Hadrontherapy Workshop - From Innovation to Implementation

Particle Therapy Experience on Central Nervous System Tumors

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University Hospital Heidelberg
Dept. of Radiation Oncology

HIT

Heidelberger Ionenstrahl-Therapiezentrum

Ion sources:
- Protons
- Carbon ions
- Helium ions

experimental:
- Oxygen ions

Ion type change: ~10 sec

Synchrotron

In room CT

2 treatment rooms horizontal beam

Experimental Beam and Laboratories

1,5 T MRT

Research

Gantry treatment room since 2012
360° rotatable
670 tons weight

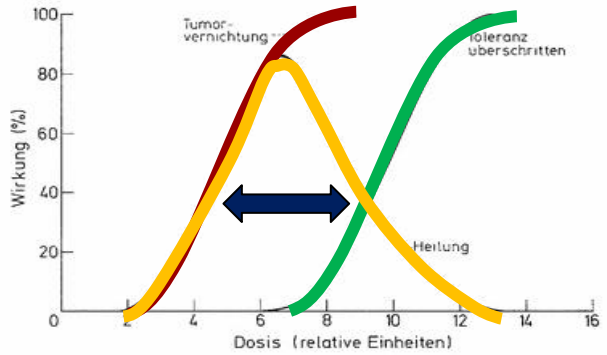
dilemma in oncology

TUMOR

-> eradication of all tumor cells

-> achieving local control

-> improving survival



NORMAL TISSUE

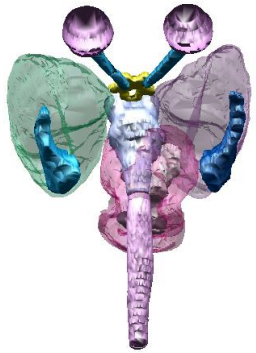
-> protection of surrounding healthy tissue

