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Principles of Pediatric radiation Oncology…how is it different from adult radiation?

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My objectives for the session…

- Understand the normal tissues in children vs adults
- Understand the tumour in children vs adults
- Treatment differences for children vs adults
- Modifications in dose/techniques
- Newer strategies for safe delivery of radiation

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Normal tissues in children

Normal tissues in children vs adults

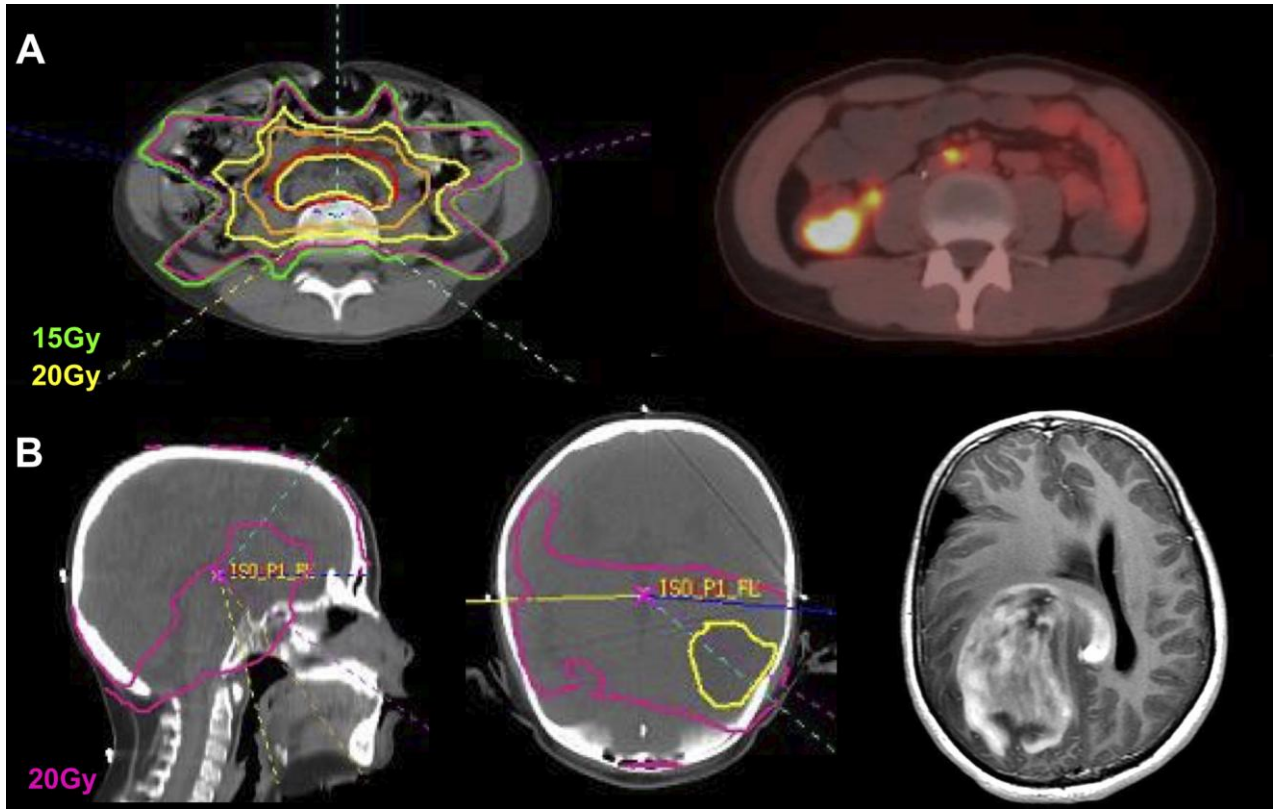
- Proliferating tissues very sensitive to radiation - developmental dynamics and maturational status of each organ, its regenerative potential are different
  - stem vs progenitor vs terminally differentiated-adults
  - Demands accurate planning and lower doses
- Acute effects in adults while late effects in children
  - Fertility issues, thyroid, breast
- CNS is same above 2 years of age
  - Motor and sensory develops earlier while intellectual functions through out childhood and adolescence

- Radiation is an independent risk factor for reduced cognition (damages the pool of neurological stem cells)
  - Avoid RT, reduce the dose, spare with technology

Secondary malignant neoplasm-factors

- Age at radiation-higher when treated at younger age
- Girls>boys
- Dose-As low as 10 cGy, increases from 15 to 60 Gy
- Time since radiation- 7-10% at 20 yrs and 25-30% at 30 yrs after HD
- Volume dependent- low dose volume as in IMRT
- Chemo also is used- alkylating agents, anthracyclines
- Predisposing conditions- retinoblastoma

- Data is based on older technique
- Newer data awaited



Tringale KR et al Second cancer risk in childhood cancer survivors treated with IMRT, An updated analysis of more than 10 years of follow-up. Pediatr Blood Cancer. 2022 May;69(5):e29600. doi: 10.1002/pbc.29600.

