
2nd Surgery
2nd Radiosurgery
Surgical Resection
Radiosurgery
Octreotide
Dopamine Agonist
GH Receptor Antagonist
Surgical Resection
Radiosurgery
Ketoconazol
Metapyrone
Adrenalectomy
Dopamine Agonists
Surgical Resection
Radiosurgery

# Pituitary Adenoma Surgical Management Algorithm



- Radiation Therapy is administered for:
  - Residual, recurrent tumors
  - Persistent post- operative hypersecretion
  - in cases where the patient is not a surgical candidate because of co-morbidities

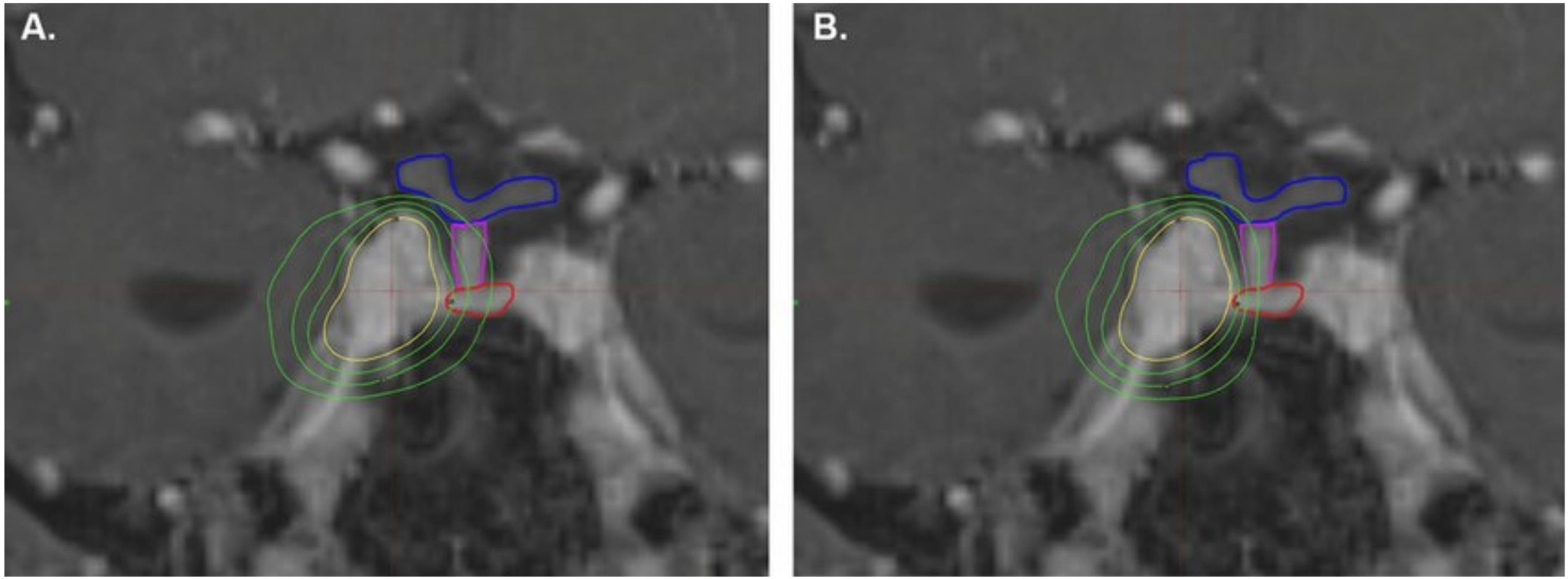
- Patient Selection for SRS or FSRT
  - For single-fraction SRS, targets should generally be: – <3 cm.
  - Not directly abutting critical OARs.
  - >3–5 mm from the optic apparatus
  - For FSRT, tumors may be larger (> 3–4 cm), in closer proximity to or involving OARs.

## Target Delieation:

The tumor bed/GTV is defined as the enhancing lesion on the post-gadolinium T1-weighted MRI.

**Table 7.4** Commonly used dose/fractionation schemes

| | Patient selection considerations | Dose/fractionation |
|---|---|---|
| SRS | Small tumor (<3 cm), >3–5 mm from optic apparatus | Nonsecretory: 12–20 Gy × 1 fx (optimally 14–18 Gy × 1 fx)<br>ACTH secreting: 15–30 Gy × 1 fx (optimally 20–25 Gy × 1 fx)<br>GH secreting: 10–35 Gy × 1 fx (optimally 20–25 Gy × 1 fx)<br>Other secretory: 15–25 Gy × 1 fx [9] |
| FSRT | Larger tumor and/or <2–3 mm from optic apparatus | 7 Gy × 3 fx, 5–5.4 Gy × 5 fx [10] |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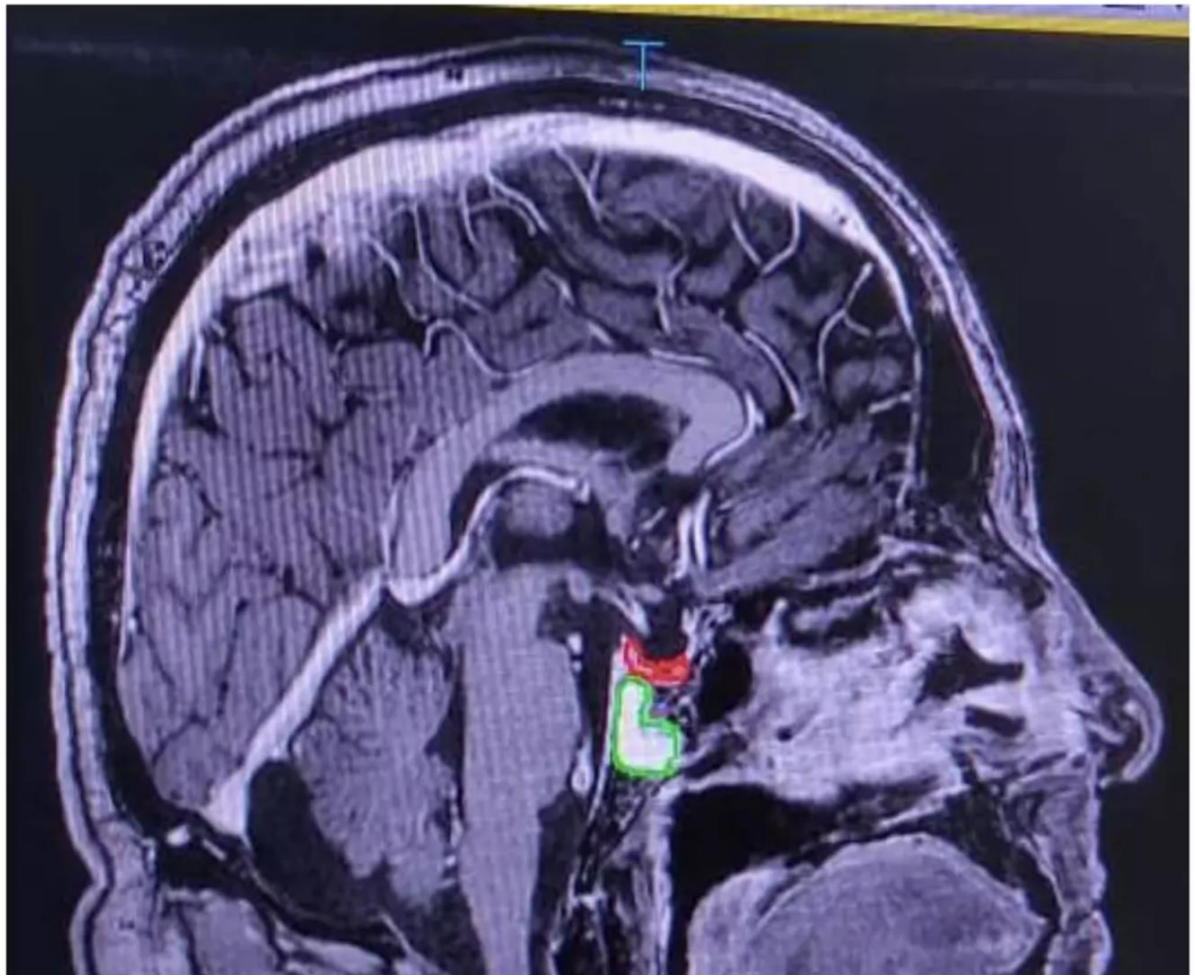
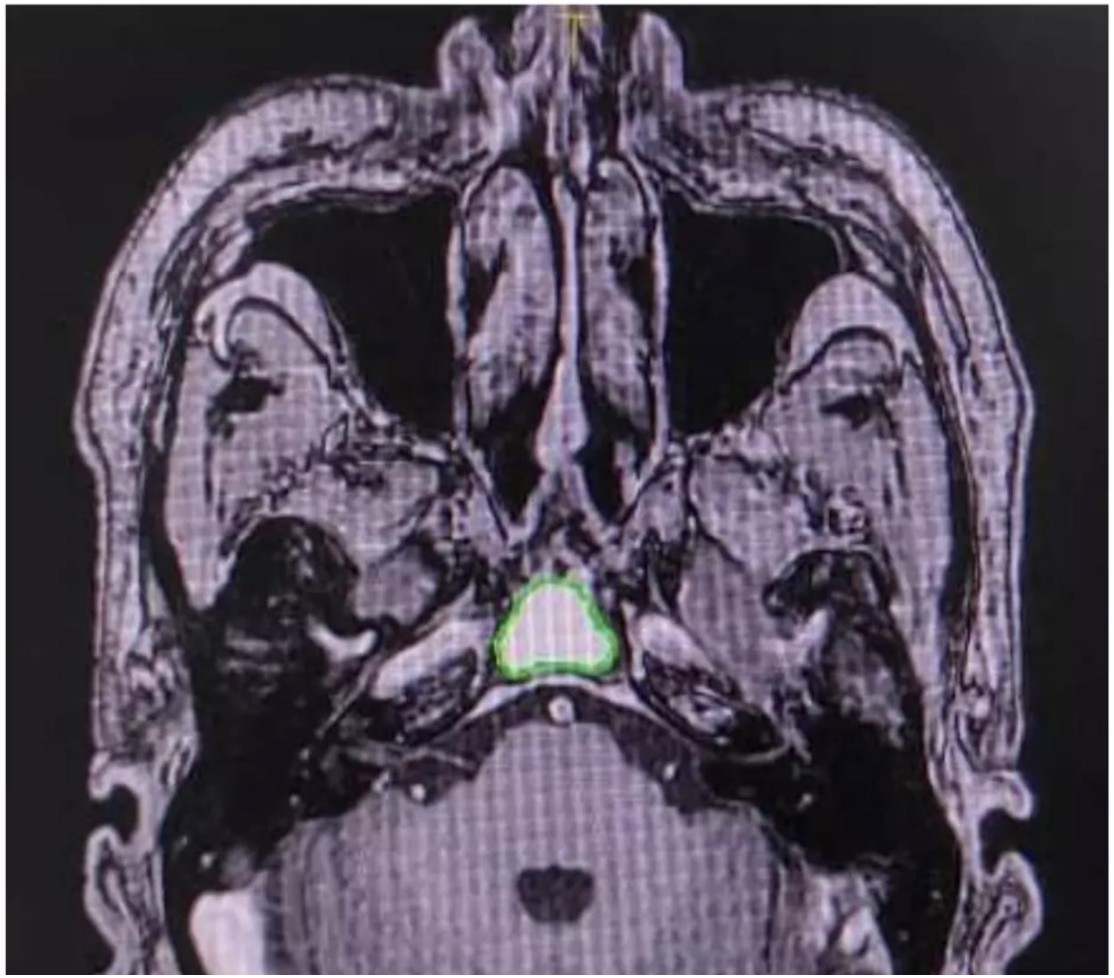
# IDENTIFYING THE PACKING MATERIAL





