HITRI plus
Heavy Ion Therapy Research Integration

PAEDIATRIC PATIENTS COMMONLY REFFERED FOR EXTERNAL BEAM RADIOTHERAPY

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AT THE HADRON THERAPY SYMPOSIUM

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

Content :

1. Pediatric Cancer RT: An Overview in
2. Common Indications for Radiotherapy
3. Treatment Planning Considerations
4. Managing Side Effects and Long-Term Outcomes
5. Future Directions in Pediatric Radiotherapy

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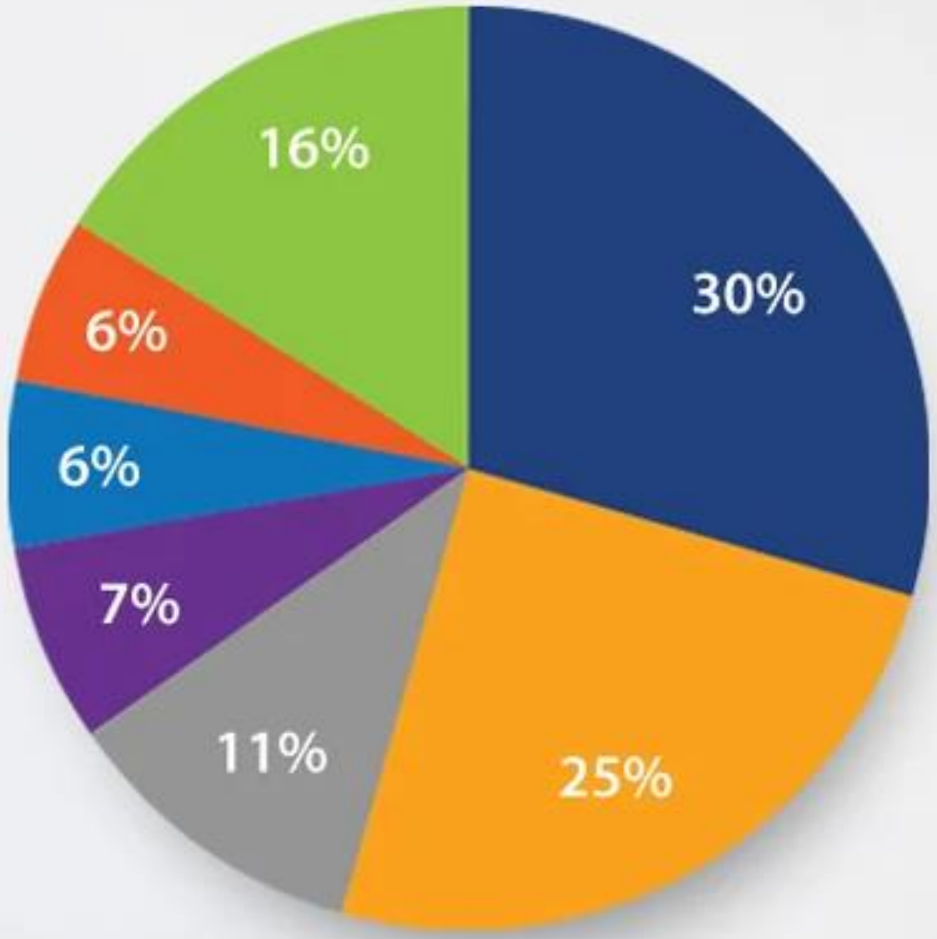

- Leukemia
- CNS tumors
- Lymphomas
- Soft-tissue sarcomas
- Neuroblastoma and other peripheral nervous cell tumors
- Renal tumors
- Other

Incidence statistics from https://publichealthmatters.blog.gov.uk/2017/02/01/childhood-cancer-statistics-what-can-we-learn-from-new-data/

Incidence

- Every 3 minutes, a child is diagnosed with cancer worldwide
- 1 in 285 children in the United States will be diagnosed with cancer before the age of 20.
- 15,400 new cases of pediatric cancer occur annually.
- Pediatric cancer is the second leading cause of death in childhood after accidents.-
- It accounts for 1% of all new cancer diagnoses in the United States.
- Pediatric cancer is very different from adult cancer.

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Paediatric cancers survival rates

Significant improvement in survival rates for pediatric cancers over the past few decades.

5-year survival rates in high-income countries exceed 80%.

Survival remains below 30% in low- and middle-income countries.

Disparities are primarily due to limited access to specialized care and radiotherapy.

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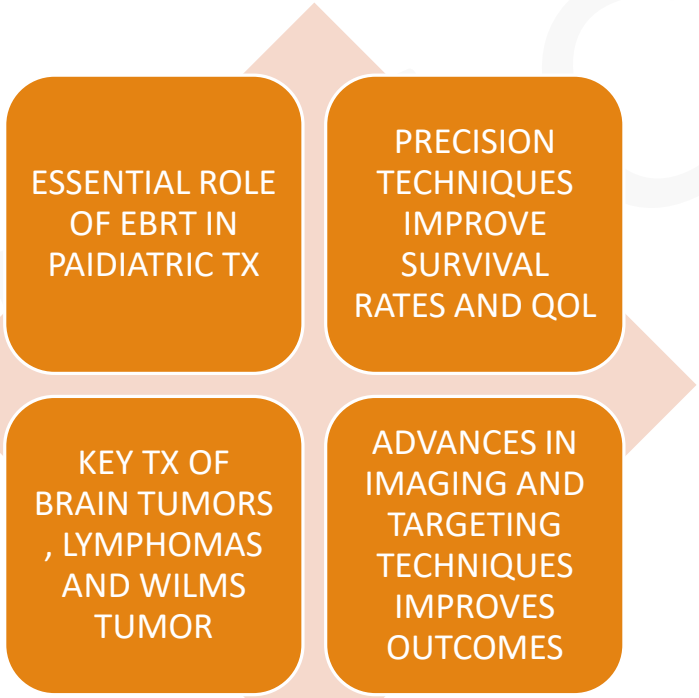
EXTERNAL BEAM RADIATION THERAPY IN PAEDIATRIC ONCOLOGY: A CRITICAL COMPONENT OF MULTIMODAL THERAPY



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1. Significant increase in survival in paediatric oncology in the last 25 years
2. Issues with child cancer tx :

Immobilization: Crucial to limit radiation to normal tissues; challenging in pediatrics due to movement

.