PENTEC similar to QUANTEC

- 150 physicians (radiation and paediatric oncologists, sub-specialists), medical physicists, mathematical modellers, and epidemiologists
- critical reviews and synthesis of quantitative data

STRUCTURE	CHILD RT LIMITING DOSE	ADULT RT DOSE LIMIT
Brain	18 Gy	35 Gy
Bones	10 Gy	> 65 Gy
Pituitary (GH)	20 Gy	NA
Ovary / Testes	10 Gy	NA
Breast CA Induction at 40 Gy	RR = 20	RR = 2
Lung MLD	> 9 Gy	17 Gy
Lens (cataract)	> 12-15 Gy	>10-12 Gy
Thyroid	Below 20 Gy up to 14 yrs age	NA

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Tumours in children

Tumours in children vs adults

- Incidence higher in adults
  - Many are under research trials
  - Better evidence

- Carcinogens cause cancer in adults vs Predisposing syndromes are common in children-Epithelial is common in adults vs mesenchymal in children

- Few mutations as compared to adults,
  - genetically more stable-success with treatment higher
  - Few targets- targeted therapy not much useful

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Basic Principles of treatment in children:

Golden Rule:

- Protect children from clinical trials (do not extrapolate from that of adults)
- Protect children with trials (encourage multi-institutional so that they get optimum therapy at the end of clinical trial)

Some statistics:

- Survival > more than 80%
- 30-year cumulative mortality for 5-year survivors- 18%
- >2-fold increased risk of mortality with radiation versus those not receiving radiation
- 75% of survivors of childhood cancer will develop one or more chronic health conditions
- 50 % will experience severe or life-threatening complications from treatment

Leads to greater years of life lost compared to adults

Rehabilitation, emotional burden management

Treatment differences in children vs adults

- Adults- outcomes are survival with preservation of organ, function etc. In addition for children-cognition, growth, endocrine
- Adults-surgery is the main vs chemo for children
- Adults- concurrent chemo radiation is common
- Risk stratification for optimization of local therapy
- Even in metastasis, radical treatment is offered
  - Ewings
- Radiation dose: Adults mostly around 60 Gy vs 20-60 Gy

Declining use of radiation over time

	1973-1976	2005-2008
ALL	57%	11%
NHL	57%	15%
Retinoblastoma	30%	2%
Brain	70%	39%
Bone	41%	21%
Wilms tumour	75%	53%
Neuroblastoma	60%	25%
HL,STS,AML	72%,40%,11%	

Cancers **2021**, *13*(11), 2607; https://doi.org/10.3390/cancers13112607.from Germany

Strategies for better therapeutic ratio in children

- Avoid Radiation- ALL, early responders HD, selected films
- Reduce the dose- HD, risk based prescription for RMS,Ewings
- Reduce the volume- boost in medulloblastoma
- Advanced technology- IMRT, Proton therapy, Brachy

- Special considerations:
  - Involving parents, surrogate consent or permission, anaesthesia, music, prepare children for daily treatment (central line, vitals monitoring, spending time with the child)
  - Remove perceived fear of radiation among our neighbour oncologists

Evaluation of risks and potential benefits

- consider child's age, developmental status apart from cancer.
  - unique fears, anxieties, perceptions of body threat
  - younger child- strange environment greater threat than the treatment
  - Adolescent- loss of privacy is more threatening than treatment.

