INDIAN COLLEGE OF RADIATION ONCOLOGY (ICRO)
PG TRAINING PROGRAMME
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Role of Highly Conformal Radiation Therapy in Benign Tumours

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WHAT DO WE COVER TODAY

		Functional category			
		Degenerative	Hyperproliferative	Functional	Focal lesion
Anatomical site	Eye		Pterygium	Graves' disease Orbital pseudotumor	
	Head and neck			Sialorrhoea	Paraganglioma
	Skin		Keloid*	Lymphatic fistula	
	Brain				Arteriovenous malformation Meningioma Acoustic neuroma Pituitary adenoma Trigeminal neuralgia
	Bones and joints	Arthritis tendinitis	Dupuytren's disease Ledderhose's disease	Heterotopic ossification	
	Heart and peripheral vascular system			Coronary stent restenosis* Vascular stent restenosis*	Refractory cardiac arrhythmias
Dose range (Gy)		2-8	3-30	6-40	12-60

Principles in using Radiotherapy for Nonmalignant Diseases

- To estimate natural course of disease.
- Potential consequences of non treatment.
- Review alternate therapies and their results.
- Risk-benefit analysis.
- Proof of failure of other conventional therapies and that indication is justified.
- Individual potential long term radiogenic risks.
- Various sites are: CNS, head and neck, eye and orbit, skin and connective tissue, skeletal system.

Brain Benign Tumours

Meningiomas

- These make up 15-20% of all primary brain tumours. Treatment of choice is radical surgical resection.

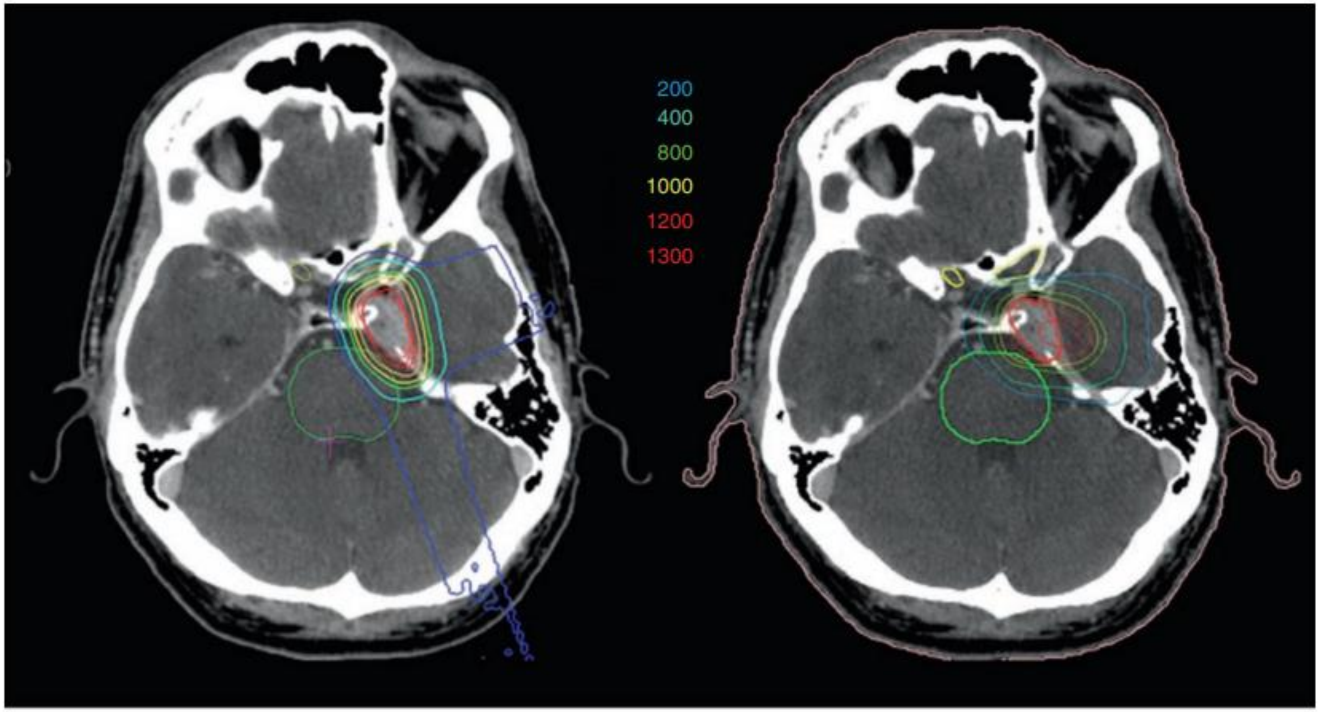
- Indications for radiotherapy:
  - Residual tumour after sub total resection.
  - Tumour relapses after previous surgery.
  - Inoperability due to proximity to critical brain structures.
  - Co-morbid conditions precluding surgery.

- Recommendations and dose of radiotherapy:
  - Primary RT in surgically inoperable cases.
  - RT post operatively after incomplete resection.
  - In case of WHO grade II / III tumours.

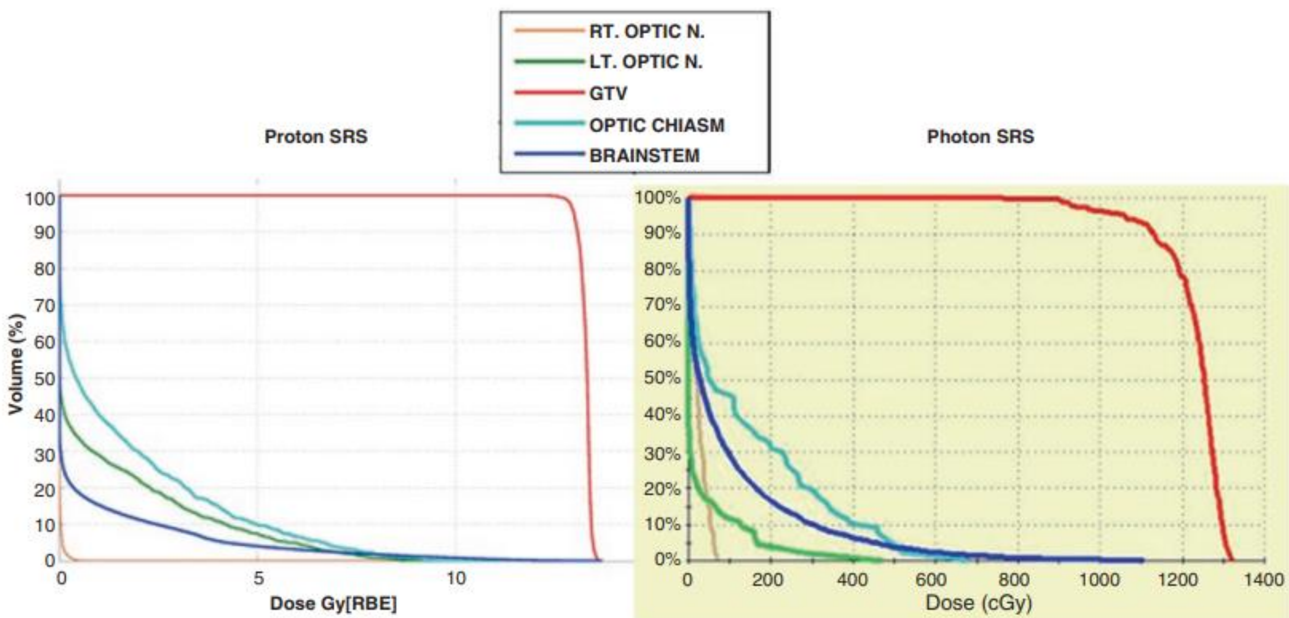
- Benign meningiomas:
  - Treatment volume is GTV + 1 cm margin.
  - Total dose given is 54 Gy in 1.8-2.0 Gy per fractions over 5.5-6 weeks.