Devices: Effective immobilization devices may be uncomfortable for pediatric patients, particularly for CNS tumors.

Anesthesia Needs: Often required for young children; propofol is the preferred anesthetic due to rapid recovery and ease of use.

Challenges: Cardiac and respiratory monitoring during anesthesia can be difficult with equipment placement.

Complications: Low complication rate (1.3%) with factors like procedure duration and total propofol dose contributing to risk.

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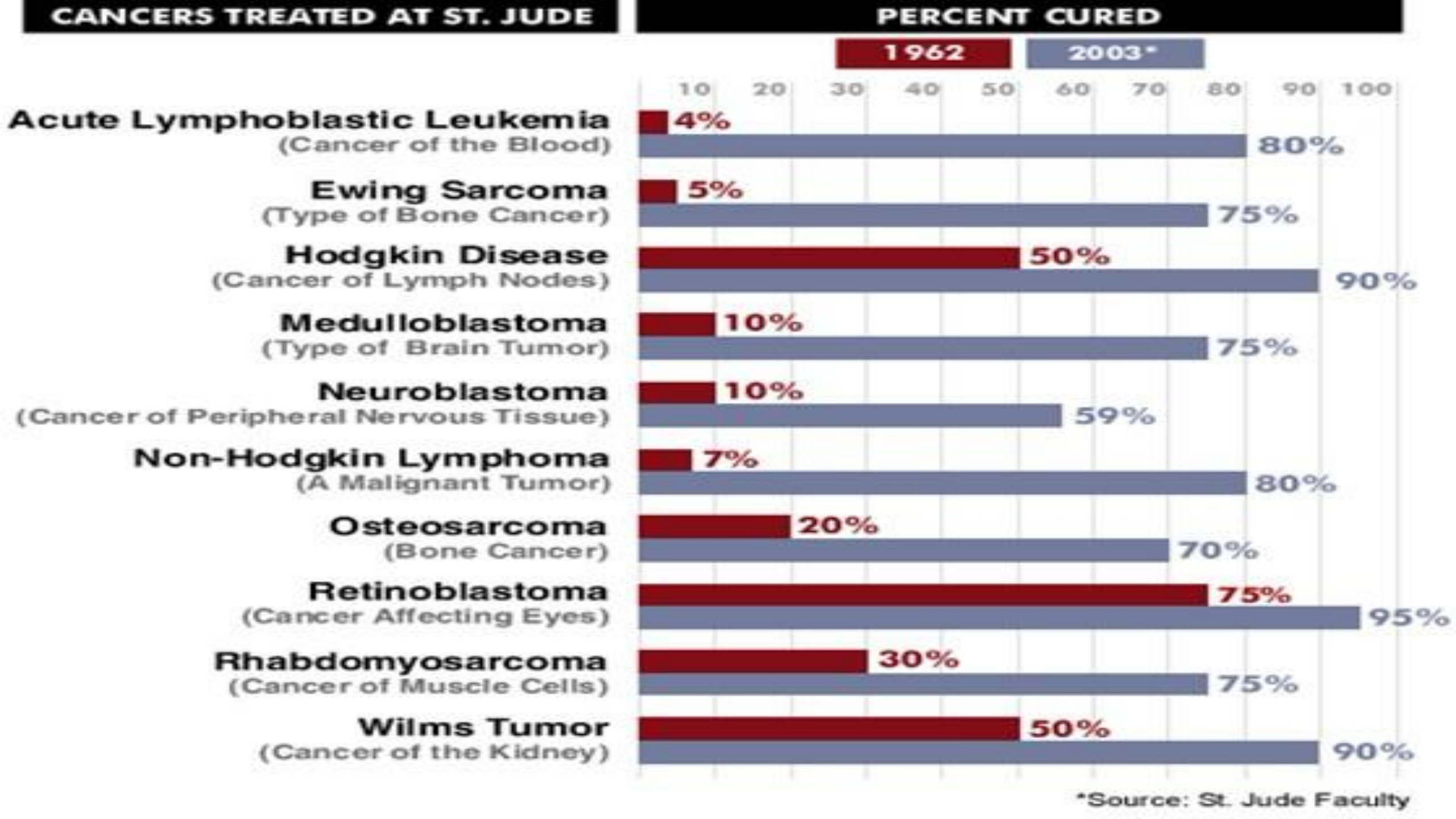
CANCERS TREATED AT ST. JUDE
PERCENT CURED
1962
2003*
10 20 30 40 50 60 70 80 90 100
Acute Lymphoblastic Leukemia
(Cancer of the Blood)
4%
80%
Ewing Sarcoma
(Type of Bone Cancer)
5%
75%
Hodgkin Disease
(Cancer of Lymph Nodes)
50%
90%
Medulloblastoma
(Type of Brain Tumor)
10%
75%
Neuroblastoma
(Cancer of Peripheral Nervous Tissue)
10%
59%
Non-Hodgkin Lymphoma
(A Malignant Tumor)
7%
80%
Osteosarcoma
(Bone Cancer)
20%
70%
Retinoblastoma
(Cancer Affecting Eyes)
75%
95%
Rhabdomyosarcoma
(Cancer of Muscle Cells)
30%
75%
Wilms Tumor
(Cancer of the Kidney)
50%
90%
*Source: St. Jude Faculty

Common indications for RT:

Brain Tumors:

- Types: Medulloblastoma, Gliomas, Ependymoma,germinoma

  - Role of EBRT: These cancers are treated using precise radiotherapy techniques to minimize damage to developing brain structures while ensuring effective tumor control.

