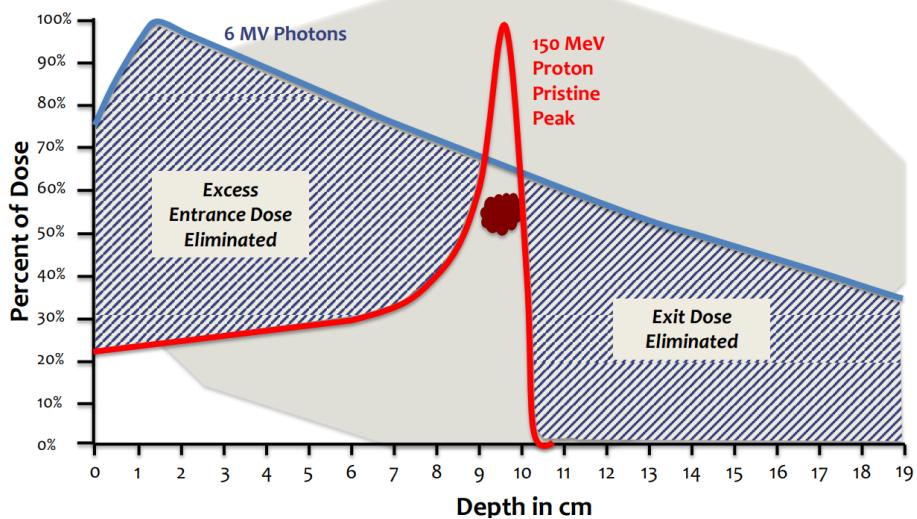
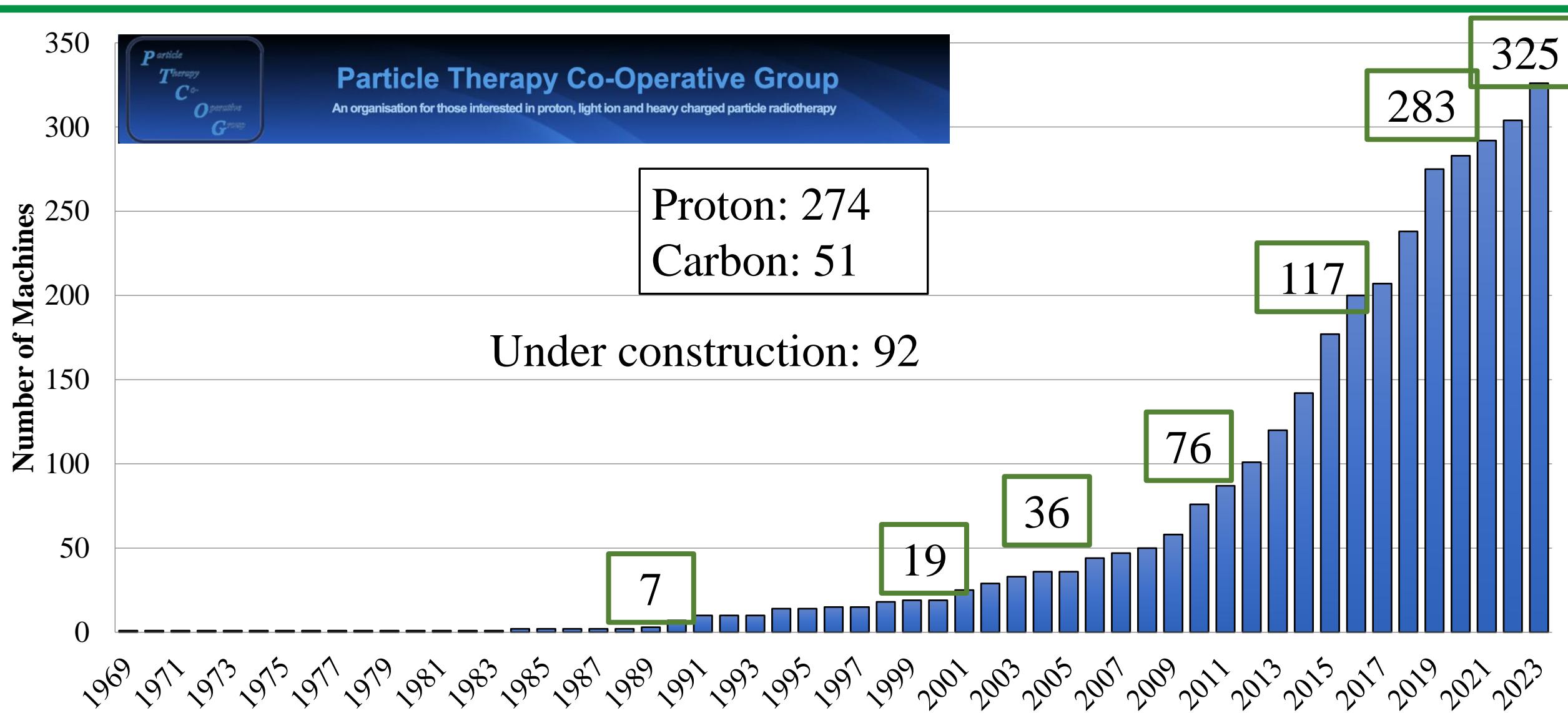


# Proton Therapy In Pediatric cancer



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# No. of Particle Machines (in operation)



# ASTRO Model Policies 2017



## PROTON BEAM THERAPY (PBT)

### Group I

#### Frequently supported the use of PBT

- Ocular tumors
- Base of skull tumors
- Primary/metastatic tumors of the spine
- Hepatocellular carcinoma
- **Childhood tumors**
- Genetic syndromes
- Malignant/benign primary CNS tumors
- Advanced unresectable H&N cancers
- Paranasal sinus tumor
- Non-metastatic retroperitoneal sarcomas
- Re-irradiation

### Group II

#### Coverage with evidence development

- Non-T4 and resectable HN cancers
- Lung cancer (M0)
- Esophageal cancer (M0)
- Mediastinal lymphomas
- Pancreatic cancer (M0)
- Biliary cancer (M0)
- Adrenal cancer (M0)
- Rectal and anal cancer (M0)
- Bladder and cervical cancers (M0)
- Prostate cancer (M0)
- Breast cancer

# ASTRO Model Policies 2023



## PROTON BEAM THERAPY (PBT)

### Group I

#### Frequently support the use of PBT

- **Benign or malignant tumors or hematologic malignancies in children aged 21 years and younger** treated with **curative intent** and **occasionally palliative intent** treatment of childhood tumors when at least one of the three criteria noted above under “indications for coverage” apply

### Group II

#### Coverage with evidence development

##### Indications for coverage

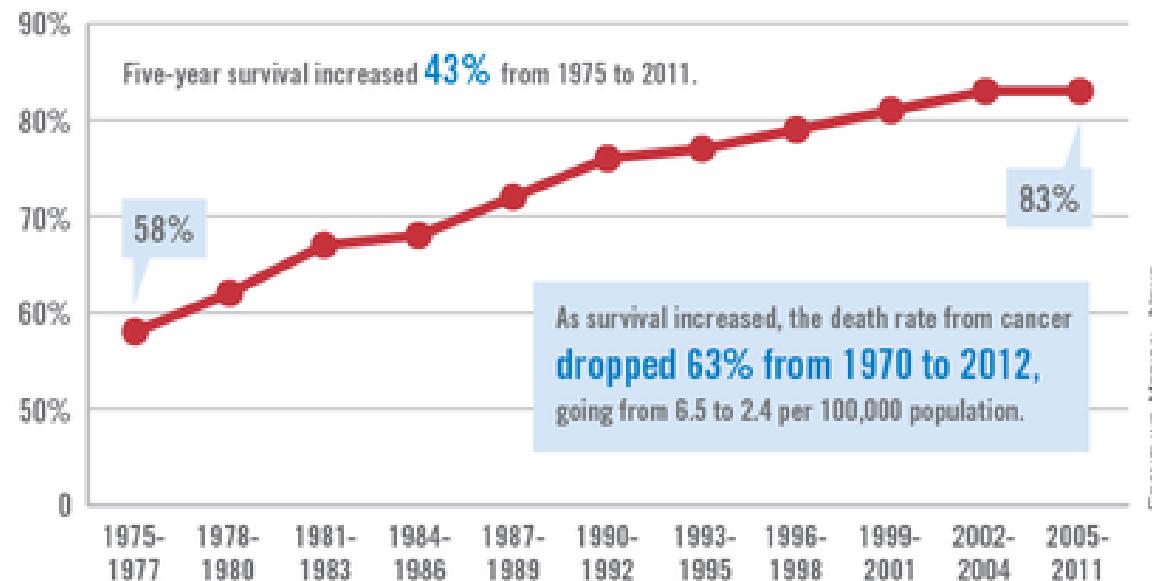
1. Target volume – near one or more critical structures and a steep dose gradient outside the target must be achieved
2. Proton technique – would decrease the probability of clinically meaningful normal tissue toxicity
3. Previously irradiated area or immediately adjacent area

# Outline

- Why proton therapy in pediatric patient?
- Treatment outcome of proton therapy in pediatric CNS tumor
- Experience of proton therapy in pediatric patient (KCMH)
- Challenging of proton therapy in pediatric cancer

# Improvement of treatment outcome of Pediatric cancer

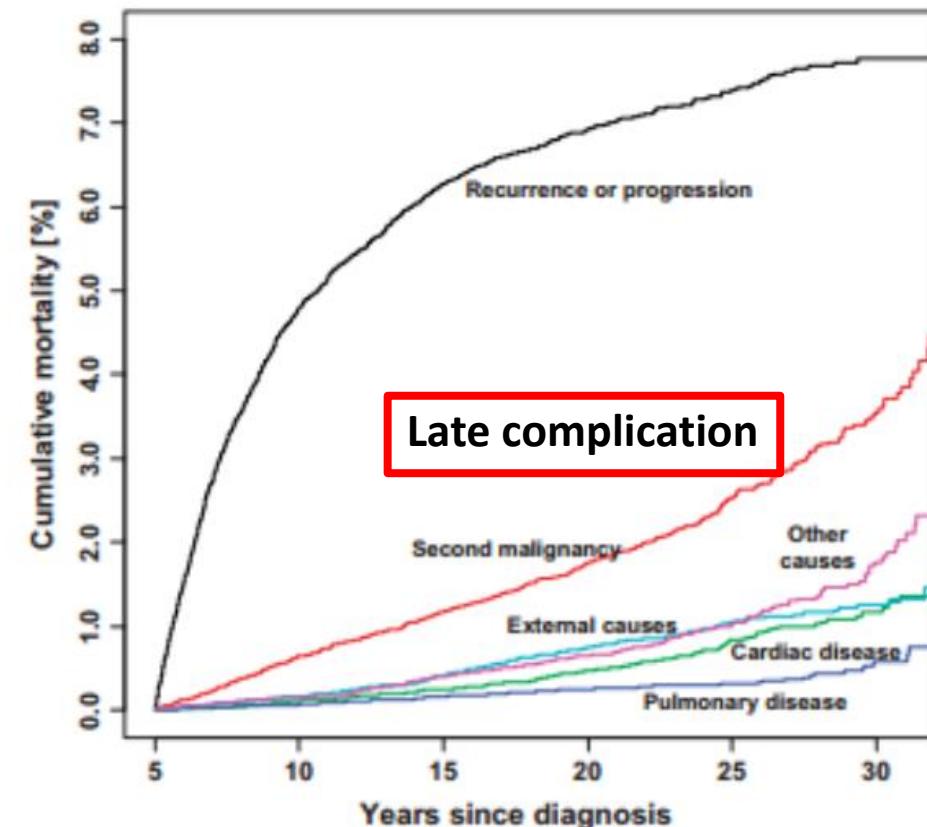
## Five-year cancer survival for children by year of diagnosis



Note: Based on data for children from birth to age 14 years from the Surveillance, Epidemiology, and End Results Program.