- For secretory adenomas, SRS is associated with faster biochemical normalization, with a mean time to normalization of 8.5 months for SRS versus 18 months for conventional fractionated radiotherapy*

- For prolactinomas,
  - The first-line therapy is a dopamine agonist such as bromocriptine/cabergoline, while surgery is second line, and SRS is reserved for patients who do not respond to or tolerate medical therapy or are not surgical candidates

  - Remission is defined as a normal serum prolactin level. Biochemical remission rates with SRS using single fraction doses above 20 Gy range from 0-84% at two years post treatment.**

  - SRS may falsely elevate the prolactin level for years after treatment postulating injury of the infundibulum.

***J Neurosurg. 2005;102(4):678–91.***

****J Neurosurg. 2006;104(6):876–83.***

- Anti-secretory medication and its effect of radiosurgery effectiveness

  - Several groups report a significantly lower hormone normalization rate for function pituitary tumour patients receiving antisecretory drugs at the time of radiosurgery.

  - It is postulated that the anti-secretory drugs interfere with phases in the tumour cells cycle making them less radiation sensitive.

  - As a result of these published studies, many centers hold antisecretory drugs 6-8 weeks before and after radiosurgery.

***J Clin Endocrinol Metab 2000;85:1287-9.***
***Neurosurgery 2006;59:255-66; discussion 255-66.***

- For ACTH secreting tumors/Cushings disease
  - The use of a 24-hour urine free cortisol is the gold standard to define cure
  - Others couple this lab result to resolution of clinical stigmata or a series of normal post treatment cortisol levels
  - The latency period following SRS is 14-18 months and hormone normalization is observed in 17-83% of patients treated*
- For GH secreting tumor/acromegaly
  - Remission is defined by a normal serum IGF-1 level and a GH levels less than 1 ng/mL in response to a glucose challenge
  - Biochemical remission rates range between 20- 96% at 2 years following single fraction treatment with SRS with does greater than 20 Gy**

***Neurosurgery 2001;49:284-91; discussion 291.***

****Pituitary 2001;4:223-30.***

**Table 7.6** Relevant Literature

| Study | Patients (*n*) | Median follow-up (year) | Mean treatment vol ($cm^3$) | Modality, median marginal dose, fractionation | LC | Remission |
|---|---|---|---|---|---|---|
| Iwai, 2005 [16] | 34<br>Nonsecretory | 5 | 2.5 | GaK,<br>14 Gy × 1 fx | 93%<br>5 years | NA |
| Mingione, 2006 [17] | 90<br>Nonsecretory | 3.7 | 4.8 | GaK, mean 18.5 Gy × 1 fx | 92% | NA |

| Study | Patients (*n*) | Median follow-up (year) | Mean treatment vol ($cm^3$) | Modality, median marginal dose, fractionation | LC | Remission |
|---|---|---|---|---|---|---|
| Voges, 2006 [18] | 175<br>– Nonsecretory (*n* = 37)<br>– GH (*n* = 64)<br>– ACTH (*n* = 17)<br>– Nelson's (*n* = 9)<br>– PRL (*n* = 13)<br>– TSH (*n* = 2) | 6.8 (mean) | 4.3 | Linac, mean 15.3 Gy × 1 fx | 97% | – 34%<br>3 years<br>– 51%<br>5 years |
| Liscak, 2007 [19] | 140<br>Nonsecretory | 5 | 3.45 | GaK,<br>20 Gy × 1 fx | 100% | NA |
| Pollock, 2008 [20] | 62<br>Nonsecretory | 5.3 | 4.0 | GaK,<br>16 Gy × 1 fx | 95%<br>7 years | NA |
| Sheehan, 2011 [21] | 418<br>– Nonsecretory (*n* = 152)<br>– GH (*n* = 130)<br>– ACTH (*n* = 82)<br>– Nelson's (*n* = 22)<br>– PRL (*n* = 32) | 2.6 | 1.9 | GaK,<br>24 Gy × 1 fx | 90% | 49-month median time to remission |
| Iwata, 2011 [10] | 100<br>Nonsecretory | 2.7 | 5.1 | CyK, 5.67–7 Gy × 3 fx or 4.4–5 Gy × 5 fx | 97% | NA |
| Puataweepong, 2015 [22] | 40<br>Secretory and nonsecretory | 3.2 | 3.35 | CyK, 5 Gy × 5 fx | 98% | 54% |

