Radiation treatment plan for pediatric cancer: a clinical view

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Outline

- Most common pediatric cancers
- Pediatric cancers statistics
- Radiotherapy in Pediatric Cancer
- Photon & Proton Therapy Common techniques
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Most common pediatric cancers

400.000 children and adolescents of 0-19 yo develop each year cancer. Most common types are:

- Leukaemias,
- Neuroblastomas,
- Wilms' tumours,
- Brain cancers,
- Rhabdomyosarcomas,
- Lymphomas,
- Retinoblastomas,
- Osteosarcomas,
- Ewing's sarcomas

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Pediatric Cancer Statistics

- **Leukaemia** accounts for approximately 35% of all childhood cancers. Although it is more common in children under the age of 10, approximately 1 in 1000 children are diagnosed with leukaemia by the age of 1.
- **Neuroblastoma** accounts for 5%-7% of all childhood malignancies and usually occurs by the age of 5.
- **Wilms' tumor** accounts for 6-7% of childhood cancer cases. It occurs in about 8 in 10^6 children < 14 yo.
- **Brain cancers** account for 15% of paediatric cancers (gliomas and medulloblastomas). The average age of glioma development is about 6 years old. Most medulloblastomas occur before the age of 10.

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Pediatric Cancer Statistics

- **Rhabdomyosarcoma** accounts for 5-8% of childhood cancers. It usually affects children between the ages of 2-6 and 15-19.
- **Lymphomas** are broadly classified as Hodgkin's and non-Hodgkin's. Hodgkin's generally occurs in individuals between 15-40 years of age.
- **Retinoblastoma** is the most common eye tumour in children and accounts for 3-4% of all childhood cancers. It usually occurs < 5yo
- **Osteosarcoma** is usually present in bones around the knee whereas Ewing's sarcoma may affect bones of the pelvis, thigh, upper arm, or ribs. Bone cancers are most common in ages 10-20 and they account for about 6% of all childhood cancers.

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Radiotherapy in Pediatric Cancer

Pediatric Cancer	Radiation Therapy
Leukaemia	Not the primary form of treatment – RT mostly used to treat metastases
Neuroblastoma	RT in the guidelines as adjuvant to chemotherapy, and/or surgery
Wilms' tumor	EBRT as part of treatment for more advanced Wilms tumors (stages III, IV, V) and earlier stage tumors with anaplastic histology
Brain cancers	Almost all brain cancers receive RT, either as monotherapy, or as part of a scheme, pre- or post-operative.
Rhabdomyosarcoma	RT to the site of the primary tumor is indicated for the HR and VHR groups, and the majority of Standard Risk Subgroup C patients (SIOP Europe)
Lymphomas	Are usually radiosensitive. RT part of therapy in Hodgking and non-Hodgkin lymphomas
Retinoblastoma	Is a radiosensitive tumor. EBRT/IMRT or Proton Beam therapy has the advantage over surgery of possibly saving vision.
Osteosarcoma	Is not usually radiosensitive. EBRT as adjuvant to surgical excision, if the tumor cannot be completely removed.

▸ Pediatr Blood Cancer. Author manuscript; available in PMC: 2022 May 1.

Published in final edited form as: Pediatr Blood Cancer. 2021 May;68(Suppl 2):e28344. doi: 10.1002/pbc.28344

Advances in radiotherapy technology for pediatric cancer patients and roles of medical physicists: COG and SIOP Europe perspectives

Chia-ho Hua [1], Anthony E Mascia [2], Enrica Servalli [3], Antony J Lomax [4], Klaus Seiersen [5], Kenneth Ulin [6]

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Photon therapy - pediatric patients

➢ The standard treatments for various pediatric cancers:

- 3D Conformal Radiation Therapy (3D-CRT),
- Intensity-modulated radiation therapy (IMRT),
- Volumetric-modulated arc therapy (VMAT),
- Helical Tomotherapy (HT),
- Stereotactic body radiation therapy (SBRT) for bone tumors, metastatic and recurrent lesions is under investigation,
- Some centers are now using high dose-rate (HDR) brachytherapy to treat pediatric sarcomas.