Source: CA Cancer J Clin. 2016 Jan;66(1):7-30

## Childhood Cancer Survivor Study



Mertens AC et al. J Natl Cancer Inst 2008

# PENTEC

## Pediatric Normal Tissue Effects in the Clinic

**Table 5 Risk of symptomatic brain necrosis: Comparing PENTEC and QUANTEC summaries**

Maximum brain dose		Risk of symptomatic necrosis
PENTEC	QUANTEC (adults)	
*	<60 Gy	<3%
~59 Gy	~72 Gy	5%
~72 Gy	*	8%
*	90 Gy	10%

Abbreviations: PENTEC = Pediatric Normal Tissue Effects in the Clinic; QUANTEC = Quantitative Analysis of Normal Tissue Effects in the Clinic.

\* Doses associated with this specific risk level were not reported.

### 5% risk of developing IQ < 85 (PENTEC)

Irradiated brain (%)	Dose (Gy)
10	35.7
20	29.1
50	22.2
100	18.1

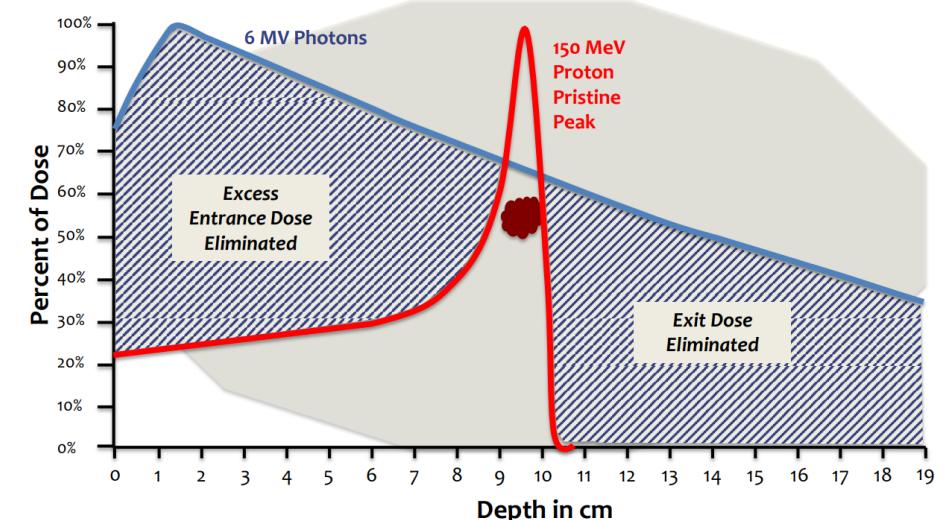
2 Gy/fx, and without use of MTX

**Pediatric – more radiosensitive**

Mahajan A, et al. *Int J Radiat Oncol Biol Phys* 2020  
Milano MT, et al. *Int J Radiat Oncol Biol Phys* 2023

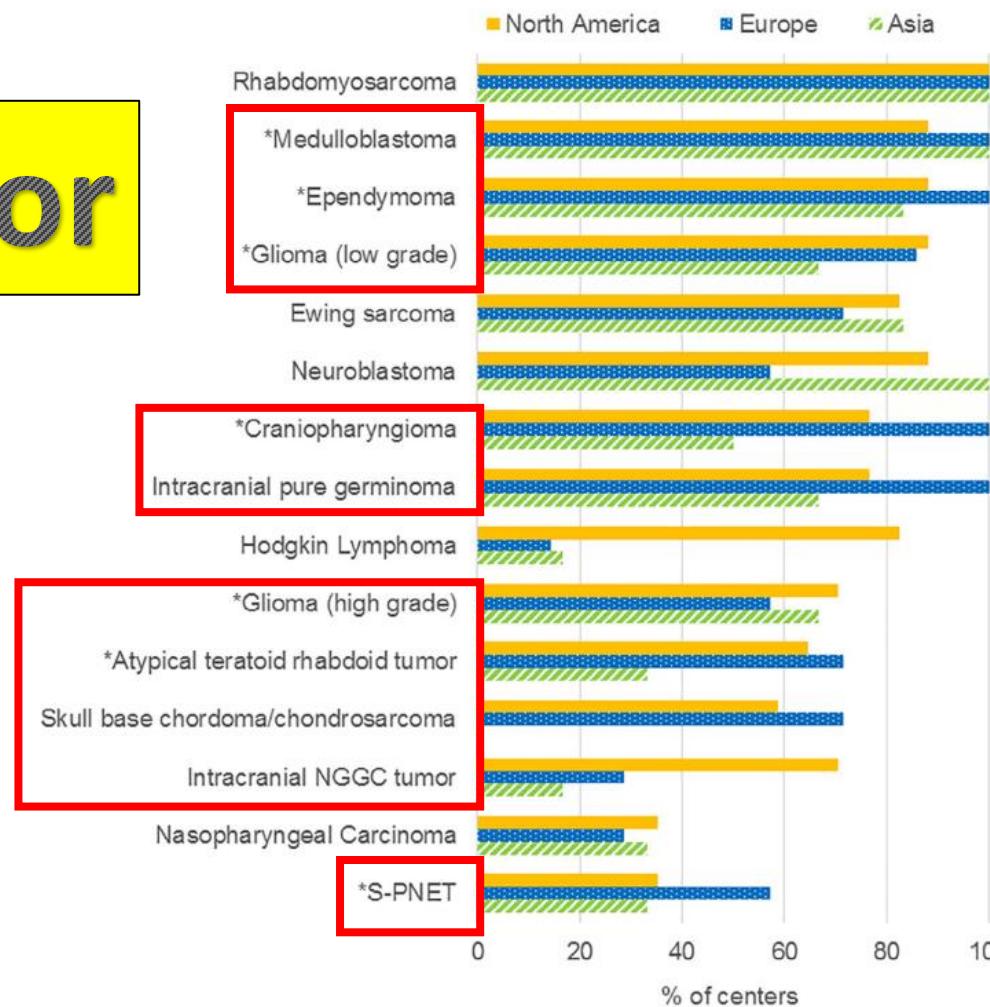
# Strategies to avoid/minimize long-term treatment side effect

- Avoidance of radiotherapy
- Delay of radiotherapy for young children
- Reduction of target volume and radiation dose
- Development of systemic chemotherapy
- Use of smaller fraction size
- Reduction of safety margin
- **Advanced RT techniques**
  - IMRT / VMAT
  - **Particle therapy**



# Pattern of Proton therapy in pediatric cancer

CNS Tumor

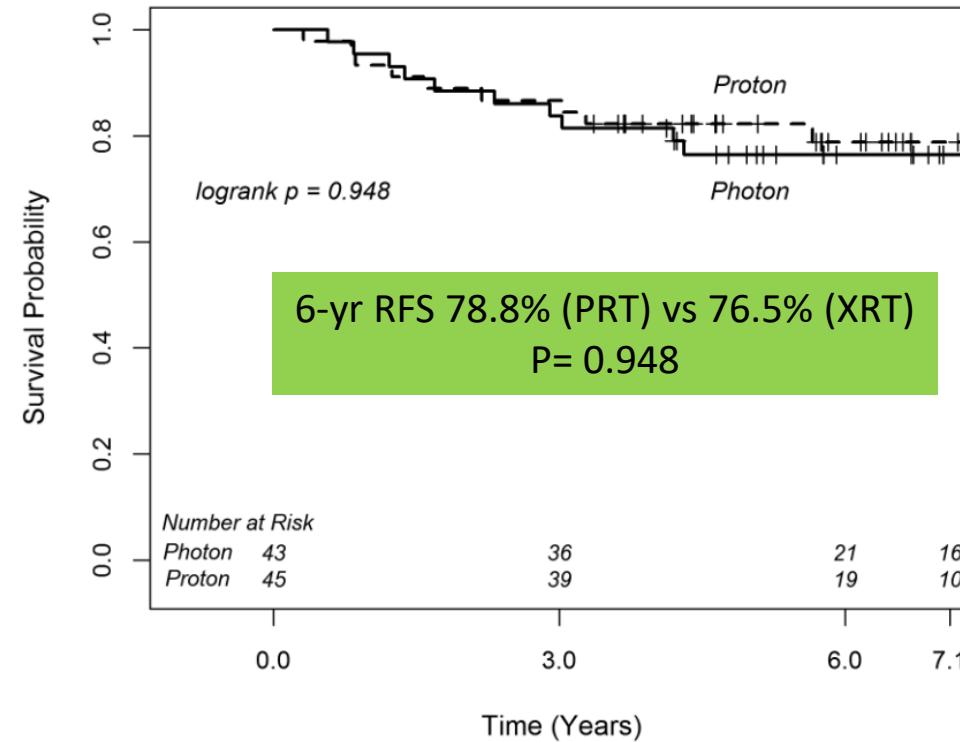
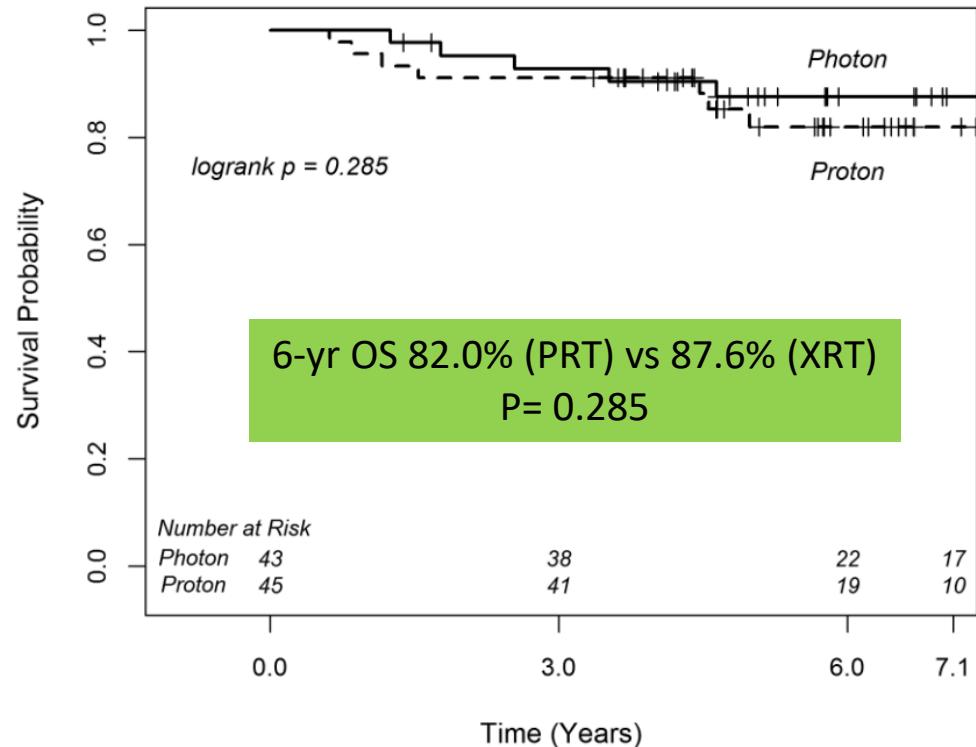


