HITRI plus
Heavy Ion Therapy Research Integration

Treatment planning for pediatric cancer tumour treatments

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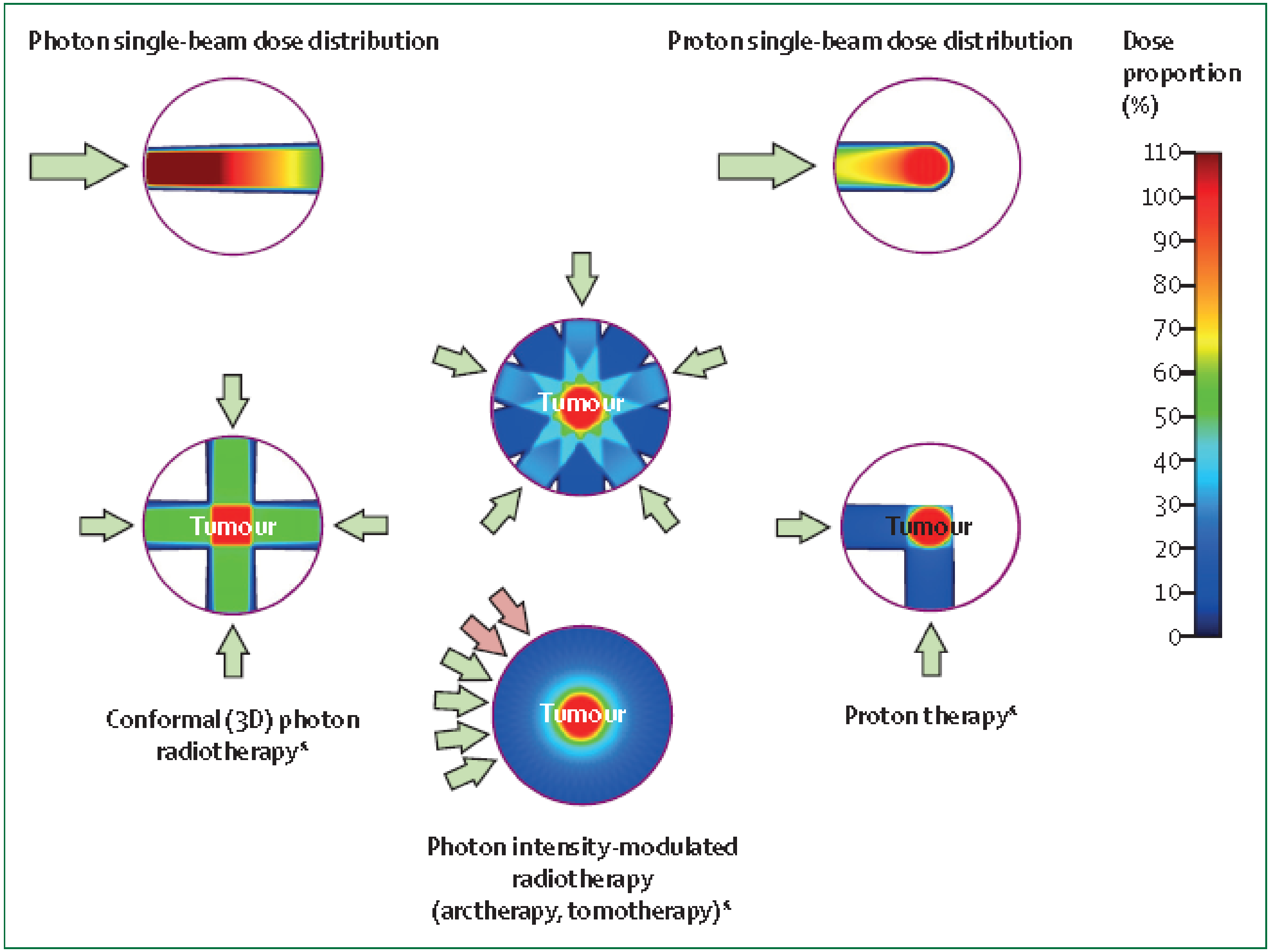
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

Outline

- Advantages over conventional radiation therapy
- Planning with protons
- Planning (childrens) with protons