-> organ preservation

-> reducing late sequelae

rationale of hadron therapy for brain tumors

potential sequelae



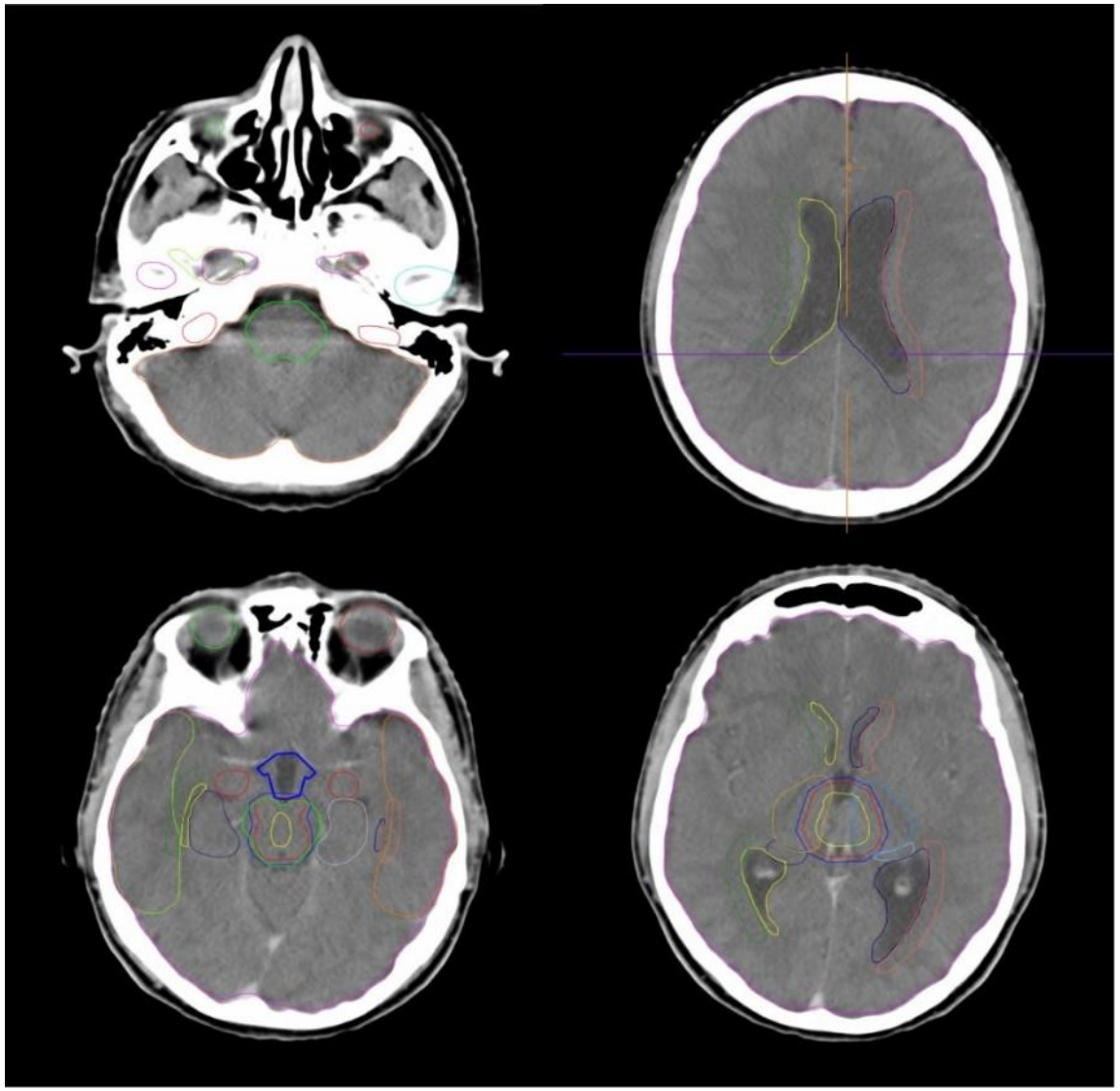