# Outline

- Why proton therapy in pediatric patient?
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- Challenging of proton therapy in pediatric cancer

# Clinical outcome PRT vs XRT in Medulloblastoma

Proton (N=45) vs Photon (N=43)



RT 2000 – 2009

Median f/u – 6.2 yr (PRT), 7.0 yr (XRT)

Eaton BR, et al. Int J Radiat Oncol Biol Phys 2016



# Side effect of Craniospinal Irradiation

- **Acute complication**
  - Hematologic toxicities
  - Nausea/vomiting
  - Esophagitis
- **Late complication**
  - Neurocognitive
  - Endocrine abnormality
  - Ototoxicity
  - Secondary malignancy

Toxicities (%)	P-CSI (n=60)	X-CSI (n=37)	P-value
<b>Leukopenia</b>			0.044
0	3.3	0	
1	16.7	8.1	
2	43.3	37.8	
3	36.7	51.4	
4	0	2.7	
<b>Neutropenia</b>			0.762
0	18.6	17.1	
1	6.8	22.9	
2	49.2	28.6	
3	22	28.6	
4	3.4	2.9	
<b>Lymphopenia</b>			<0.0001
0	0	0	
1	0	0	
2	23.7	0	
3	59.3	32.4	
4	16.9	67.6	

**Proton-CSI – Significant lower hematologic toxicity**

# QOL studies of pediatric cancer treated with PRT

Reference	No.	Tumor status	Dose, Gy RBE	QOL/PRO parameters	End points	Conclusions	Criticisms and confounders
Kuhlthau et al., 2012 (41)	142	Primary brain tumors, most commonly PNET (35%), ependymoma (22%), LGG (14%); CSI in 43% PBT only (7%), PBT/surgery (31%), PBT/ chemo (9%), tri-modality (53%)	≥45 (96%)	PedQoL: core (functioning), brain tumor (sensorimotor, neurocognitive), cancer modules (psychosocial) Also utilized Wechsler IQ scale, BASC and SIB-R (behavioral), and cross-comparison with scores provided by both parents and children Measured during the first and last weeks of PBT and annually thereafter	QOL rose from start to end of PBT in both CSI and non-CSI, but comparatively less rise from end of PBT to 3 y post-PBT During treatment, lowest scores for school and emotional functioning, anxiety/worry, communication, physical health Worse QOL scores at start statistically correlated with baseline IQ and behavioral	QOL increases during PBT Noteworthy clinical factors associated with poorer QOL scores	Heterogeneous population with unclear dosing and likely equally heterogeneous treatment volumes Did not assess baseline home/socioeconomic situation Analyzed PBT dose as a binary (noncontinuous) variable with imbalanced cutoff No association with receipt of anesthesia or lack thereof
Weber et al., 2015 (42)	15	Primary ATRT, resection in 93%, concurrent chemo in 47%	54	PedQoL: physical, emotional, social, school, psychosocial, composite Measured before PBT and compared with measurement at 2 mo	Numerically higher physical, emotional, school scores Numerically lower social score	QOL does not deteriorate at median 33 mo after PBT	Mean (no median) values of QOL scores reported, without statistical comparisons Did not assess baseline home/socioeconomic situation Isolated comparison at just 2 mo post-PBT difficult to interpret regarding long-term QOL
Leiser et al., 2016 (43)	93	Rhabdomyosarcoma, concurrent chemo in 89%, anesthesia in 66%	54	PedQoL measured at baseline and 2 mo post-PBT, and annually thereafter; matched with proxy normal population Questionnaire given to 34 patients	Lower QOL at beginning of PBT vs normal population QOL improves (all domains) at 2 mo post-PBT and continues to 2 y; most notable improvement in first year post-PBT At 2 y, most QOL parameters comparable (or higher) with normal population	QOL increases after PBT	Details regarding surgery missing Excluded patients age < 5 y from QOL analyses Did not assess baseline home/socioeconomic situation Unclear matching of comparison with proxy normal population

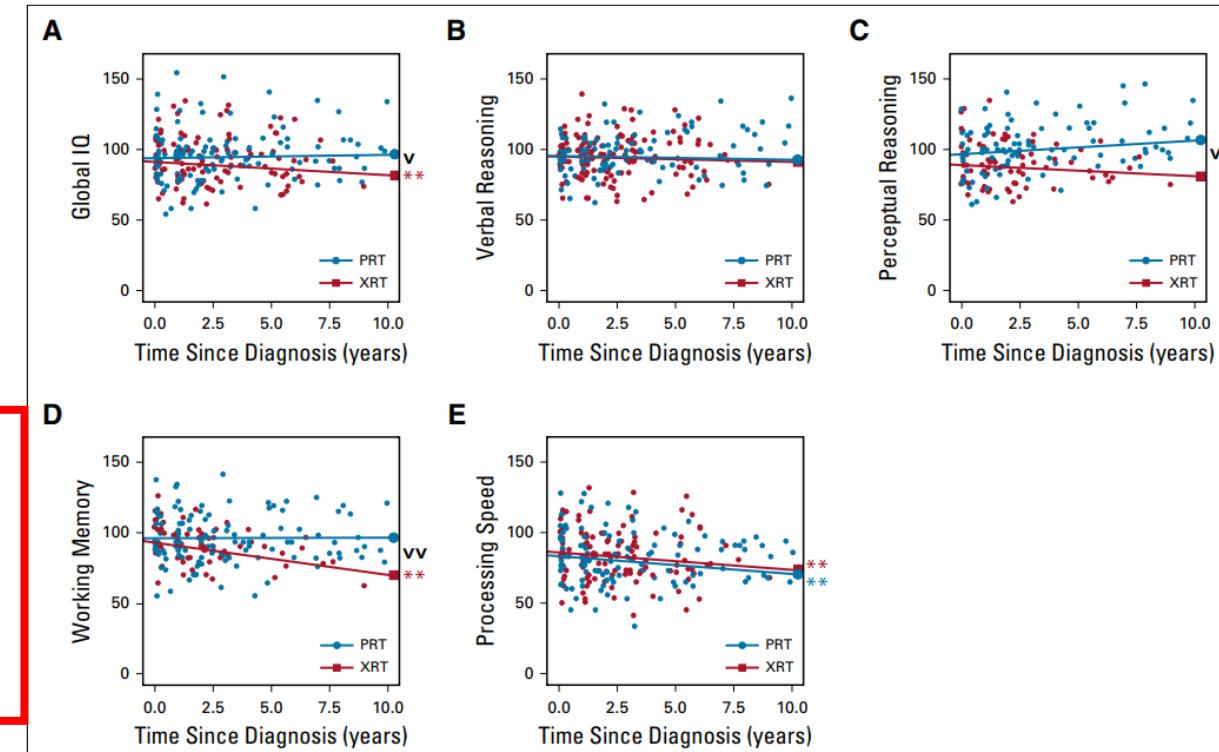
QOL increases during and after PBT

# Endocrine outcome PRT vs XRT in MB

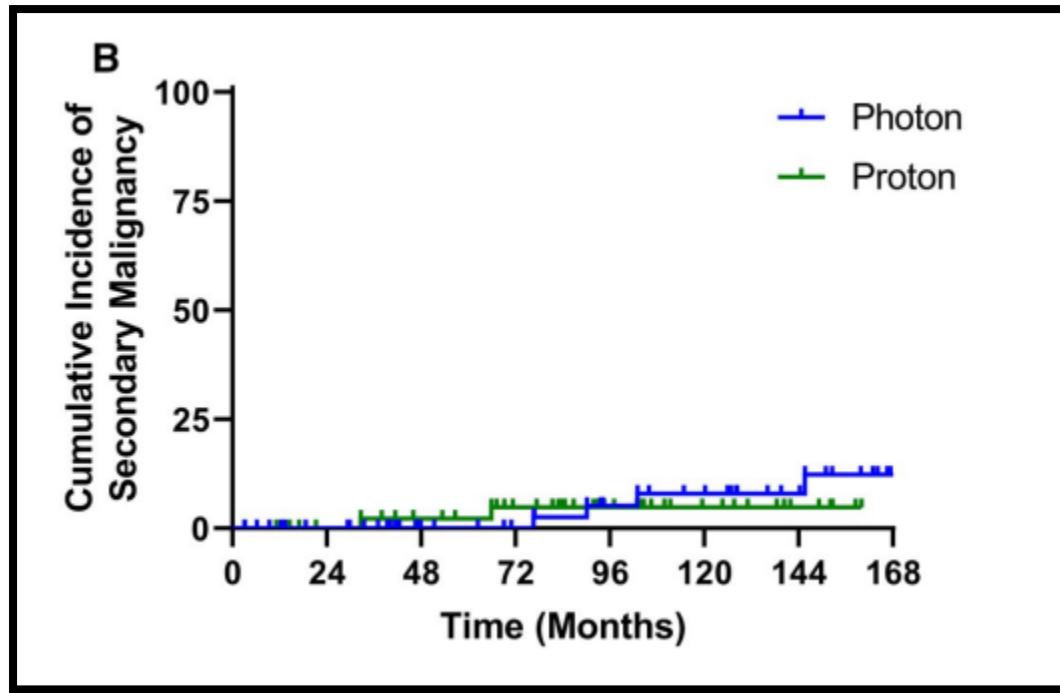
	PRT (N=40)	XRT (N=37)	P value
Median age	6.2 yr	8.3 yr	0.01
Median f/u	5.8 yr	7.0 yr	0.01
<b>Hypothyroidism</b>	<b>23%</b>	<b>69%</b>	<b>&lt; 0.001</b>
<b>Sex hormone deficiency</b>	<b>3%</b>	<b>19%</b>	<b>0.025</b>
<b>Endocrine Replacement Rx</b>	<b>55%</b>	<b>78%</b>	<b>0.03</b>
GH deficiency	53%	57%	0.708
Adrenal insufficiency	5%	8%	0.667
Precocious puberty	18%	16%	0.881

# Superior Intellectual Outcomes after PRT vs XRT in MB

- 79 patients, between 2007 - 2018
  - 37 PRT (MDACC)
  - 42 XRT (Sick Kids, Canada)
- Tumor bed boost margin
  - XRT – 1 cm margin
  - PRT – 1 cm margin (62%) and 0.5 cm margin (38%)
- Proton RT – superior long-term outcomes in
  - Global IQ
  - Perceptual reasoning
  - Working memory
- Comparable rate of relapse



# Risk of secondary malignant neoplasm In pediatric medulloblastoma



SMN	X-ray (N= 63) 1996-2005	Proton (N=52) 2006-2014
f/u time (yr)	12.8	8.7
At 10 yr	8% (4 pt)	4.9% (2 pt)

Passive scatter

# Outline

- Why proton therapy in pediatric patient?
- Treatment outcome of proton therapy in pediatric CNS tumor
- Experience of proton therapy in pediatric patient (KCMH)
- Challenging of proton therapy in pediatric cancer



