Radiation Therapy in Benign Diseases

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Introduction

- Benign disease- localized tumour having low potential for progression , not metastasize to distant sites and not invade surrounding tissue
- Pathologically –well differentiated cell
- Treatment requires – secretory effects and bothersome mass
- 1920-1960 received RT for H&N benign disease
- Over past decade decrease RT use – sequelae normal tissue and radiation carcinogenesis
- Indications & guidelines have only recently been streamlined & are still evolving

Risk of Second Malignancy

- Risk of cancer attributed to stochastic effect
- Increasing radiation dose will increase probability of cancer but not severity of cancer

Types	Absolute life time risk
Basal cell carcinoma	0.1% for 100 cm2
Osteosarcoma	0.0001% for 1Gy
Leukaemia	1% for 1Gy TBI
Brain tumour	0.2% after 20Gy
Thyroid Ca	1% for 1Gy (less than 10Yr)
Breast Ca	5% for 1 breast for 1Gy
Lung Ca	1% for 1Gy

The Rationale

- Connective tissue: suppressing differentiation; cell proliferation
- Vascular system: endothelial modulation – ICAM-1, PG release (low dose) & sclerosis, obliteration of vessels (high doses)
- Painful Processes: reduces inflammation & pain
- RT induced modulation of NO production and Oxidative burst in macrophage- modify immune
- Inflammation by Ag-Ab reaction- RT suppress T-lymphocyte

Mechanisms and dose

Mechanism of Action	Single Dose(Gy)	Total Dose(Gy)
Cellular gene & protein expression	< 2	< 2
Inhibition of inflammation in lymphocytes	0.3-1.0	2-6
Inhibition of fibroblast proliferation	1.5-3.0	8-12
Inhibition of proliferation in benign tumors	1.8-3.0	46-60

Benign Diseases

Further qualified as

(A) Benign Tumors and

(B) Benign Conditions

Indications, Techniques & Doses

The Nervous System

- Meningioma
- Pituitary Adenoma
- Craniopharyngioma
- Chordoma
- Acoustic Neuroma
- Arteriovenous Malformations

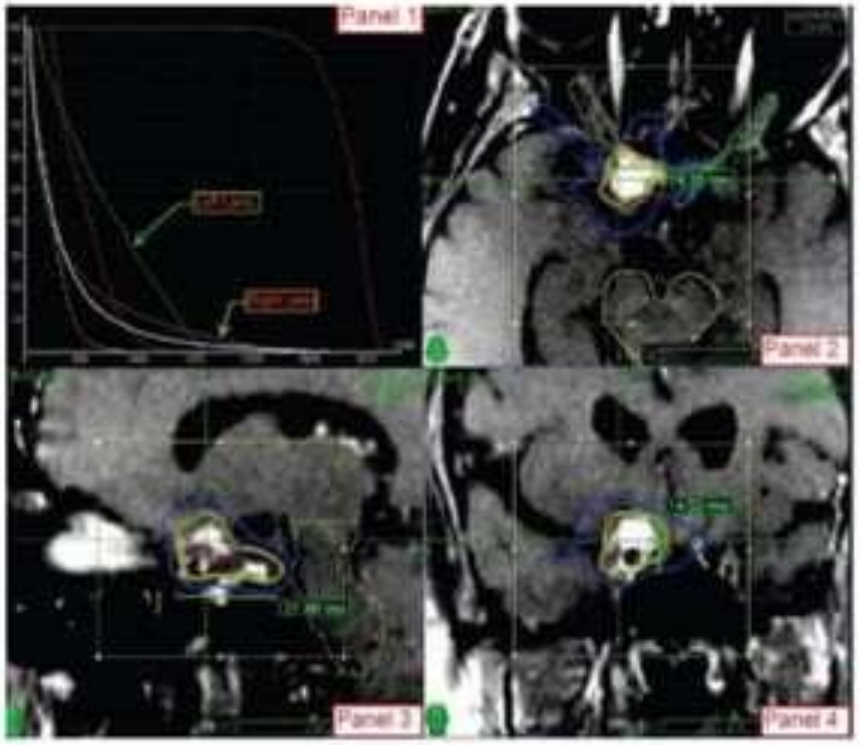
Meningioma

- Most common benign tumor of Brain
- Peak incidence 6^{th}-7^{th} decade of life (twice in female)
- Well-circumscribed, firm, greyish lesion
- Surgery main treatment
- After GTR- For grade I- relapse rate is 10%(5yr) & 20%(10Yr) and 40% for incomplete resection(5yr)
- For Grade II,III- 40-100% recurrence after GTR (5yr)
- Primary RT- where complete resection not possible(optic Nv, cavernous sinus), poor candidate for Surgery