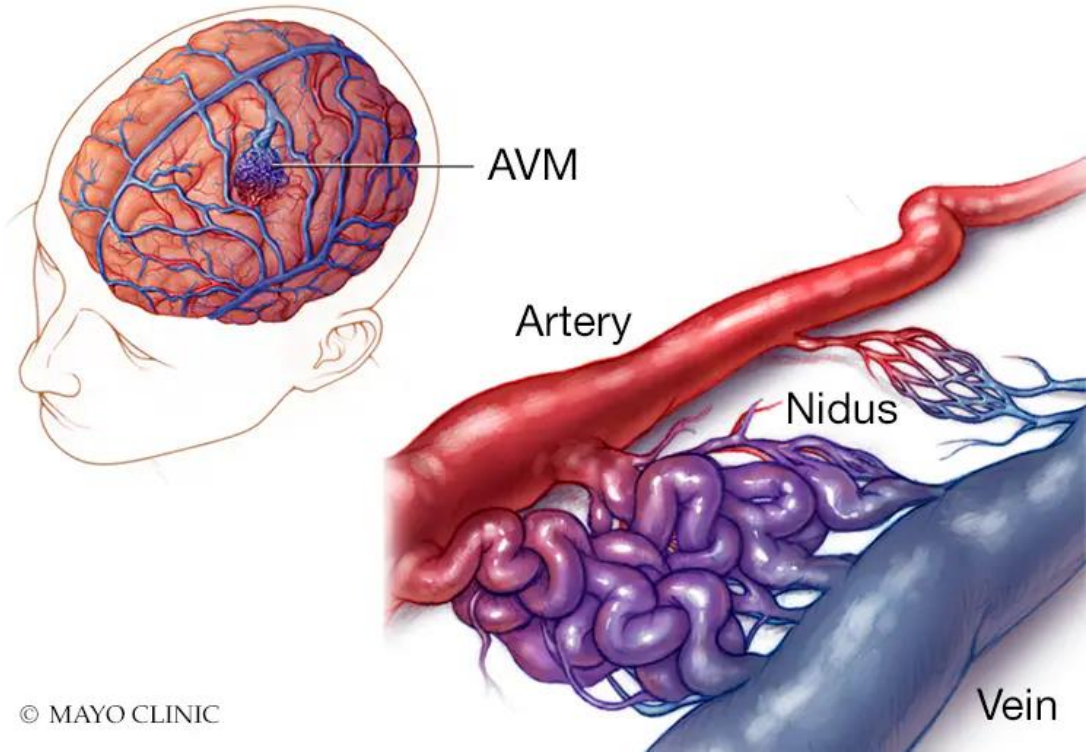
*Vol* volume

# Arterio Venous Malformations (AVM)

- Cerebral AVMs are abnormal vascular lesions that bypass the capillary network by shunting blood from feeding arteries to draining veins via a tortuous nidus of vascular connections.

- Generally considered sporadic congenital malformations
- Multiple AVMs is predictive of hereditary hemorrhagic telangiectasia (also termed Osler-Weber-Rendu syndrome).

- The most common presenting symptoms are:
  - Intracranial hemorrhage (usually intraparenchymal)
  - Seizure (more likely with large, cortical AVMs with superficial drainage)
  - Headaches
  - Focal neurologic deficits (secondary to mass effect, hemorrhage, or vascular steal)




- OBSERVATION
- EMBOLIZATION
- MICOSURGERY
- RADIOSURGERY

Even when discovered in the asymptomatic setting, patients are often encouraged to pursue therapy because of the devastating implications of a hemorrhagic event.

- Annual rate of spontaneous hemorrhage ~2–6 %, with morbidity 20–30 % and mortality 10–15 % per event; after angiographic obliteration, lifetime risk of hemorrhage ≤1 %.

- The strongest predictors of hemorrhage include prior hemorrhage (at presentation, or clinically silent), deep location, exclusively deep drainage, and associated aneurysms.

- SRS induces vascular wall hyperplasia and luminal thrombosis, but requires several years to achieve full effect.

- AVMs differ from cavernous malformations insofar as the latter are composed of sinusoidal vessels without a large feeding artery, and therefore have a low-pressure gradient

Grading Systems

| Spetzler-Martin Grading | Points | Supplementary Grading |
|---|---|---|
| Size, cm | | Age, y |
| <3 | 1 | <20 |
| 3-6 | 2 | 20-40 |
| >6 | 3 | >40 |
| Venous drainage | | Bleeding |
| Superficial | | |
| Deep | | |
| Eloquence | | |
| No | | |
| Yes | | |
| Total | | |

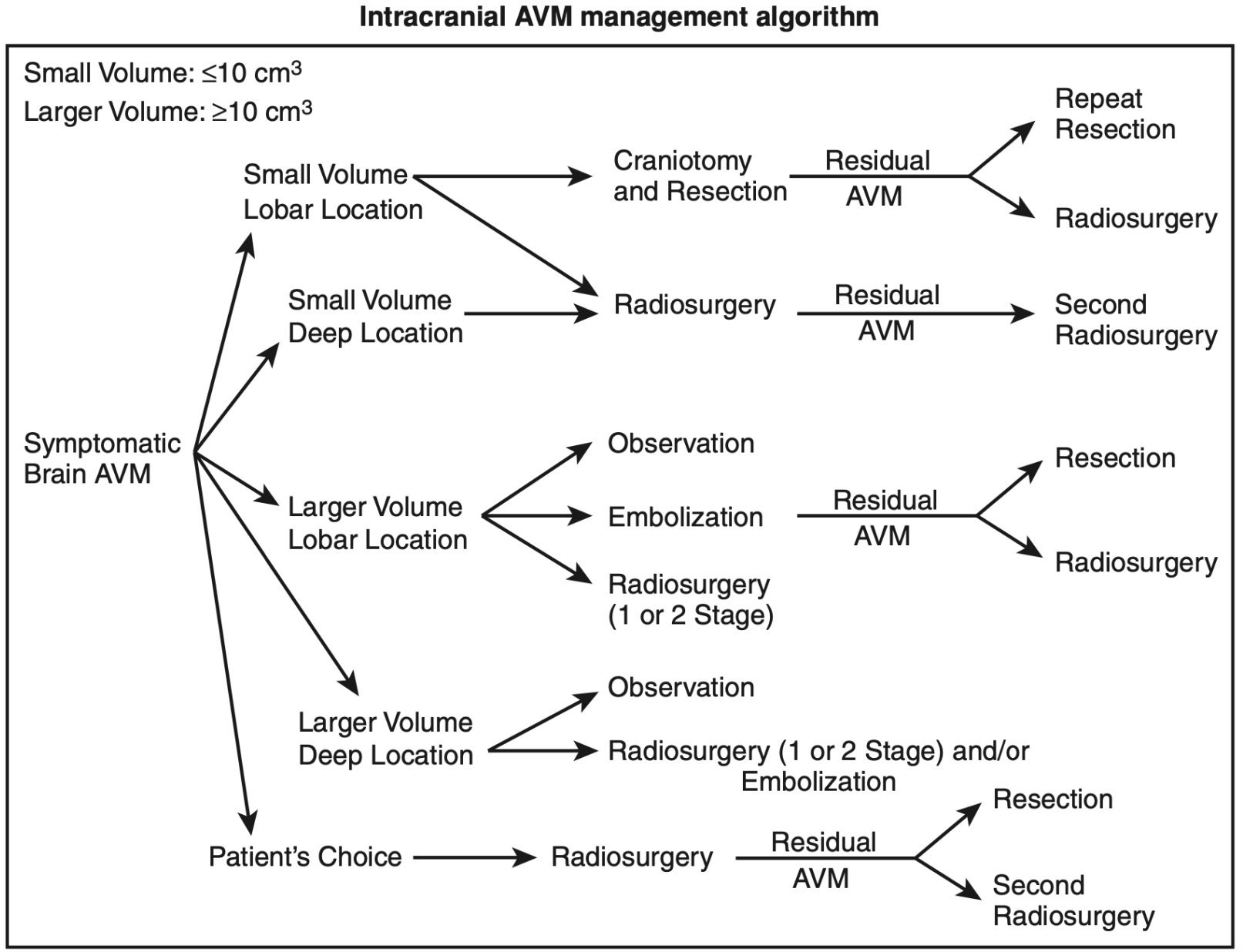
- **Modified Pollock Flickinger AVM score**