- Malignant aggressive disease:
  - Treatment volume is GTV + 2-3 cm margin.
  - Total dose given is 68 Gy in 1.8-2.0 Gy per fractions over 6.5-7.5 weeks.

- SRS / SRT / IMRT can be used to treat smaller lesions or those lying near critical organs.



Dose distribution comparison for a proton and photon SRS treatment for a left cavernous sinus meningioma



Pituitary adenomas

- Therapeutic options include surgery, radiotherapy, drugs or surveillance.

- Indications for radiotherapy:
  - Given post operatively: After sub total resection.
  - Tumour relapses after previous surgery.
  - In clinically relevant persisting hormone secretion even after surgery.
  - Primary RT in surgically inoperable cases.

- Recommendations, volume, technique and dose of radiotherapy:
  - Total dose given is 50 Gy in 1.8 Gy per fraction for 6 weeks.
  - Adjuvant RT, post operatively after incomplete resection.
  - MRI- or CT- based planning is done; 6-18 MV photons are used.

- In Fractionated RT:
  - Total doses are 45 Gy (microadenomas) and 50.4 Gy (macroadenomas) @ 1.8 Gy per fraction.
  - Dose to rest of chiasma and pituitary gland is kept below 50 Gy, to brain tissue below 60 Gy and to brainstem below 50 Gy.

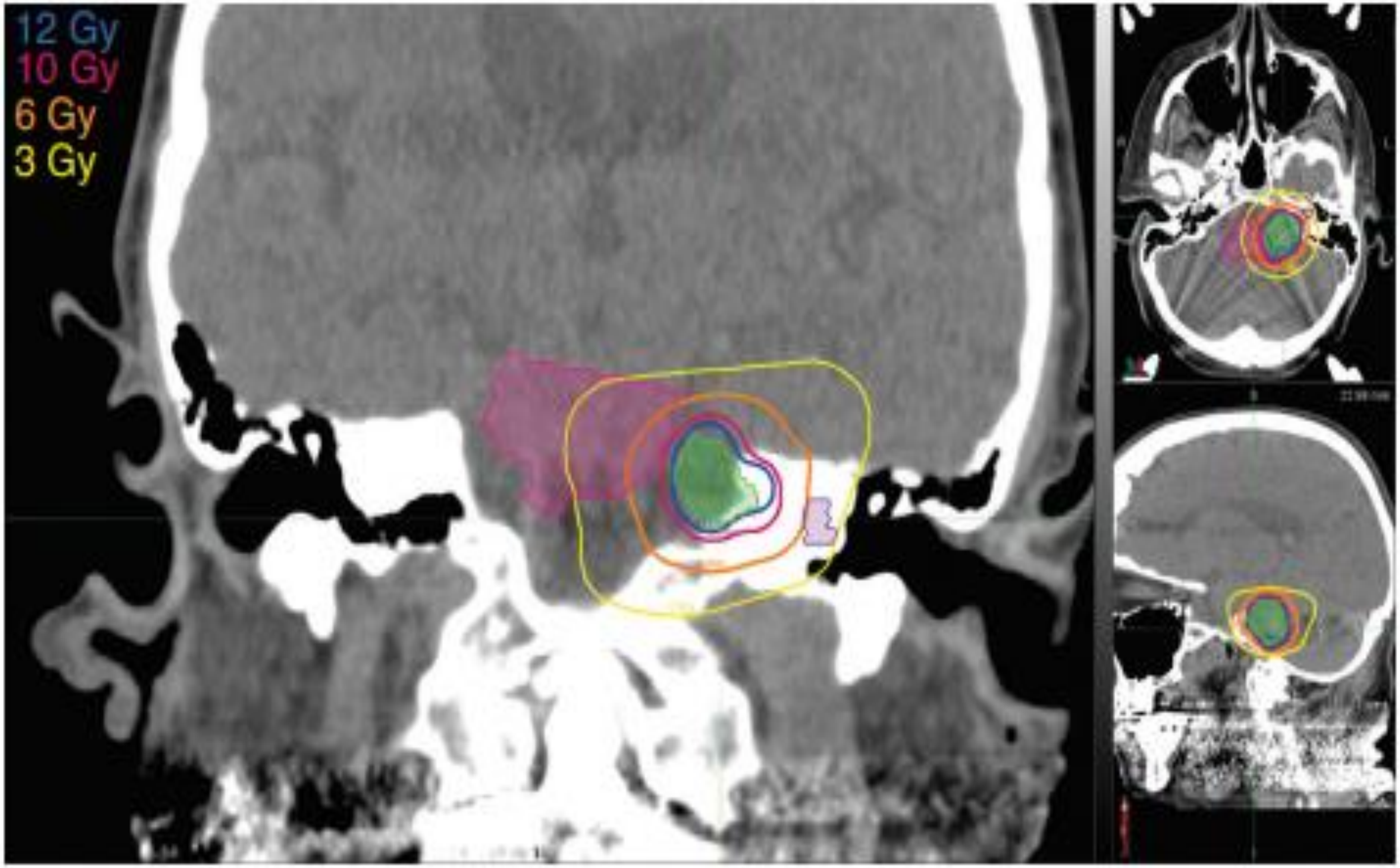
- In Radiosurgery:
  - Total doses are >12-13 Gy (for STH-secreting and inactive adenomas) and 15 Gy (for all other adenomas).
  - Dose to rest of chiasma and pituitary gland is kept below 8 Gy and to 10 mL of brain tissue below 10 Gy.

CRANIOPHARYNGIOMAS / SELLAR TUMOURS:

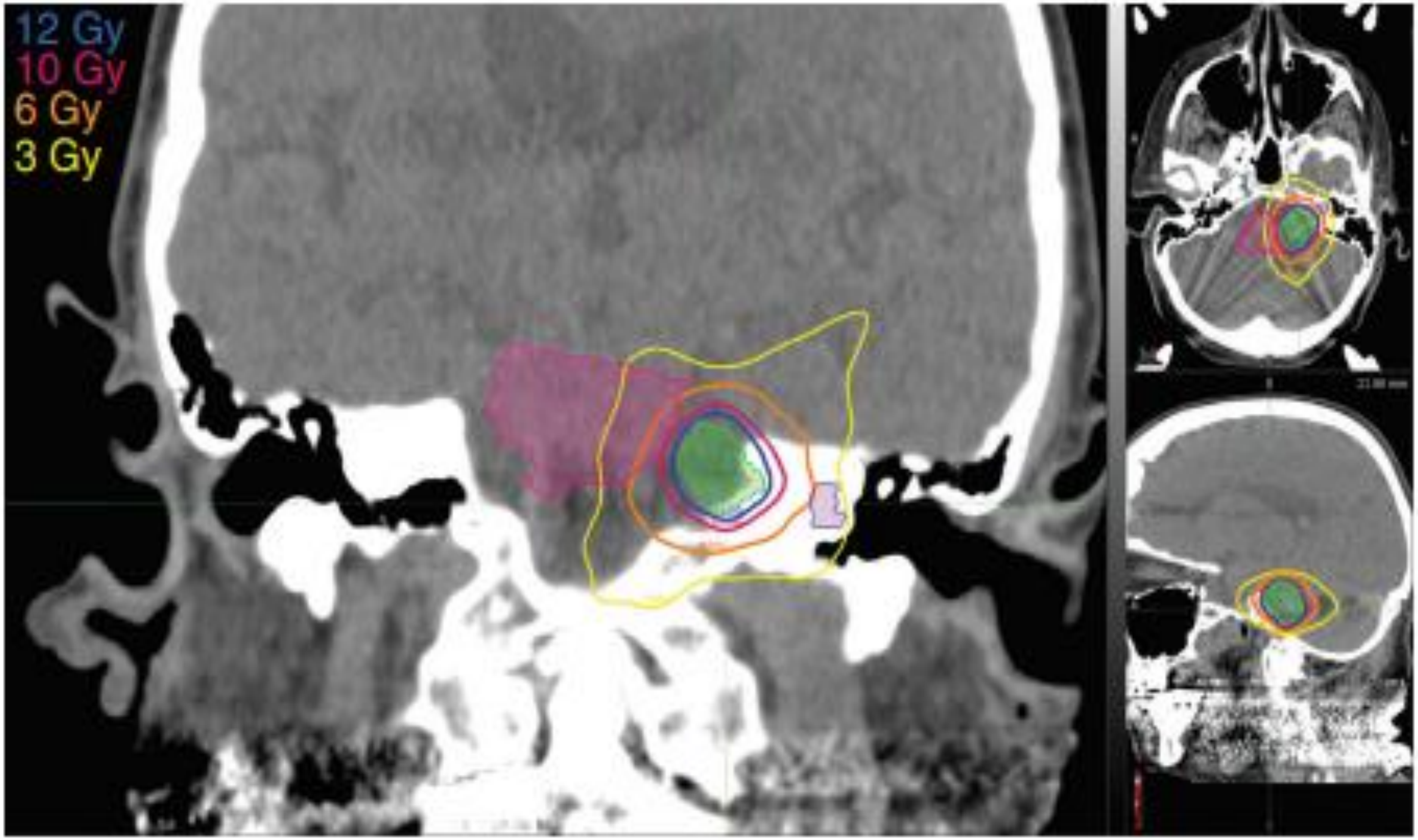
- Craniopharyngiomas are among the most common suprasellar tumours in children and young adults. Surgery is treatment of choice.
- **Indication for RT**:
  - Sub-totally resected tumour.
  - Recurrence after total excision.
- **Dose**:
  - 54 Gy / 30 # / 6 weeks @ 180 cGy per fraction by two parallel opposed fields with 6 MV photons for craniopharyngiomas; 50.4 Gy / 28 # / 6 weeks for other sellar tumours.
- **Radiotherapy target volume**:
  - GTV: includes the whole tumour (solid plus cystic areas) based on pre-operative imaging and any macroscopic residual disease.
  - CTV: GTV plus 1 cm.
  - PTV: CTV plus 0.5 cm.

Acoustic Neuroma

- Surgery- Total or near total resection.
  - If subtotal resection; postop RT is recommended.
  - Preservation of cranial Nerve VII- >60%
  - Preservation of useful hearing- 30-50%
- SRS- 12-13 Gy single fraction.
  - Preservation of cranial Nerve VII- >90%
  - Preservation of useful hearing- 75%
  - Preservation of cranial Nerve V- >90%
- Radical RT- 54Gy in28 #
  - Preservation of cranial Nerve VII- >95%
  - Preservation of useful hearing- 75%
  - Preservation of cranial Nerve V- >95%



A Gamma Knife based SRS plan for a vestibular schwannoma. Tumor–solid green; brainstem–solid pink; cochlea–solid purple



A linac-based SRS plan made with three non-coplanar VMAT arcs for a vestibular schwannoma. Tumor–solid green; brainstem–solid pink; cochlea–solid purple

Organ	Fractionation	Dose (Gy) or dose/volume parameters	Toxicity rate (%)	Type of toxicity
Brain	3-fraction SRS	18 (6 Gy/fx) to <26 ml	<3%	Symptomatic necrosis
Brainstem	3-fraction SRS 5-fraction SRS	18 (6 Gy/fx) to <1 ml, maxPD 23 (7.67 Gy/fx) 26 (5.2 Gy/fx) to <1 ml, maxPD 31 (6.2 Gy/fx)	<3%	Permanent cranial deficit or necrosis
Optic nerve/ chiasm	3-fraction SRS 5-fraction SRS	15 (5 Gy/fx) to <0.2 ml, maxPD 19.5 (6.5 Gy/fx) 20 (4 Gy/fx) to <0.2 ml, maxPD 25 (5 Gy/fx)	<3%	Optic neuropathy
Cochlea	3-fraction SRS 5-fraction SRS	maxPD 20 (6.67 Gy/fx) maxPD 27.5 (5 Gy/fx)	NA	Hearing loss
Medulla oblongata	3-fraction SRS 5-fraction SRS	18 (6 Gy/fx) to <0.25 ml, maxPD 22.5 (6.67 Gy/fx) 22.5 (4.5 Gy/fx) to <0.25 ml, maxPD 30 (6 Gy/fx)	1%	Myelopathy

Normal tissue dose constraints for multifraction SRS

GAMMA KNIFE PLANNING GOALS

- **Radiation Therapy Oncology Group (RTOG) Conformity Ratio (PITV)**: The ratio of the volume encompassed by the prescription dose to the tumor target volume. Should be less than or equal to 2 (except for very small targets). For tumor targets that are adjacent to critical structures, the PITV should be less than or equal to 1.5.
- **RTOG Homogeneity Ratio (MD/PD)**: The ratio of the maximum dose within the treatment volume to the prescription dose has to be less than or equal to 2.
- **Target coverage ratio**: the ratio of the target volume getting the prescribed dose to the target volume.
- **Selectivity ratio**: the ratio of the target volume getting the prescribed dose to the whole volume getting the prescribed dose.
- **GK Vs Linac**: Linac can treat multiple lesions with single isocentre unlike GK

- **Paddick conformity index (PCI)**: target coverage ratio multiplied by selectivity ratio. PCI is inversely proportional to RTOG conformity index with proportionality constant equal to the square of target coverage. When the target coverage is 100%, the PCI is the inverse of the PITV conformity ratio.
- **Gradient Index**: The ratio of the volume getting half of the prescribed dose to the volume getting the prescribed dose. This index should be less than 3 but is not as critical as conformity and inhomogeneity ratios.
- Coverage of the target should be 99% to 100%.
- Usually, GK plans have been prescribed to the 50% IDL. This is due to the shot profile having the sharpest dose falloff at 50% IDL. Usually, 50% is a minimum isodose that can be prescribed to, and still maintain the required inhomogeneity ratio less than or equal to 2.
- Higher prescription IDLs can be used to minimize treatment time or reduce the size of a shot. But increase the spread of low dose which is reflected in a higher gradient index

GLOMUS JUGULARE

- **Indications for Radiotherapy:**
  - Pre-operatively or post operatively.
  - Post surgery recurrence
  - Tumours with destruction of petrous bone, jugular fossa, occipital bone.
  - Patients with jugular foramen syndrome (paralysis of cranial nerves IX – XI).

- **Dose of Radiotherapy:**
  - Total dose of 45-55 Gy in 5 weeks for benign glomus tumours and 65 – 70 Gy in 6.5 weeks for malignant glomus tumours to the PTV @180-200 cGy per fraction 5 times a week is generally sufficient in more than 80% cases for local control.

- **Volume and technique of Radiotherapy:**
  - 3D-CRT or IMRT may be considered for better dose distribution.
  - 15 – 18 MeV electrons used alone or in combination with 4 – 6 MV photons are used (photons for 20 – 25% of total tumour dose). In case of posterior fossa spread, 6 – 18 MV photons used.