Secondary malignancies

Visual impairment / loss of hearing

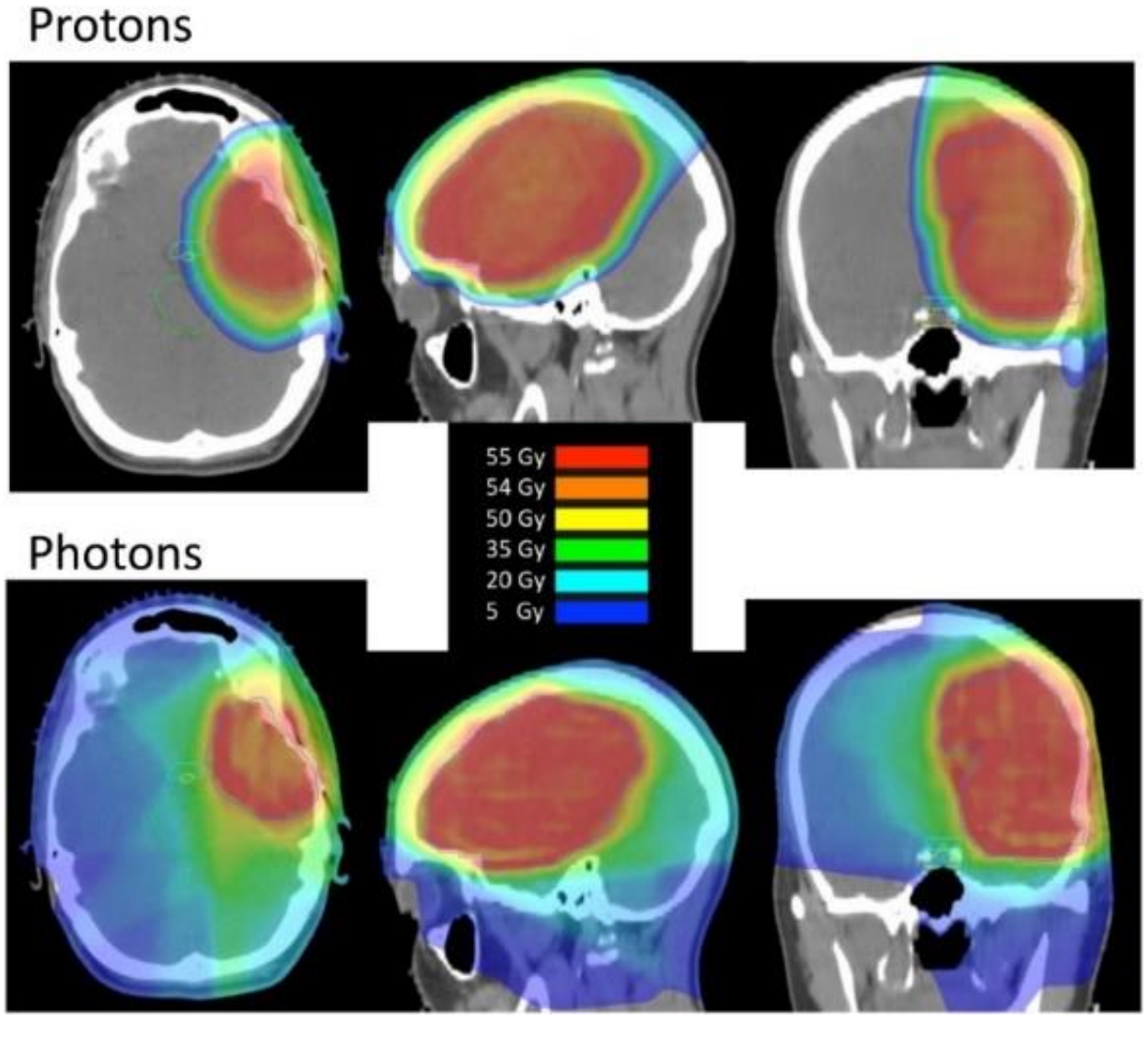
Quality of life ↓

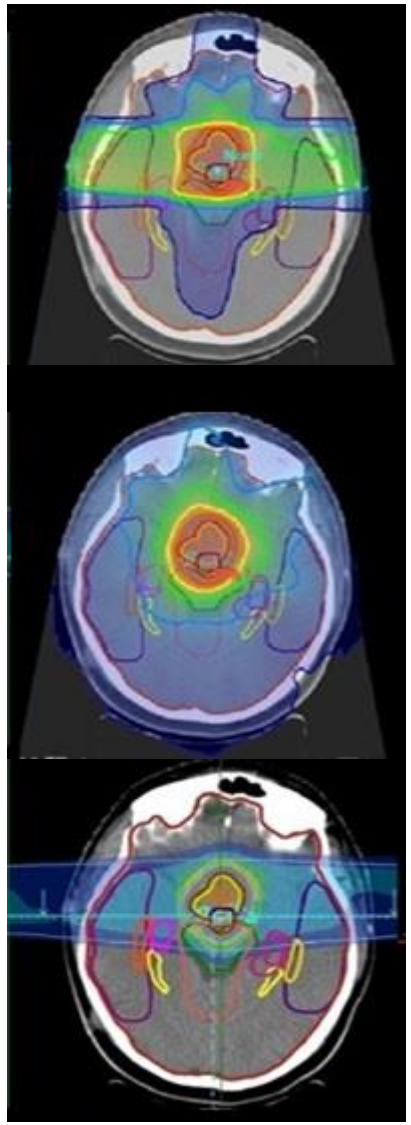
Hypopituitarisms