Lymphomas:

  - Hodgkin's and Non-Hodgkin's Lymphoma.

  - Radiotherapy's Role: Often used after chemotherapy to consolidate treatment, especially for bulky or residual disease.

Wilms Tumor:

  - A common childhood kidney cancer.

  - Use of EBRT: Administered post-surgery to destroy any remaining cancer cells, particularly in cases

where the tumor has spread.

Sarcomas:

  - Types: Ewing sarcoma, Rhabdomyosarcoma.

  - EBRT Use: Critical for local control in high-risk or surgically unresectable tumors.

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Medulloblastoma Radiation Therapy

Indications: Post-surgery radiation is standard for medulloblastoma to prevent recurrence.

1. Risk Classification:

- Standard Risk: No metastasis, near-total or total resection, and age >3 years.

-High Risk: Presence of metastasis, residual tumor (>1.5 cm^2 post-resection), or age <3 years.

2. Radiation Dose:

- **Craniospinal Irradiation (CSI):**
  - Standard Risk: 23.4 Gy to the entire craniospinal axis, typically delivered in 1.8 Gy fractions.
  - High Risk:36-39.6 Gy to the craniospinal axis, depending on the patient's age and risk features.
- **Boost to Posterior Fossa/Tumor Bed:**
  - Standard Risk:After CSI, a boost of 54-55.8 Gy is given to the posterior fossa or tumor bed.
  - High Risk: 54-55.8 Gy boost to the tumor bed or any areas with residual disease, sometimes extending to cover metastasis sites.

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3. Timing:

- Radiation typically starts within 4-6 weeks after surgery, depending on the patient's recovery and any concurrent chemotherapy.

4. Young Children:

- For children younger than 3 years old, radiation therapy is often delayed due to concerns about neurocognitive side effects. Chemotherapy is used initially to control the disease, and radiation may be introduced later as a reduced-dose protocol.

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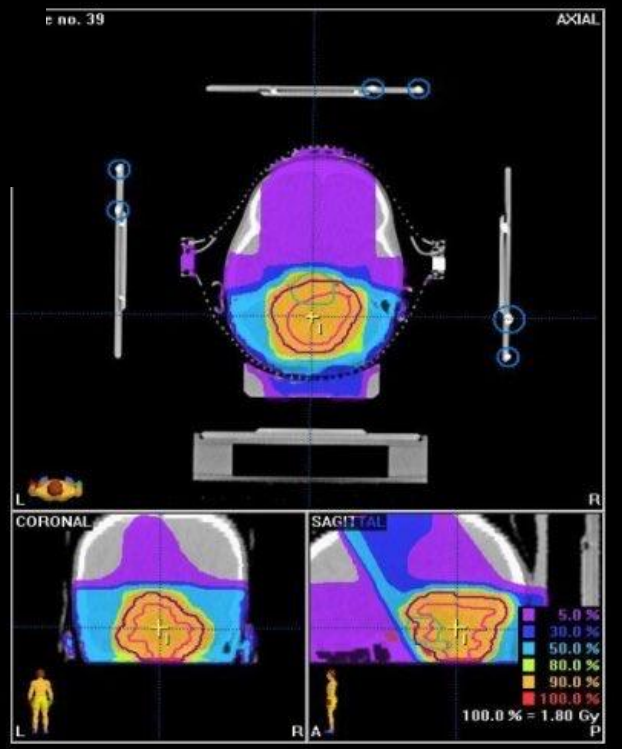
MEDULLOBLASTOMA
POST. Fossa boost