Method	Patients (n)	Tumor volume	Dose	Follow-up	Tu. growth control	Tu reduction	Complications
Gamma-knife [4]	46	Median 3.6 cm^3	Median 20 Gy	Median 118 months	98 %	77 %	4 %
Gamma-knife [5]	58	Mean 12 cm^3, median 9.3 cm^3	Mean marginal 13.6 Gy	Mean 86.4 months	91.4 %	67.2 %	8.6 %
LINAC [6]	1 1	NA	Median 15 Gy	Median 5.3 years	81 %	NA	0 %
LINAC [7]	2 7	Median 9.5 ml	Median 15 GY	Median 9.6 years	100 %	37.5 %	3.7 %
CyberKnife [8]	3 31	10 cm^3	25GY/5 fractions	Median 24 months	100 %	49 %	19 %
CyberKnife [9]	8	NA	Mean 12.5 GY	Mean 20 months	100 %	NA	0 %

Arteriovenous Malformation

- Resection – Microsurgical or SRS
- Entire nidus is treated but not feeding arteries or draining vessels.
- Dose- 21 Gy when treated with SRS.

Trigeminal Neuralgia

- Medical management - Carbamazepine, gabapentin, antidepressants, etc.
- Surgical options - Nerve blocks, partial sensory rhizotomy, balloon decompression of Gasserian ganglion, microvascular decompression and peripheral nerve ablation.
- SRS may also be used Dose ~ 80 Gy.

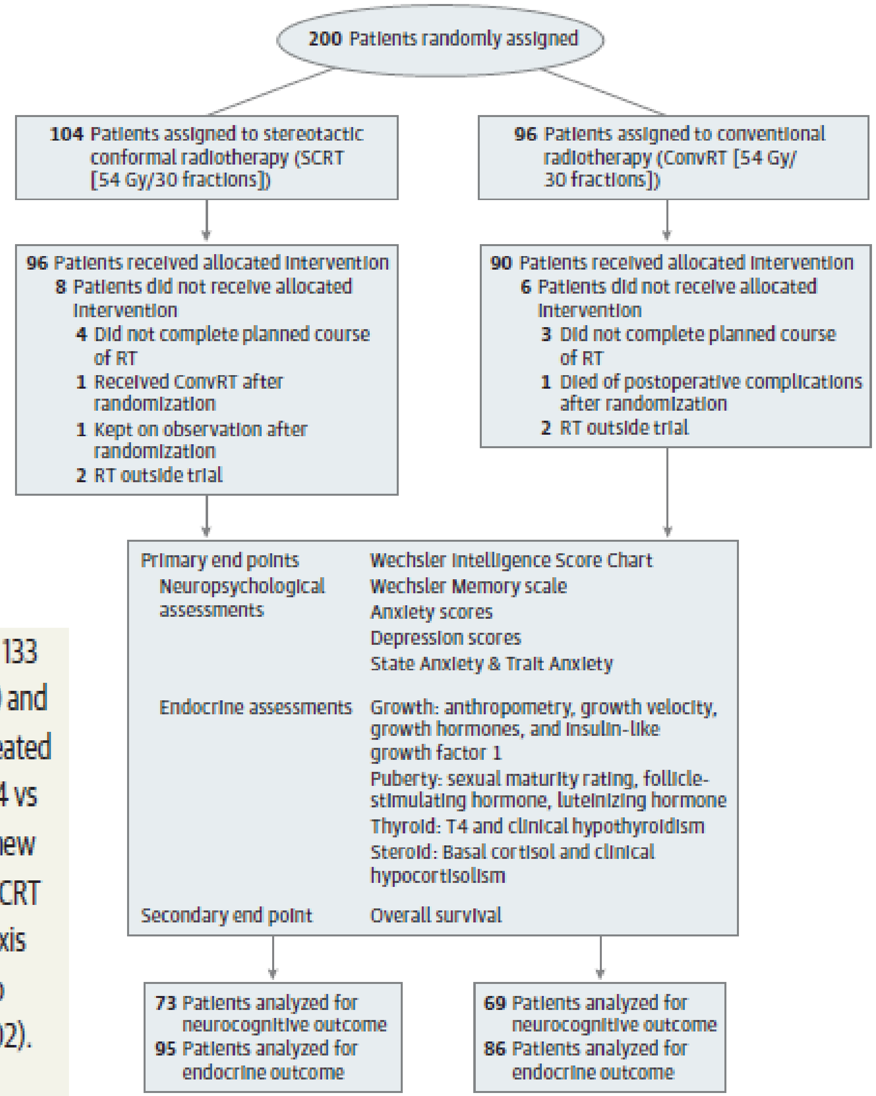
Brain Benign Tumours

- IMRT / IGRT / SBRT: These techniques may be used to improve dose delivery to target volumes and reduce dose to the many dose-limiting OARs within the cranium, including the optic chiasm, right and left optic nerves, both globes, the brainstem, the right and left inner ear, the area postrema, and uninvolved normal brain, especially optic cortex and right and left temporal lobes.
- Reducing dose to the area postrema may reduce the incidence of treatment-related nausea. IMRT in craniospinal axis irradiation can homogenize dose and improve conformality.
- Higher doses to the left temporal lobe and, more precisely, the limbic structures (hippocampus and the parahippocampal gyrus) have shown statistically significant positive correlation with decline in cognitive function, especially in verbal learning and auditory learning domains

RECENT DEVELOPMENTS

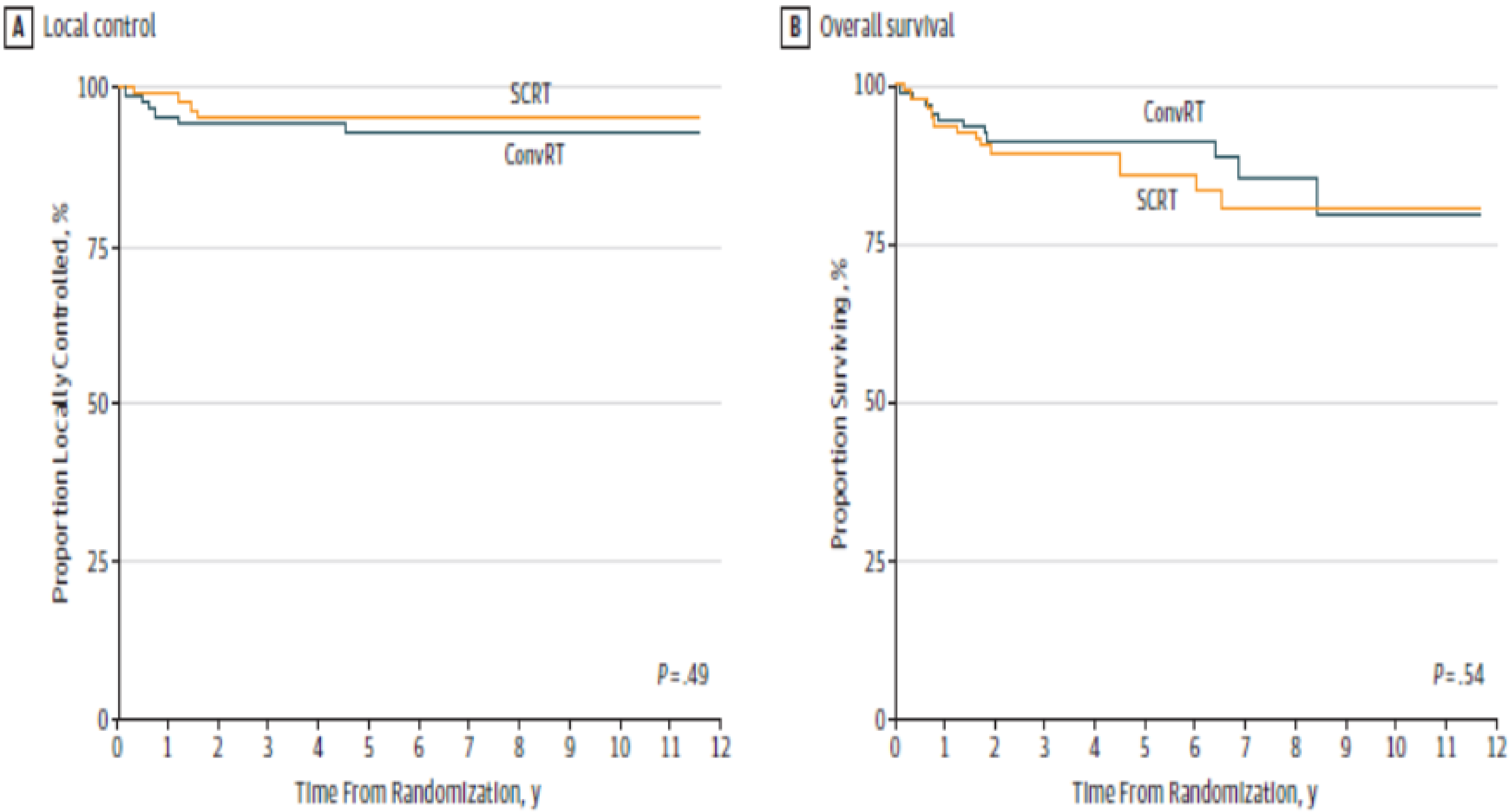
Efficacy of Stereotactic Conformal Radiotherapy vs Conventional Radiotherapy on Benign and Low-Grade Brain Tumors