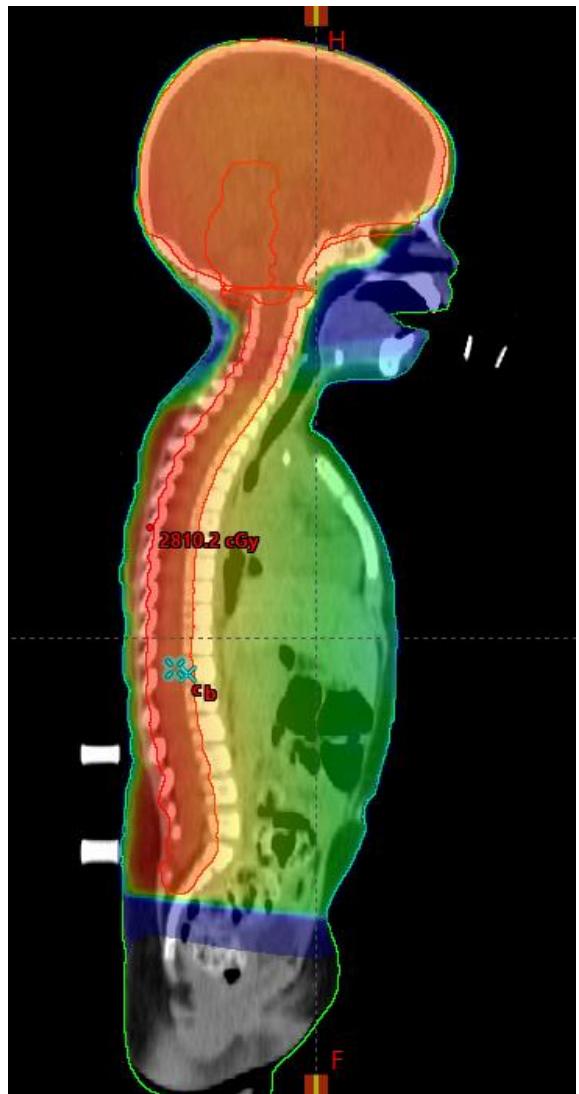
August 1, 2021

# Number of pediatric cancer cases treated with radiotherapy at KCMH

	2021	2022	2023
<b>Treated with RT/year</b>	66	65	76
- XRT	62	57	61
- PRT	4	8	15
<b>Type of tumor treated</b>			
<b>With proton</b>			
- Medulloblastoma	1	2	4
- Germ cell tumors	1	1	3
- Neuroblastoma	1	1	2
- Ependymoma	1	1	1
- Rhabdomyosarcoma		2	1
- Meningioma		1	1
- ATRT			2
- Esthesioneuroblastoma			1

CSI 13 cases

# Dosimetric comparison: Craniospinal Irradiation



3D

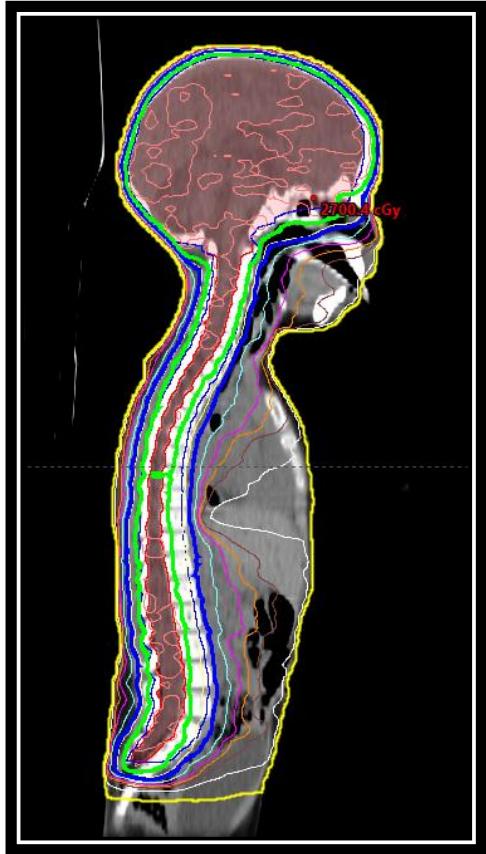


VMAT

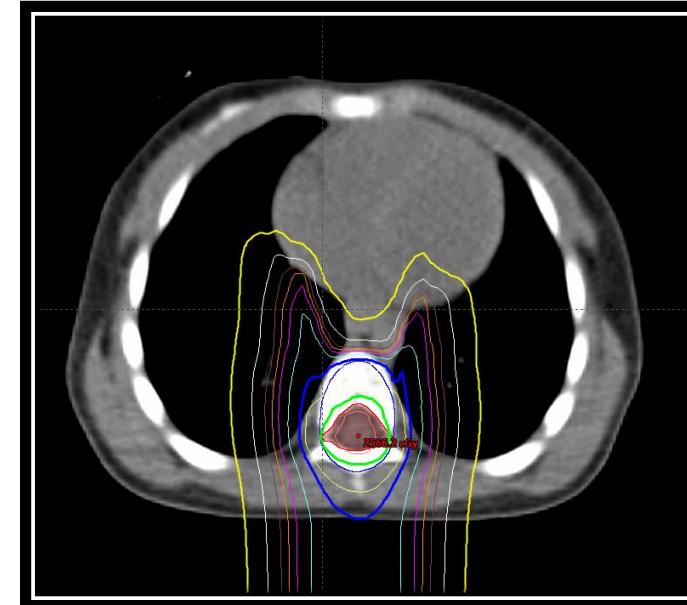
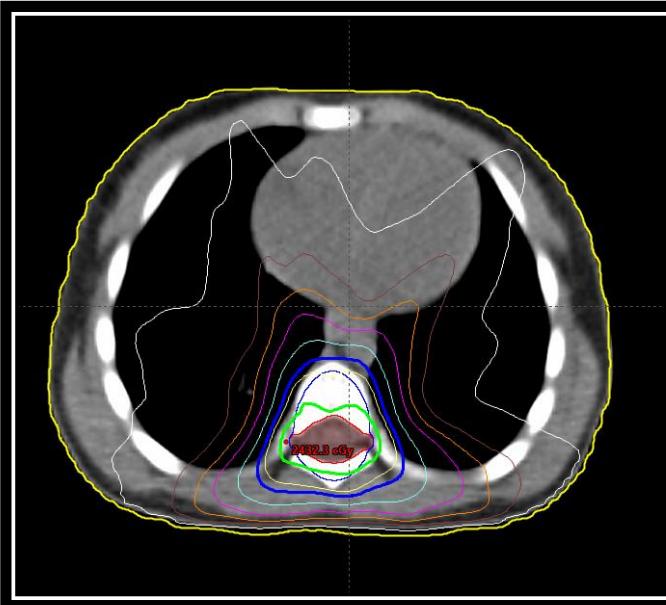


Proton

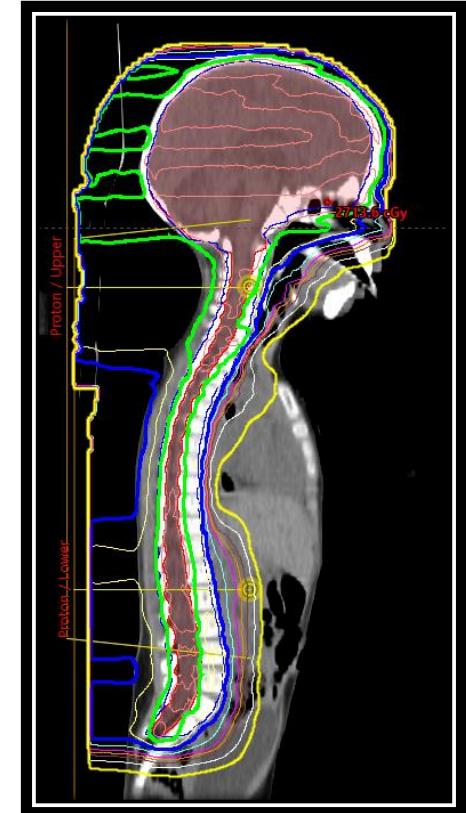
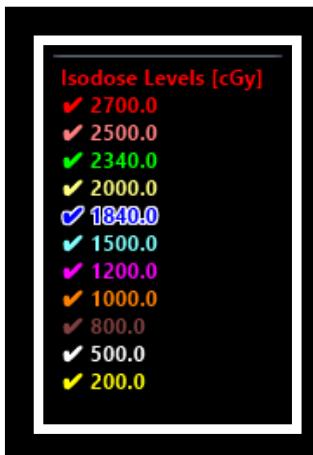
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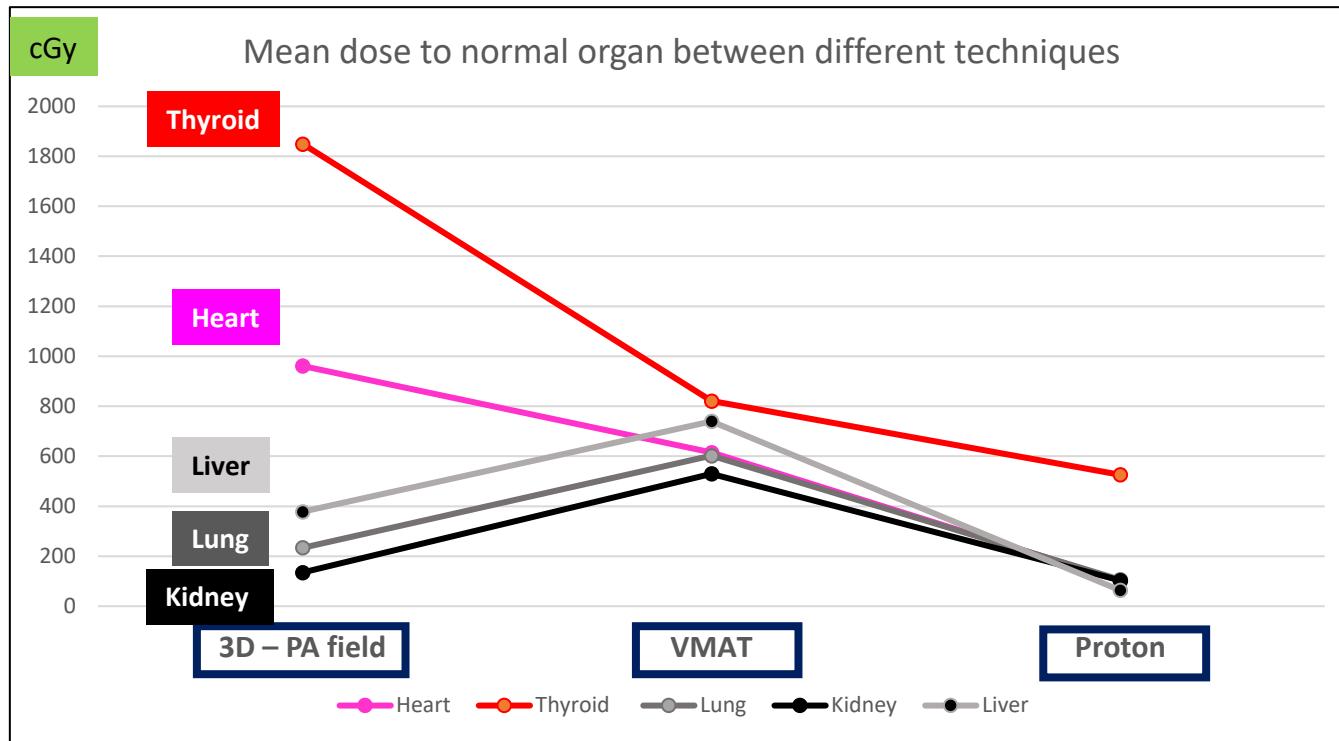
VMAT 23.4/18.4