3-D conformal with dynamic mMLC & IMRT



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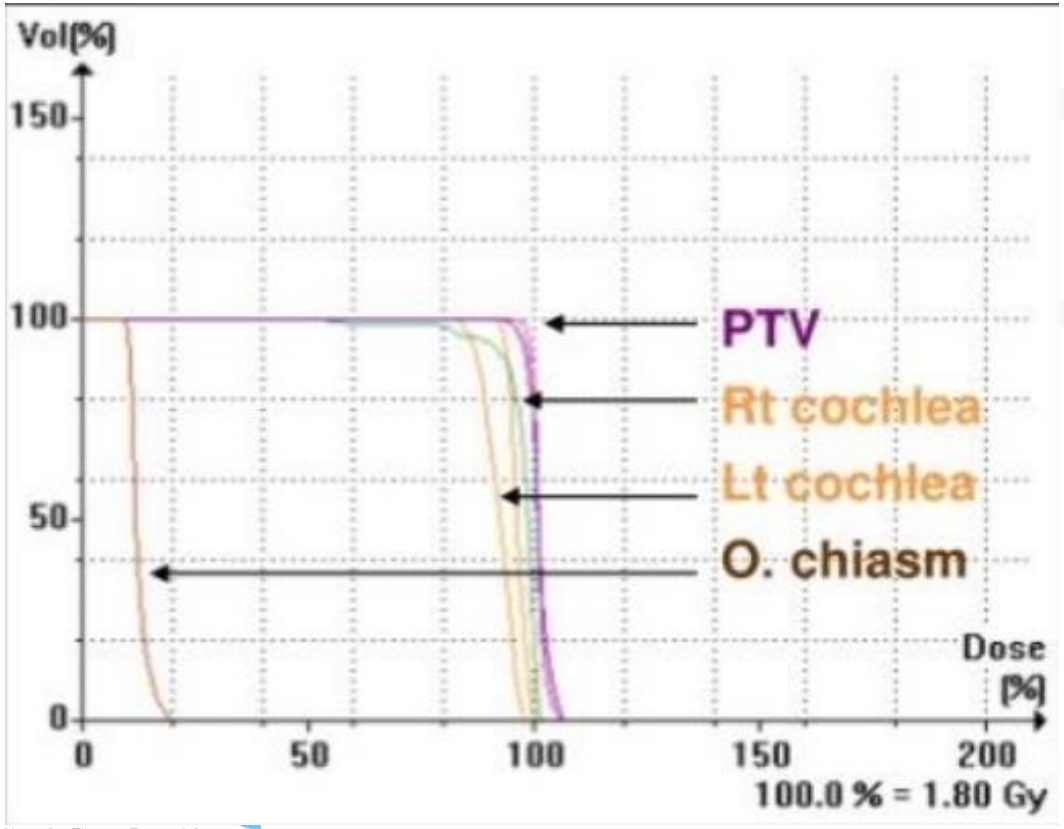
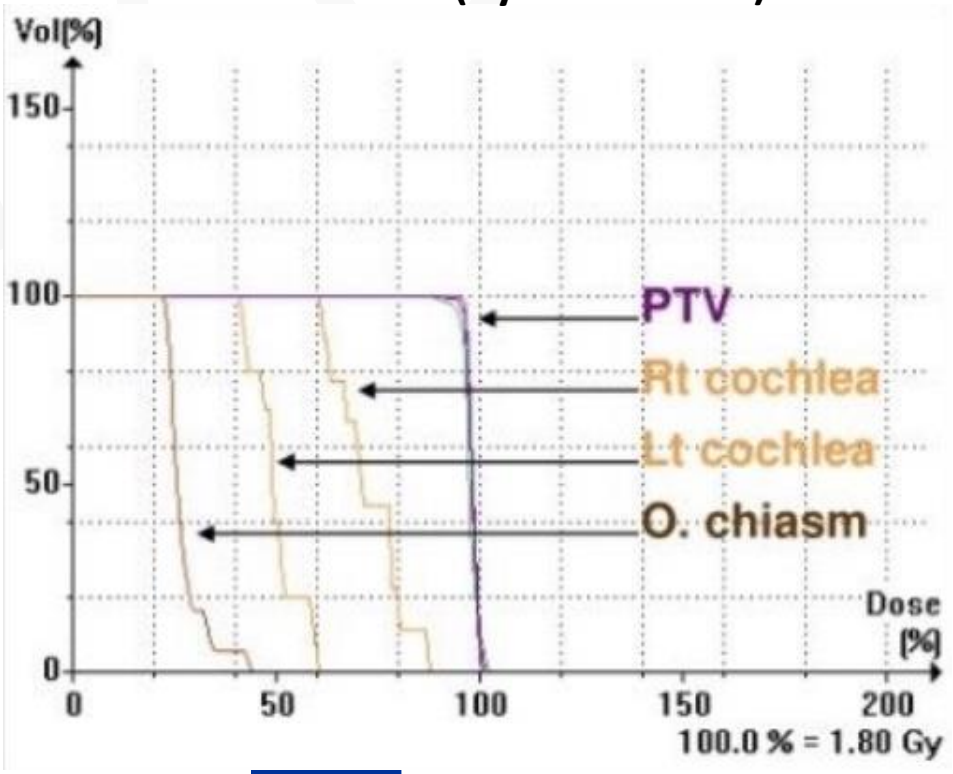
Comparative planning

3-D mMLC (CRT)



3-D mMLC (dynamic IMRT)