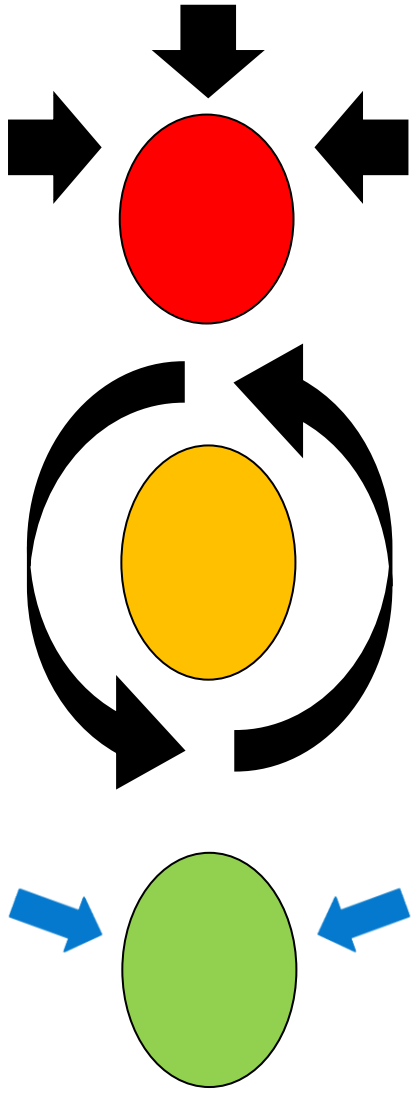
neurocognitive function ↓



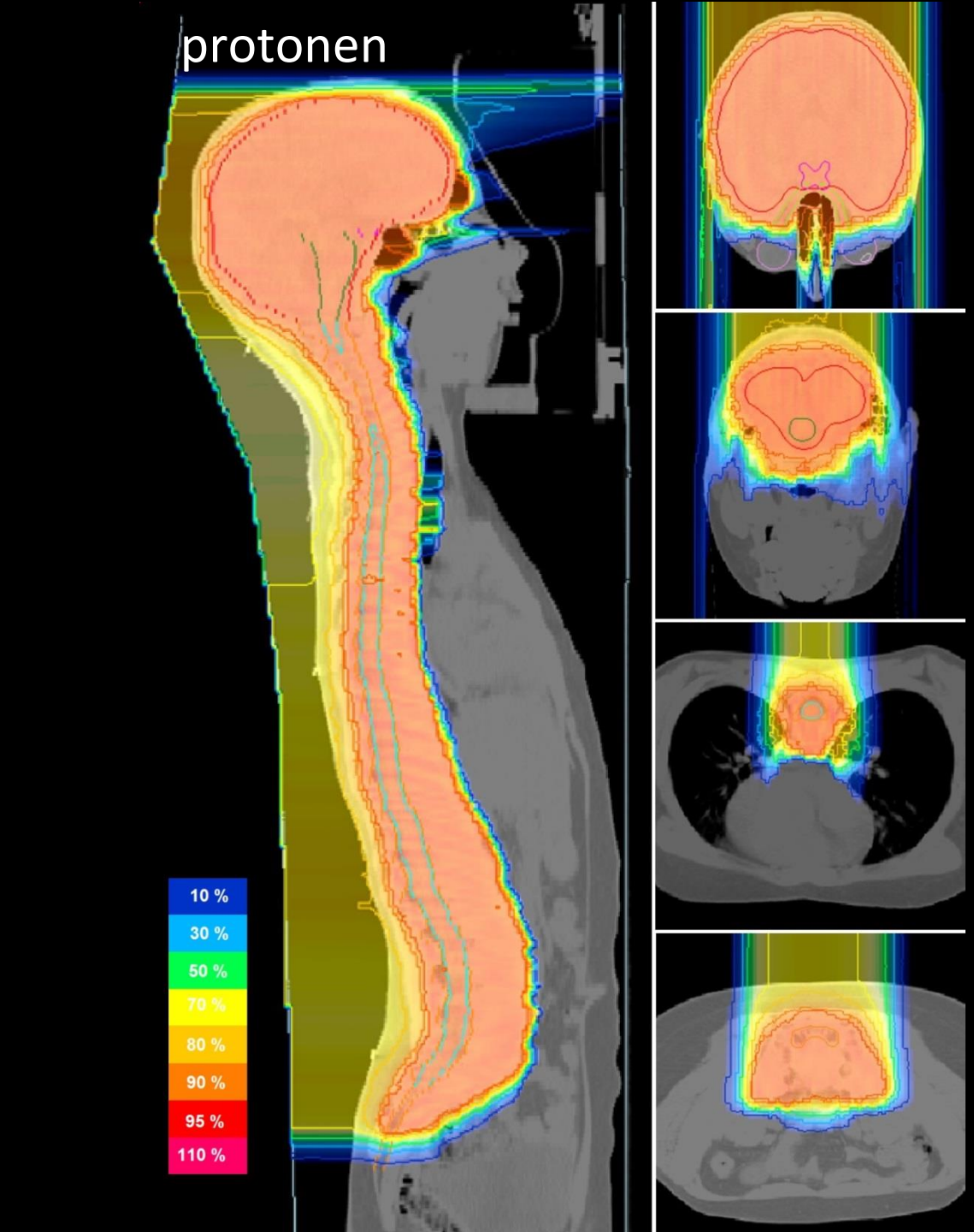
quantification of the dosimetric potential