- Adjuvant RT-Subtotal resection, recurrent disease, WHO Grade II, III
- Grade I lesions(80%): 50-54 Gy – improves local control, time to recurrence and survival
- Grade II (atypical, clear, chordoid) & III(anaplastic, rhabdoid, papillary) lesions: up to 59.4-63 Gy improved local control
- In grade I- 5yr local control rate 89-98% (3DCRT) and 98-100% in SRS, and Grade II/III-20-80%
- Frame based SRS- 12-16Gy (50% isodose line)
- FSRT choice for optic sheath meningioma for visual acuity preservation

- Worse outcome after SRS if following are present

1. Male
2. Conformality index less than 1.4
3. Size more 10ml



Pituitary adenoma

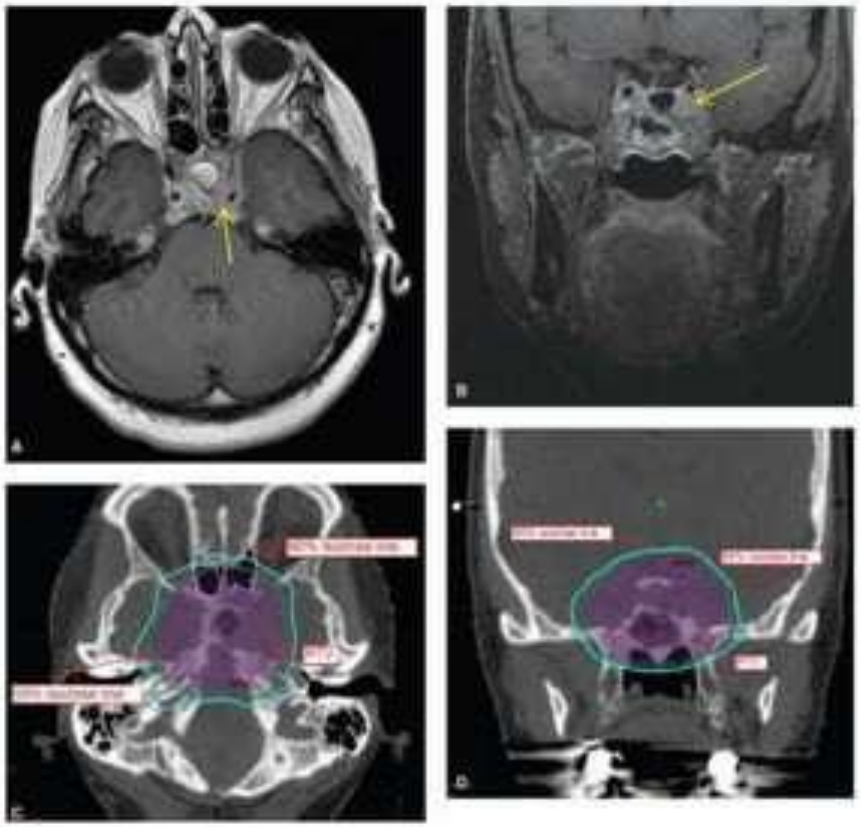
- 10-15% of all intracranial neoplasm
- 75% functional (present in female)(MC-prolactinoma, GH releasing adenoma)
- Size classification- Pico<.3cm; Micro<1cm; Macro>1cm
- Surgery main treatment-transsphenoidal or frontal craniotomy
- Local control rate-50-80% after surgery
- Bomocriptine, cabergoline, octreotide, ketoconazole are pharmacotherapy

- RT- adjuvant after subtotal resection or recurrence , persistent hormone elevation after surgery or primarily for inoperable lesions
- Options: Conventional fractionated RT or SRS
- Technique: single fraction SRS or 3D CRT ,FSRT, IMRT
- Dose used-16-20Gy for nonfunctional adenomas and 20-25Gy for functional tumors in frameless robotic radiosurgery

Doses

- Prolactinoma: Radiation has a limited role; Median dose SRS:20 Gy: 0-84% prolactin normalization
- ACTH secreting:50.4-54Gy:57% remission at 10 yrs
- GH secreting:50.4-54Gy: 25-96% endocrine cure rates
- Non-functioning adenoma: standard indications and doses up to 45-50Gy
- FSRT used for lesion >3cm, or near critical structure(<1-2mm from chiasm)
- 5 yr local control 92-100%