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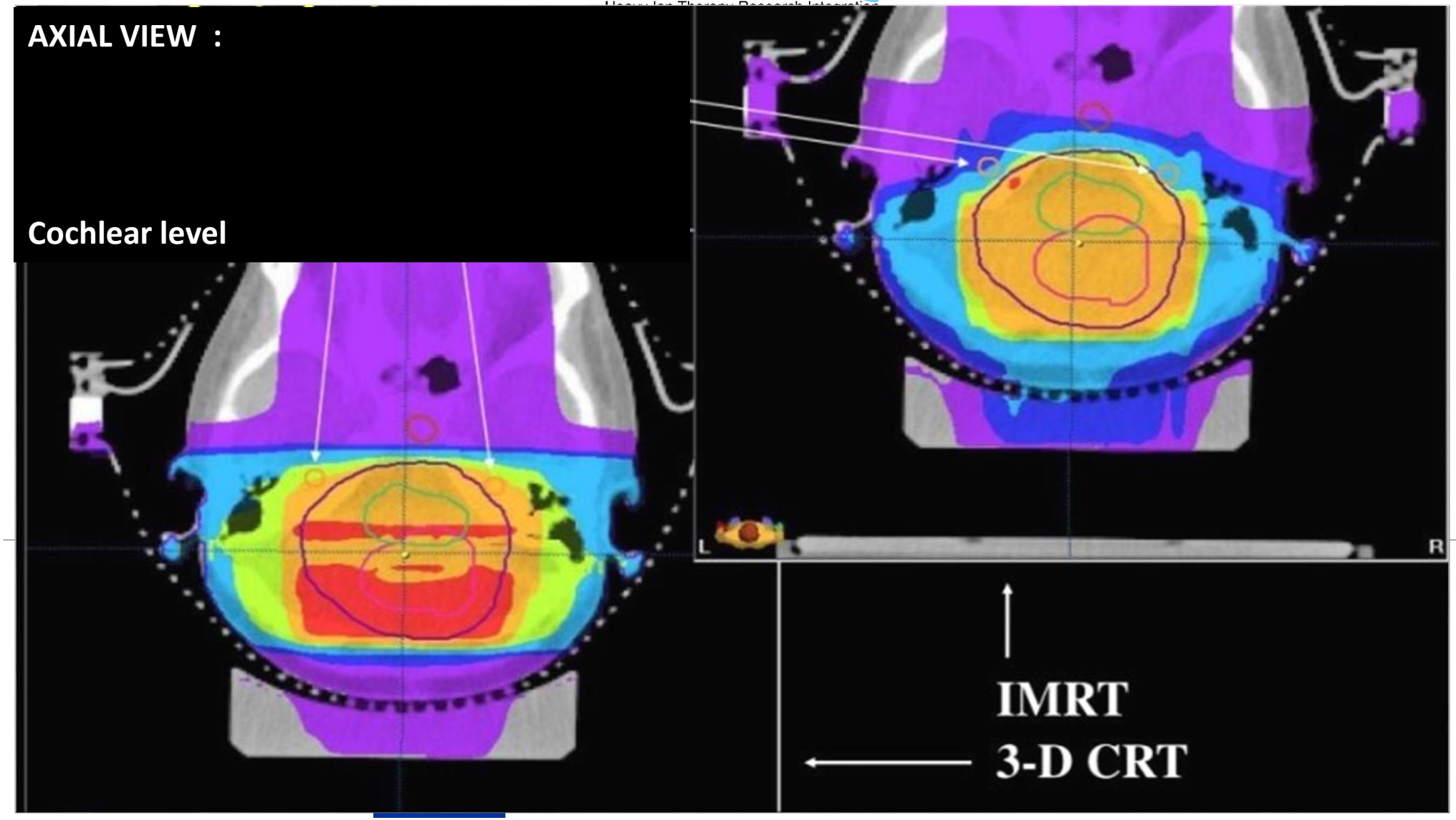
AXIAL VIEW :

Cochlear level



Risk of G-3/G-4 ototoxicity versus dose after RT to the posterior fossa in children

RT technique	Dose to the cochlea	Risk (%)
3-D CRT	54.2 Gy (mean)	64%
IMRT	36.7 Gy (mean)	13%

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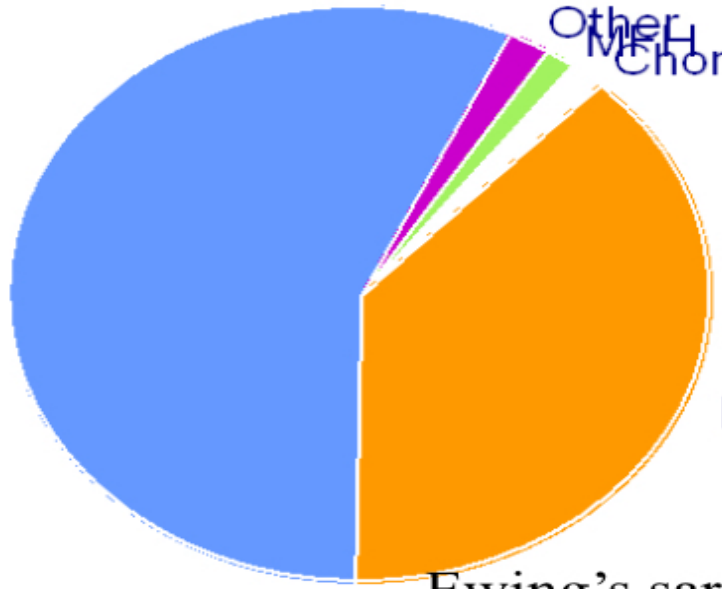
Pediatric Malignant Bone Tumors by Histology (n=664)

Other 13 (2.0%)
MFH 10 (1.5%)
Chondrosarcoma 11 (1.7%)



Osteosarcoma 377 (57%)

Ewing's sarcoma family of tumors 253 (38%)

Ewing osteosarcoma

Age range: 5–25 years

Predominantly affects white individuals

Commonly affects the diaphysis of bones and soft tissues

25% of patients have metastatic disease at diagnosis

Common metastatic sites: lung, bone, bone marrow

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Indications: Used for unresectable tumors, residual disease post-surgery, or metastatic cases

Goal: Achieve local tumor control while minimizing damage to healthy tissue.-

Dosage: Typically 45-55 Gy, balancing effective control with reduced toxicity.

Challenges: Potential for growth disturbances and late effects, especially in children; proton therapy may help minimize risks.-