**AVM score = (0.1) (volume, ml) + (0.02) (age, yr) + (0.5) (location)**
basal ganglia/thalamus/ brainstem = 1

| AVM score | Excellent outcome | Decline in MRS |
|---|---|---|
| ≤1.00 | 89% | 0% |
| 1.00 - 1.50 | 70% | 13% |
| 1.51 – 2.00 | 64% | 20% |
| > 2.00 | 46% | 36% |

Neurosurgery 63:239–243, 2008

- Imaging workup:
  - CT: Lesions are typically identified on CT, which demonstrate strong contrast enhancement and appear as isodense or hyperdense tortuous vessels. There may be areas of haemorrhages surrounding the nidus. More sensitive imaging (see below) is usually required.
  - MRI/MRA: Increased sensitivity for evaluating the nidus, which demonstrate strong contrast enhancement and appear as hypointense flow voids on both T1- and T2-weighted series.
  - DSA: The gold standard modality for AVM diagnosis and nidus delineation.




IRSA intracranial AVM management algorithm.

- Factors influencing treatment recommendations include patient age, medical comorbidities, cranial nerve deficits, AVM size and/or growth rate, presenting symptoms, competing symptoms (i.e., contralateral hearing or vision loss), and proximity to critical OARs

- Single-fraction SRS for low-grade or small-volume AVMs (SM Grade I–II, low AVM score, nidus volume <10–15 cc), including those in eloquent or deep locations not amenable to surgical resection.

# Target delineation

- Target is the entire nidus, delineated by co-registration with brain MRI/MRA and/or CT angiography. Draining veins best visualized during arterial phase of angiogram are not part of the target.

- CT scans assist in the detec- tion of hemorrhage, and CTA assists in evaluating vascular detail, whereas MRI/MRA allows the best assessment of the surrounding brain parenchyma. Angiography is the most accurate method of categorizing the extent of aneurysms, obstructions, or outflow abnormalities and allows grading of the AVM on the basis of Spetzler–Martin scale.

- The target is the nidus (GTV = CTV).

**Table 3.3** Commonly used dose/fractionation schemes

| Commonly used dose/fractionation schemes | | |
|---|---|---|
| | Patient selection considerations | Dose/fractionation |
| SRS | SM Grade I–II, low risk | 15–24 Gy × 1 fx [10, 11] |
| FSRT | Large lesion, high risk | 12–28 Gy, in 2–4 fx ≥7 days apart [6, 12] |
| Volume staged | Large lesion, high risk | 13–18 Gy, in 2–4 sessions, 3–9 months apart [7, 8] |

*SM* Spetzler-Martin

For large or high-risk AVMs, the optimal treatment approach remains controversial, but includes FSRT versus volume-staged SRS:
FSRT: Total dose is divided into ≥2 equal fractions delivered approximately weekly*
Volume-staged SRS: The AVM nidus is divided into several regions based upon branches of vascular flow (typically 2–4), each of which is treated to an effective single-fraction dose, commonly with a 3–9-month break interval**