  - Do everything to minimize fear, anxiety, discomfort eg.. Chemo port.
  - parents' perceptions are important -views of the possible benefits vs risks. greater risks for some toxicities (e.g., neurocognitive effects, breast tissue damage).
  - child's developmental stage, other treatments such as chemotherapy, and underlying genetic predispositions, maldevelopment of musculoskeletal tissue, teeth, breasts, and reproductive organs,

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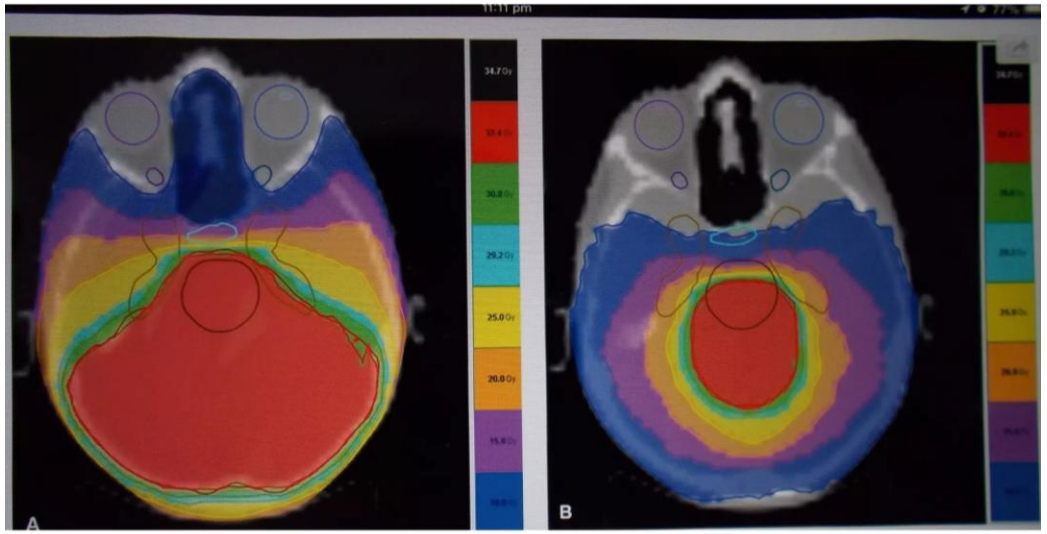
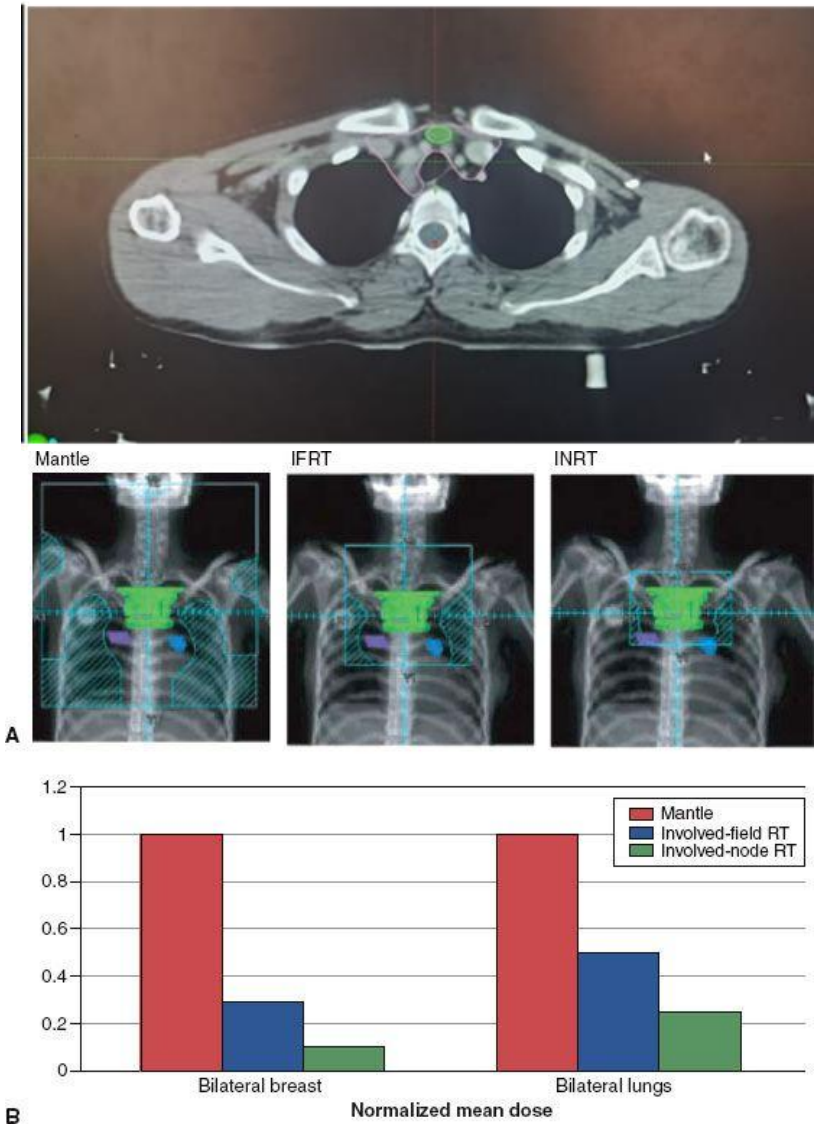
Reduction in volume..