A Randomized Clinical Trial



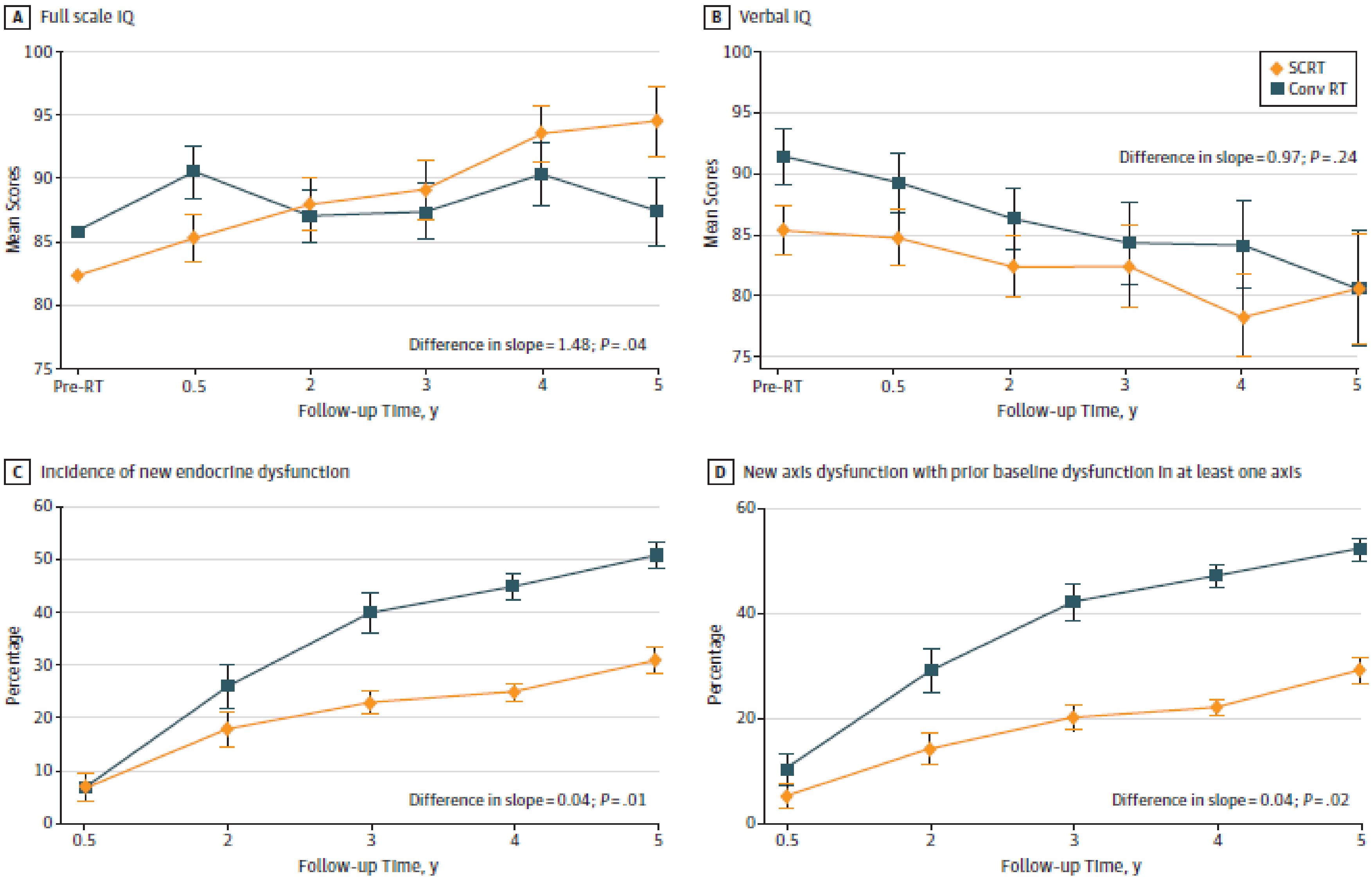
RESULTS In total, 200 young patients (median [interquartile range] age, 13 [9-17] years; 133 males and 67 females) were enrolled. Mean full-scale or global intelligence quotient (IQ) and performance IQ scores over a period of 5 years were significantly superior in patients treated with SCRT compared with those treated with ConvRT (difference in slope = 1.48; *P* = .04 vs difference in slope = 1.64; *P* = .046, respectively). Cumulative incidence of developing new neuroendocrine dysfunction at 5 years was significantly lower in patients treated with SCRT compared with ConvRT (31% vs 51%; *P* = .01) while developing a new neuroendocrine axis dysfunction in patients with preexisting dysfunction in at least 1 axis at baseline was also significantly lower in the SCRT arm compared with the ConvRT arm (29% vs 52%; *P* = .02). Five-year OS in SCRT and ConvRT arms was 86% and 91%, respectively (*P* = .54).

Jalali et al. JAMA Oncology 2017;3(10):1368-76.



A, The local control rate was 95% (95% CI, 88%-98%) for stereotactic conformal radiotherapy (SCRT) and 93% (95% CI, 85%-97%) for conventional radiotherapy (ConvRT) (*P* = .49). B, The overall survival rate was 86% (95% CI, 76%-92%) for SCRT and 91% (95% CI, 83%-95%) for ConvRT (*P* = .54).

Jalali et al. JAMA Oncology 2017;3(10):1368-76.