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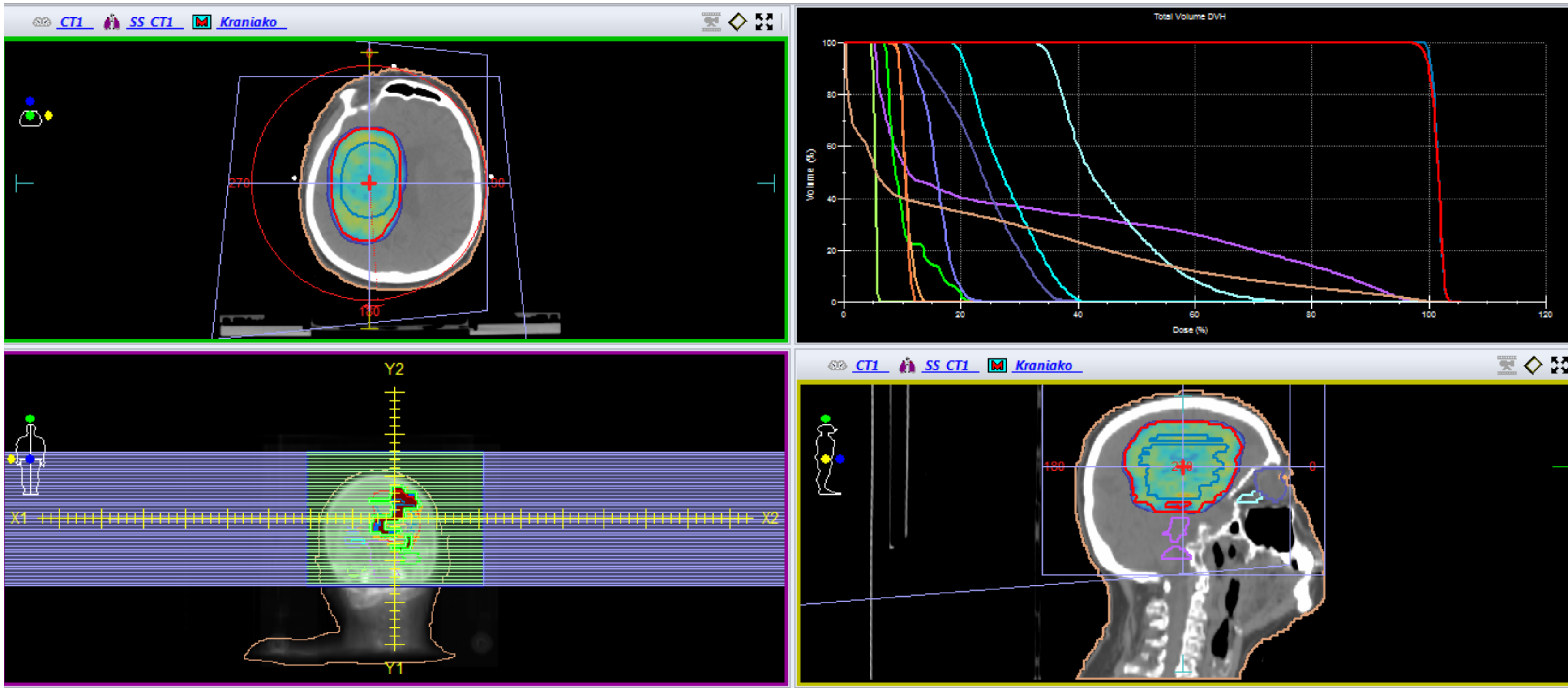
Brain Irradiation



VMAT technique delivers the radiation dose continuously as the treatment machine rotates