***Radiol Oncol. 2013;47(1):50–6.***
****J Neurosurg. 2016;124(1):163–74.***

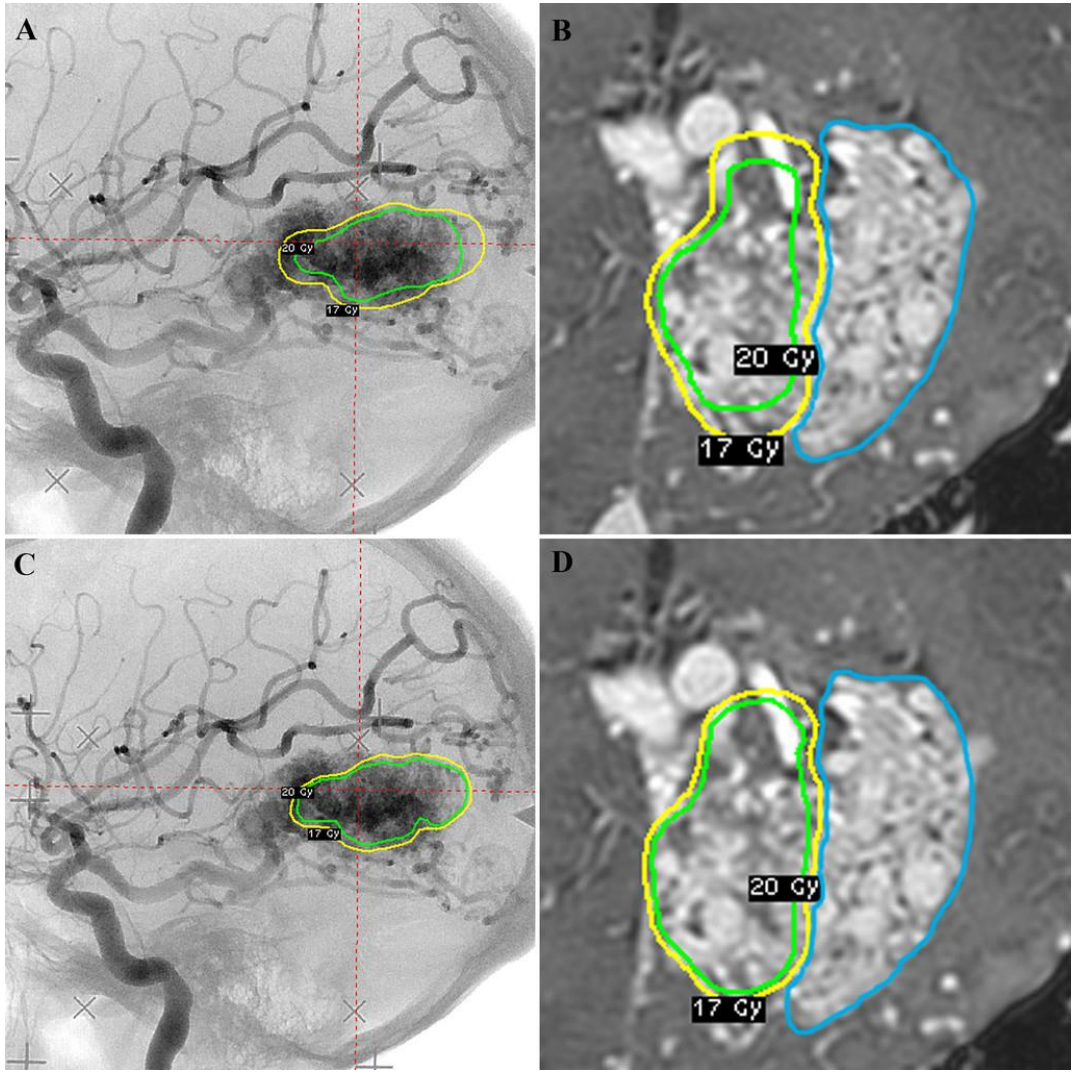
# RADIOSURGERY FOR LARGE CEREBRAL AVM

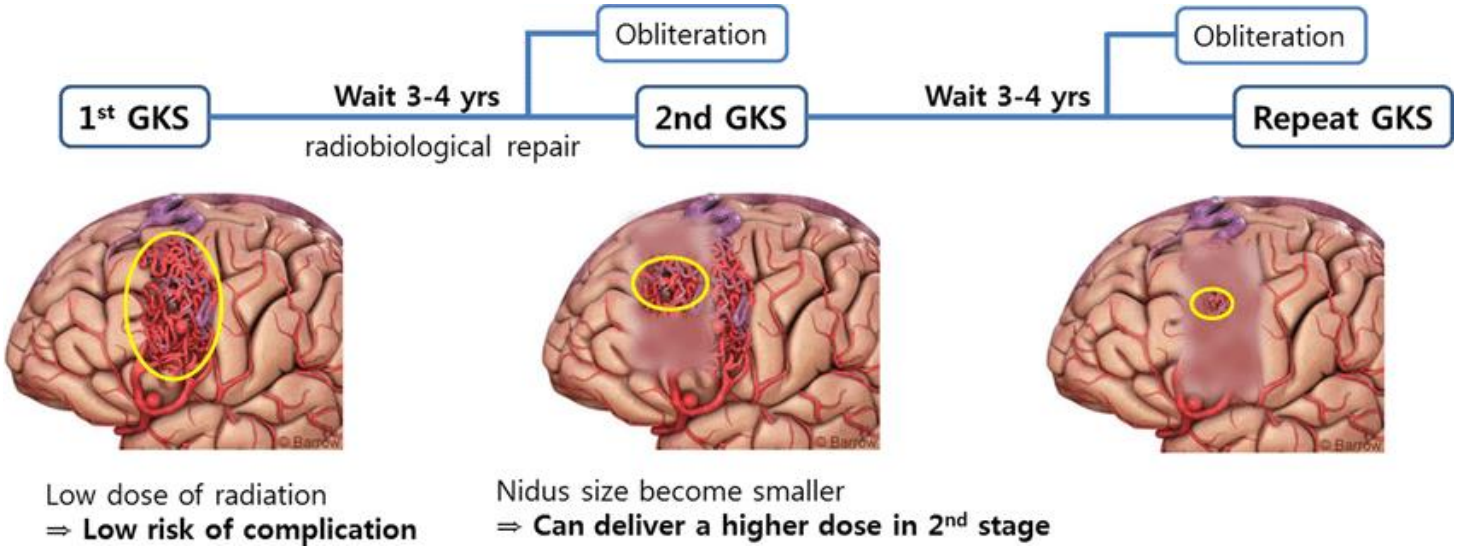
- SRS after Embolization

- Volume Staged Radiosurgery (33-53%)
  - The interval of each radiosurgery sessions are usually from 3 to 6 months.
  - The each session volume is decided on the chance of develop- ing a radiation-induced complication based on the 12-Gy volume
  - Volume staging can be based on different feeding arterial area on planning an- giogram and major draining veins is treated last session

- Dose staged Radiosurgery (0-70%)
  - Repeated radiosurgery of the whole nidus using low doses for each single session over an interval period of 3–4 years41)