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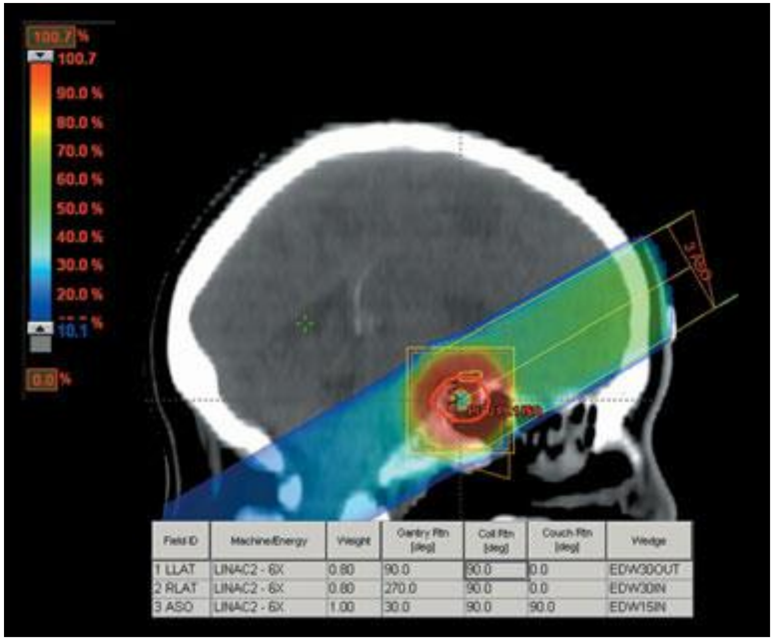
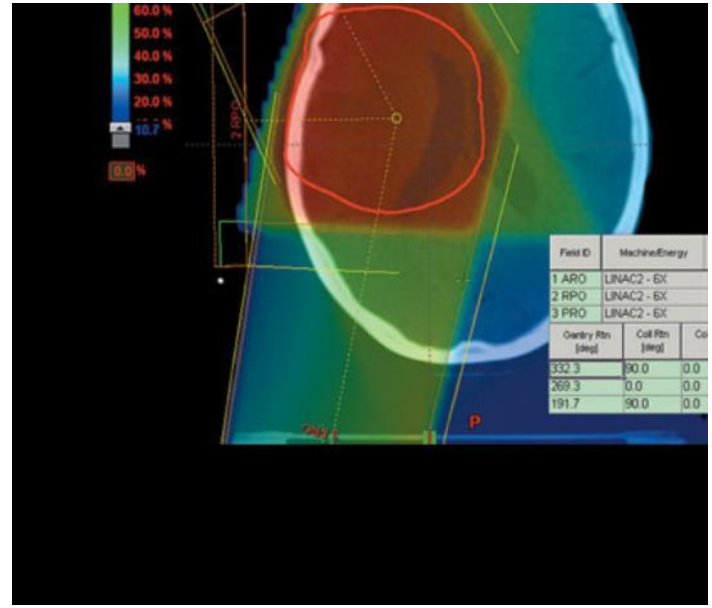
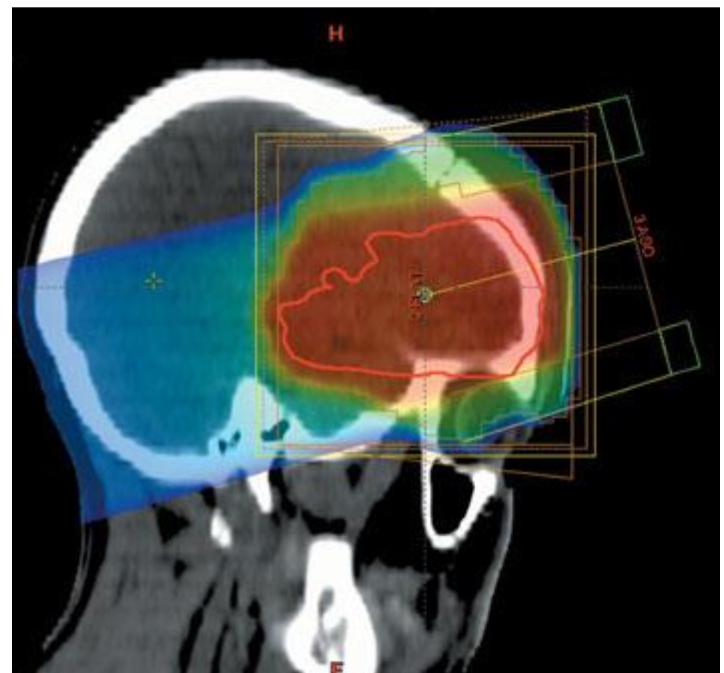




Patient positioning: A neutral head position with the patient supine is easily reproducible. Noncoplanar beams can be used to avoid entry and exit dose to organs at risk (OAR).

IMRT: improves dose delivery to target volumes and reduces dose to the dose-limiting OARs within the cranium.

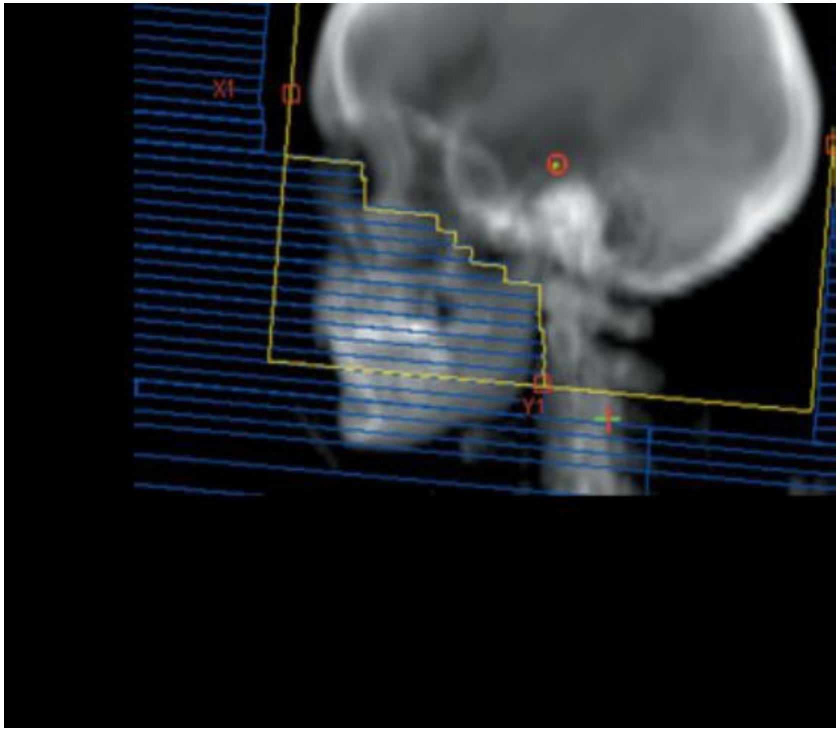


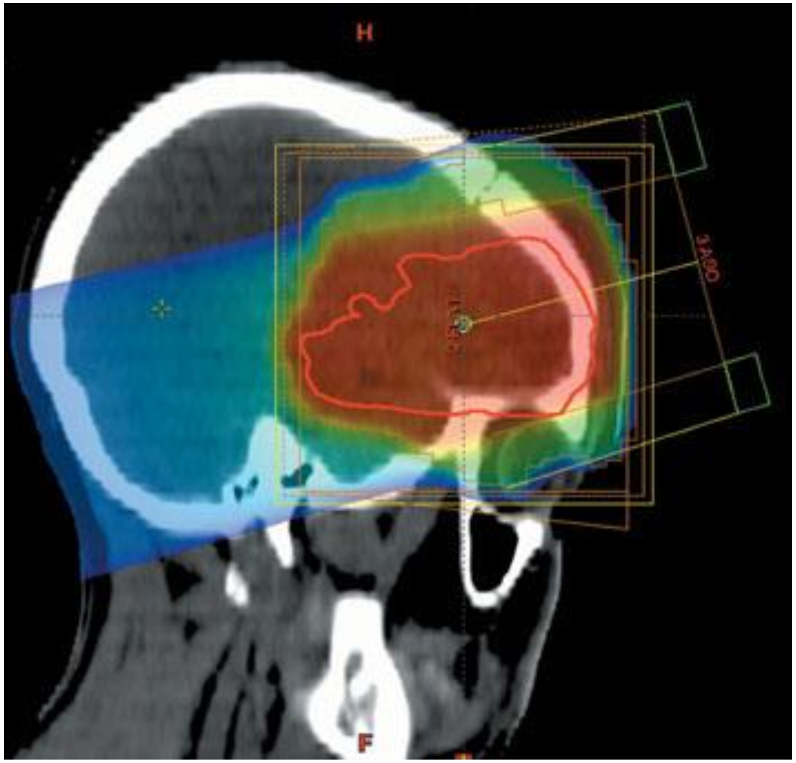
- **Immobilization:** Variability of setup not more than 2-3 mm with thermoplastic mask. More accurate and/or rigid head positioning and immobilization can be obtained by a modified stereotactic head frame with noninvasive multiple-point head fixation.