Shih et al Cancer (2015) 121(10):1712-9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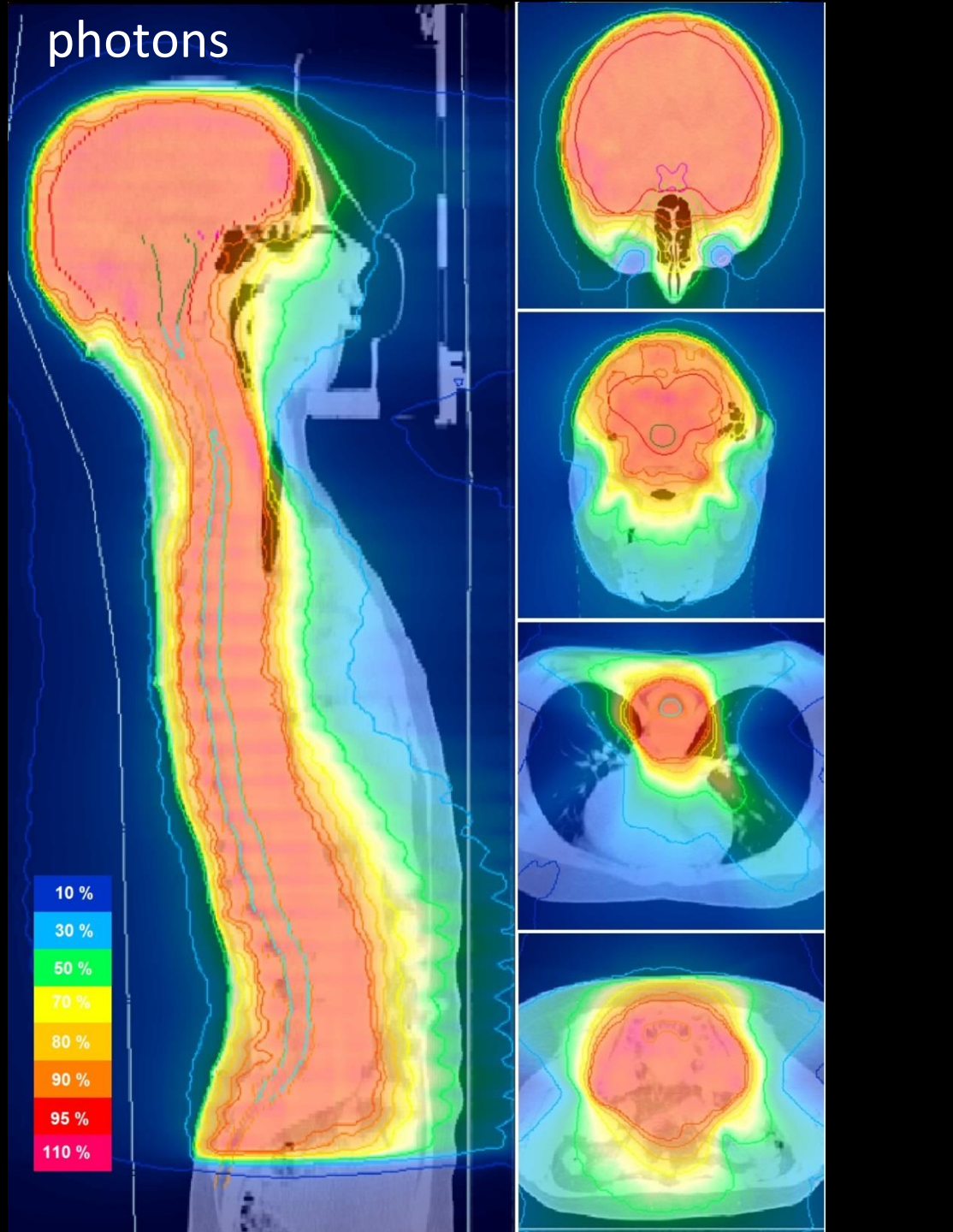
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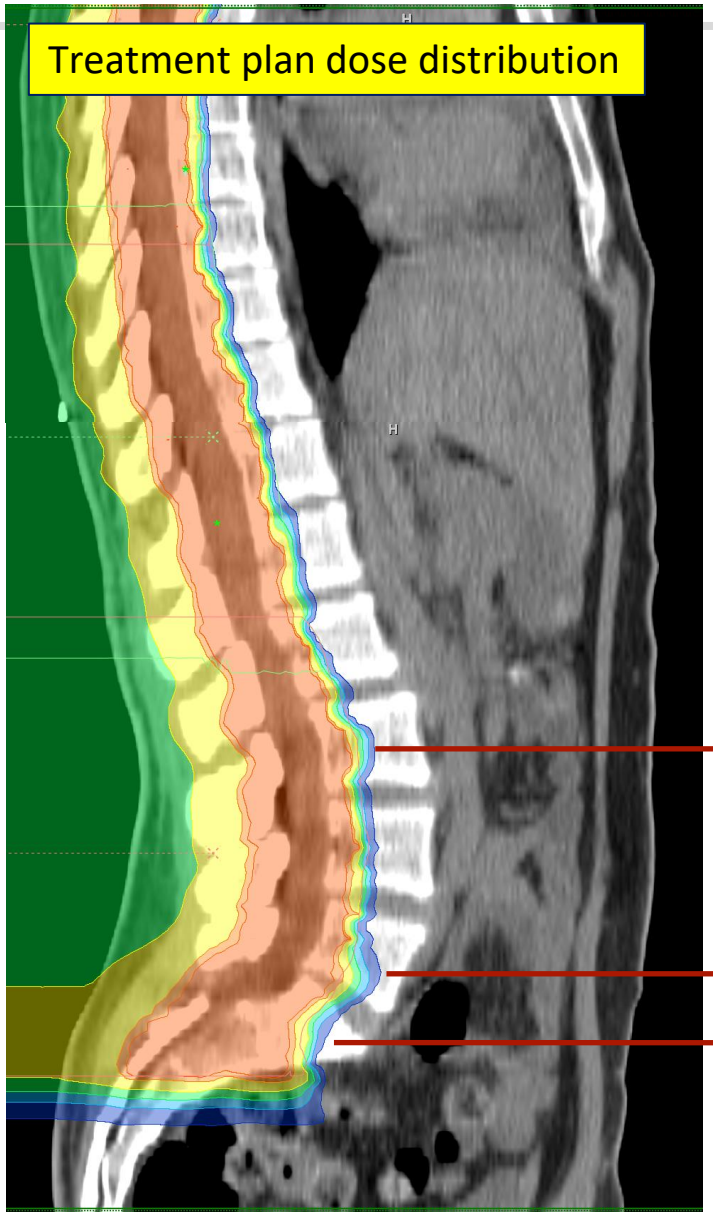
clinical outcome