- HfRT (5-74%)
  - BED to a single-session radiosurgery 15 Gy

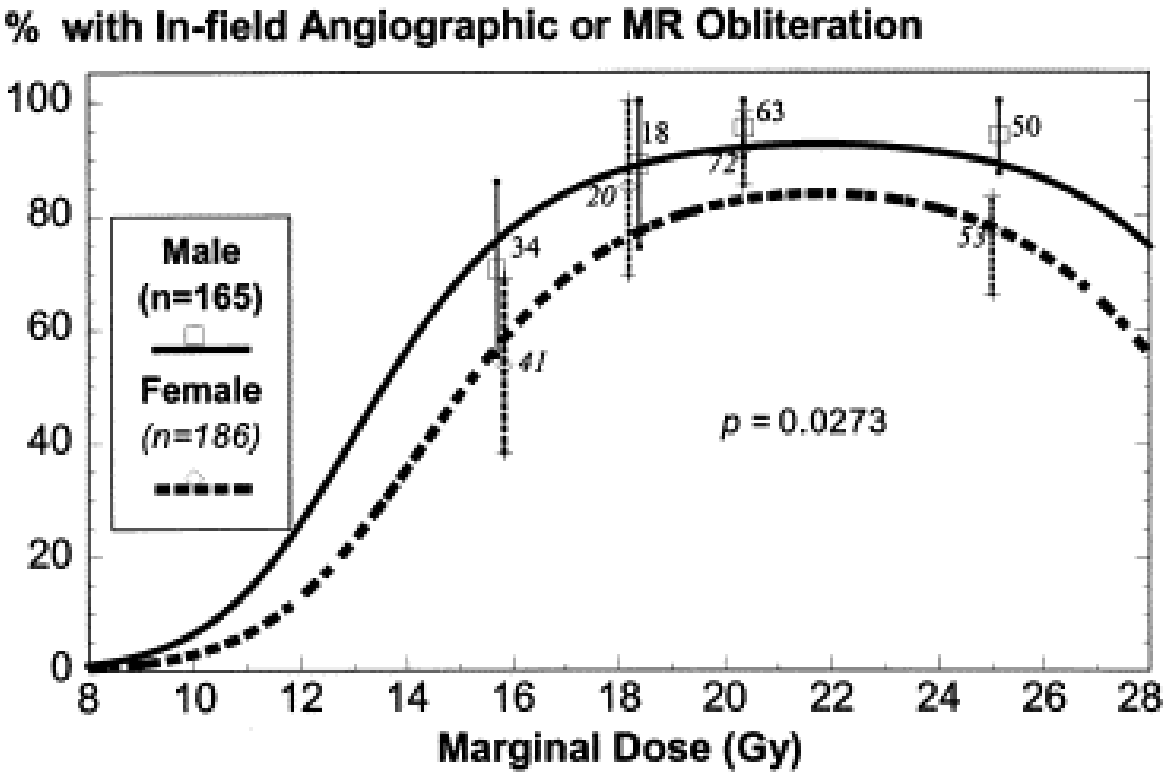


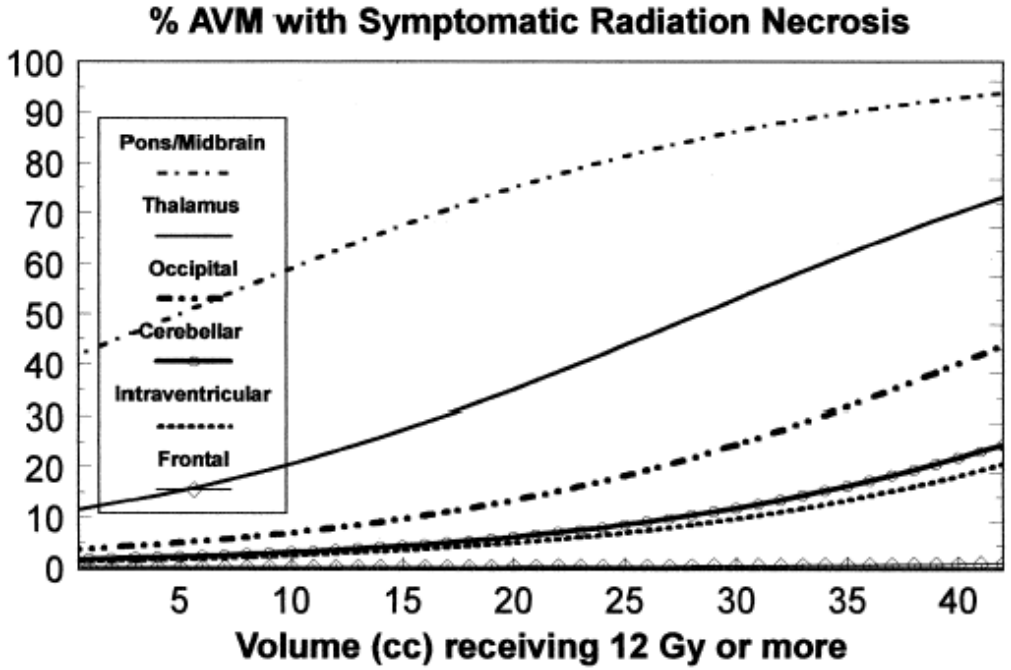




Low dose of radiation
⇒ **Low risk of complication**

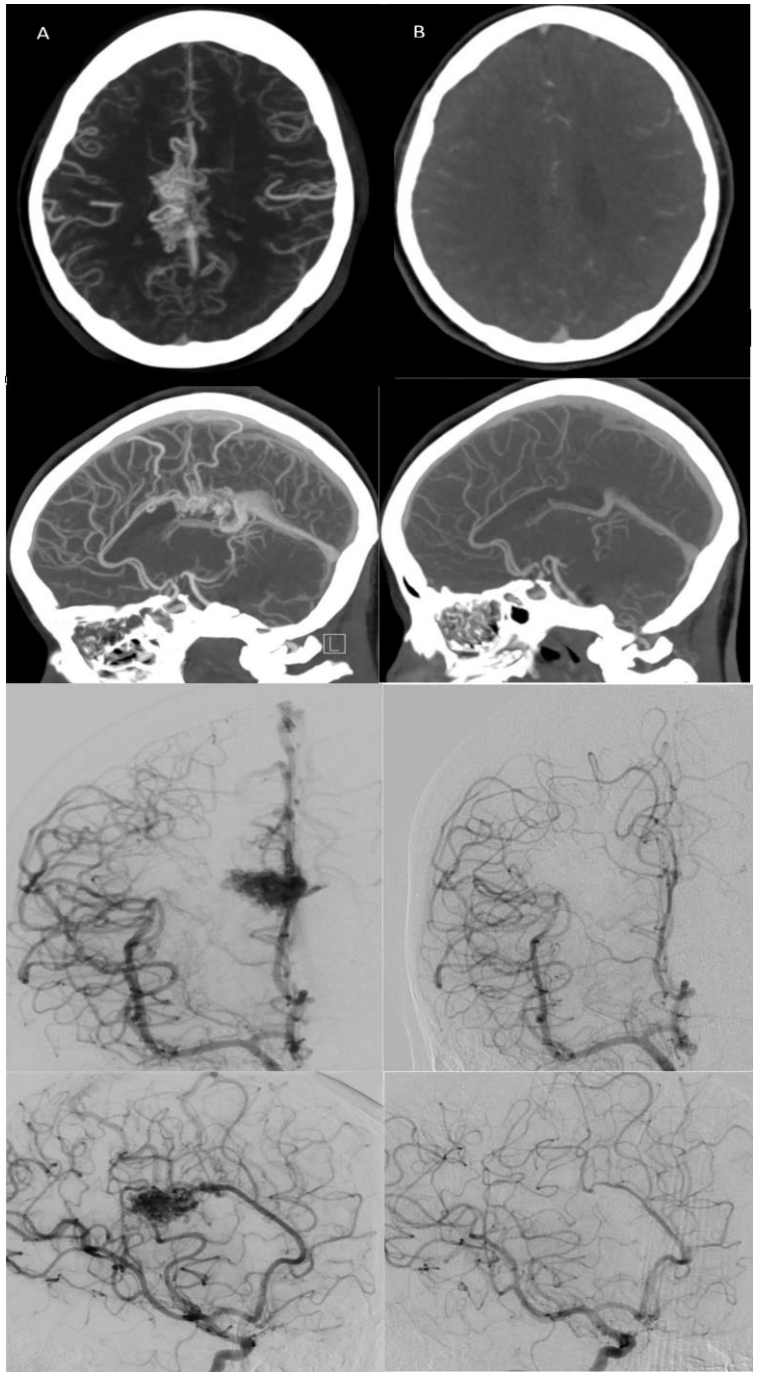
Nidus size become smaller
⇒ **Can deliver a higher dose in 2nd stage**

# FLICKINGER'S MODEL



| Study | Patients (*n*) | Median follow-up (months) | Median AVM vol ($cm^3$) | Modality, median marginal dose, fractionation | Obliteration rate (%) |
|---|---|---|---|---|---|
| Pan (2000) [22] | 240 | 26 (12–73) | 32% >10 | GaK, 15–18 Gy × 1 fx | – vol 10–15 $cm^3$: 77% at 40 months<br>– vol >15 $cm^3$: 25% at 40 months<br>– 58% at 50 months |
| Flores (2011) [23] | 213 | 48 | 2.1 (mean) | Linac, 14 Gy × 1 fx | – 66% at 3 years<br>– 82% at 5 years |
| Kano (2012) [18] | 217 (SM I-II) | 64 | 2.3 | GaK, 22 Gy × 1 fx | – 58% at 3 years<br>– 87% at 4 years<br>– 90% at 5 years<br>– 93% at 10 years |
| Stark (2013) [24] | 1012 | 96 | 3.5 (mean) | GaK, mean 21.1 Gy × 1 fx | 69% overall |
| Hattangadi-Gluth (2014) [11] | 248 | 35 | 3.5 | Protons, 15 Gy (RBE) × 1 fx | – 65% at 2.9 years<br>– 70% at 5 years |
| Ding (2014) [10] | 502 (SM I-II) | 48 (radiographic) 62 (clinical) | 2.4 | GaK, 23 Gy × 1 fx | – 66% at 5 years<br>– 80% at 10 years |
| Silander (2004) [19] | 26 | NA | 13 | Protons, FSRT, 20–25 Gy (RBE) total in 2–4 fx | – vol <25 $cm^3$:70%<br>– vol ≥25 $cm^3$: 30% |
| Vernimmen (2005) [25] | 64 | 62 | 41% <14, 59% ≥14 | Protons, FSRT, 2–3 fx<br>– Volume <14 $cm^3$: Minimum target vol total dose—15 Gy (RBE)<br>– Volume ≥14 $cm^3$: Minimum target vol total dose—10.4 Gy (RBE) | – vol <14 $cm^3$: 75%<br>– vol ≥14 $cm^3$: 43% |
| Hattangadi (2012) [12] | 59 | 56 | 22.9 | Protons, FSRT, 8 Gy (RBE) × 2 fx | Total 15%, partial 34%, stable 51% |
| Blamek (2013) [6] | 49 (37% SM III) | 29 | 18 | 19.9 Gy total dose in 2–4 fx | 1 year 7%<br>2 years 11%<br>3 years 21% |



2-Year obliteration rate for single- fraction treatment:
<2 cm 90–100 %, >2 cm 50–70 %

To note, there remains an inherent risk of hemorrhage until obliteration occurs, including any hemorrhage (LG 0–6%, HG 2–22%) and fatal hemorrhage (LG 0–3%, HG 0–15%)

## Comparison of treatment modalities

| | Ablation | Time | Seizures | | New defecits |
|---|---|---|---|---|---|
| | | | Old | new | |
| Surgery | 96% | Immediate | 66 -76% | 4-15% | 2.5 – 17% |
| Curative embolization | 5-20% | Immediate | | | 10 - 14 % |
| Radiosurgery | 80% at 2 Yrs at marginal dose of 25 Gy | Years | | | 5 – 10 % |
| | | | | | |