Proton 23.4/18.4



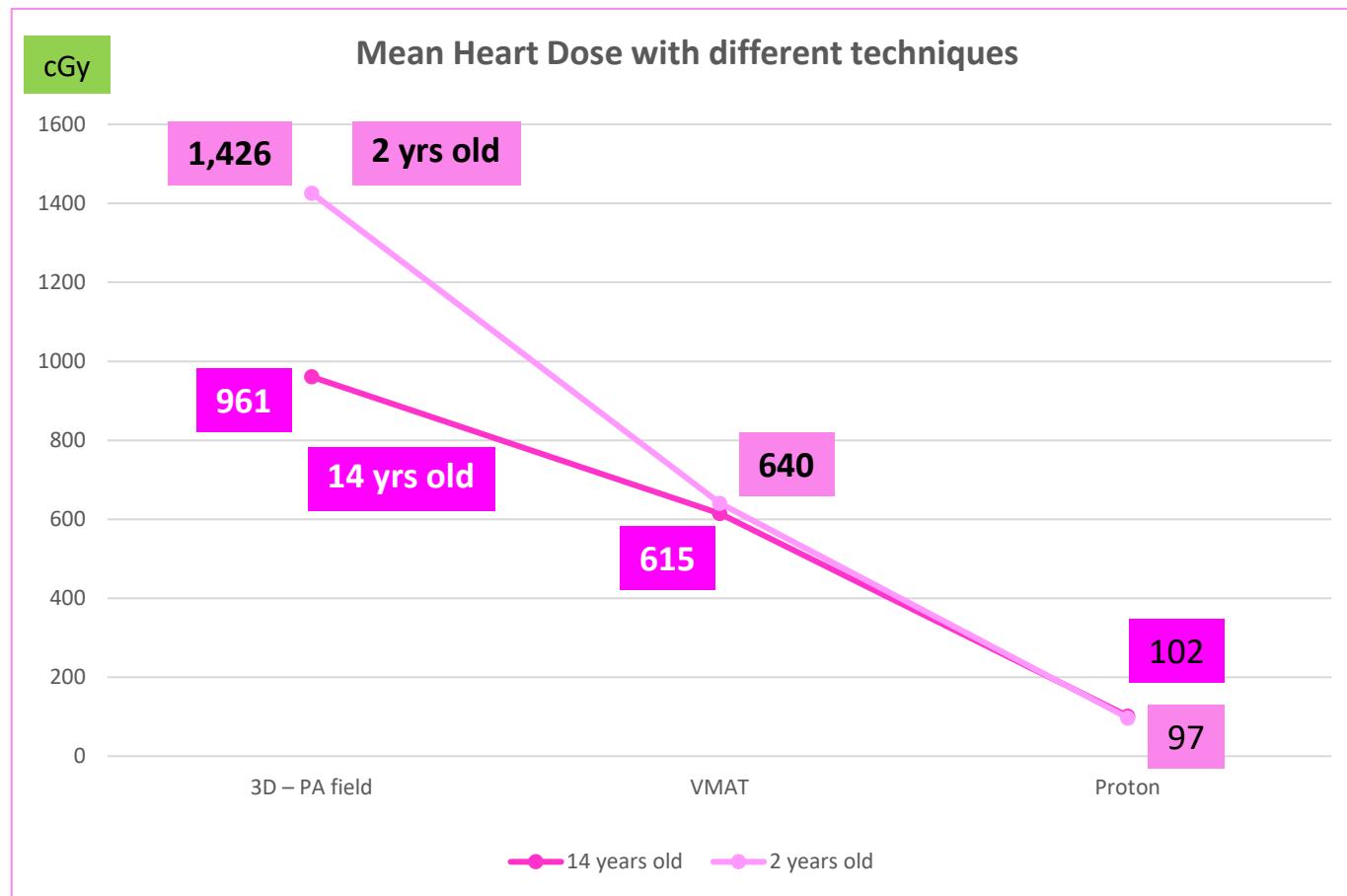
# Less radiation exposure with proton



14-year-old male, CSI dose : 2,340 cGy

Organ	3D – PA field (cGy)	VMAT (cGy)	Proton (cGy)
Thyroid	1,849	821	526
Heart	961	615	102
Liver	378	740	64
Lung	234	602	106
Kidney	135	530	103

# More benefit in younger patient





## RELATIVE RISK OF CARDIAC MORTALITY AND DOSIMETRIC COMPARISON AMONG THREE-DIMENSIONAL RADIOTHERAPY, VOLUME MODULATED ARC THERAPY AND PROTON BEAM IN VERTEBRAL BODY-REDUCED-DOSE CRANIOSPINAL IRRADIATION

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### Background and Aims

We aimed to compare dose to organs at risk (OARs), and the relative risk (RR) of cardiac mortality among three-dimensional conformal radiotherapy (3D-CRT), volume modulated arc therapy (VMAT) and pencil beam scanning proton therapy (PT) in craniospinal irradiation (CSI).

### Methods

CSI plans of 3D-CRT, VMAT and PT were generated. To reduce dose to OARs and avoid spinal abnormality, vertebral body-reduced-dose (VBRD) CSI according to SIOP recommendation was used for VMAT and PT. We delineated 2 sets of target volumes, i.e., clinical target volume1 and planning target volume1 (CTV1, PTV1) for brain and thecal sac and CTV2, PTV2 for vertebral body. Two sets of CSI dose, i.e., 23.4 and 36 Gy were prescribed to each technique. For VMAT and PT, 23.4/18.4 Gy and 36/20 Gy for PTV1/PTV2 (CTV1/CTV2 for PT) were optimized in 13 and 20 fractions, respectively. For 3D-CRT, we prescribed 23.4 and 36 Gy, to cover only PTV1. To evaluate the relative risk (RR) of cardiac mortality compared with normal population, we incorporated the mean heart dose (MHD) with the linear model.

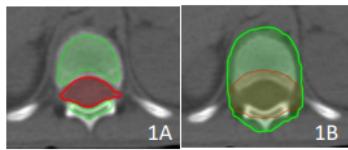


Figure 1A: CTV1 (red)  
Figure 1B: CTV2 (green)

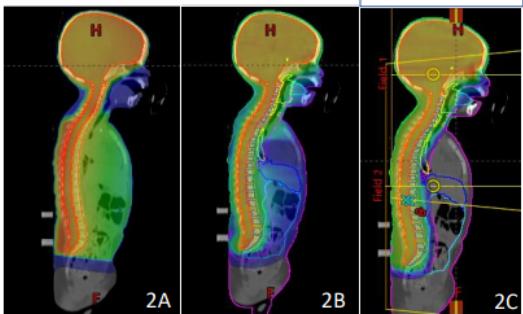


Figure 2: Dose color wash of 3D-CRT (2A), VMAT (2B), PT (2C)

### Results

In total of 8 patients, 48 treatment plans, i.e., 8 plans for each technique of each dose set, were generated. PT showed the lowest mean dose to all OARs, i.e., heart, lungs, liver, kidneys, esophagus, oral cavity, stomach, thyroids, and vertebral body. MHD of 3D-CRT, VMAT and PT were 12.15, 3.99 and 0.9 Gy for 23.4 Gy-prescription, and 18.6, 5.7, and 1.2 Gy for 36 Gy-prescription, respectively. PT showed significantly less RR of cardiac mortality compared with 3D-CRT and VMAT, 1.54, 8.92 and 3.40 for 23.4 Gy-prescription ( $p<0.001$ ) and 1.74, 12.19, 4.40 for 36 Gy-prescription ( $p<0.001$ ), respectively.

### Tables

Table 1: Dose to organs at risk (23.4 Gy-prescription)

Mean dose	3D-CRT (Gy)	VMAT (Gy)	PT (Gy)	p-value
Heart	12.15	3.99	0.9	<0.001
Lung	3.64	6.59	1.95	<0.001
Esophagus	21.59	14.57	11.66	<0.001
Oral cavity	3.39	7.65	2.16	0.002
Thyroid	17.19	14.06	7.82	<0.001
Stomach	4.26	6.17	0.28	<0.001
Vertebral body	24.44	22.59	21.11	<0.001
Kidneys	2.83	5.8	2.18	<0.001
Liver	5.23	5.96	0.44	<0.001

Table 2 Dose to organs at risk (36 Gy-prescription)

Mean dose	3D-CRT (Gy)	VMAT (Gy)	PT (Gy)	p-value
Heart	18.6	5.7	1.2	<0.001
Lung	5.6	9.06	2.6	<0.001
Esophagus	33.12	17.22	14.28	<0.001
Oral cavity	4.76	10.63	2.64	0.002
Thyroid	25.28	18.08	10.41	<0.001
Stomach	6.54	8.13	0.29	<0.001
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Liver	7.07	8.19	0.52	<0.001

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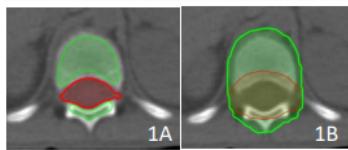
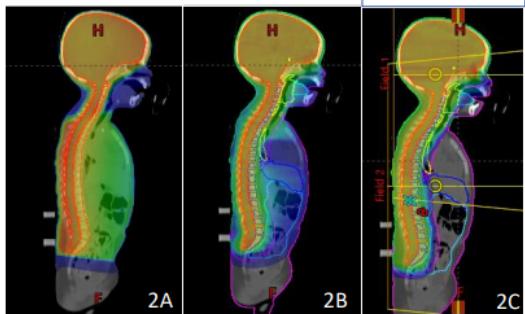


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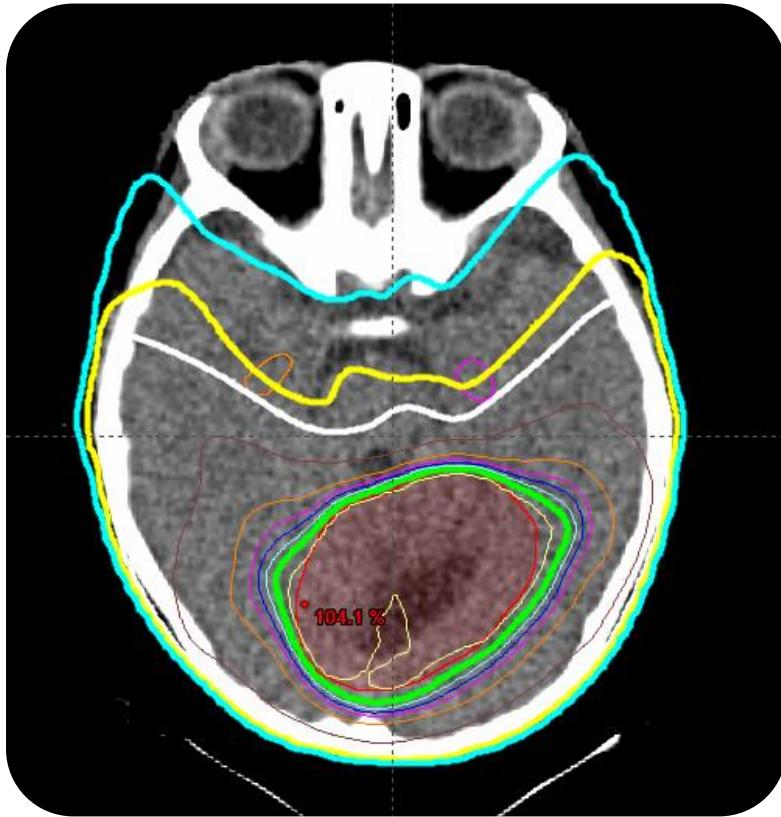
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# RR of cardiac mortality