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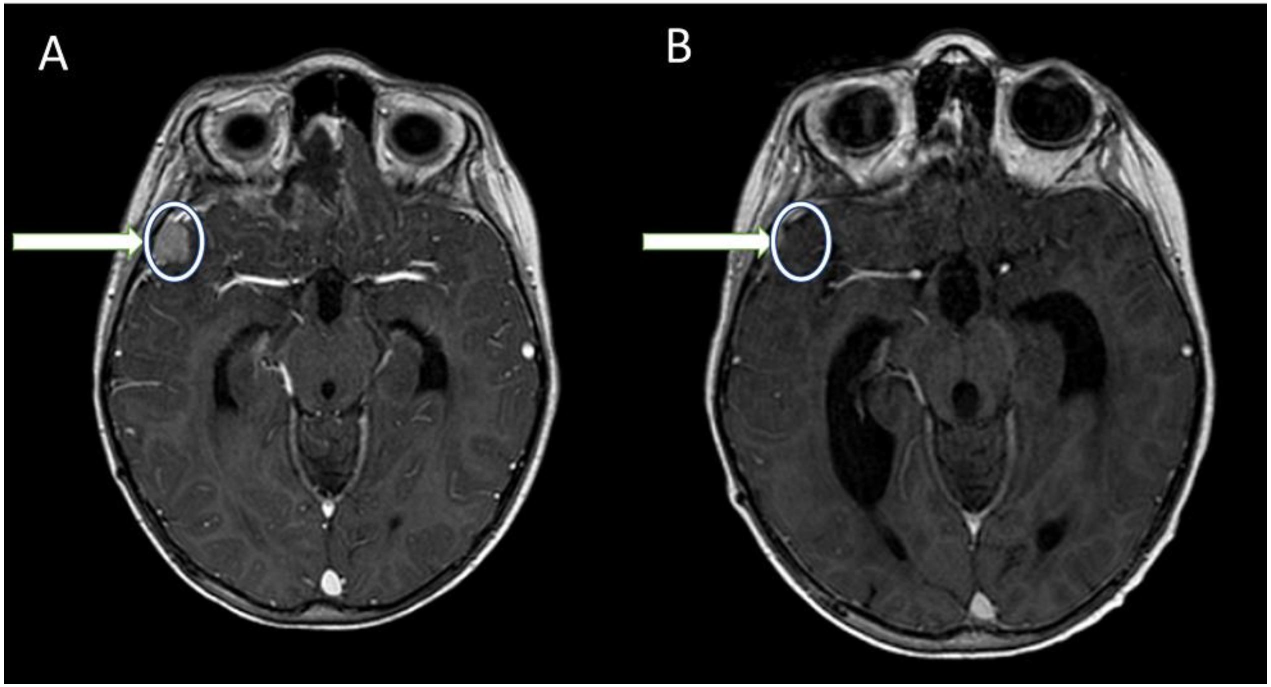
Re-irradiation of Pediatric Medulloblastoma



A: Recurrence of medulloblastoma, B: Three months after VMAT re-irradiation.

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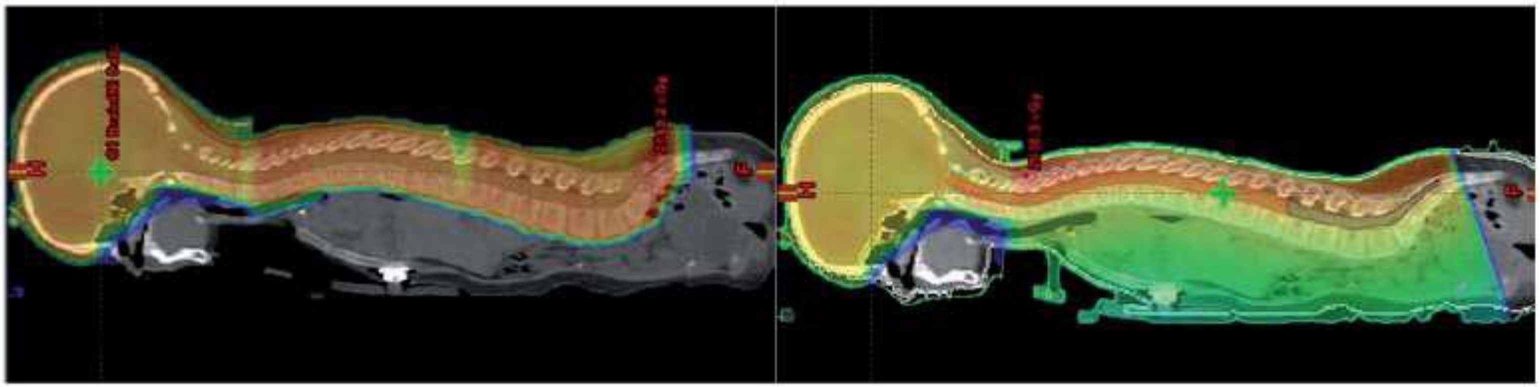
Craniospinal Irradiation



Proton CSI

Photon CSI

{Source: St. Clair, et al (2004)}

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Proton therapy - pediatric patients

- Pencil-Beam Scanning (PBS)
  - Conformity
  - Flexibility
- Intensity-Modulated Proton Therapy (IMPT)
  - More Complex
  - Highly Modulated
  - Highly Conformal

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History of Proton Beam Radiation Treatment

1899: The First Use of Radiation Therapy to Cure Cancer.