Whole post fossa Vs Reduced Volume Boost



Hodgkins Lymphoma



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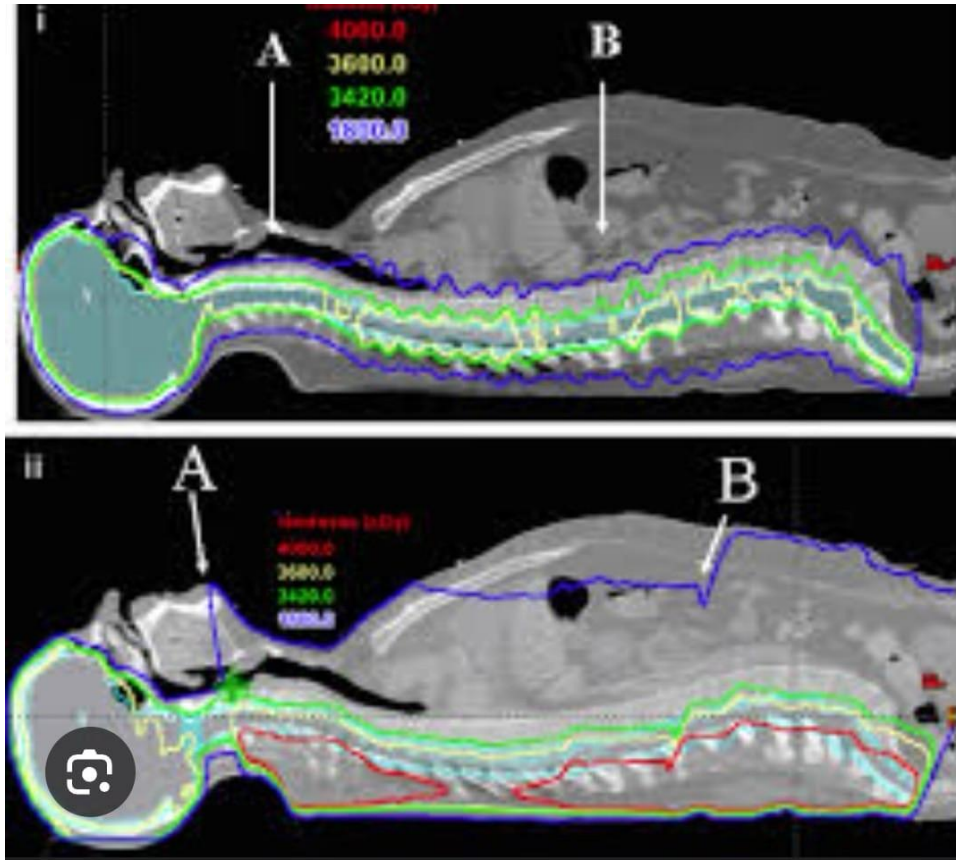
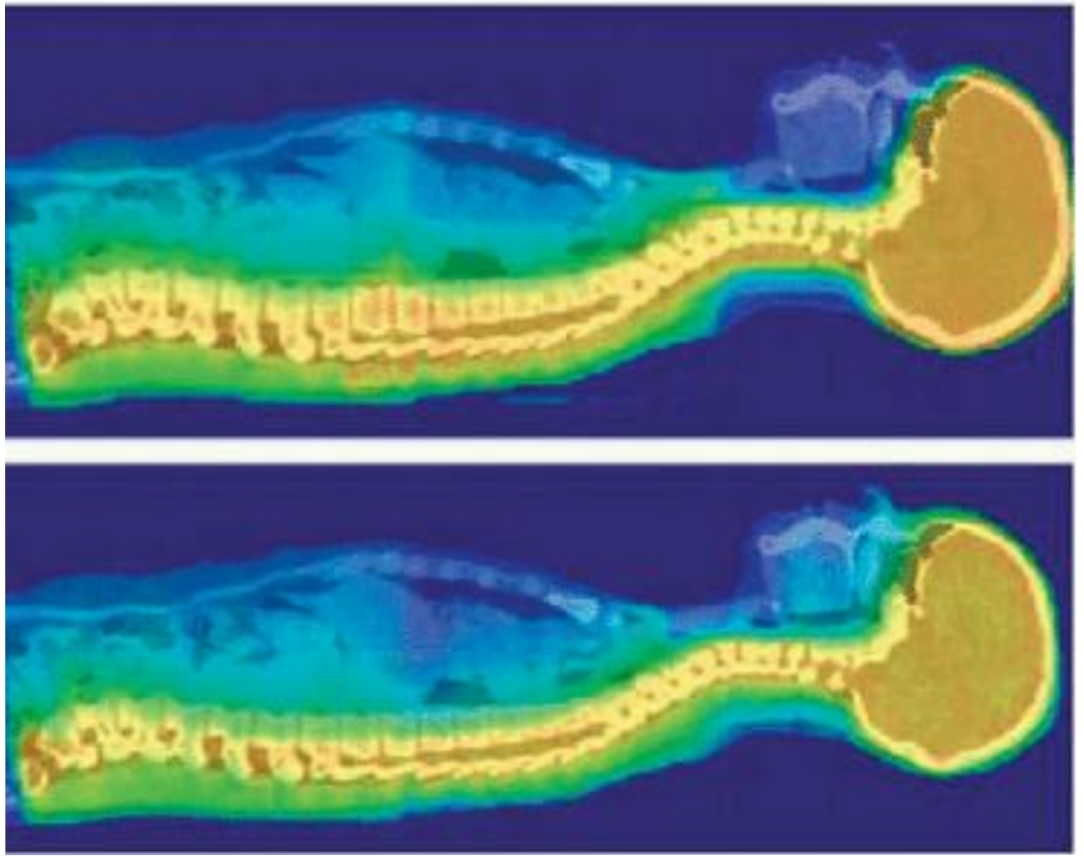
Therapeutic benefit with technology:

Protons



3DCRT

IMRT



VMAT

Summary of key differences..

	Children	**Adults**
Occurence	4% of adult cancers	100/lakh
Aetiology	Unknown/lesser mutation	Carcinogen/multiple mutations
Type of cancer	Mesenchymal origin	Epithelial origin
Association	Familial syndromes/germline mutation	Lifestyle/smoking/somatic mutation
Diagnosis	Difficult-overlapping symptoms	Follows set pattern
Treatment	Primarily surgery	Primarily chemotherapy
Trials	Multi-institutional	Very common
Response to treatment	Very good	Relatively lesser
Outcome-survival	Excellent upto 80-90%	Okay
Long term-sequelae	Very common	Lesser

Conclusion: Children are not adults

- Aim is to have a near normal adult later in life following therapy for childhood cancer.
- Since the incidence is very low extra care is required at every step of radiation process.
- Lesser doses, lower volumes, higher technique will help in achieving better therapeutic ratio.
- Avoidance of radiation as in early responders of Hodgkin's, reduced dose of radiation as in PCI, lower volume as in lymphoma, use of high end technology as with protons for CSI, risk stratification as in Ewings, RMS.

- Equally important are close follow up for late sequelae, early recognition and prompt rehabilitation

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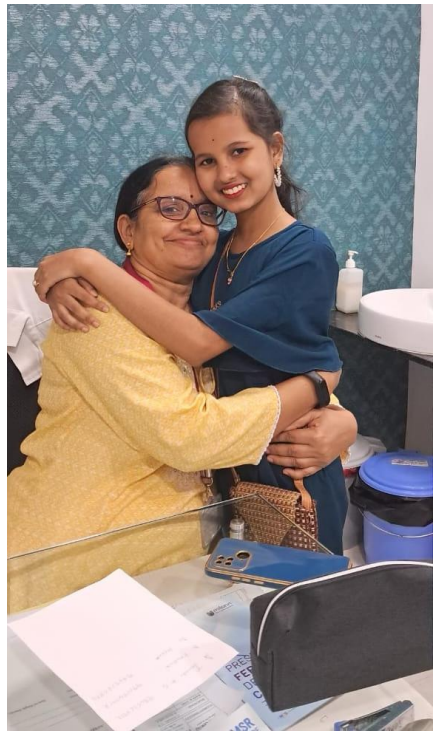

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My heartfelt appreciation to all my Technologists and nurses who make the journey of these kids absolutely smooth!!!