- GTV-residual tumour
- CTV-GTV+1-1.5cm
- PTV- 3-5mm



Craniopharyngioma

- Origin: remnant of Rathke's pouch i.e hypophyseal-pharyngeal duct (supraseller)
- 6-10% pediatric CNS tumor
- Median age-5-10 yr and 2nd peak at 40Yr
- GTR has neurologic sequelae, visual impairment
- So maximal safe resection with adjuvant RT preferred
- RT- 3DCRT, IMRT, FSRT, proton therapy, intralesional RT with β emmitor (P-32,Y-90)

- Primary inoperable / subtotal resection needs adjuvant radiation
- Long term control with primary RT or biopsy + RT up to 54 Gy is comparable to complete resection
- Fractionated Stereotactic RT(6GyX3) is preferred to single fraction RT
- β-emitter dose- 200-250Gy to cyst wall
- Cyst may regrow during treatment so routine imaging during treatment is recommended (1)

1. Int J Radiat Oncol Biol Phys 2009 Mar 716-21

Acoustic Neuroma:

- 5-8% primary CNS tumor
- From Schwann cell of neurilemma of CN VIII
- Progressive & symptomatic primary or recurrent AN- need RT
- SRS is preferred for better dose localization
- 12-14 Gy to tumor periphery: 95% local control
- FSRT also used: 5Gyx5, 10Gyx3, 2Gyx25, have been used
- SRT as effective as surgery with fewer adverse effects
- Proton Beam therapy- 12GyE in single fraction

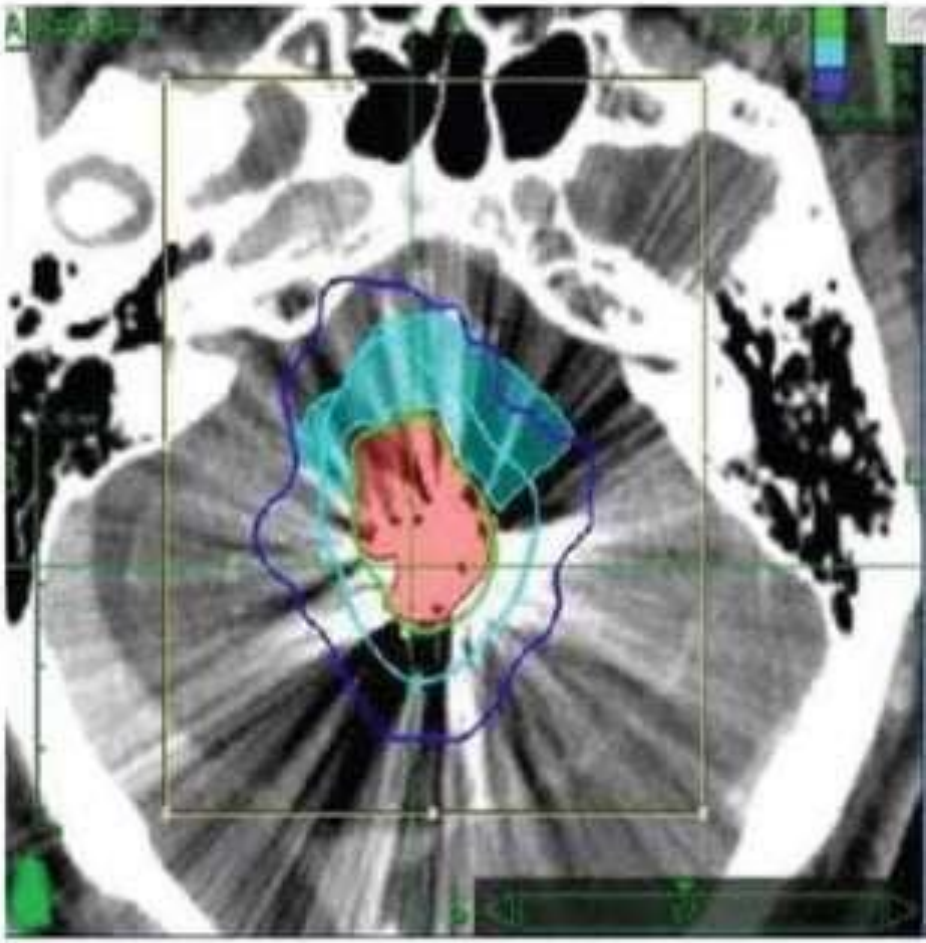
Chordoma

- Slow growing, midline tumors from embryonal notochord: clivus 35%, vertebral column 15%, sacrum 50%
- Inoperable / incomplete resection mandates RT
- Sacral chordomas: role of pre-op RT
- Dose – effect relation: > 65 Gy improves local control
- Protons are useful for dose escalation