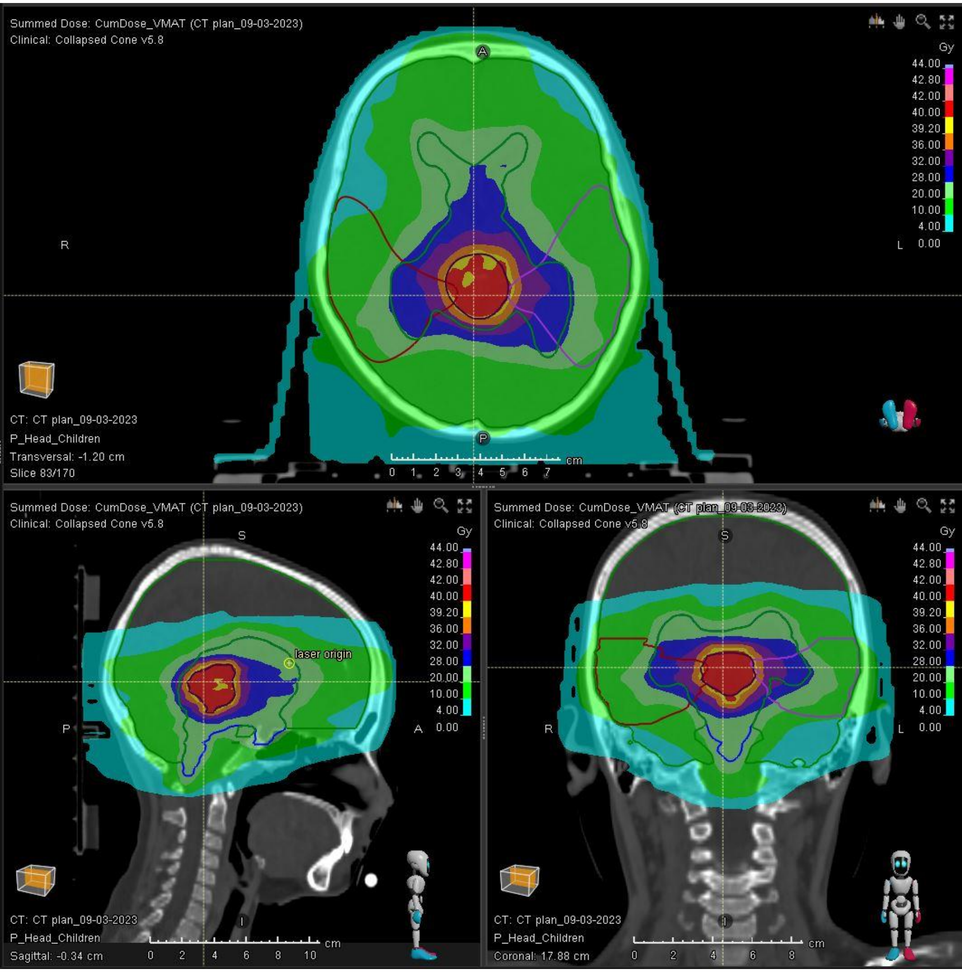
RATIONAL - PHYSICS

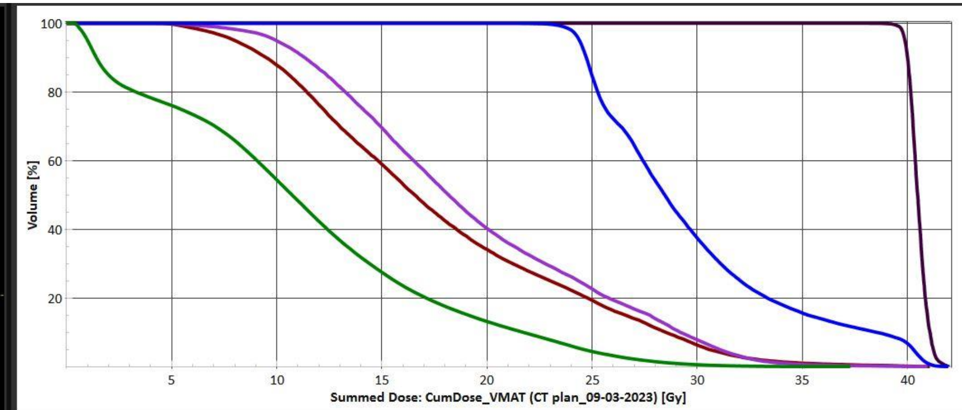


Thariat J. The Lancet 2021

Protons versus photons: WVI

VMAT





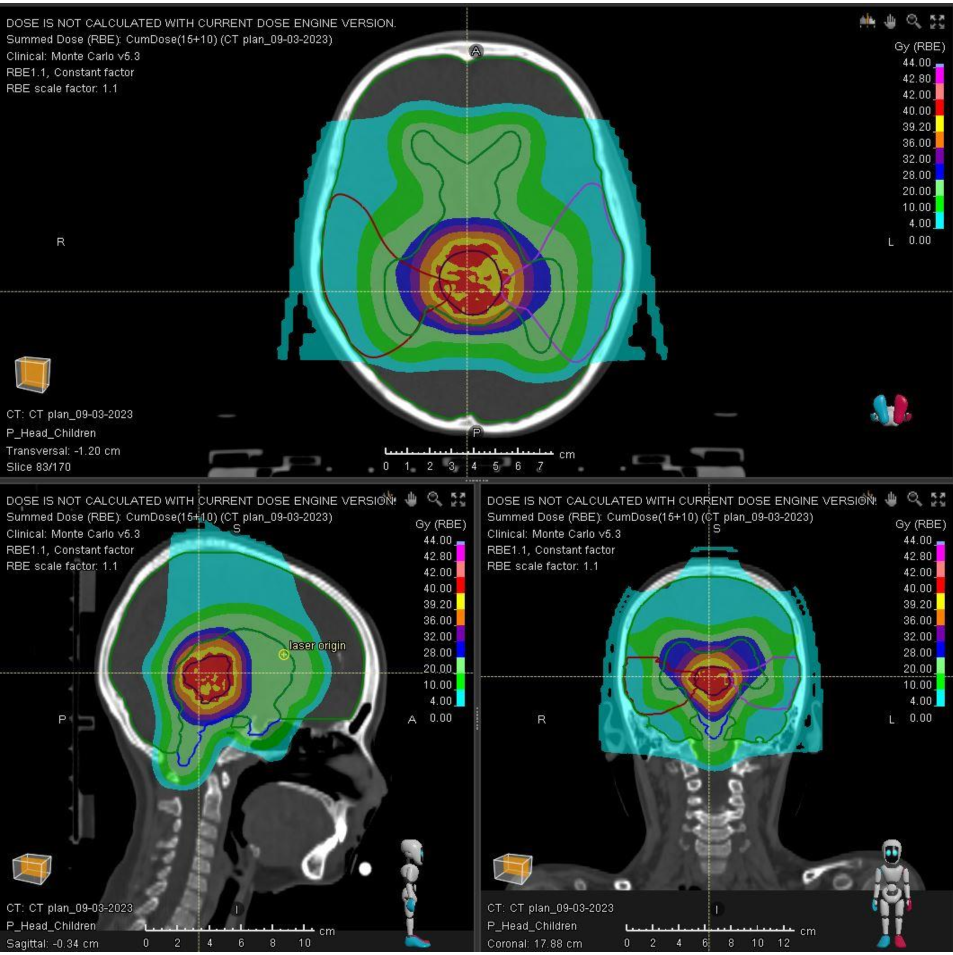
Dose axis: Absolute | Gy | Volume axis: Relative max

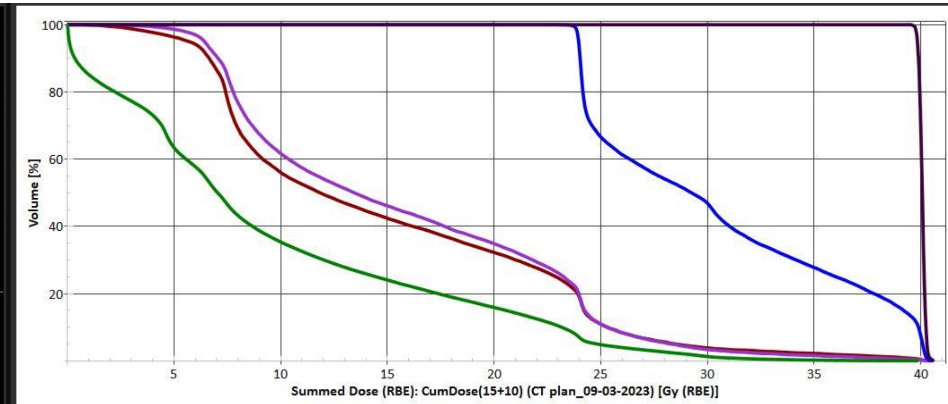
Dose statistics | Clinical goals | Biological response | Plan fraction sche... | Beams (Current) | Control points (Cu... | BEV (Current)

ROI statistics | POI statistics

Name	ROI	ROI vol. [cm³]	Dose [Gy] D99	D98	D95	Average	D50	D2	D1	% ou
Summed Dose: CumD...	Brain-Brainstem-CTV-WVI	1350.40	0.56	0.69	1.00	11.14	10.72	27.22	28.80	
Summed Dose: CumD...	CTVBoost	12.43	39.62	39.73	39.88	40.51	40.49	41.42	41.56	
Summed Dose: CumD...	CTV-WVI	194.84	23.64	24.01	24.40	29.70	28.45	40.72	40.94	
Summed Dose: CumD...	Lobe_Temporal_L	104.77	6.98	8.27	9.97	19.28	18.17	32.72	34.09	
Summed Dose: CumD...	Lobe_Temporal_R	118.78	5.68	6.47	8.00	17.83	16.56	32.95	34.97	

Protons CNAO (fixed beams)





Dose statistics | Clinical goals | Biological response | Plan fraction sche... | Beams (Current) | Control points (Cu... | BEV (Current)

ROI statistics / POI statistics

Name	ROI	ROI vol. [cm³]	Dose [Gy (RBE)] D99	D98	D95	Average	D50	D2	D1	% ou
Summed Dose (RBE):...	Brain-Brainstem-CTV-WVI	1350.40	0.02	0.03	0.09	9.52	7.04	28.97	30.52	
Summed Dose (RBE):...	CTVBoost	12.43	39.76	39.79	39.85	40.08	40.08	40.35	40.40	
Summed Dose (RBE):...	CTV-WVI	194.84	23.84	23.89	23.97	30.34	29.25	40.20	40.26	
Summed Dose (RBE):...	Lobe_Temporal_L	104.77	4.63	5.51	6.43	15.56	13.44	33.33	37.22	
Summed Dose (RBE):...	Lobe_Temporal_R	118.78	2.78	3.74	5.69	14.87	11.83	35.56	39.01	

- Lower mean dose to healthy brain than VMAT
- Lower mean dose Temp. Lobes than VMAT
- Similar (even better) CTV coverage than VMAT

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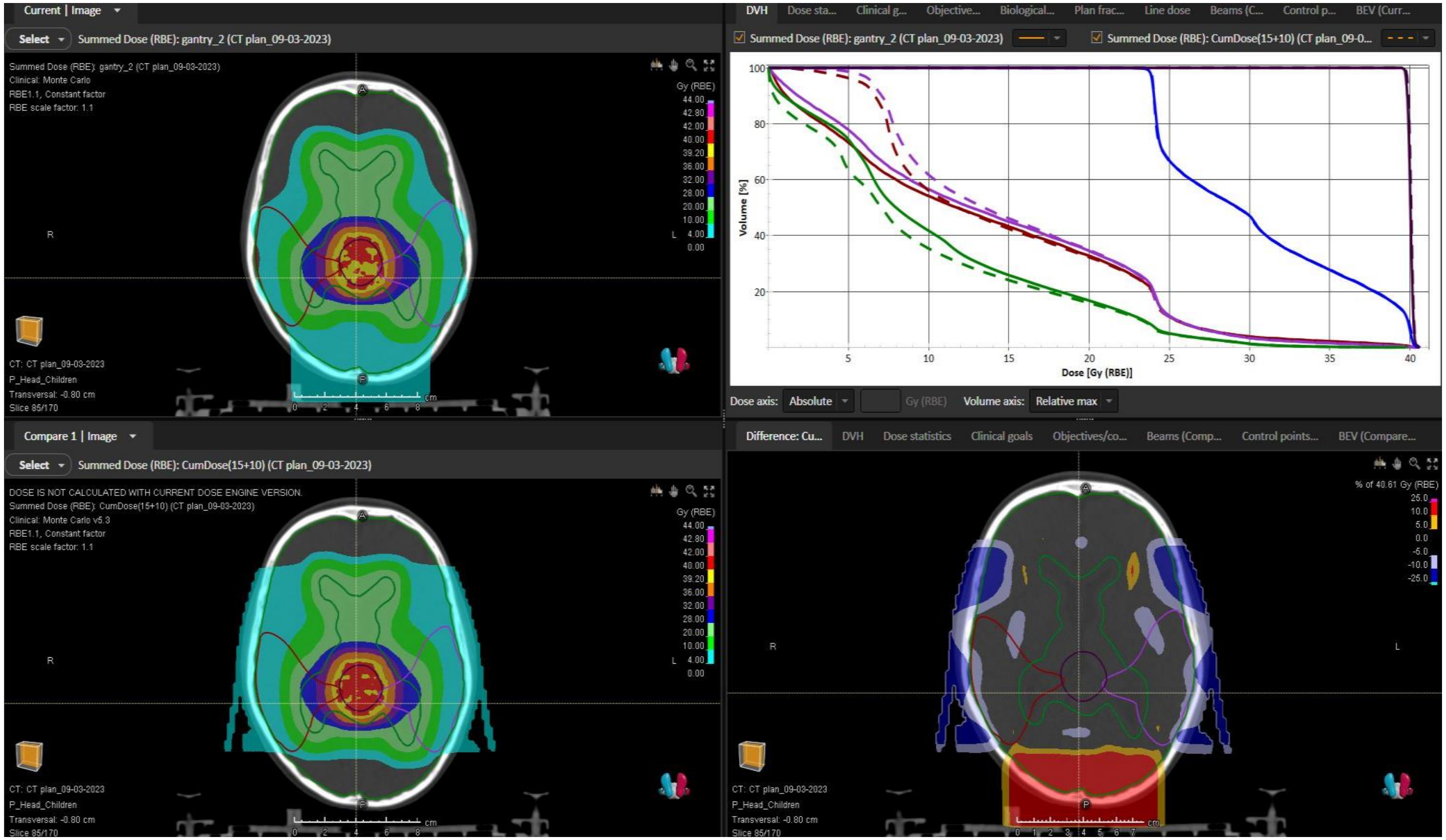
Protons fixed vs Gantry