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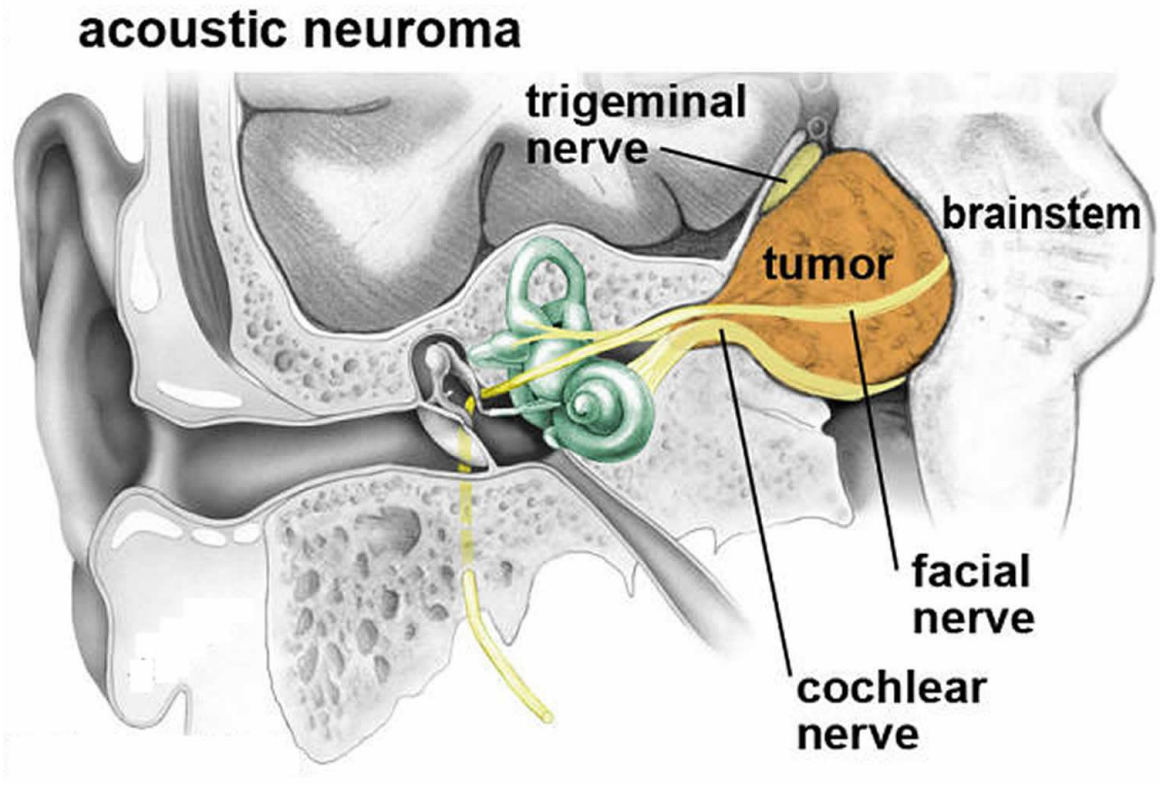
# Vestibular schwannomas/Acoustic Neuroma

- Unilateral/Sporadic… B/L …NF2
- Origin: and refer to a rare slow growing benign tumour usually arising from the vestibular branch and less often the cochlear branch of the 8th cranial nerve.
- The average VS growth rate has been estimated between 1 and 3 mm/year, with approximately 5% of VS remaining stable or regressing during surveillance
- The natural history is characterized by progressive growth within the internal auditory canal, extending to the cerebellopontine angle with associated compression of nearby cranial nerves most notably the facial and trigeminal nerves as well as the brainstem



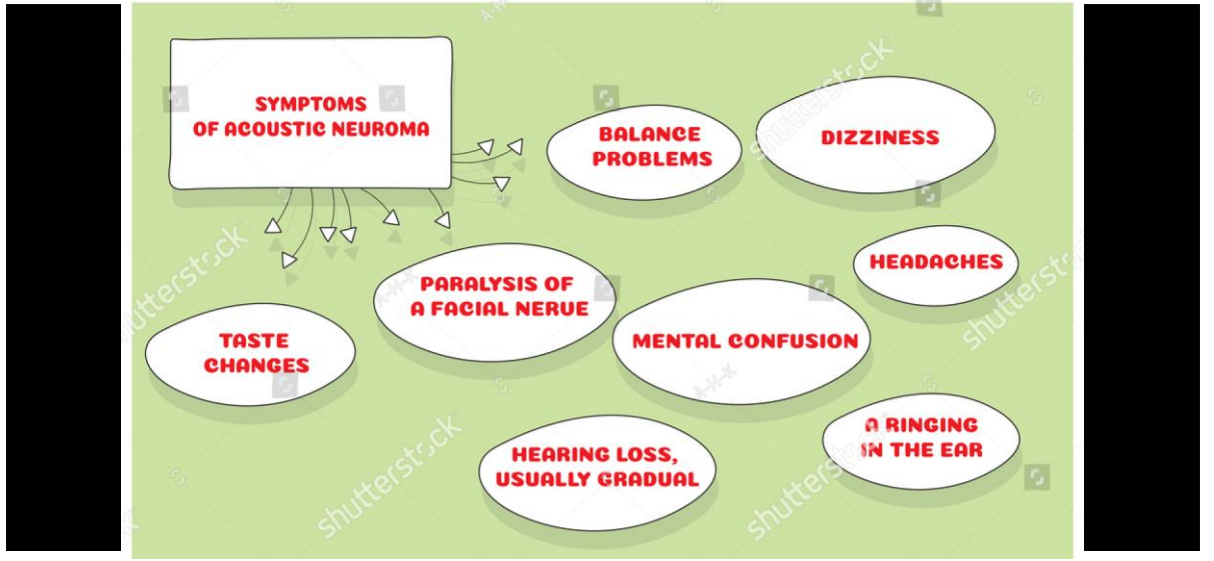



**Table 6.1** Koos Grading System for Vestibular Schwannomas

| Koos grading system for vestibular schwannomas[a] | |
|---|---|
| Grade | Tumor localization/extension |
| I | Purely intracanalicular |
| II<br>IIA<br>IIB | Extension into the CPA (without contacting the brainstem):<br>≤ 10 mm from the porus acusticus<br>11–18 mm from the porus acusticus |
| III | Large tumor extending to the CPA cistern without brainstem displacement |
| IV | Very large tumor with displacement of brainstem and/or cranial nerves |

[a]Modified from Koos et al. [4]. *CPA* cerebellopontine angle

# Work-up

- Pure Tone Audiometry: Initial screening test of choice, most commonly revealing asymmetric sensorineural hearing loss, preferentially at higher frequencies.

- Imaging workup:
  - CT: Appear as a well-defined isodense, contrast-enhancing mass within the internal auditory canal with variable extension into the cerebellopontine angle, and rarely harbor calcifications (as opposed to meningiomas).

  - MRI: Gold standard imaging modality; typically appear iso- or hypointense to the pons on T1-weighted images, heterogeneously hyperintense on T2-weighted images, and strongly and homogenously contrast enhancing.

  - Post-contrast T1-weighted images with thin (1 mm) sectioning through the internal auditory canal are ideal. High-resolution constructive interference in steady state (CISS) or 3D fast imaging employing steady-state acquisi- tion (FIESTA) sequences can show enhanced visualization of structures surrounded by CSF, thereby assisting in delineation of the tumor and cranial nerves.

# Treatment:

- Goals of therapy are to maximize local tumour and preservation of function (i.e., minimizing hearing loss and other cranial nerve deficits such as facial or trigeminal nerve dysfunction).

- Management options include surveillance, surgical resection, SRS, FSRT, or conventionally fractionated radiotherapy.

- No prospective randomized multi-institutional study has directly compared microsurgery with radiosurgery; however, retrospective single-institution series indicate similar oncological outcomes.

- Large tumors, more symptomatic tumors, and tumors presenting with hydrocephalus generally require microsurgical resection.

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0360-3016/10/$–see front matter

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# DIFFERENCES IN CLINICAL RESULTS AFTER LINAC-BASED SINGLE-DOSE RADIOSURGERY VERSUS FRACTIONATED STEREOTACTIC RADIOTHERAPY FOR PATIENTS WITH VESTIBULAR SCHWANNOMAS

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**Purpose:** To evaluate the outcomes of patients with vestibular schwannoma (VS) treated with fractionated stereotactic radiotherapy (FSRT) vs. those treated with stereotactic radiosurgery (SRS).

**Methods and Materials:** This study is based on an analysis of 200 patients with 202 VSs treated with FSRT ($n = 172$) or SRS ($n = 30$). Patients with tumor progression and/or progression of clinical symptoms were selected for treatment. In 165 out of 202 VSs (82%), RT was performed as the primary treatment for VS, and for 37 VSs (18%), RT was conducted for tumor progression after neurosurgical intervention. For patients receiving FSRT, a median total dose of 57.6 Gy was prescribed, with a median fractionation of 5 x 1.8 Gy per week. For patients who underwent SRS, a median single dose of 13 Gy was prescribed to the 80% isodose.

**Results:** FSRT and SRS were well tolerated. Median follow-up time was 75 months. Local control was not statistically different for both groups. The probability of maintaining the pretreatment hearing level after SRS with doses of ≤13 Gy was comparable to that of FSRT. The radiation dose for the SRS group (≤13 Gy vs. >13 Gy) significantly influenced hearing preservation rates ($p = 0.03$). In the group of patients treated with SRS doses of ≤13 Gy, cranial nerve toxicity was comparable to that of the FSRT group.