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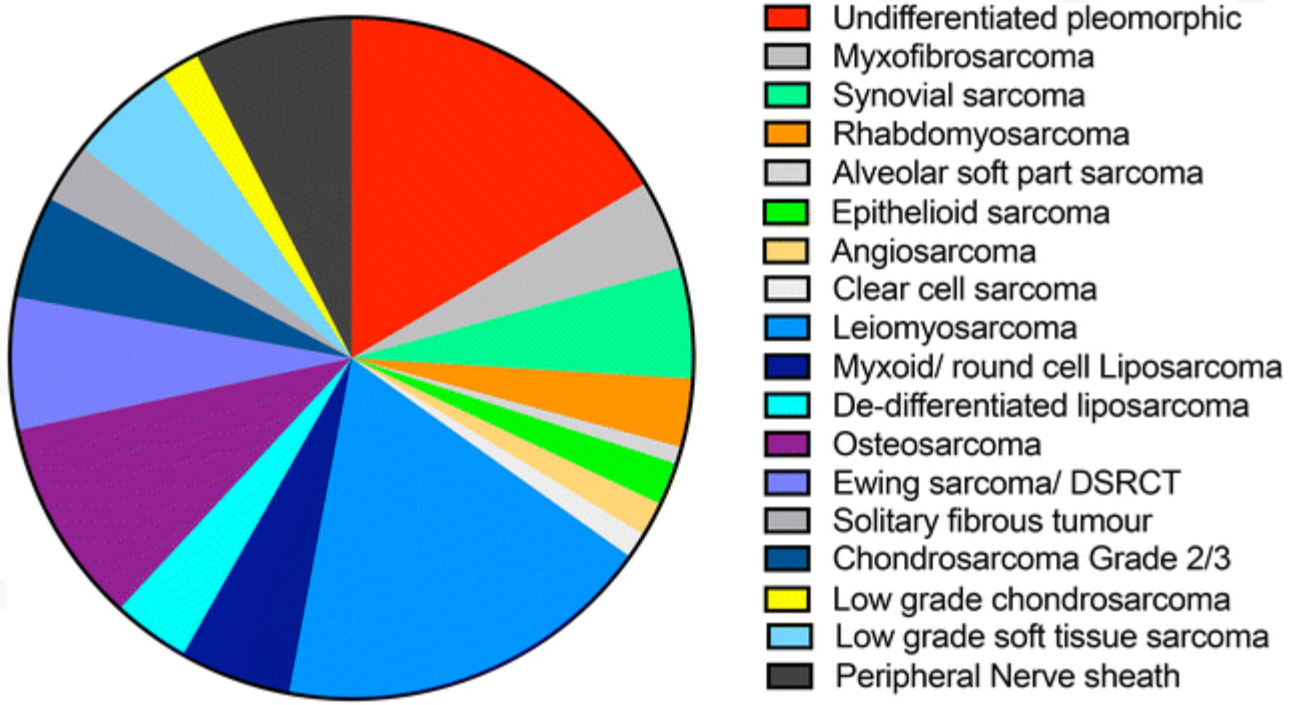
Soft tissue sarcomas



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Rhabdomyosarcoma radiation therapy:

Indications for Radiation Therapy: Radiation therapy is used in cases where complete surgical resection is not possible, for residual disease, or in patients with high-risk features.

- **Primary Radiation Dose:**

36-50.4 Gy, depending on the tumor site, size, and resection status. Treatment generally starts about 6-12 weeks after chemotherapy.

- Boost Dose: 41.4-50.4 Gy total, delivered if there is residual tumor post-surgery or if complete resection wasn't possible.

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Lymphoma (Hodgkin's and Non-Hodgkin's)

- **Indications:** Used with chemotherapy for residual or bulky disease.

Low-Risk Hodgkin's Lymphoma:

- Radiation Dose: 20-25.5 Gy to involved sites after chemotherapy.

High-Risk Hodgkin's Lymphoma:

- Radiation Dose: 30-36 Gy to bulky sites or areas with residual disease.

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Non-Hodgkin’s Lymphoma

- Radiation is typically used for residual disease or CNS involvement.

  - **Radiation Dose:** 24-30 Gy depending on the residual tumor size and location.

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Wilms tumor / nephroblastoma :

- Stage III Disease (Local Residual Tumor) or Stage IV (Metastatic Disease):

  - **Radiation Dose to Flank**: 10.8-20 Gy, generally starting within 10 days after surgery.

  - **Boost Dose:** May receive an additional boost to a total dose of 20-30 Gy in case of residual disease or high-risk features.

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Leukemia (ALL) :

Indications for Radiation: Used selectively for CNS prophylaxis, CNS involvement, testicular relapse, or as part of stem cell transplant preparation (TBI).

- CNS Prophylaxis for ALL:

  - **Radiation Dose:** 12-18 Gy, commonly used in combination with intrathecal chemotherapy.

- CNS Relapse or High-Risk CNS Disease:

  - **Radiation Dose**: 18-24 Gy, depending on patient risk factors and treatment response.

- Total Body Irradiation (TBI) for Transplant Preparation: (in the past)

  - **Dose:** 12-14 Gy in 6-8 fractions over 3-4 days is typical as part of conditioning before hematopoietic stem cell transplantation.

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Ways to reduce the risk of radiation induced endocrine dysfunction

1. Total dose and/or field size reduction
2. Total/partial shielding of the gland(s) at risk
3. More than 1 small fraction a day (hyperfractionation)
4. Free radical scavengers (radio protectors)
5. Better dose distribution (computer based optimisation of 3-D treatment planning + new highly performant treatment techniques)

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Total dose and/or field reduction

1. “Mantle” RT for Hodgkin disease :