Details:

Upper part (continous lines) for Gantry

Lower part (dashed lines) for fixed beams

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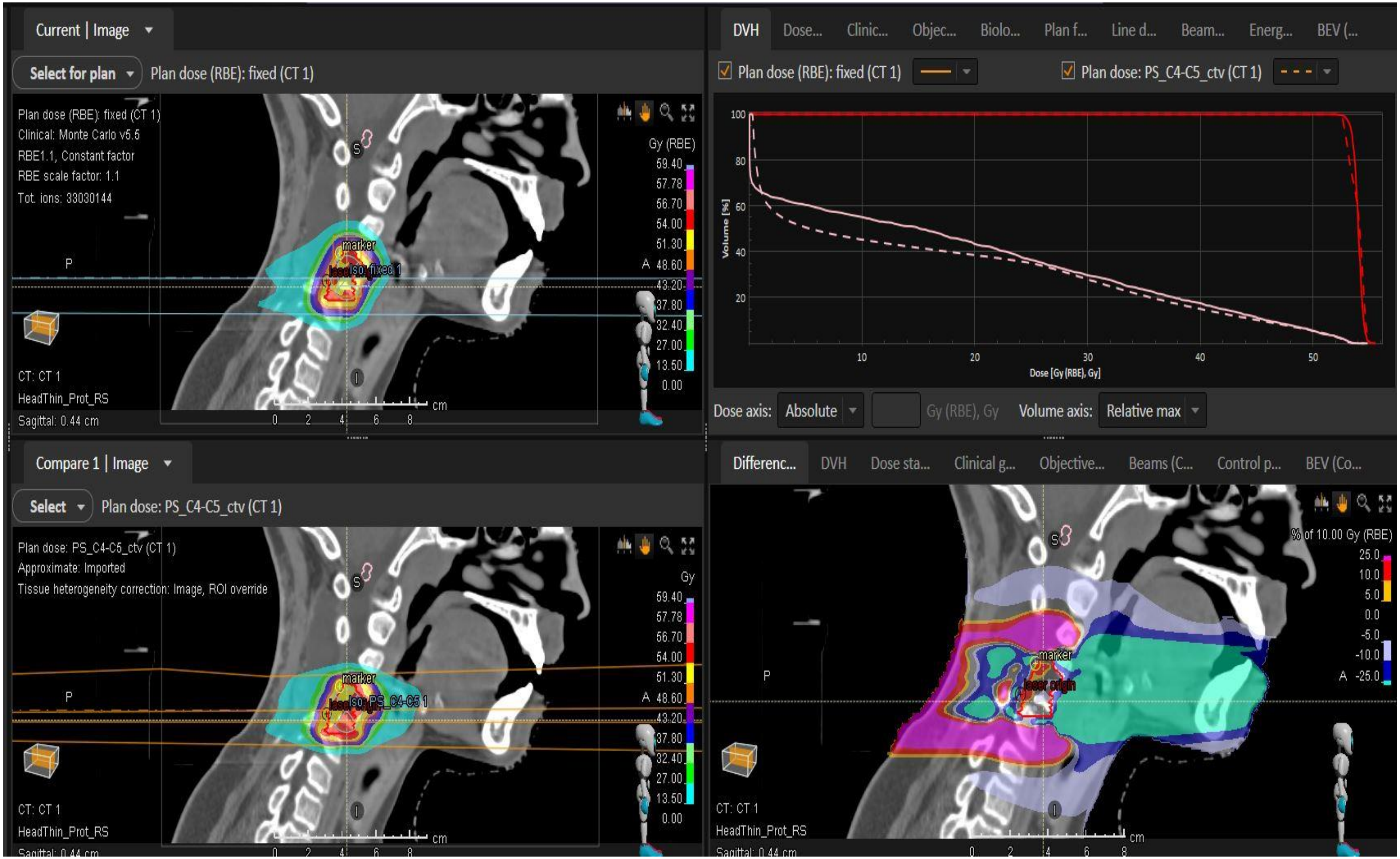
Protons versus photons: Schwannoma



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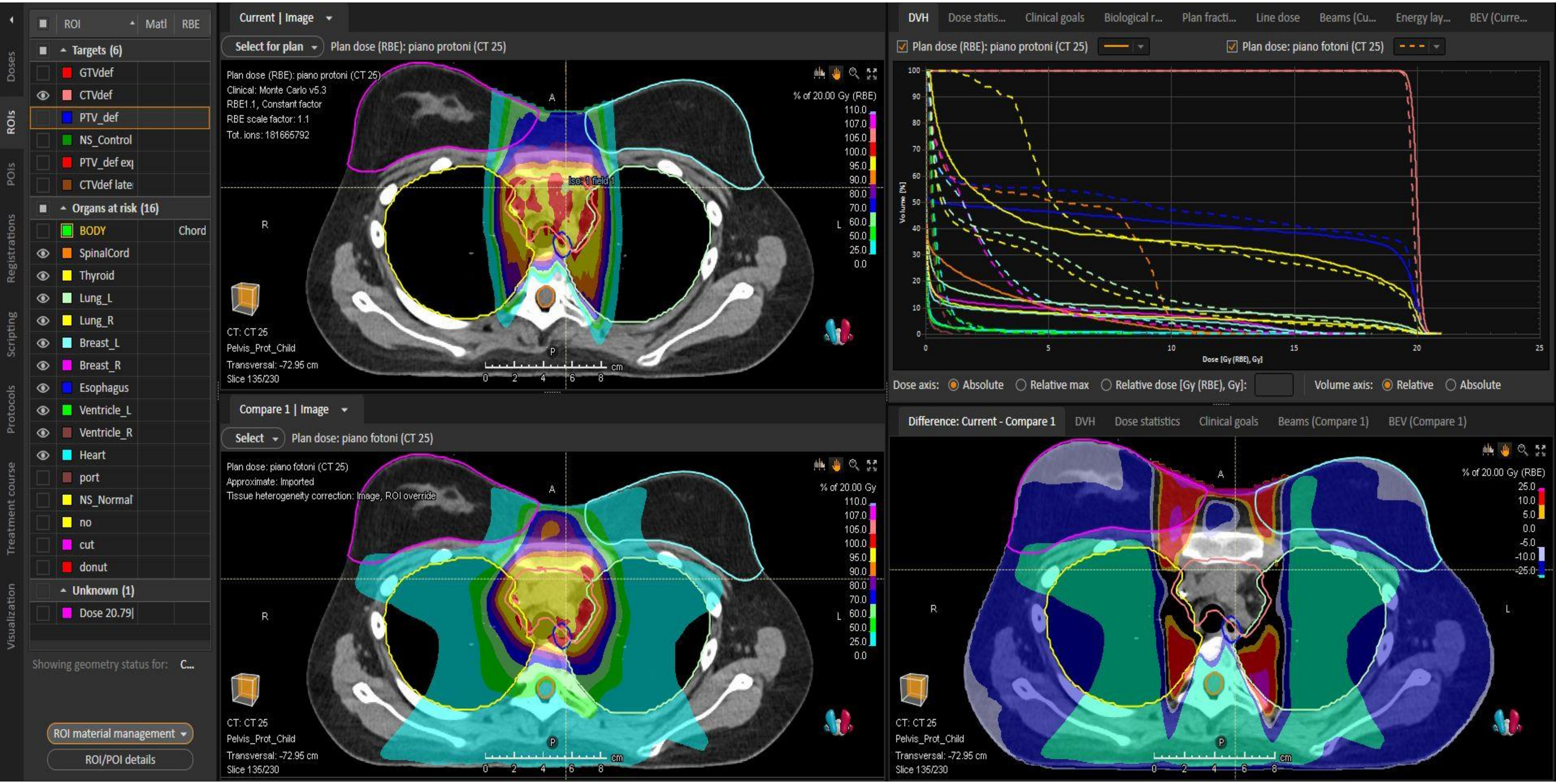
Protons versus photons: Lymphoma