**Conclusions:** FSRT and SRS are both safe and effective alternatives for the treatment of VS. Local control rates are comparable in both groups. SRS with doses of ≤13 Gy is a safe alternative to FSRT. While FSRT can be applied safely for the treatment of VSs of all sizes, SRS should be reserved for smaller lesions. 

Acoustic neuroma, Precision radiotherapy, Local control, Hearing preservation.

# SRS/SRT

- Factors influencing treatment recommendations include patient age, medical comorbidities, cranial nerve deficits, tumor size and/or growth rate, presenting symptoms, competing symptoms (i.e., contralateral hearing loss), and proximity to critical organs at risk (OAR, such as brainstem, cochlea).

- For single-fraction SRS, targets should generally be <3 cm.

- For FSRT, tumors may be larger (>3–4 cm), in closer proximity to or involving OARs.

- Patients with non-serviceable hearing (typically <50% speech discrimination at >50 dB) may not benefit from therapeutic approaches to preserve hearing.

## Target Delineation:

The tumor bed/GTV is defined as the enhancing lesion on the post-gadolinium T1-weighted MRI.

## Margins:

GTV = CTV.
PTV = CTV plus 0–2 mm uniform expansion for a stereotactic frame.

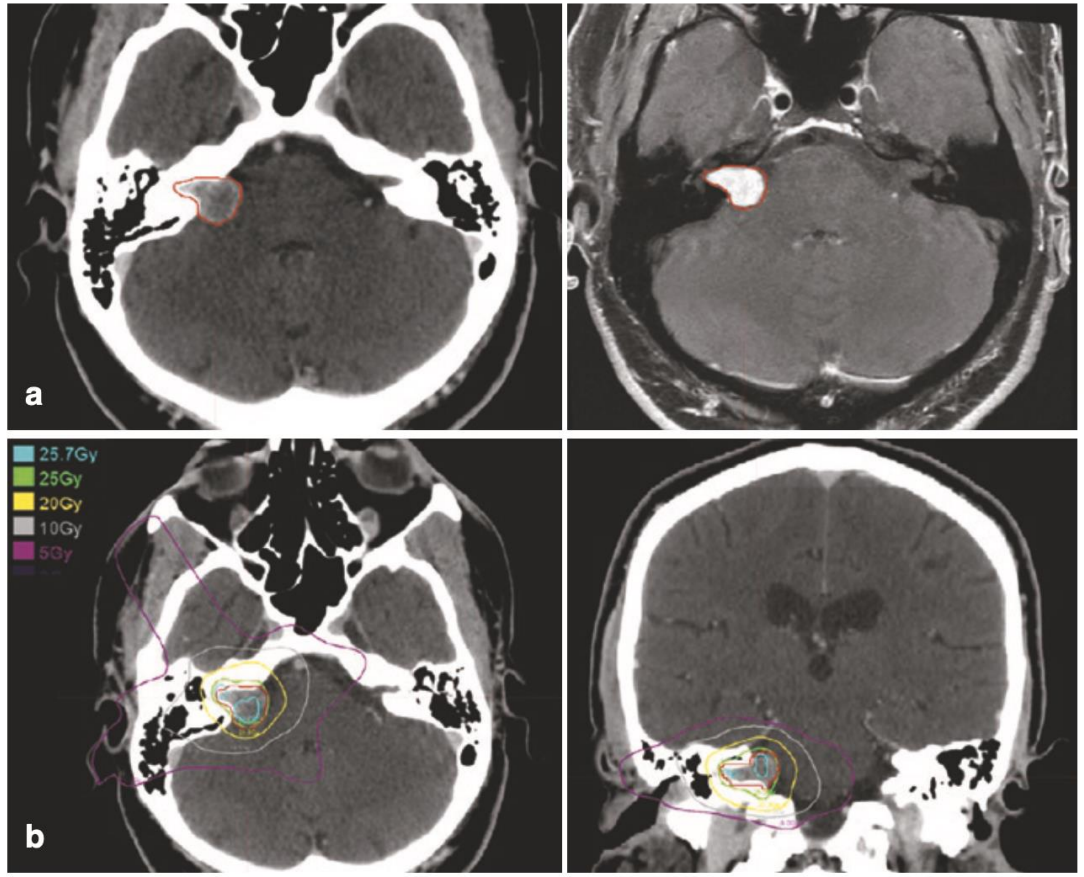


**Table 6.3** Commonly utilized dose/fractionation schemes for SRS and FSRT

| | Patient selection considerations | Dose/fractionation |
|---|---|---|
| SRS | Small, <3 cm | 12–13 Gy |
| FSRT | Larger, >3–4 cm | 5 Gy × 5 fx, 3 Gy × 10 fx [8, 9] |

*Fx* fraction(s)

- Thirty to 40% of patients with useful hearing treated with SRS, loose hearing over 6-24 months.
- Other chronic side effects include a less than 5% risk of injury to the facial/trigeminal nerve function as well as headaches, imbalance and tinnitus.
- 10% of patients experience acute treatment complications or worsening of pre-treatment symptoms from treatment related tumor edema with further compression of the nerves or artery.
- The edema can occur weeks after treatment and persist up to 18-24 months.
- Radiographic treatment success is a stable or reduced tumour size with central loss of contrast enhancement seen on subsequent MRI's. Imaging studies are routinely obtained at 6 months, 12 months, and then every other year thereafter.
- All patients are advised to obtain audiological testing at the time of their MRI studies.

**Table 6.5** Relevant literature

| Study | Patients (*n*) | Median follow-up (year) | Mean tumor vol ($cm^3$) | Modality, dose, fractionation | PFS | Hearing preservation (%) |
|---|---|---|---|---|---|---|
| Prasad 2000 [15] | 153 | 4.3, (mean) | 2.6–2.8 | GaK, 13 Gy × 1 fx | 93% | 58[a] |
| Hasegawa 2005 [16] | 317 | 7.8 | 5.6 | GaK, 13.2 Gy × 1 fx | – 93% 5 years<br>– 92% 10 years | 13(>13 Gy)[a]<br>68(≤13 Gy)[a] |
| Friedman 2006 [17] | 295 | 3.3 | 2.2, (median) | Linac, 12.5 Gy × 1 fx | – 98% 2 years<br>– 90% 5 years | NA |
| Chopra 2007 [18] | 216 | 5.7 | 1.3 | GaK, 13 Gy × 1 fx | – 98% 10 years | 44, 10 years[a] |
| Fukuoka 2009 [13] | 152 | >5 | 2.0 | GaK, 12 Gy × 1 fx | – 94% 5 years<br>– 92% 8 years | 71 |
| Murphy 2011 [14] | 103 | 3.1 | 1.95 | GaK, 13 Gy × 1 fx | 91% | NA |
| Kalapurakal 1999 [19] | 19 | 5.4 | 3.5 cm (mean diameter) | Linac, 6 Gy × 6 weekly fx ($n = -6$); 5 Gy × 6 weekly fx ($n = 13$) | 100% | 100 |
| Williams 2002 [8] | 150 | 1.9 | 1.5 (≤3 cm), 8.7 (3–4 cm), 26.3 (≥4 cm) | Linac, 5 Gy × 5 fx (≤3 cm, $n = 131$), 3 Gy × 10 fx (3–4 cm, $n = 18$), 2 Gy × 20 fx (>4 cm, $n = 1$) | 100% | 72[a] |
| Meijer 2003 [20] | 80 | 2.8 | 2.5 cm, (mean diameter) | Linac, 4 Gy × 5 fx (1992–1995), 5 Gy × 5 fx (1995–2000) | – 94% 5 years | 61 |
| Kapoor 2011 [9] | 385 | 4.7 | 2.66, (mean) | Linac, 5 Gy × 5 fx ($n = 340$) or 3 Gy × 10 fx ($n = 36$) | – FFS 97%<br>– FFRP 70%<br>– 7.6 years median time to progression | NA |

[a]Gardner-Robertson Class I–II.; *vol* volume, *FFS* freedom from surgery, *FFRP* freedom from radiologic progression

Thanks