- Patient is placed in the positioning device, and scanned, typically with radio-opaque reference markers placed at the setup isocenter.

- Verification films taken before treatment; and include orthogonal radiographs to verify the isocenter, + films of any custom-shaped portal fields.

- **Simulation**: patient is immobilised and scanned with three radio-opaque reference markers placed on the thermoplastic mask.
- A prone setup may be considered for posterior fossa tumors.
- An optimum beam arrangement typically consists of 3 to 7 non opposed shaped beams. When applicable, the contralateral uninvolved hemisphere of the brain should be spared as much as possible.
- A true vertex beam should be avoided, if possible, due to exit dose into the body; a 5 to 10 degree gantry rotation should be considered instead.





HEAD AND NECK TUMOURS

Chordomas

- These are rare slow growing midline tumours, originating from embryonal notochord rest in base of skull, clivus, vertebral column or sacral region.
- Complete surgical excision is the treatment of choice.
- Indications for RT:
  - Inoperability
  - After incomplete resection.
- Dose: more than 65 Gy
- Proton beams, Gamma knife or IMRT are particularly useful in treating small tumours near vital structures.

- The emerging technology committee of the American Society of Radiation Oncology (ASTRO) found evidence for a benefit of proton beam radiation therapy over photon therapy in large chordomas

- Other authors, however, observed similar results with proton- and photon-based radiotherapy.

Di Maio S et al. J Neurosurg. 2011;115(6):1094–105.

Jahangiri A et al. Neurosurgery. 2015;76(2):179–1986.

- Complications of proton beam radiotherapy for clival chordomas such as delayed optic nerve neuropathy and blindness have been described

	Proton beam therapy	Carbon ion therapy
Proton advantages over carbon	• Lower cost. • Able to be delivered via gantry, allowing multiple beam angles. • More narrow range of RBE (1–1.1) and greater certainty leading to smaller variations in actual delivered dose. • Decreased risk of late normal tissue damage due to lower RBE.	• Higher cost (2–3 x proton therapy). • Usually delivered via a fixed beam, not permitting multiple angles. • There are uncertainties in the RBE (1.5–3.4) which may cause large variations in the actual delivered dose. • Potential for increased risk of late normal tissue damage due to higher/variable RBE.
Carbon advantages over proton	• RBE is similar to photon radiation and increased tumor control would not be expected. • Larger lateral penumbra which can cause greater dose to normal tissue structures than carbon ion.	• Higher RBE particularly at distal edge of Bragg peak which may permit greater tumor control. • Smaller lateral penumbra which may permit a more conformal dose laterally and limit normal tissue damage.
Similarities of both therapies	• Both proton and carbon ion limit the integral dose and therefore are predicted to reduce the risk of secondary malignancies over photon therapy, particularly in the pediatric population.	• Both proton and carbon ion research is limited, largely consisting of small series of patients where definitive conclusions are difficult to make.

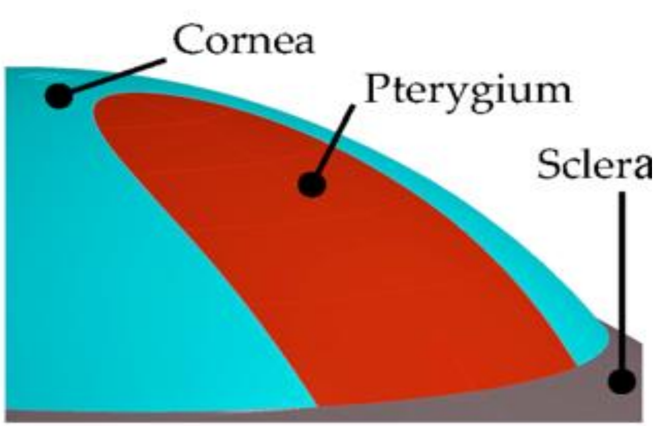
Juvenile Nasopharyngeal Angiofibroma

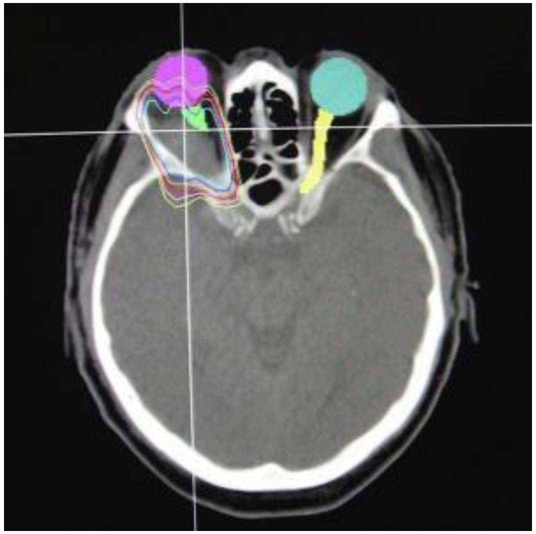
- This is a rare, benign vascularised tumour in the head and neck, mainly affecting males; and develops in the sphenoethmoidal suture and spread from epipharynx and nasal cavity to the sphenopalatine foramen and pterygopalatine fossa.
- Intra cranial spread occurs in 25% of cases.
- Surgery combined with embolization is the treatment of choice.
- Indications for radiotherapy:
  - Stage IV tumour with intra-cranial spread.
  - Residual tumour after sub total resection.
  - Tumour relapses after previous surgery.
  - Tumour rests.
- Recommendations, volume, technique and dose of radiotherapy:
  - Primary RT in stage IV cases. Total dose given is 55 Gy in 1.8 Gy per fraction for 6 weeks.
  - MRI- or CT- based planning is done; 6-18 MV photons are used.
  - Fractionated SRT or IMRT used to protect vital structures.

EYE

Pterygium

- It is a wing shaped fibrovascular proliferating tissue at the border between conjunctiva and cornea originating mostly from the medial corner of the eye. Corneal involvement can lead to blindness. Complete surgical excision is the treatment of choice.
- **RT indicated** in pre-operative, primary treatment, relapse after surgery.
- **Doses**: 10 Gy per week x 6 such fractions / 25 Gy single fraction using Orthovoltage machines or Strontium-90 brachytherapy.





Pterygium receiving beta ray therapy

Choroidal Hemangioma

- These are slow growing benign tumours originating from the choroidal vessels. Photodynamic therapy with verteporfin is the treatment of choice especially in lesions away from the centre.