Cardiotoxicity model-based patient selection for Hodgkin lymphoma proton therapy. *Acta Oncologica, 0(0), 1-8*

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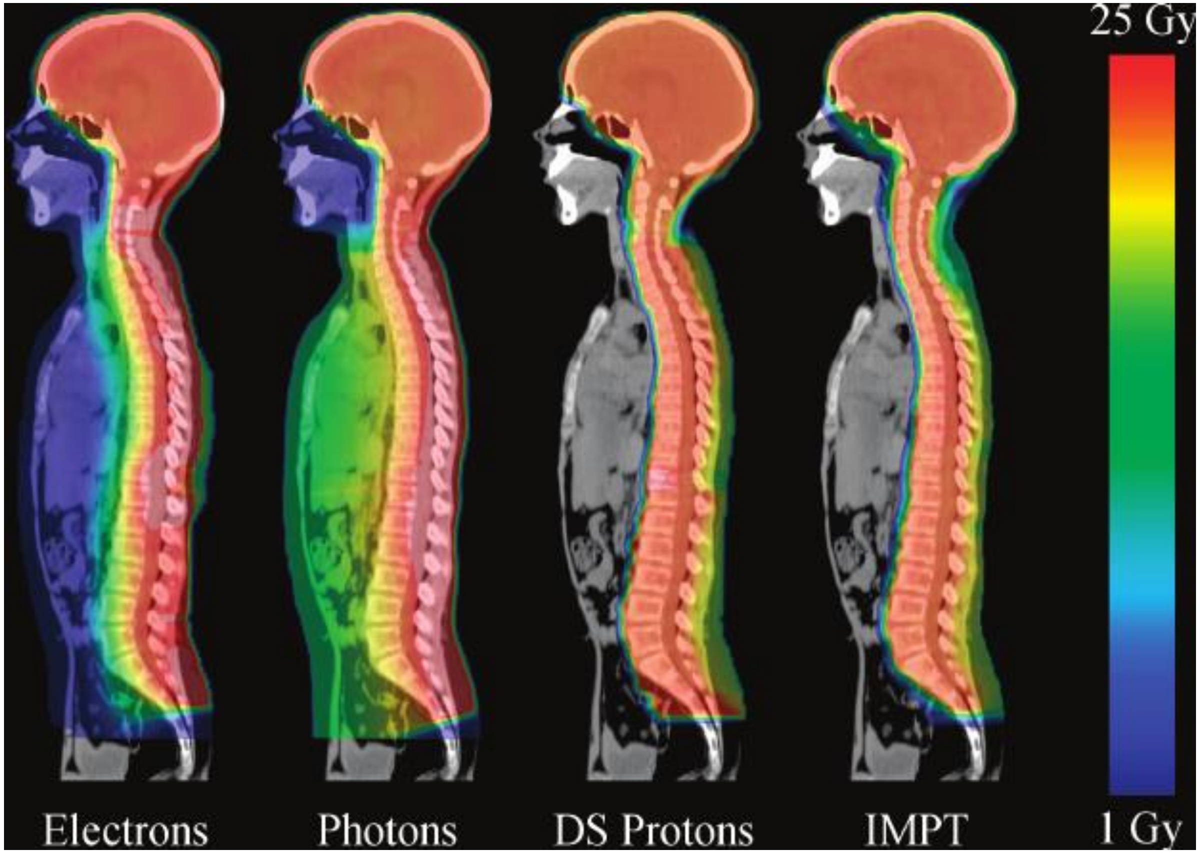
Protons versus photons: CSI



Estimated risk of radiation-induced cancer following paediatric cranio-spinal irradiation with electron, photon and proton therapy. DOI: 10.3109/0284186X.2014.928420

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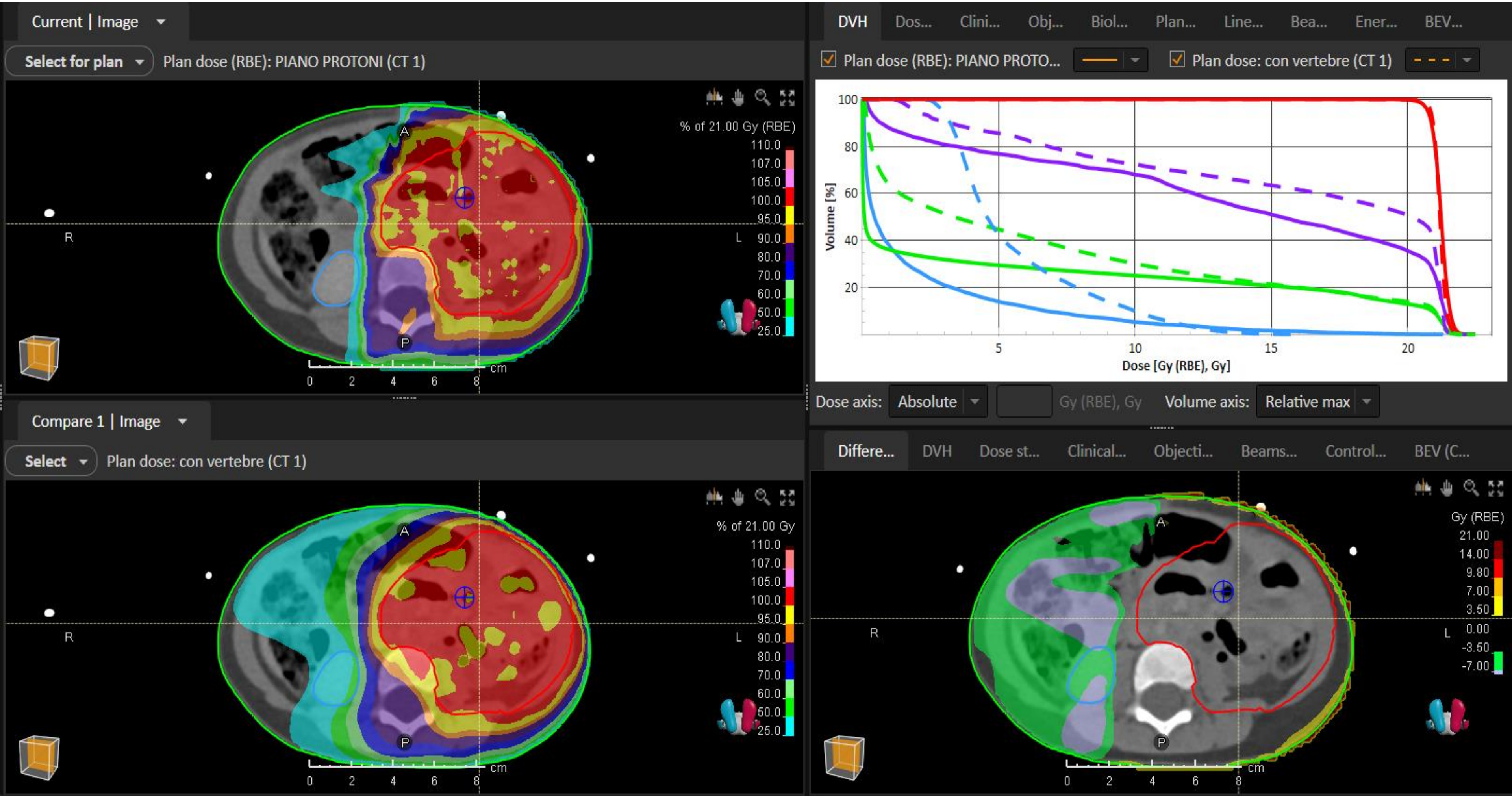
Protons versus photons: NBL



Dosimetric Comparison Between Proton and Photon Radiation Therapies for Pediatric Neuroblastoma. *International Journal of Particle Therapy*, 100100. Mirandola et al. 2024

Cognitive Sparing in Proton versus Photon Radiotherapy for Pediatric Brain Tumor Is Associated with White Matter Integrity: An Exploratory Study

by Lisa E. Mash [1,2], Lisa S. Kahalley [1,3,*], Kimberly P. Raghubar [1,2], Naomi J. Goodrich-Hunsaker [4], Tracy J. Abildskov [4], Luz A. De Leon [1,2], Marianne MacLeod [1,2], Heather Stancel [1,2], Kelley Parsons [1,2], Brian Biekman [5], Nilesh K. Desai [6,7], David R. Grosshans [8], Arnold C. Paulino [8], Zili D. Chu [6,7], William E. Whitehead [9], Mehmet Fatih Okcu [10], Murali Chintagumpala [10] and Elisabeth A. Wilde [4,11]

Research has shown that children who undergo radiotherapy for brain tumors are at risk for long-term changes in both their thinking and brain structure. Compared to photon radiotherapy (i.e., X-rays), proton radiotherapy may cause less damage to healthy brain tissue and result in fewer cognitive problems. This study compared cognitive functioning and white matter damage in survivors of pediatric brain tumors who were treated with proton or photon therapy. The results showed that patients who received photon therapy had more cognitive problems and showed more white matter change than those who received proton therapy. Patients who underwent proton therapy, on the other hand, were similar to healthy individuals with no history of brain tumors. This study suggests that proton therapy may protect healthy brain tissue, leading to better long-term cognitive outcomes.