1929: Cyclotron invented by Ernest O. Lawrence as a way to accelerate nuclear particles to very high speeds

1946: Robert R. Wilson proposed the use of proton beams for treating cancer.

1948: Berkeley Radiation Laboratory conducts extensive studies on protons and confirms predictions made by Wilson.

1954: First patient treated with protons at Berkeley Radiation Laboratory.

1957: Treatment successfully duplicated on patients in Uppsala, Sweden.

1961: Harvard treats first patient in its cyclotron

1972: UC Davis cyclotron team develops the first method for making pure iodine-123, employed in thyroid imaging and to detect tumors.

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History of Proton Beam Radiation Treatment

1974: Los Alamos National Laboratory cyclotron treats first patient with pi-meson beam.

1975: Use of ionized particle beams to treat eye cancers pioneered by team of scientists using the Harvard cyclotron.

1978: UCSF and Lawrence Berkeley Laboratory team begins clinical trials of choroidal melanoma treatment with ionized helium beam.

1988: Proton therapy approved by FDA as radiation-treatment option for certain tumors.

1990: Loma Linda University opens first hospital-based proton-beam clinic. The 250 MeV machine is designed and built by Fermilab, where Wilson was the founding director, with $19.6 million in federal funding.

2001: Northeast Proton Therapy Center at Massachusetts General Hospital treats first patient.

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AI-assisted Systematic Review - Methods

- Pubmed and Cochrane Library
- Search terms: “proton beam therapy” AND “pediatric cancer”
- Inclusion Criteria
  - Language: English
  - Type of publication: Original studies and meta-analyses
  - Population: adults < 18 years old
  - Last 10 years
- Exclusion Criteria
  - Type of publication: case reports, reviews, letter to the editor
  - Population: Adult

Mourad Ouzzani, Hossam Hammady, Zbys Fedorowicz, and Ahmed Elmagarmid. Rayyan — a web and mobile app for systematic reviews. Systematic Reviews (2016) 5:210, DOI: 10.1186/s13643-016-0384-4.

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AI-assisted Systematic Review - Results

- Literature search results: 584 articles
- Duplicates deleted: 2
- Included articles = 37
- Excluded articles = 545
  - Wrong study design = 452
  - Case Reports = 25
  - Wrong population = 35
  - Animal study = 12
  - Wrong publication type = 21

Mourad Ouzzani, Hossam Hammady, Zbys Fedorowicz, and Ahmed Elmagarmid. Rayyan — a web and mobile app for systematic reviews. Systematic Reviews (2016) 5:210, DOI: 10.1186/s13643-016-0384-4.

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Guidelines ???

Cancer Treatment Reviews 98 (2021) 102209

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journal homepage: www.elsevier.com/locate/ctrv

ELSEVIER

Anti-tumour Treatment

Proton beam therapy for children and adolescents and young adults (AYAs): JASTRO and JSPHO Guidelines

Check for updates

Masashi Mizumoto [a], Hiroshi Fuji [b], Mitsuru Miyachi [c], Toshinori Soejima [d], Tetsuya Yamamoto [e], Norihiro Aibe [f], Yusuke Demizu [d], Hiromitsu Iwata [g], Takayuki Hashimoto [h], Atsushi Motegi [i], Atsufumi Kawamura [j], Keita Terashima [k], Takashi Fukushima [l], Tomohei Nakao [m], Akinori Takada [n], Minako Sumi [o,ae], Junjiro Oshima [p], Kensuke Moriwaki [q], Miwako Nozaki [r], Yuji Ishida [s], Yoshiyuki Kosaka [t], Keisuke Ae [u], Ako Hosono [v], Hideyuki Harada [w], Etsuyo Ogo [x], Tetsuo Akimoto [i], Takashi Saito [a], Hiroko Fukushima [y], Ryoko Suzuki [y], Mitsuru Takahashi [z], Takayuki Matsuo [aa], Akira Matsumura [ab], Hidekazu Masaki [ac], Hajime Hosoi [c], Naoyuki Shigematsu [ad], Hideyuki Sakurai [a,*]