- **RT indicated in:**
  - Nonresponding cases
  - Lesions in proximity to macula or papilla.
  - In advanced cases, to maintain the eye as a whole

- **Recommendations, volume, technique and dose of radiotherapy:**
  - Earlier the RT starts, the better. Head mask and vacuum contact lenses used for better eye fixation.
  - In localised type (age 30-50 years), total dose recommended is 18-20 Gy in 10 fractions of 1.8 -2.0 Gy each.
  - In diffuse type (age 5-10 years), total dose recommended is 30 Gy in 15 fractions.
  - Brachytherapy used in localized lesions. Iodine-125, cobalt-60 and ruthenium-106 are used; of which Iodine-125 is preferred. Dose delivered is 30-240 Gy from apex to base of lesion.

Age Related Macular Degeneration

- This is one of leading causes of blindness in developed countries. Nicotine abuse is an important risk factor. **Typical signs are: (a) drusen (yellow spots of cellular detritus) (b) retinal pigment epithelium changes (c) serous or haemorrhagic retinal detachment and (d) choroidal neovascularization**.

- **Recommendations, volume, technique and dose of radiotherapy**:
  - Protons and brachytherapy with ruthenium-106, palladium-103 and strontium-90 are used; these provide protection for eye structures.
  - Photon therapy using linear accelerator with mask fixation via lateral semicircular field is also used. The unaffected eye is spared by 10-degree posterior gantry tilt.

- **Doses**:
  - By photons: 2 Gy fractions to a total dose of 12-16 Gy (Max 20 Gy) or 4-5 fractions of 4 Gy each to a total dose of 20 Gy.
  - By protons: 2 fractions to a total dose of 20-24 CGE.

Endocrine Orbitopathy (Graves' disease)

- It is an autoimmune inflammatory fibrosing eye disease related to hyperthyroidism, toxic struma and Hashimoto's thyroiditis. Auto antibodies are formed against TSH receptors in eye muscles; leading to their inflammation and fibrosis, causing edema and proptosis.

- **RT indicated in:**
  - Medium dose RT is indicated in progressive and recurring disease.
  - Low dose RT is very effective in early inflammatory disease.

- The goals of RT are: Bring about clinical remission; Reduce / eliminate functional deficits; Improve cosmesis; Avoid or decrease side effects of other treatment modalities like surgery, long term steroids, immuno-suppressives like cyclosporine, plasmapharesis.

- **Volume, technique and dose of radiotherapy:**
  - Both orbits are irradiated by opposing lateral opposing fields with 6-10 MV photons.
  - CT planning done; Half beam block or lateral fields with 10-degree posterior tilt used to spare opposite lens / posterior eye chamber.
  - Blocks are used to spare paranasal sinuses and intra cranial structures.
  - The central beam and anterior field border is daily adjusted to 5-6 mm behind iris or pupil on both sides.
  - The posterior field border covers the ring of Zinn at superior orbital fissure.

Diseases of Bones, Tendons and Joints:

- RT is a last resort approach after failure of other non-invasive treatments, but before surgery. There is reduction of pain, but the patho-morphologic changes are not removed.
- **Recommended doses**: 0.5 – 3.0 Gy daily doses for acute inflammation, 2-3 times a week; and upto 6 Gy for chronic inflammation. If response is seen, a second course is repeated after 6 weeks.
- **Indications for RT**
  - **Degenerative Osteoarthritis**: Affected joints are irradiated by enface or opposing fields. Dose reference point is at the centre of the joint.
  - **Tendonitis and Bursitis / Rotator Cuff Syndrome**: Opposing fields are used. Dose reference point is at the centre of the joint.
  - **Tennis / Golfer's Elbow**: using low energy photons. Opposing fields are used. Dose reference point is at a depth of 5 mm.
  - **Calcaneodynia / Achillodynia**: Pain syndromes of heel and achilles' tendon. Affected area is treated by low energy photons, using stationary (plantar area) or opposing (dorsal area) fields to deliver a dose of 0.5-1.0 Gy x 3-6 fractions. Dose reference point is at depth of 5 mm for plantar field and at centre of joint for dorsal field.

Heterotropic Ossification

- It consists of real bone located in the periarticular soft tissue; and about one third of all patients with this condition have undergone total hip replacement. Prophylactic RT (in post operative period, 24-48 hrs after surgery). Dose recommended is 6-7 Gy in single fraction.
- Pre-operative RT of 7 Gy in single fraction is recommended.
- Target volume includes the typical localizations of heterotropic ossification with cranial border 3 cm above acetabulum and lower border including two-third of shaft.
- The dose reference point is central beam at the center of the target volume.

SKIN AND FASCIA

Desmoid (Aggressive Fibromatosis)

- Are benign connective tissue disorders of deep muscular aponeurotic structures in muscle fascias, aponeuroses, tendons and scar tissues. Are of two types: extra- and intra-abdominal. Surgical removal with a margin of 2-5 cm is treatment of choice.
- RT is indicated in:
  - Inoperable cases
  - After R2 resection.
  - After R1 resection if repeat surgery is done.
- Total dose recommended for primary RT is 65 Gy @2 Gy per fraction; while post operatively recommended dose is 55 Gy @ 2 Gy per fraction.

Keloids and Hypertrophic scars

- Are excessive tissue proliferation around scars after skin injury caused by surgery, burns, chemicals, and inflammation or even spontaneous.
- Recommended total dose is 40 Gy @ 2 Gy per fraction. Electrons / brachytherapy commonly used.

Morbus Peyronie

- This is a chronic, usually progressive, inflammatory tissue proliferation of the penile tunica albuginea; in men 40-60 years age with formation of hard plaques, lumps or cords and can involve entire penile shaft.
- RT is best given in early stages and delays induration; leading to reduction in pain, bends and function loss; with sparing of glans penis.
- Non erected penis is treated via dorsal field with 6 MeV electrons with 5-10 mm bolus.
- HDR brachytherapy used in cases with extensive induration.
- Total dose recommended is 20 Gy in 10 fractions @ 2 Gy per fraction. Hypofractionated RT can also be given with dose 12-15 Gy in 3-4 fractions.

Morbus Dupuytrens and Morbus Ledderhose

- Connective tissue disorders affecting palmar and plantar aponeurosis. Prophylactic use in early stages shows good response.
- Goal: avoid further progression and later surgery.
- 6 MeV Electrons used in treating. Margin of 1 cm laterally, 2 cm proximally and distally is given to avoid field edge recurrences. Dose recommended is 20-30 Gy in 10-15 fractions @ 2 Gy per fraction.
- End point of therapy is softening of lumps and strands with improvement in function.

TAKE HOME MESSAGE

- The overarching principle is to minimise the volume of irradiated normal tissue. Highest doses given is not more 45-50 Gy hence acute toxicities may not occur much.

- Current radiotherapy techniques and modern imaging can allow more accurate target definition and other developments in immobilisation and image guidance can allow reduced margins.

- Techniques such as intensity modulated radiotherapy, can achieve better conformality to complex target volumes, although this may increase the volume of tissue receiving lower doses.

- In some sites, particularly the skull base, dose distributions achievable with proton therapy may have advantages.

- But there is currently only limited data regarding the application of modern radiotherapy techniques to the treatment of benign conditions, including the implications for RIC risks from treatments such as IMRT.

- The decline in the use of radiotherapy for benign conditions is probably multifactorial.
- Long-term cognitive function in brain radiotherapy survivors is a major issue in clinical practice.
- These can be increased availability of alternative medical therapies, advances in surgery and concerns as to the potential risk, if very small, of Radiation Induced Cancers.
- This is exemplified by the increased incidence of leukaemia after radiotherapy for ankylosing spondylitis.

Thank you