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Adv Radiat Oncol. 2023 Nov-Dec; 8(6): 101273. PMCID: PMC10692298
Published online 2023 May 21. doi: 10.1016/j.adro.2023.101273 PMID: 38047226

The Pediatric Proton and Photon Therapy Comparison Cohort: Study Design for a Multicenter Retrospective Cohort to Investigate Subsequent Cancers After Pediatric Radiation Therapy

Amy Berrington de González, DPhil,[a,*] Todd M. Gibson, PhD,[a] Choonsik Lee, PhD,[a] Paul S. Albert, PhD,[a] Keith T. Griffin, MS,[a] Cari Meinhold Kitahara, PhD,[a] Danping Liu, PhD,[a] Matthew M. Mille, PhD,[a] Jungwook Shin, PhD,[a] Benjamin V.M. Bajaj, MPH,[b] Tristin E. Flood, MS,[b] Sara L. Gallotto, MS,[b] Harald Paganetti, PhD,[b] Safia K. Ahmed, MD,[c] Bree R. Eaton, MD,[d] Daniel J. Indelicato, MD,[e] Sarah A. Milgrom, MD,[f] Joshua D. Palmer, MD,[g] Sujith Baliga, MD,[g] Matthew M. Poppe, MD,[h] Derek S. Tsang, MD,[i] Kenneth Wong, MD,[j,k] and Torunn I. Yock, MD[b]

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Sources of uncertanties in particle therapy: general

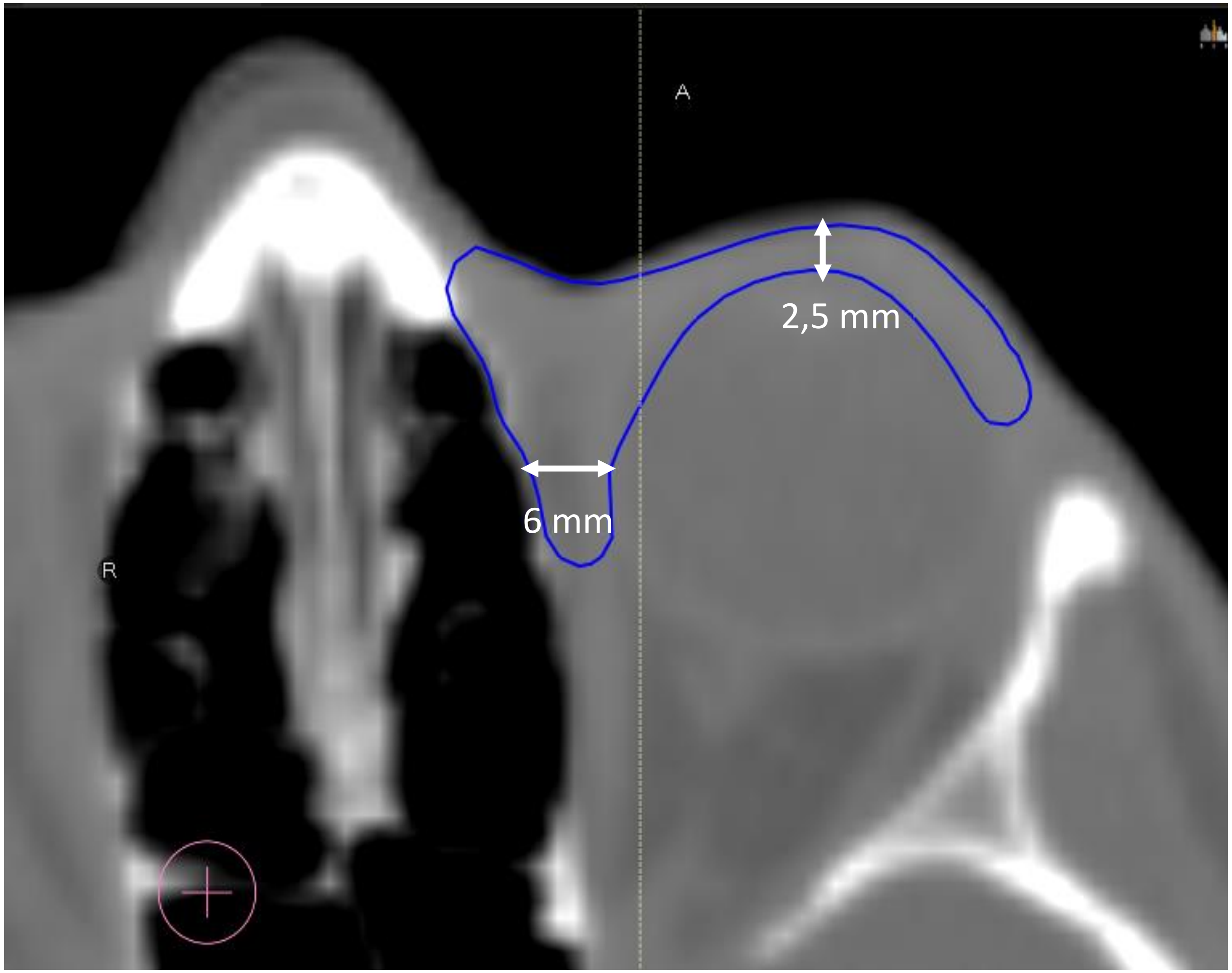
- Measurement uncertainty in water for commissioning
- Stopping power / mean excitation energy of water in beam modeling
- Beam reproducibility
  - energy constancy
  - momentum spread
- Patient setup
  - Organ motion
  - Anatomical changes
- CT imaging and calibration
- CT conversion to tissue
  - rWEPL-to-energy dependence
  - Metal implants
- Biology

Treatment planning aspects specific for pediatrics

Secondary cancer
Small volumes (both targets and OARs in general)
Growth during the treatment course and from the simulation CT
Density variations
Higher radiosensitivity respect to the adults for specific diseases
Patient comfort and fast deliverability (for anesthesia)

↓

Fiew beam entrances for IMPT/SFUD plans
Plan robustness
LET optimisation



Adults:

- **3-5 mm spot spacing**
- **Minimum Np = 1,5E06**

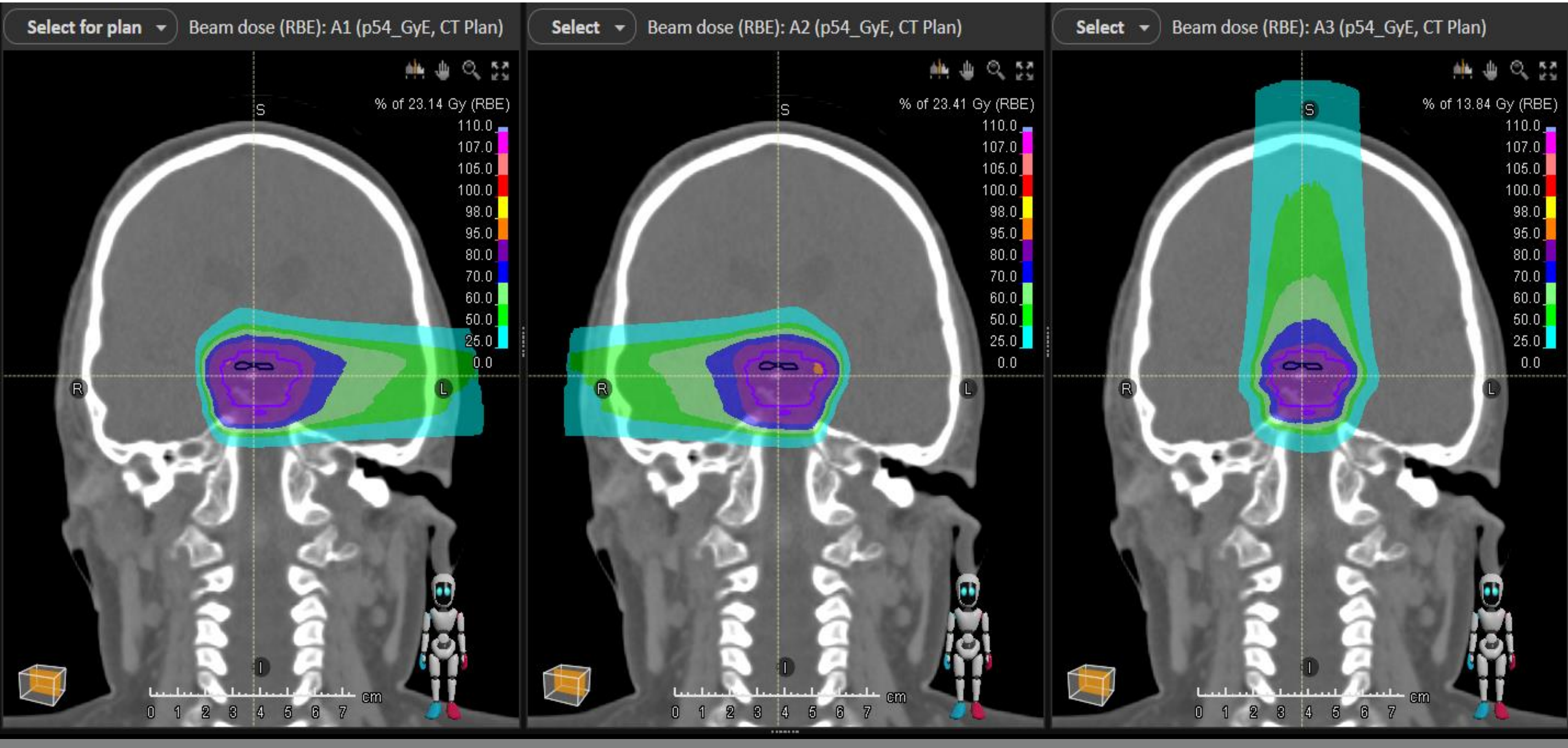
Higher modulation

Childrens:

- **Down to 1 mm spot spacing**
- **Minimum Np = 1,0E06**

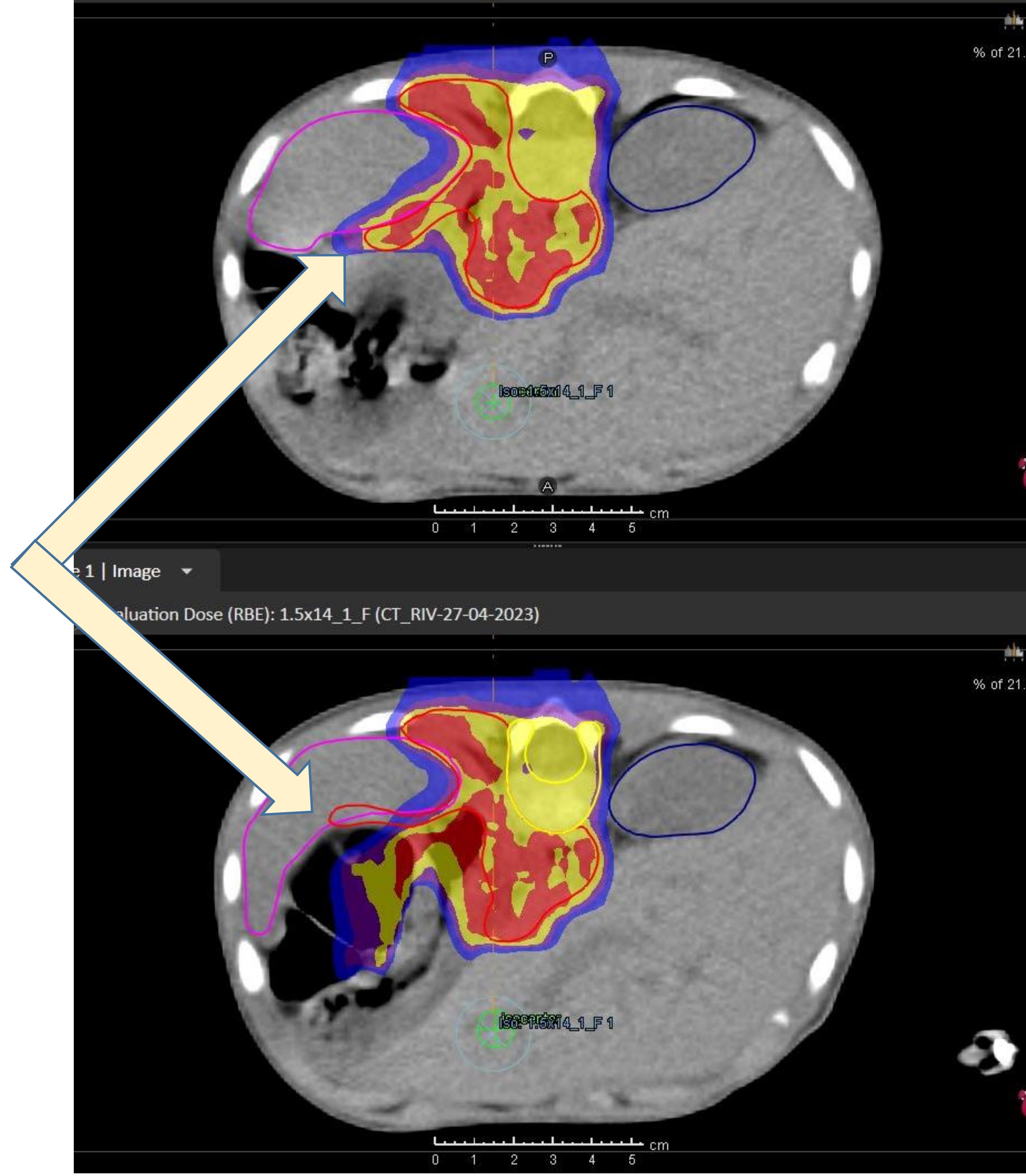
SFUD

It can be helpful for increasing robustness: Craniopharyngioma.
"The combination of individually optimised fields, each of which deliver a (more or less) homogenous dose across the target volume. SFUD is the spot scanning equivalent of treating with 'open' fields" (T.Lomax)



Small changes, big impacts

NBL patient:
peritoneal cavity and stomach emptying/filling → target displacement



OFF-LINE PLAN ADAPTATION

CNAO - 221 patients (6 months – no eye)

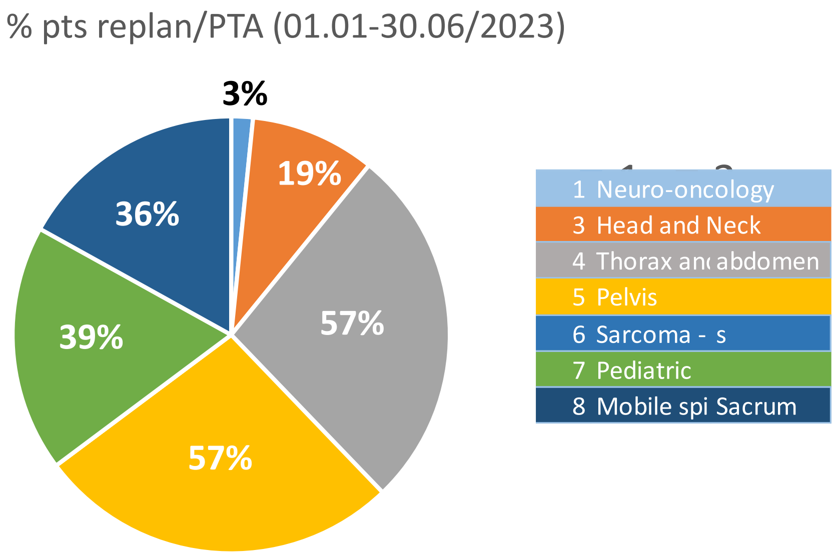
→ 154 (70%) RE-CT (at 22 days on average)