	3D-CRT	VMAT	Proton
<b>CSI 23.4 Gy</b>	<b>8.92</b>	<b>3.4</b>	<b>1.52</b>
<b>CSI 36 Gy</b>	<b>12.19</b>	<b>4.4</b>	<b>1.74</b>

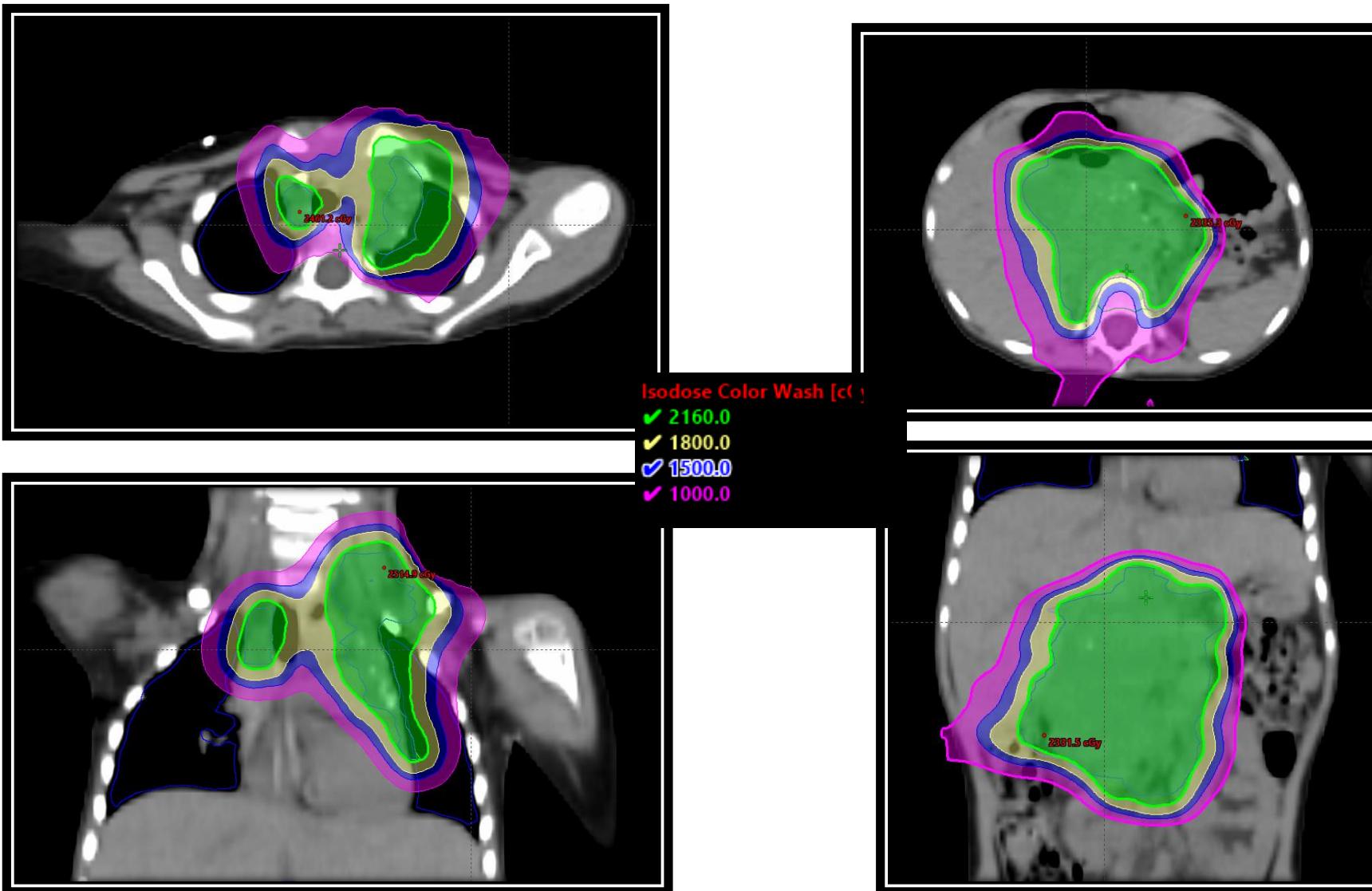


**VMAT boost**

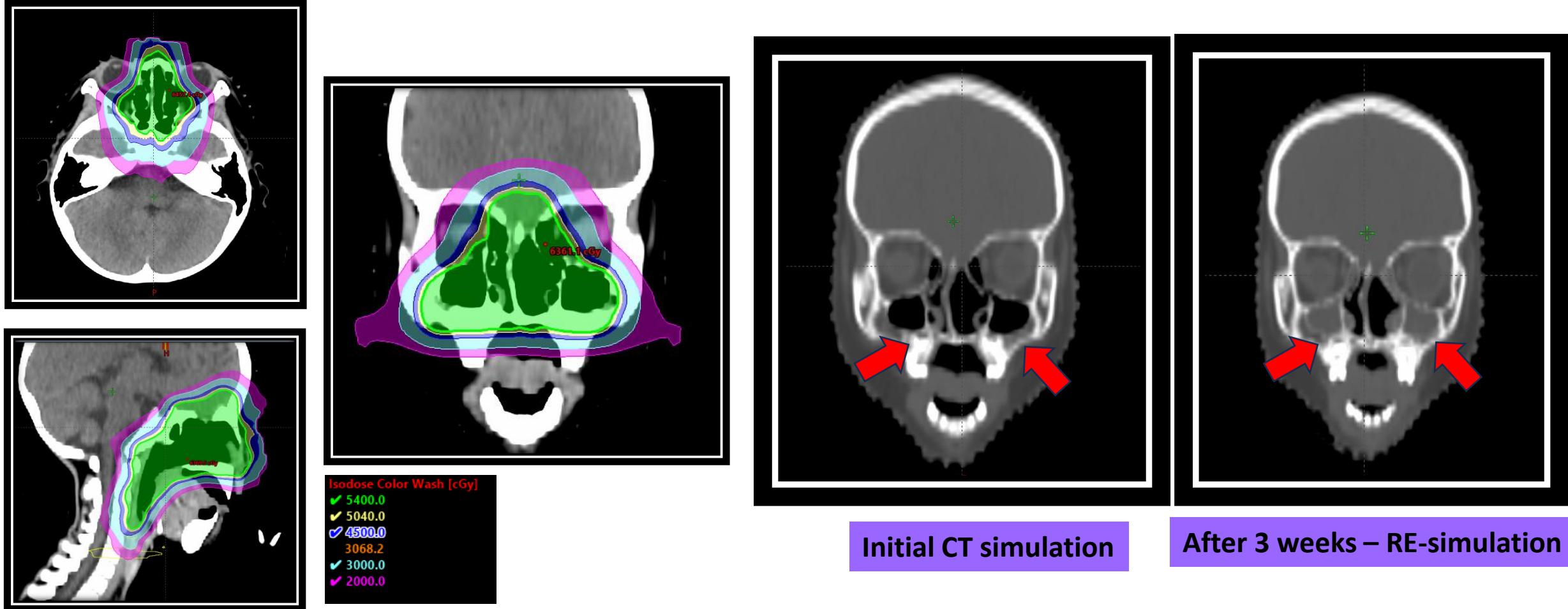


**Proton boost**

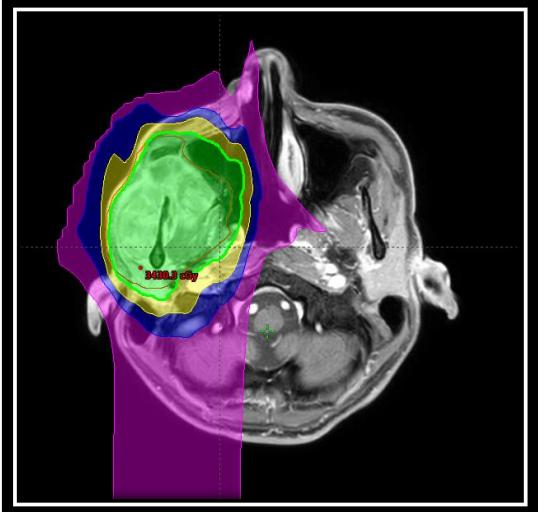
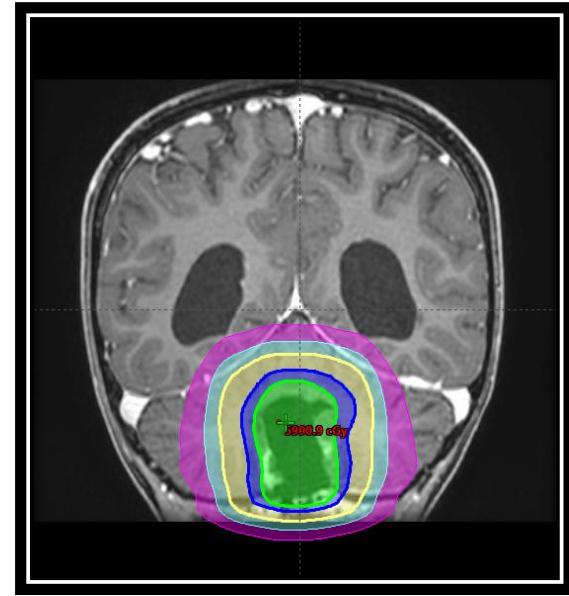
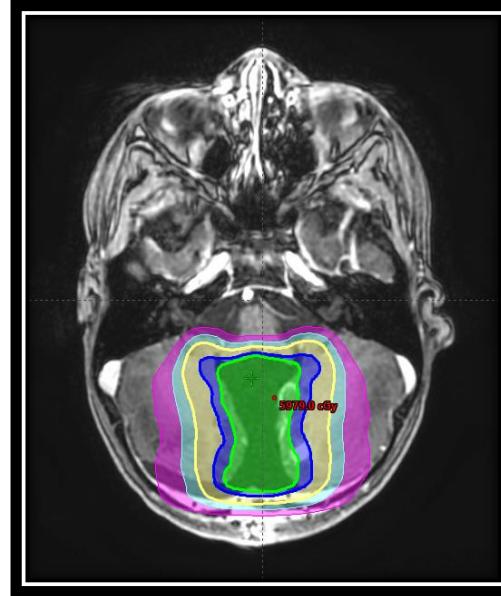
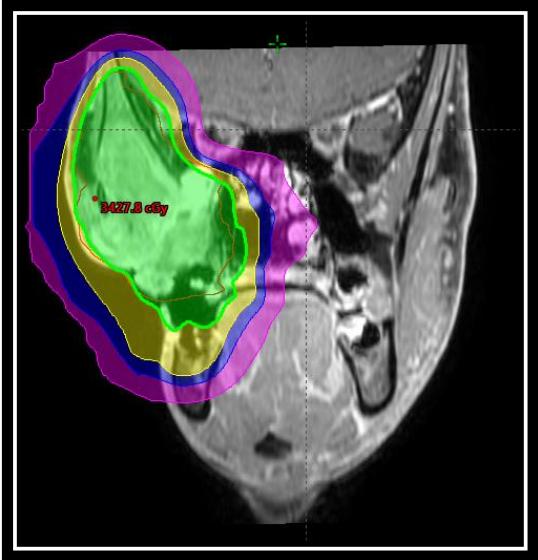
# Neuroblastoma