   Dose lowered from 44Gy to 20Gy and field size reduced. Still excellent survival

   Sparing primary hypothyroidism

2. Prophylactic cranial irradiation in paediatric lymphoblastic leukaemia or medulloblastoma:

   Dose lowered to 18 Gy

   Sparing GH dysfunction

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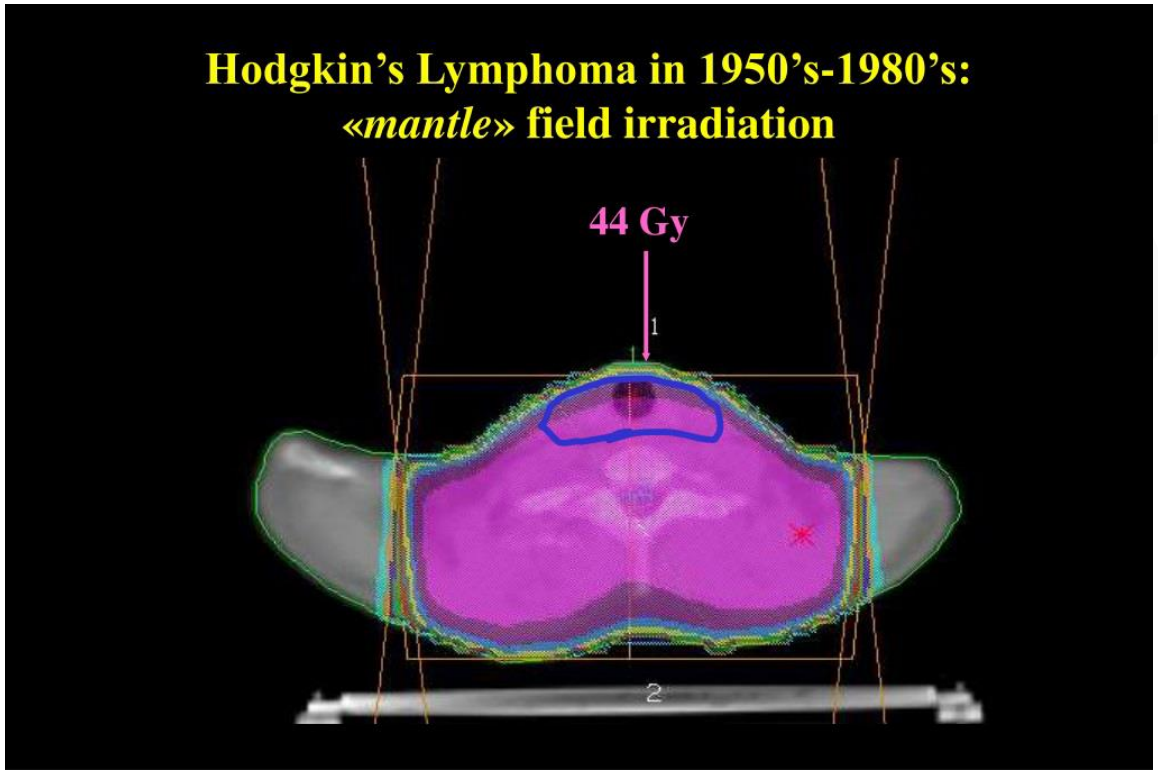

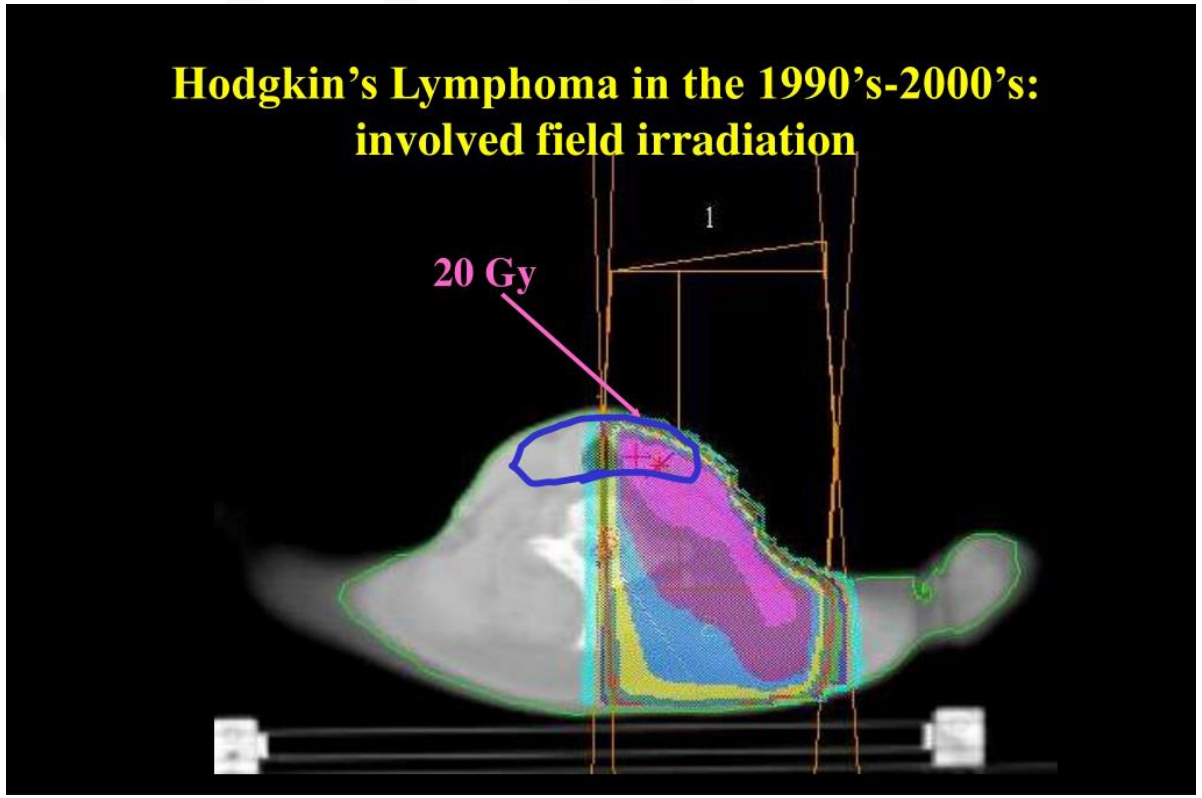

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Total/partial shielding of the gland(s) at risk

1. Head and neck tumors :

Usually high doses to the neck (50-70 Gy)

Sparing primary hypothyroidism

Sparing pituitary dysfunction

2. Pelvic tumors in males :

Shielding of the testicles

Dose <3 Gy **(sparing fertility)**

Dose < 20 Gy **(sparing leydig-cell function)**

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Dose-volume relations for thyroid dysfunction in head and neck tumors