→ 57 1 RP

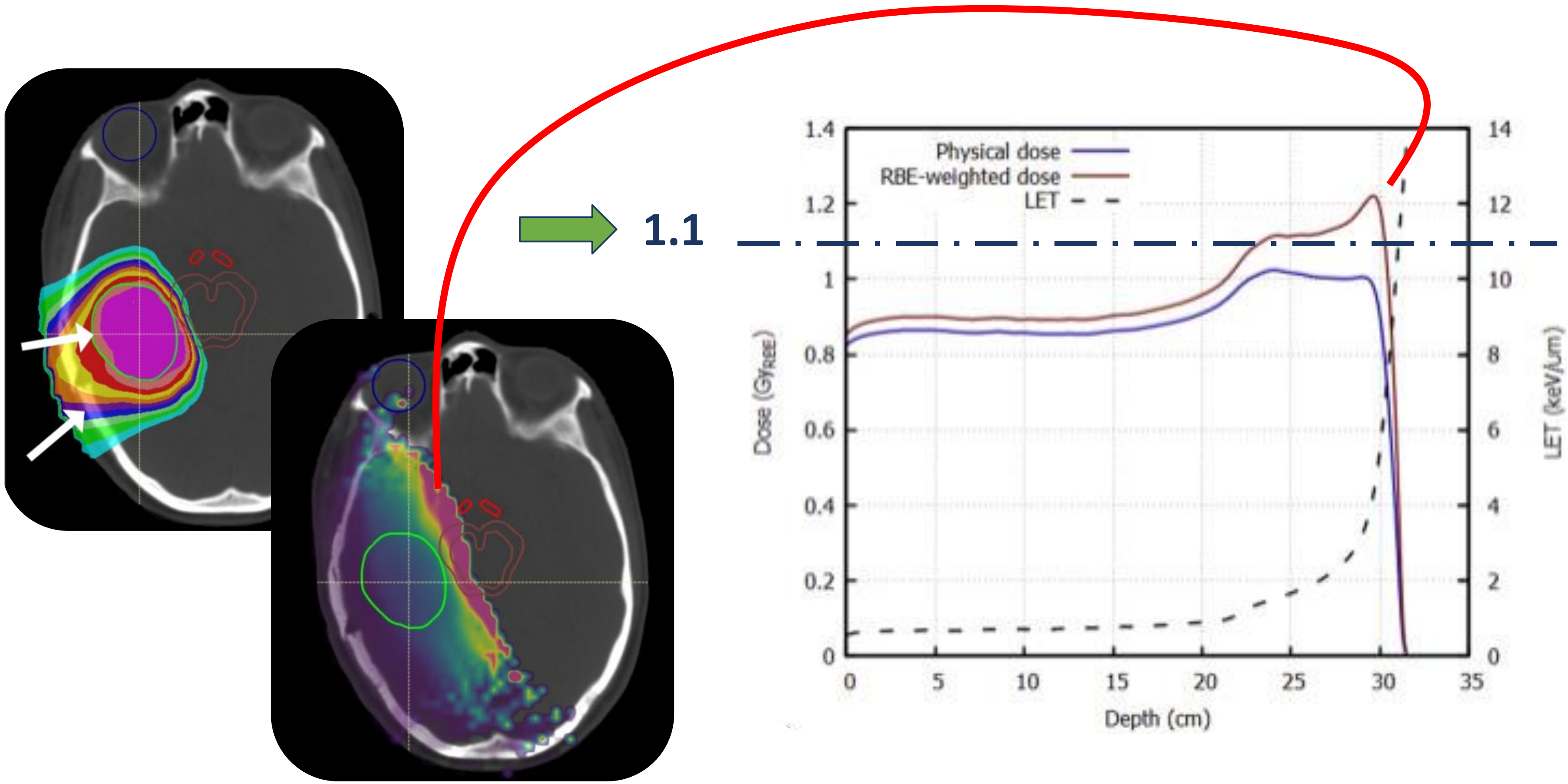
→ 25 >1 RP

37% (p≈C)

→ 78% Target coverage

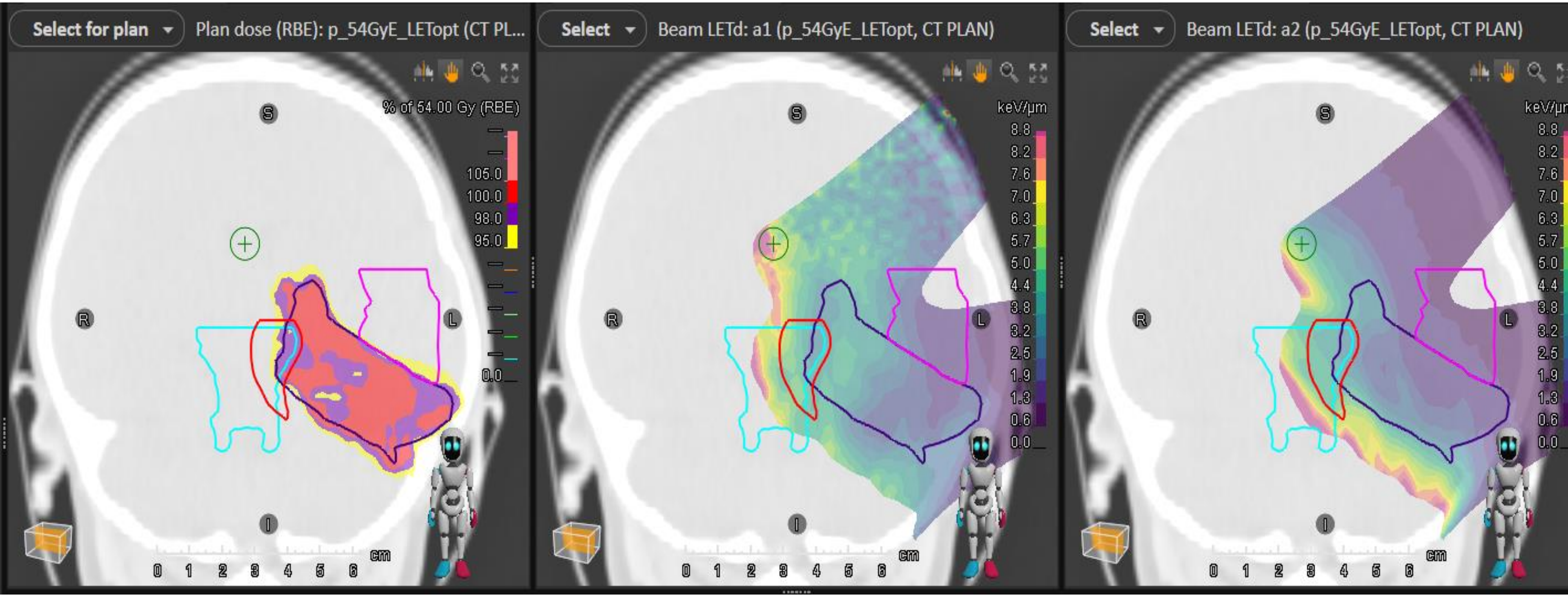


Courtesy of A. Vai



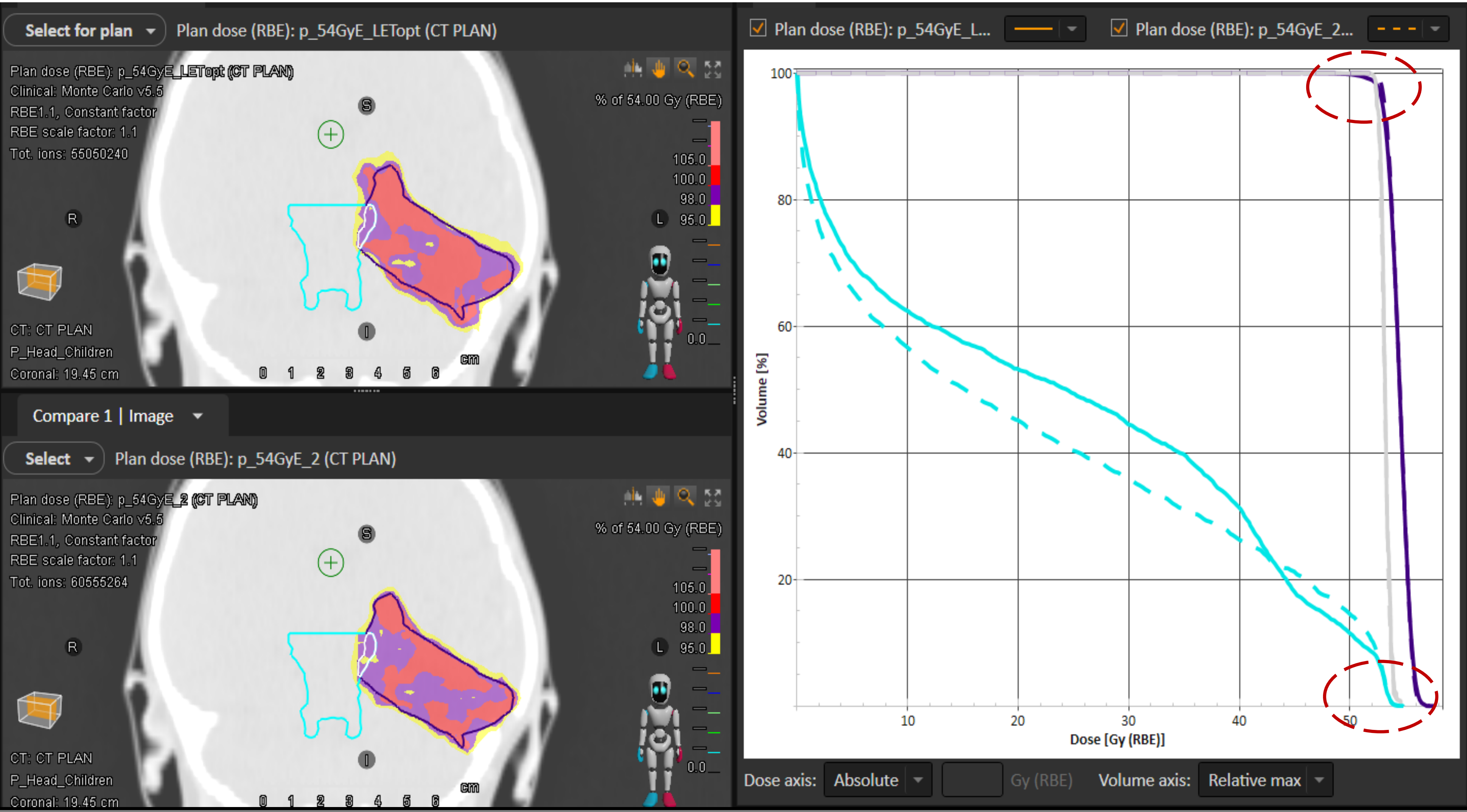
1.1
Physical dose
RBE-weighted dose
LET
Dose (Gy_{RBE})
LET (keV/μm)
Depth (cm)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
0
5
10
15
20
25
30
35
0
2
4
6
8
10
12
14