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Recommendation and Evidence level

Clinical	Strength of Recommendation
Medulloblastoma	B (Moderate)
Ependymoma	C (Low)
Unresectable/Postoperative Persistent Craniopharyngioma	C (Low)
Whole Ventricle Irradiation and Craniospinal Irradiation for Intracranial Germ Cell Tumor	D (Very Low)
Rhabdomyosarcoma	C (Low)
Postoperative radiotherapy for a Primary Lesion of Neuroblastoma	D (Very Low)
Unresectable/Incompletely Resectable Pediatric Osteosarcoma	C (Low)
Ewing’s Sarcoma Family of Tumors (ESFT)	D (Very Low)
Unresectable/Incompletely Resectable Spinal Chordoma and Chondrosarcoma	C (Low)

20
48

Comment > Clin Oncol (R Coll Radiol). 2023 May;35(5):292-300. doi: 10.1016/j.clon.2023.02.009. Epub 2023 Feb 16.

Outcomes of Patients Treated in the UK Proton Overseas Programme: Non-central Nervous System Group

E Hwang [1], S Gaito [2], A France [3], A M Crellin [4], D I Thwaites [5], V Ahern [6], D Indelicato [7], B Timmermann [8], E Smith [9]

Affiliations + expand

PMID: 36813694 DOI: 10.1016/j.clon.2023.02.009

Free article

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- 86.1% survival rate and 90.3% local control for non-CNS tumors in children.
  - Grade 3 toxicity rate 12.6%
  - Cataracts most common complication.
- Effective disease control,
- Acceptable toxicity rates,
  - Especially for rhabdomyosarcoma and Ewing sarcoma

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ELSEVIER

Practical Radiation Oncology

Available online 10 August 2024

In Press, Corrected Proof ⓘ What's this?

Basic Original Report

Evolution of Proton Radiation Therapy Brainstem Constraints on the Pediatric Proton/Photon Consortium Registry

Dora Correia MD [a b c 1], Daniel J. Indelicato MD [d], Arnold C. Paulino MD [e], Ralph Ermoian MD [f], Stephen Mihalcik MD [g], Stephanie M. Perkins MD [h], Christine Hill-Kayser MD [i], Victor S. Mangona MD [j], Jae Lee MD [k], John Han-Chih Chang MD [l], Nadia N. Laack MD, MS [m], Young Kwok MD [n], John Perentesis MD [o], Ralph Vatner MD [p], Ronak Dave MD [q r 1], Sara L. Gallotto MS [a], Miranda P. Lawell MS [a], Benjamin V.M. Bajaj MA [a], Keith W. Allison MS [a], Alisa Perry BSN [a]...
Torunn I. Yock MD, MCH [a]

Received: 17 February 2018 | Revised: 8 March 2018 | Accepted: 19 March 2018

DOI: 10.1002/pbc.27095

Check for updates

RESEARCH ARTICLE

WILEY Pediatric Blood & Cancer SIOP aspho The American Society of Pediatric Hematology/Oncology

Meta-analysis of the incidence and patterns of second neoplasms after photon craniospinal irradiation in children with medulloblastoma

Abhishek Bavle[1,2] | Sayani Tewari[1,2] | Amy Sisson[3] | Murali Chintagumpala[4,5] | Michael Anderson[2,6] | Arnold C. Paulino[7]

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Proton Beam vs Photon Beam THx

Aspect	Proton Beam Therapy	Photon Beam Therapy
Radiation Type	Protons (charged particles)	Photons (X-rays, electromagnetic waves)
Energy Deposition	Energy peaks at Bragg peak, sparing tissue beyond the tumor	Energy is deposited along the entire path (before, in, and after the tumor)
Precision	Highly precise, minimal damage to healthy tissue	Less precise, affects more surrounding tissue
Side Effects	Fewer side effects, especially long-term	More side effects, potential for secondary cancers
Clinical Use	Pediatric cancers, tumors near critical structures	Common cancers, broader applications
Cost and Availability	More expensive, limited availability	More affordable, widely available

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THANK YOU

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