The whole thyroid in the treatment field

Risk of thyroid dysfunction: **29%**

Partial shielding of the thyroid

Risk of thyroid dysfunction: **5%**

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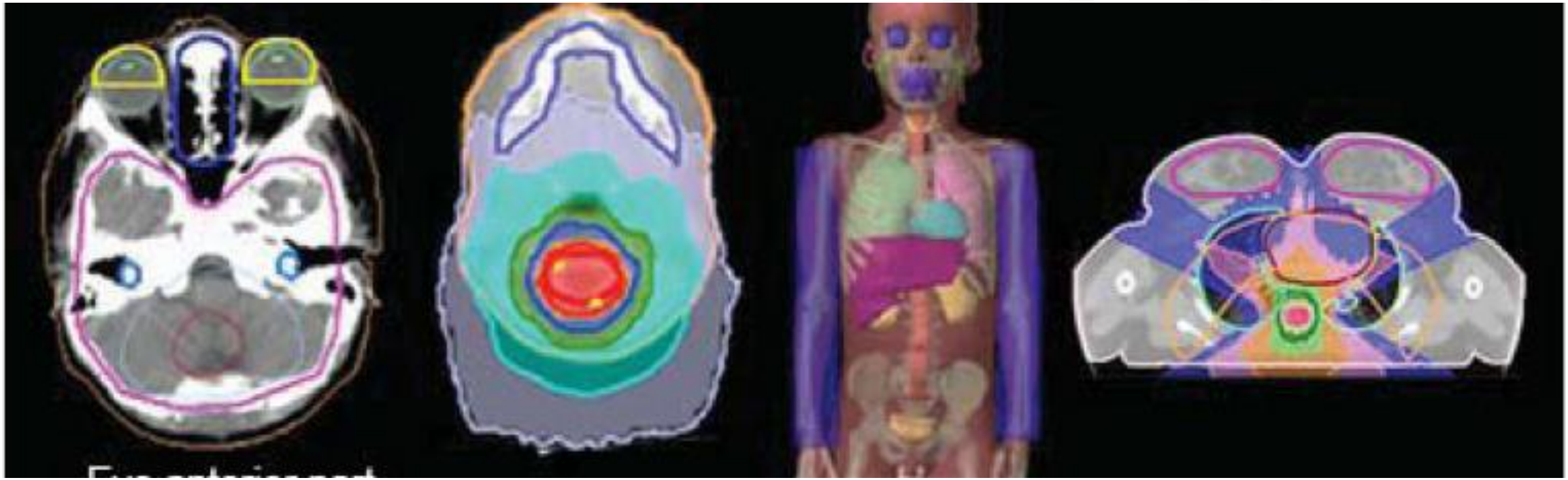
If OARS are not contoured , process doesn’t matter !



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3-D conformal RT

Shapes the prescription dose to the tumor avoiding normal tissues (critical organs) .

The system relies on 3 – dimensional imaging to define and target the tumor

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..is further optimisation possible ?

New treatment technologies such as **intensity modulated X-ray beams** and **proton beams** can provide an even superior dose distribution compared to conventional 3-D conformal RT

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Intensity Modulated Radiation Therapy

IMRT is a highly conformal RT technique whereby many beamlets of varying radiation intensity within one treatment field can delivered

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Quality of life in CNS tumor survivors: XRT vs no-XRT

Measure	% Survivors	Odds ratio
Never employed		
XRT	21	16.0
No-XRT	8	4.5
Emotional problems		
XRT	16	3.0
No-XRT	8	1.6
Fair of poor health		
XRT	30	13.1
No-XRT	10	1.0

Non operative strokes in children with CNS tumors

Incidence : 13/807 patients (1,6 %)

Occurrence : 2,3 years from diagnosis

Increased risk : - treatment with RT

- optic pathways gliomas

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Secondary cancers

Observed / expected ratios (95% CI) :

- Hodgkin disease : 9.7 (8.1 – 11.6)
- Soft tissue sarcoma : 7.0 (4.9 - 9.7)
- Neuroblastoma : 6.6 (3.3 – 11.8)
- CNS tumors : 4.4 (1.8 – 5.4)

Increases risk : female & young age

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Estimation of 2nd cancer incidence

Based on ICRP #60 guidelines

$$M = S(t)\, M(t)\, H(t)/L(t)$$

M: probability in % of 2nd cancer incidence (sv-1) total
Mt : probability in % of fatal 2nd cancer (sv-1) organ specific

Ht: average dose (sv) in the outlined organ
Lt: organ specific cancer lethality

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RMS: Estimated absolute yearly rate (%) of 2nd cancer

	Xrays	IMXT	Protons	IMPT
Yearly	0.06	0.05	0.04	0.02
RR compared to X-rays	***1***	***0.8***	***0.7***	***0.4***

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MDB: Estimated absolute yearly rate (%) of 2nd cancer

Tumor site	X-rays	IMXT	Protons
Oesophagus & stomach	0.15	0.11	0.00
Colon	0.15	0.07	0.00
Breast	0.00	0.00	0.00
Lung	0.07	0.07	0.01
Thyroid	0.18	0.06	0.00
Bone & soft tissue	0.03	0.02	0.01
Leukemia	0.07	0.05	0.03
All	0.75	0.43	0.05
RR (compared to X-rays)	**1**	**0.6**	**0.07**

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Proton beams may reduce the expected incidence of radiation-induced 2nd cancers by factor of > 2 (RMS) or > 8 (MDB)

With a lower risk of 2nd cancers the cost of life saved may be significantly reduced

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Conclusion : The future of paediatric radiation therapy

External Beam Radiation Therapy remains essential in paediatric cancer management

Advances in technology improves outcomes while reducing long term risks

Holistic approach ensures better survival rates and quality of life

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Thank you

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