Ependymoma: 17 months old

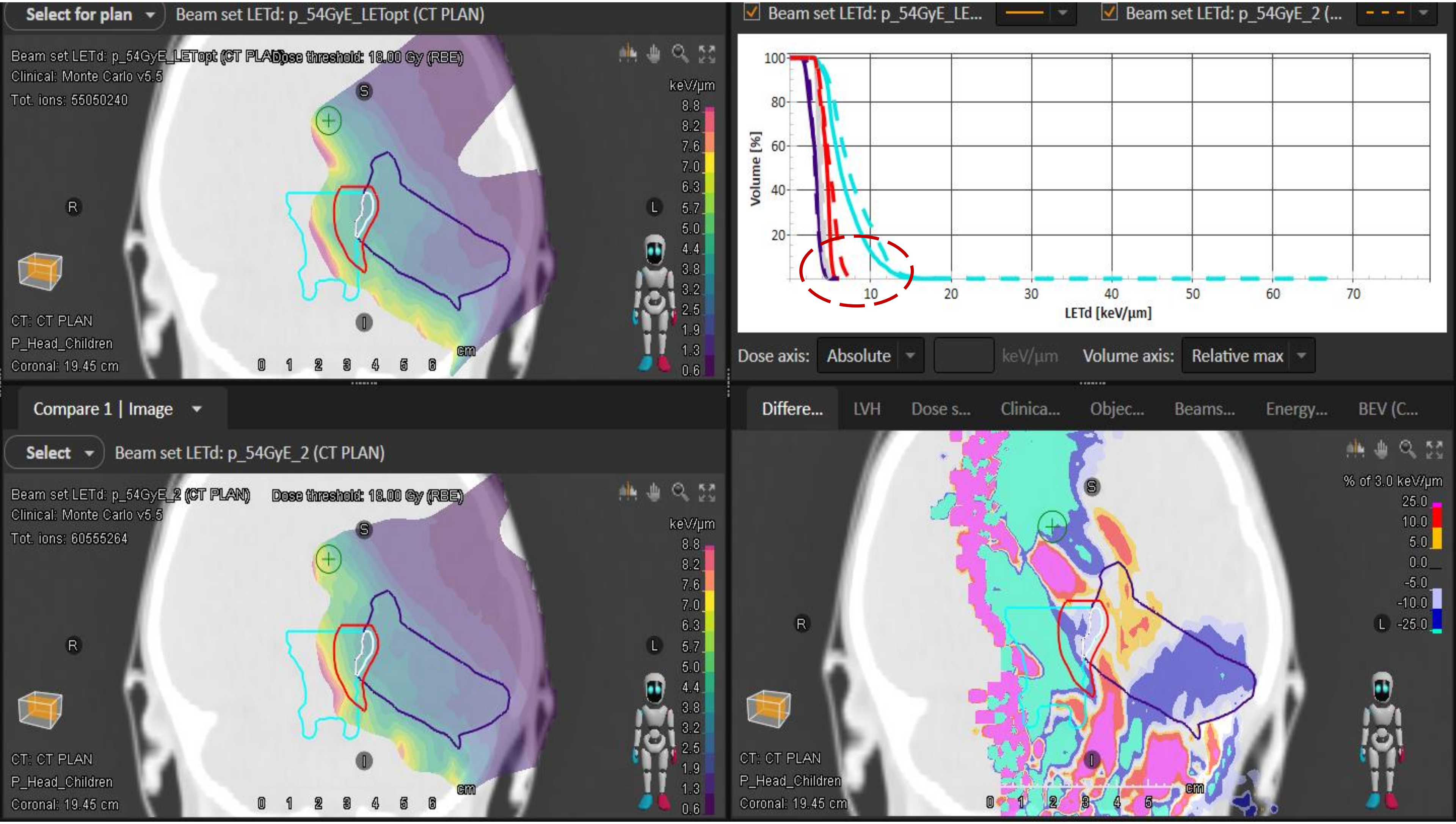


Red area: High risk area for LET in Brainstem (light blue), distally to the target (blue contour)

Both plans are clinically acceptable in terms of CTV coverage and OARs sparing but…



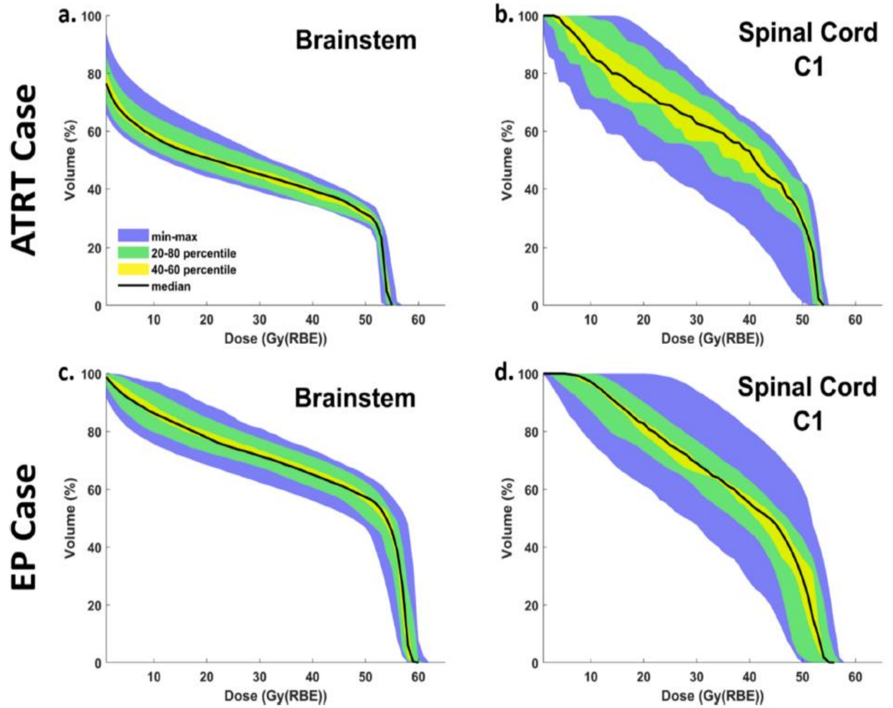
but… different LET distribution in critical OARs → potentially higher RBE



Clinical practice in European centres treating paediatric posterior fossa tumours with pencil beam scanning proton therapy

Toussaint et al. Radiotherapy and Oncology 198 (2024) 110414

	Optimization		Evaluation	
	Type	Parameters	Type	Parameters
1	Robust	3 %/3mm	Worst-case	3 %/2mm
2	Robust	3 %/3mm	Worst-case	3 %/1.5 mm
3	Robust	3.5 %/2mm	Worst-case	3.5 %/2mm
4	Robust	3.5 %/2mm	Worst-case	3.5 %/2mm
5	Robust	3 %/3mm	Voxel-wise	3 %/3mm
6	Robust	3.5 %/3mm	Worst-case	3.3 %/2.8 mm
7	Robust	3.5 %/3mm	Worst-case	3.5 %/3mm
8	Robust	3 %/3mm	Worst-case	3 %/3mm
9	Robust	3.5 %/3mm	Worst-case	3.5 %/3mm
10	Robust	3.5 %/3mm	Worst-case	3.5 %/3mm
11	PTV	3 mm	Worst-case	3 %/2mm
12	Robust	3.5 %/2mm	Worst-case	3.5 %/4mm
13	Robust	3.5 %/2mm	Worst-case	3.5 %/2mm
14	Robust	3.5 %/1–2 mm	Worst-case	3.5 %/1–2 mm
15	PTV	3 mm	None	
16	PTV	5 mm	None	



High variability in beams arrangment among 16 centers partecipating in the survey

Future perspectives

- Proton Arc Therapy?
- New ions, maybe Helium?
- Multi-Ion Radiotherapy?

"Even when laws have been written down, they ought not always to remain unaltered."