Arteriovenous Malformations

- Congenital vessel anomaly- widened artery connected to normal capillary bed
- Nidus- made up of tangled artery and vein that are connected by fistulas
- Age-20-40 years
- Complete surgical excision, Embolization to decrease bleeding (not curative)
- The risk of hemorrhage from AVMs ≈ 2% to 3% per year
- The mortality rate 10% & rises with each subsequent bleed

- SRS more effective if smaller than 3 cm & all feeder are irradiated.
- Complication rates low unless a large volume is treated or re-irradiated
- Recommended dosing is 16-24Gy in one fraction or 20-22Gy in 2# for spinal AVM
- After SRS time for obliteration of vessel 1-4 yr, bleeding risk reduced by 90%



Langerhans Cell Histiocytosis

- Accumulation and proliferation of Langerhans skin like cell, tissue damage by cytokine
- Affect single or multiple system
- Higher incidence in children(better outcome)
- Symptomatic lesion by curettage , excision, intralesional steroid
- RT given-relapse, no healing after treatment, pain relief, cord compression
- For children- 5-10Gy for bony lesion
- For Adult-6-15Gy for untreated cases and 8-15Gy for recurrent cases

Orbits and Optic apparatus

- Graves Ophthalmopathy
- Pseudotumor
- Choroidal hemangioma
- Pterygium
- Age related Macular Degeneration

Graves Ophthalmopathy

- Autoimmune disease by activated T-lymphocyte
- RT- for who are symptomatic & not responded to a course of high-dose systemic steroids
- MC dose of RT- 20 Gy, which is administered using lateral fields with posterior angulation including extraocular muscle (split lens)
- Overall response rate-98%

Pseudotumor orbitae

- Lymphoid disease of orbit that cause inflammation of tissues within orbit or surrounding - resembling a tumor
- 5^{th} -6^{th} decade of life
- Biopsy is necessary to differentiate benign and malignant one
- Radiation is the treatment of choice for cases in which there is a contraindication to, a poor response to, or recurrence after steroid treatment, recurrent lesion after surgery

- Local control rates generally are high response of 90%, morbidity is minimal
- External-beam irradiation 20Gy in 10# generally used

Choroidal Hemangiomas

- Origin: choroidal vessels
- Types: circumscribed & diffuse
- RT indicated when no response to photocoagulation particularly for lesions near to the macula & papilla
- Earlier RT: better long term results
- 18-20 Gy local type and 30 Gy diffuse type fractionated RT
- Brachytherapy with Iodine-125 for localized hemangiomas:25-30Gy

Pterygium

- Fibrovascular degenerative process arises from conjunctival-corneal junction
- Surgery - primary therapy but recurrence rates are high up to 20% to 67%
- PORT using a Strontium-90/Yttrium-90 β-emitting contact applicator - reduce recurrence rates significantly, to 20% or less
- Local control is best when the radiation is given immediately after surgery
- RT- as a nonsurgical treatment & reducing size

Age Related Macular Degeneration

- ARMD leading cause of blindness
- The two common forms are dry and wet
- Dry AMD is MC- accounting for 90% of all AMD
- Wet macular - more severe than dry form.
- Prevent the proliferation of endothelial cells necessary for neovascularization
- Side effects is radiation retinopathy, which is dose dependent
- 6- to 9-MV photons with lateral-port half-beam technique

The Head and Neck Region

- Paraganglioma
- Nasopharyngeal Angiofibroma
- Trigeminal Neuralgia

Paraganglioma

- Rare neuroendocrine neoplasm
- chromogranin, synaptophysin, neuron specific enolase positive
- Primary RT: functional or inoperable tumors
- Adjuvant for R1/R2 resections or recurrences
- 3D-CRT up to 45-55 Gy
- Local control:88-93%; dose response relation: >40 Gy 1.4% recurrence vs. 22% with <40 G
- Linac based SRS- 15-25Gy

Nasopharyngeal Angiofibroma

- Vascularised tumor, 25% intracranial, male adolescent
- From sphenoethmoidal suture
- Surgery with embolization
- Sx has local control rate 100% (for Stage I,II,III)