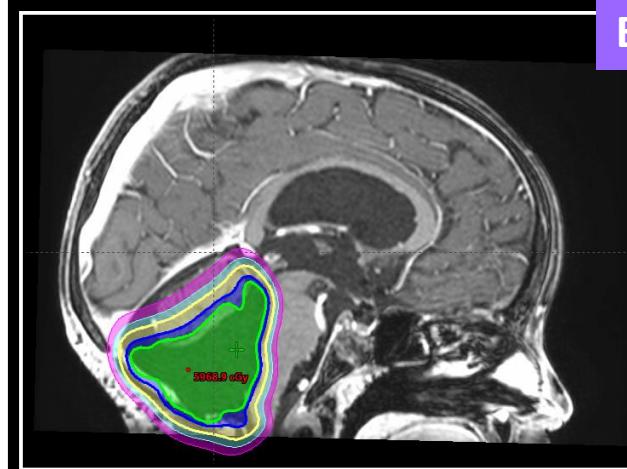
# Esthesioneuroblastoma



# Re-irradiation



Leiomyosarcoma

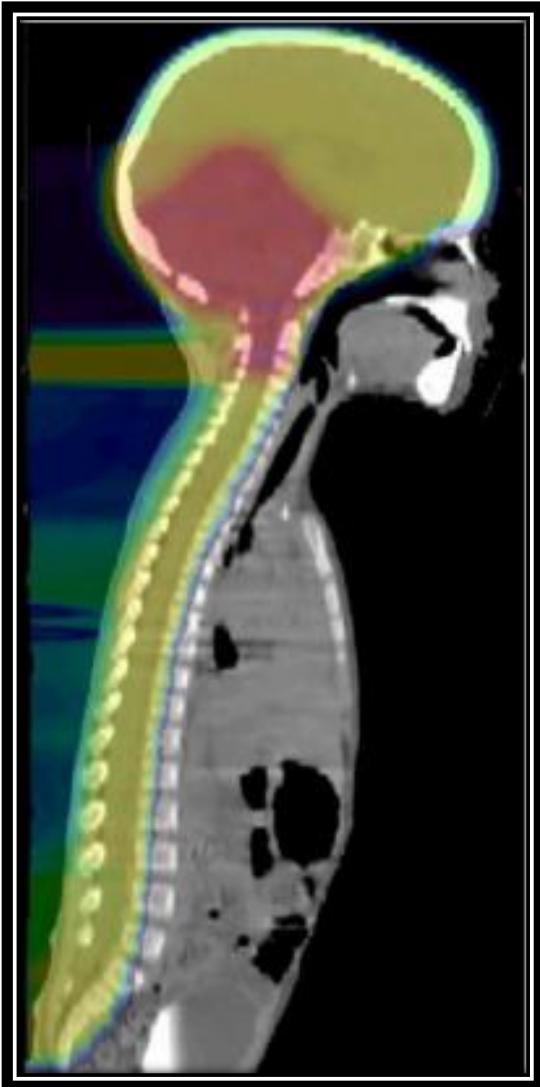


Ependymoma

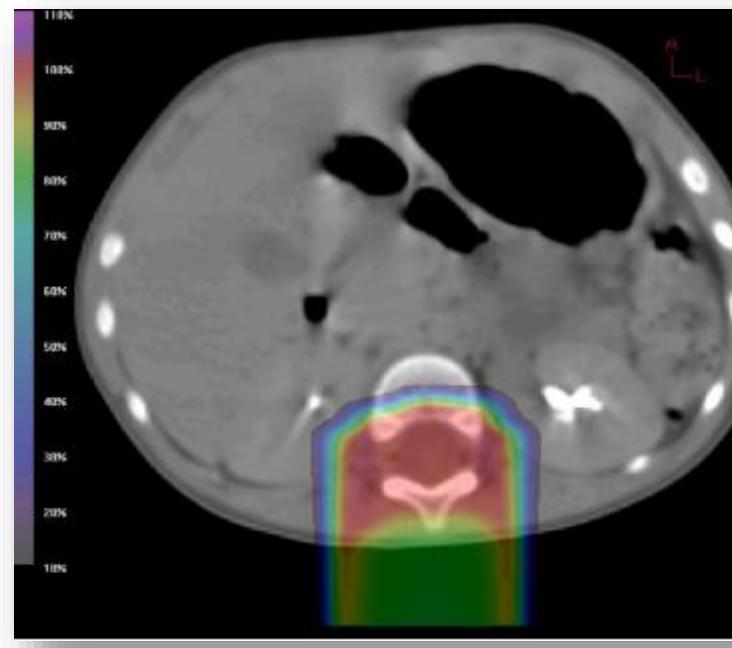
# Outline

- Why proton therapy in pediatric patient?
- Treatment outcome of proton therapy in pediatric CNS tumor
- Experience of proton therapy in pediatric patient (KCMH)
- Challenging of proton therapy in pediatric cancer

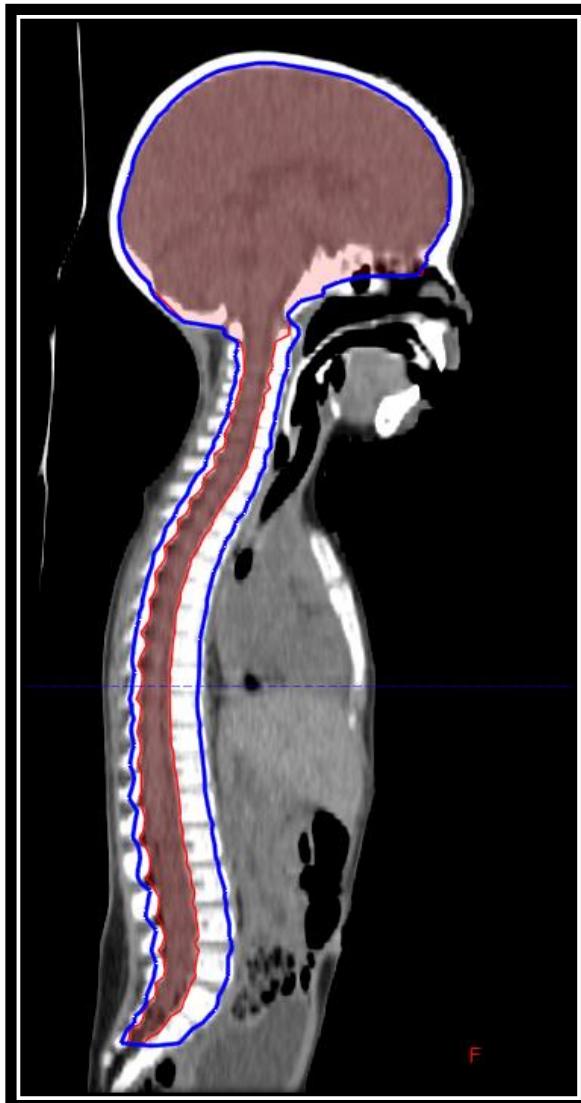
# Vertebral body dose in Craniospinal Irradiation



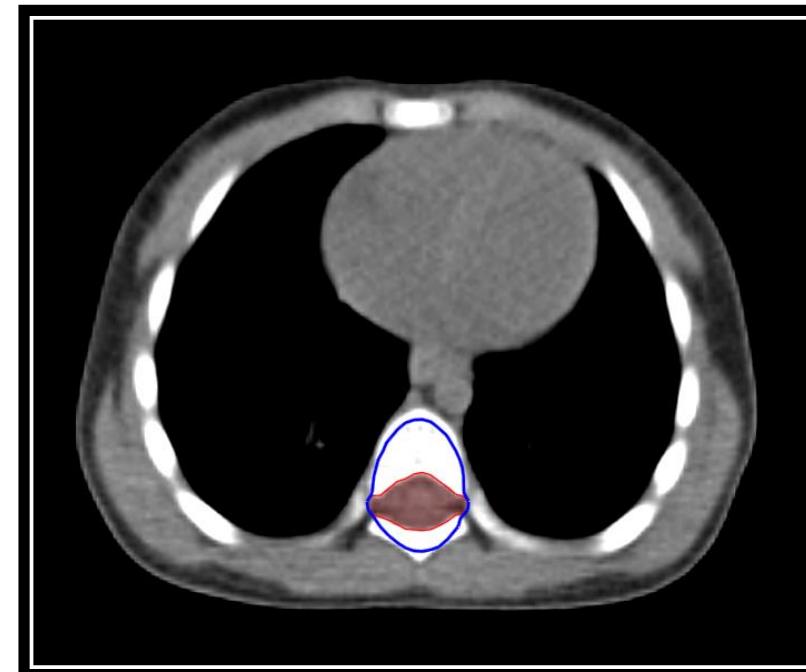
Vertebral body sparing



# Craniospinal Irradiation: Reduced-dose vertebral body



**CSI/vertebral body dose**  
- 23.4/18 Gy  
- 36/20 Gy



# Challenging of proton therapy in pediatric patient

- Vertebral body dose in CSI
- Brain stem necrosis

# Brainstem injury in Posterior fossa Pediatric Brain tumor

- Brain stem injury rate
  - Photon : 0-6.7%
  - Proton : 2-16%
- Is there a different tolerance of the brainstem between XRT and PRT?
  - Variation of RBE at the Bragg peak
- COG ACNS 0831 protocol, Brainstem dose criteria

	XRT	PRT
D50%	$\leq 6,100/6,200$ cGy	$\leq 5,240/5,400$ cGy
D10%	$\leq 6,300/6,400$ cGy	$\leq 5,660/5,800$ cGy

Goal/Maximum

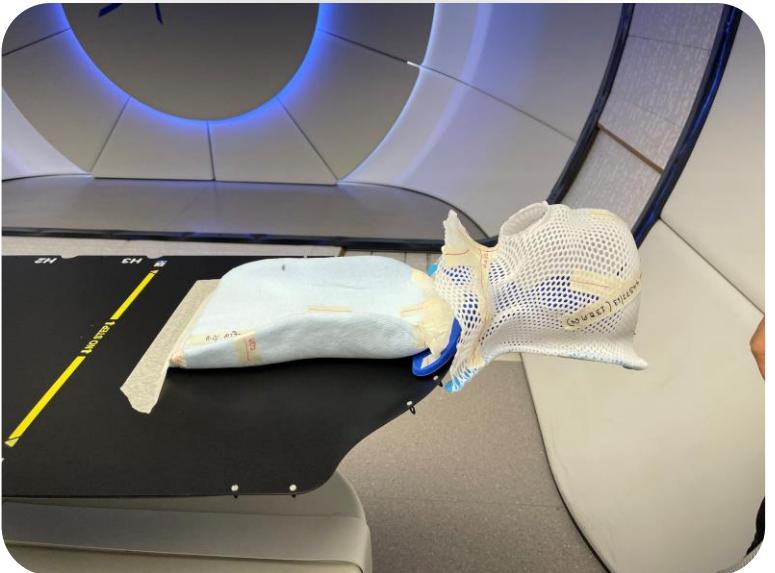
- PBT techniques – multiple beam arrangement, IMPT