Chandler Stage	Description
I	Confined nasopharyns
II	Into nasal cavity, sphenoid sinus
III	≥1 structure; cheek, ITF, ptrygomaxillary fossa, etmoid sinus, maxillary antrum
IV	Intracranial extension

- RT is very effective; intracranial disease, tumor rests, inoperability or recurrences need RT
- Fractionated IMRT technique of choice
- Dose: 35-50Gy effective: local control: 80-100%
- After remission is slow and late recurrence may occur

Trigeminal Neuralgia

- RT is an ablative procedure for this indication
- Results of Stereotactic Radiosurgery are comparable with those of other ablative techniques
- Maximal level of pain relief after Radiosurgery is achieved within one month
- Stereotactic Radiosurgery is the safest technique , although probably not the most effective

Functional Disorder

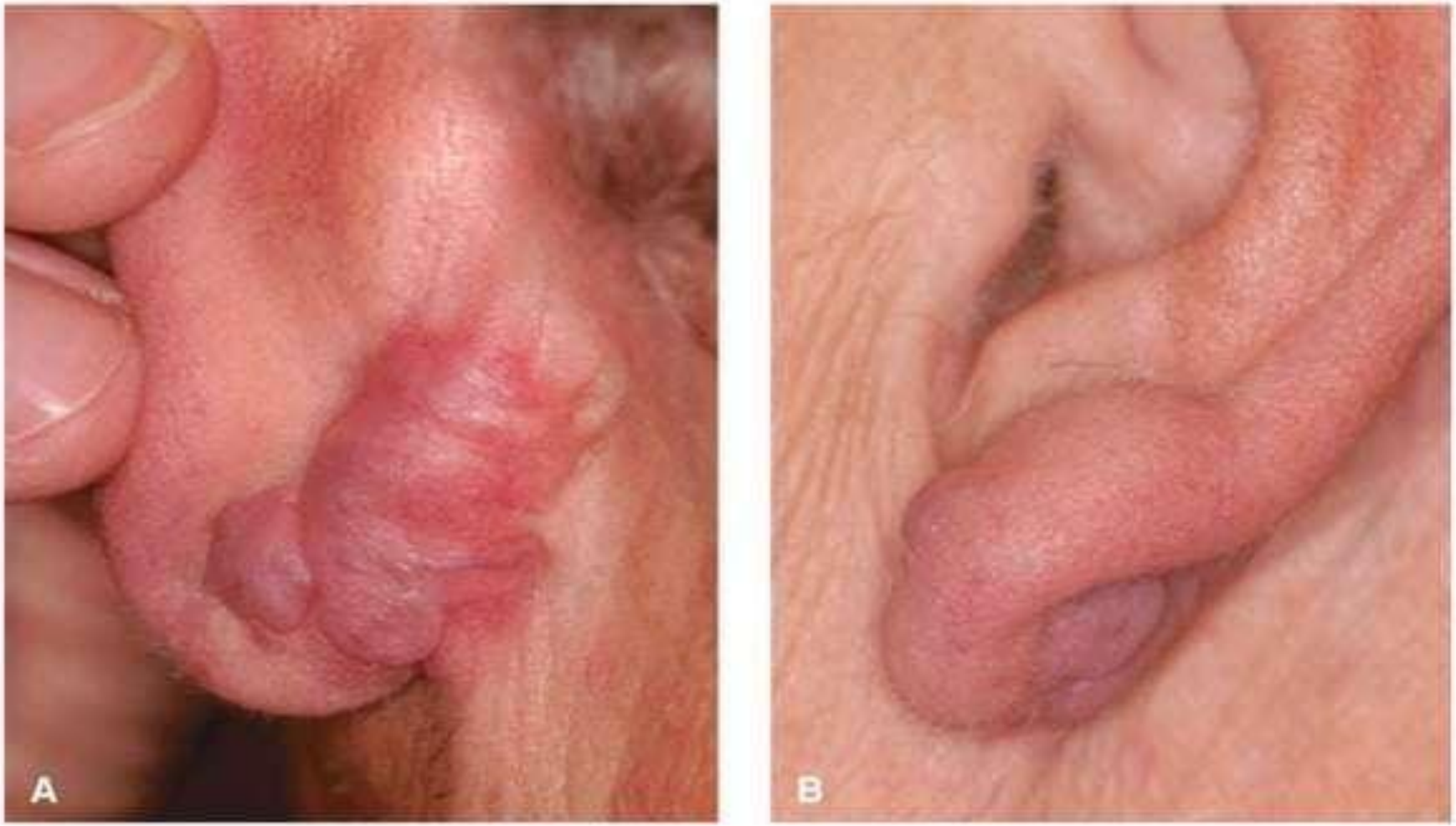
- Epilepsy
- Parkinson disease
- Psychiatric disorder

The Skin and Soft tissues

- Keloids, Hypertrophic scar
- Desmoids / Aggressive Fibromatosis
- Peyronie's Disease
- Gynecomastia

Keloids

- Excessive tissue proliferative disorder from surgery, burn, heat, inflammation
- Surgery has recurrence rate 50-100%
- Immediate PORT most effective and reduces recurrence rate to 20-25%
- Single fraction 7.5-10Gy or 12-20Gy in 3-4 fractions
- RT initiated 24 hour after Sx with scar and 1cm margin



Keloid behind ear lobule, following Sx and 4x4Gy RT

Desmoids / Aggressive Fibromatosis

- Benign connective tissue growth from muscle fascia, tendon; locally infiltrative
- Similar to low grade fibrosarcomas
- Indications: Inoperability, R1 resection with recurrence, R2 resections
- 50 Gy doses reduce recurrence for 60-80% to 10-30%
- 50-55 Gy: PORT
- 60-65 Gy: Gross disease

Peyronie's Disease

- Inflammatory connective tissue disorder involving penile tunica albugenia
- 40-60 yr of age
- Low-dose RT- relieve pain and to improve plaque resolution
- RT – orthovoltage, electron, photon used
- Doses ranging from 20-30Gy
- Special care must be given to gonadal protection and shielding.

Gynecomastia

- Most common pathologic cause - anti-androgens for treatment of prostate cancer.
- 90% of patients antiandrogen and 15% of patients receiving LHRH agonists
- Hormone-induced gynecomastia is usually bilateral and often is painful.
- RT-prevent pain, growth of gland but cannot reverse it
- Electron irradiation is preferred due shallow depth–dose characteristics.
- 8-12Mev electron with dose of 12-15Gy

The Skeletal System

- Aneurysmal Bone cysts
- Pigmented Villonodular Synovitis
- Morbus Dupuytren and Morbus Lederhose
- Myositis Ossificans

Aneurysmal Bone Cysts

- Vascular osteolytic cystic lesion in metaphysis
- Complete resection (no recurrence) or curettage cause recurrence of 60%
- Unresectable lesions i/v/o location, size or post curettage need RT
- Progression/recurrence need RT as well
- Young age: 10-19 yrs mandates lowest possible dose
- 10-20 Gy fractionated RT is considered adequate

Pigmented Villonodular Synovitis

- Proliferative disorder of synovial tissue
- Diffuse and localized
- Surgical excision is rarely complete especially in the large joints like the knee
- Risk factors: microscopic residual, gross disease, size >10cm, recurrent lesions, skin infiltration with ulceration
- Radiotherapy dose- 35-50 Gy is adequate

Conclusion

- Radiation for benign diseases has evolved with time
- Radiation often is not the first treatment in almost all cases
- Radiation is quite effective for indicated case
- Risk-benefit analysis with RT treatment in most conditions are not life threatening

Thank You

Epilepsy

- Recurrent seizure, 1% total population
- SRS- alternative to surgery (for refractory disease mainly temporal lobe epilepsy) in medically refractory cases
- Dose- Temporal lobe 24-25Gy in single fraction
- Response rate of 70% in 3years

Psychiatric disorder

- Disease like OCD, bipolar disorder, major depressive disorder
- In OCD- bilateral anterior capsule to dose of 120-140Gy
- Active area of investigation, mainly institutional protocol

Morbus Dupuytren and Morbus Lederhose

- Spontaneous connective tissue diseases affecting palmar and plantar aponeurosis
- Radiosensitive fibroblasts and inflammatory cells are the target for RT
- 20 Gy in 2 Gy fractions or 3-4 Gy per fraction up to 12-15 Gy recommended
- 70-80% show stabilization but only 20-30% show disease resolution

Myositis Ossificans

- Develops in 10-80% of cases with surgery and/or trauma around the hip joint
- Believed to arise from pluripotent mesenchymal stem cells that differentiate eventually into myositis ossificans
- RT dose- 20Gy in divided dose or 8-10Gy single fraction