# Challenging of proton therapy in pediatric patient

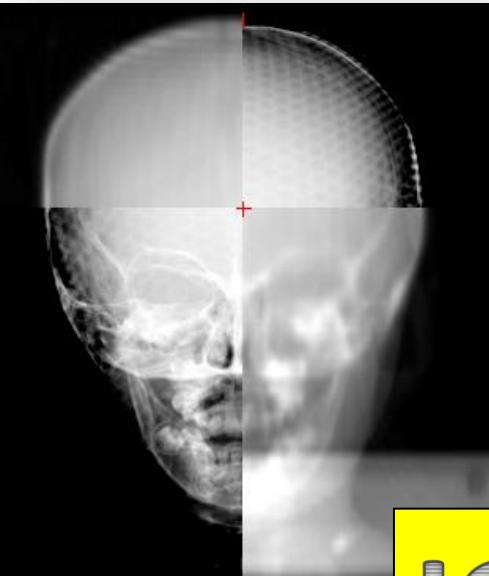
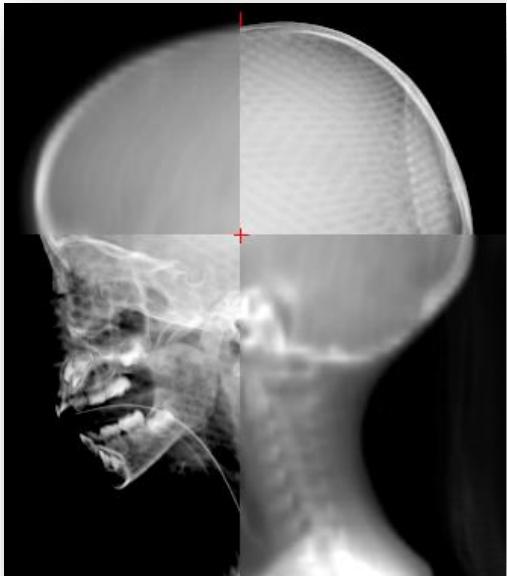
- Vertebral body dose in CSI
- Brain stem necrosis
- Spend longer time in the treatment room
  - Need sedation and general anesthesia
  - IGRT



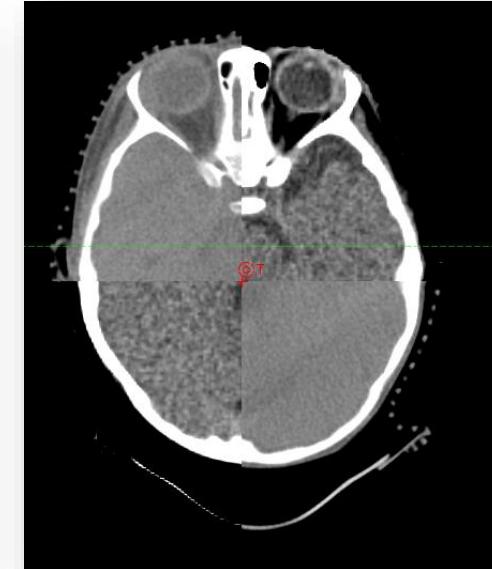
# General Anesthesia



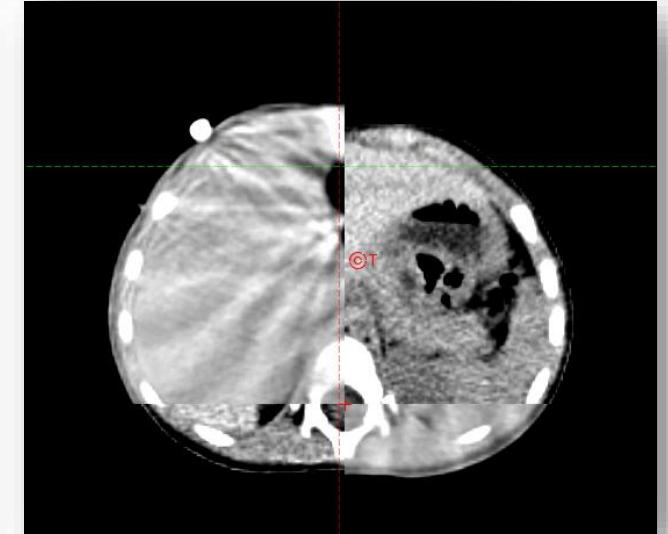
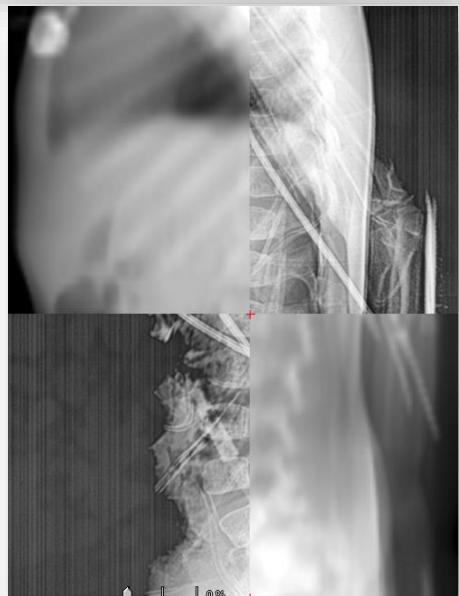
KV Image



CBCT



IGRT



# Challenging of proton therapy in pediatric patient

- Vertebral body dose in CSI
- Brain stem necrosis
- Spend longer time in the treatment room
  - Need sedation and general anesthesia
  - IGRT
- Treatment cost



ขอเชิญผู้มีจิตศรัทธาร่วมบริจาคเพื่อสนับสนุน  
โครงการเฉลิมพระเกียรติ

## สมเด็จพระกนิษฐาธิราชเจ้า กรมสมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมารี



**1** บริจาคผ่านระบบ โดยสแกน QR Code ผ่าน E-Donation\* | Mobile Banking Application ได้ทุกรายการ



**2** บริจาคด้วยเงินสด  
หรือโอนเงิน เข้าบัญชีชื่อบัญชี  
“โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย (พ.จพ. สะพานบุญ)”  
ธนาคารกสิกรไทย สาขาโรงพยาบาลจุฬาลงกรณ์  
เลขที่ 059-1-93894-0

หมายเหตุ

- หากท่านประสงค์ขอรับใบเสร็จรับเงิน สามารถส่งหลักฐานการโอนเงิน ผ่านช่องทางไลน์ของฝ่ายการเงิน โรงพยาบาลจุฬาลงกรณ์ Line ID : @478ebxxn หรือ E-mail: lorchulasaphanboon@gmail.com
- ผู้ที่บริจาคผ่านระบบ E-Donation ระบบจะส่งข้อมูลการบริจาคไปยังกรมสรรพากรโดยอัตโนมัติ \*

พ.อ.พ.ส.พ.บุญ โครงการร่วมเหลือ  
บุญเบิกประโยชน์สืบต่อของบุญภาพที่ปลดปล่อย

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ฝ่ายประชาสัมพันธ์ โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย

# Her Royal Highness Princess Maha Chakri Sirindhorn Proton Center

## Division of Radiation Oncology

### King Chulalongkorn Memorial Hospital



# กรมบัญชีกลางปรับปรุงอัตราค่าบริการ สาธารณสุข **ด้านค่าบริการรังสีรักษา**

ที่เก็บเงินเข้ารับบริการในโรงพยาบาลของรัฐ  
และกรณีโรงพยาบาลของรัฐส่งไปรับบริการในโรงพยาบาลเอกชน



ปรับปรุงอัตราค่าบริการสาธารณสุข เพื่อใช้สำหรับ  
การเบิกจ่ายค่ารักษาพยาบาลในสถานพยาบาลของ  
การราชการ **หมวดที่ 8 ค่าตรวจวินิจฉัยและรักษา**  
การรังสีวิทยา ด้านค่าบริการรังสีรักษา



ที่มา : หนังสือกรมบัญชีกลาง  
กําหนด 0416.2/ว 146  
ลงวันที่ 9 มิถุนายน 2566



เพิ่มรายการค่าบริการรังสีรักษา **จากเดิม 30 รายการ**  
ปรับเพิ่มเป็น **50 รายการ**

(เช่น ค่าบริการการฉายรังสีโปรตอน ค่าบริการการฉายรังสี  
วิเล็กตรอน ค่าบริการการฉายรังสีแบบรังสีร่วมพักรัด และ  
ค่าบริการการฉายรังสีแบบ 4 มิติ เป็นต้น )

อัตราค่าบริการสาธารณสุขเพื่อใช้สำหรับการเบิกจ่ายค่ารักษาพยาบาลในสถานพยาบาลของทางราชการ

**หมวดที่ 8 ค่าตรวจวินิจฉัยและรักษาทางรังสีวิทยา**

มีผลใช้บังคับสำหรับค่ารักษาพยาบาลที่เกิดขึ้น ตั้งแต่วันที่ 1 มิถุนายน 2566 เป็นต้นไป

## ลำดับที่ 8.8.48 การฉายรังสีโปรตอน

(Proton Beam Therapy)

ใช้สำหรับข้อบ่งชี้ ดังนี้

- เนื้องอกและมะเร็งในเด็ก (อายุไม่เกิน 15 ปี) ที่หวังหายขาด

(Primary or benign solid tumors in children treated with curative intent)

- เนื้องอกและมะเร็งที่ไม่สามารถรักษาด้วยรังสีเอกซ์/โฟตอนได้อย่างปลอดภัย เนื่องจากมีโอกาส  
เกิดภาวะแทรกซ้อนที่เป็นอันตรายต่อชีวิต (CTCAE ความรุนแรงระดับ 4-5)

(Tumors that cannot be achieved with OARs constraint by photon due to possibility  
of life-threatening complications (CTCAE grade 4-5 complications))

# ข่าวดี บอร์ด สปสช. อนุมัติสิกธิประโยชน์ “รักษาเมะเริง ด้วยօบุภาคโปรต้อน”

แชร์   

อ่าน继续

⌚ 25 ธันวาคม 2566



บอร์ด สปสช. อนุมัติสิกธิประโยชน์รักษาเมะเริงจายแสงด้วยօบุภาค<sup>โปรต้อน</sup> ดูแลผู้ป่วยเมะเริงสิกธิบัตรทอง จ่ายชดเชยค่าบริการเหมาจ่าย 50 ล้านบาท/ปี ให้แก่ รพ.จุฬาลงกรณ์ ซึ่งให้บริการรักษาด้วยօบุภาค<sup>โปรต้อน</sup>เพียงแห่งเดียวของไทย

ทั้งการรักษาเมะเริงด้วยօบุภาค<sup>โปรต้อน</sup>เป็นวิธีรักษาเมะเริงที่มีประสิทธิผล มีอัตราการควบคุมโรคเฉพาะที่และการลดชีวิตที่สูงในกลุ่มโรคเมะเริง สมองในเด็ก ช่วยลดผลข้างเคียงในทุกด้านเมื่อเปรียบเทียบกับการฉายรังสีไฟฟ่อนแบบเดิม โดยการรักษาต้องใช้บุคลากรทางการแพทย์และผู้เชี่ยวชาญ ประกอบด้วย 医師รังสีรักษา 医師รังสีวินิจฉัยแพทย์เวชศาสตร์นิวเคลียร์ กุมารแพทย์ทางโลหิตวิทยาและรังสี (กรณีผู้ป่วยเด็ก) วิสัญญีแพทย์ นัก พิสิกส์การแพทย์ นักรังสีเทคนิค พยาบาล และวิศวกร

# Conclusion

- Proton beam therapy in pediatric cancer
  - Comparable treatment outcome
  - Decrease dose to adjacent normal tissues
    - Expected to improve treatment-related side effect
  - Lower integral dose
    - Potential to reduce risk of secondary malignancy
- Challenging
  - Treatment technique
  - Treatment cost



Thank you