Fatty changes
in irradiated part
of vertebral bodies

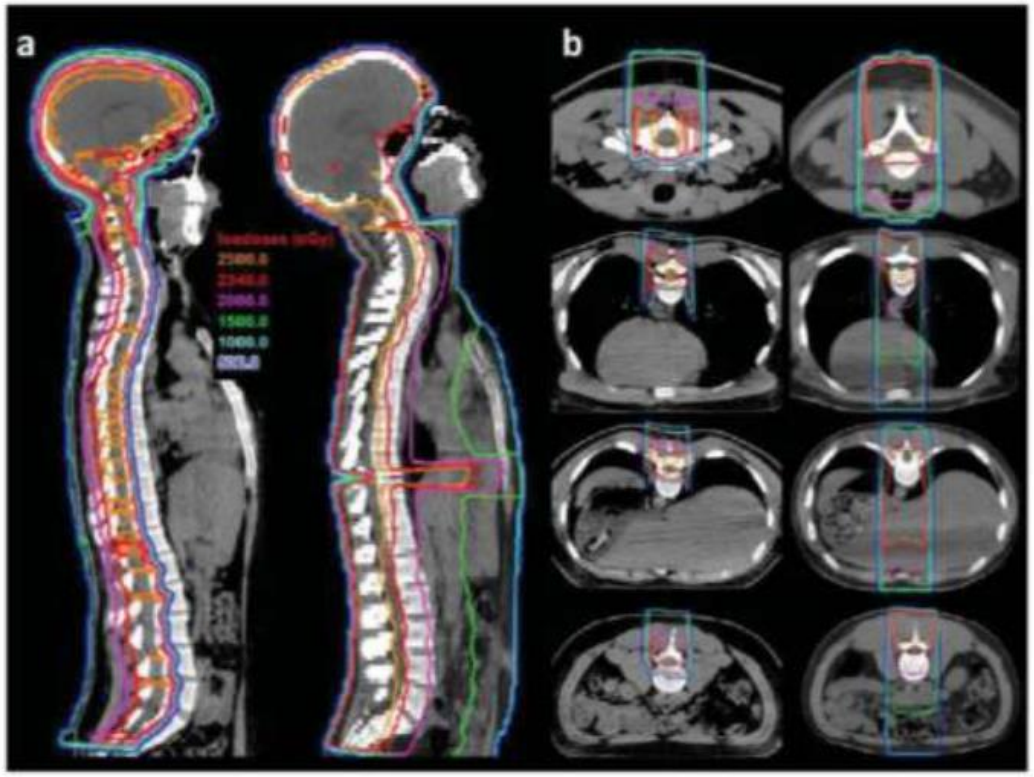
~6 month
after
Proton RT

Proves entire treatment chain, incl. patient positioning, beam application

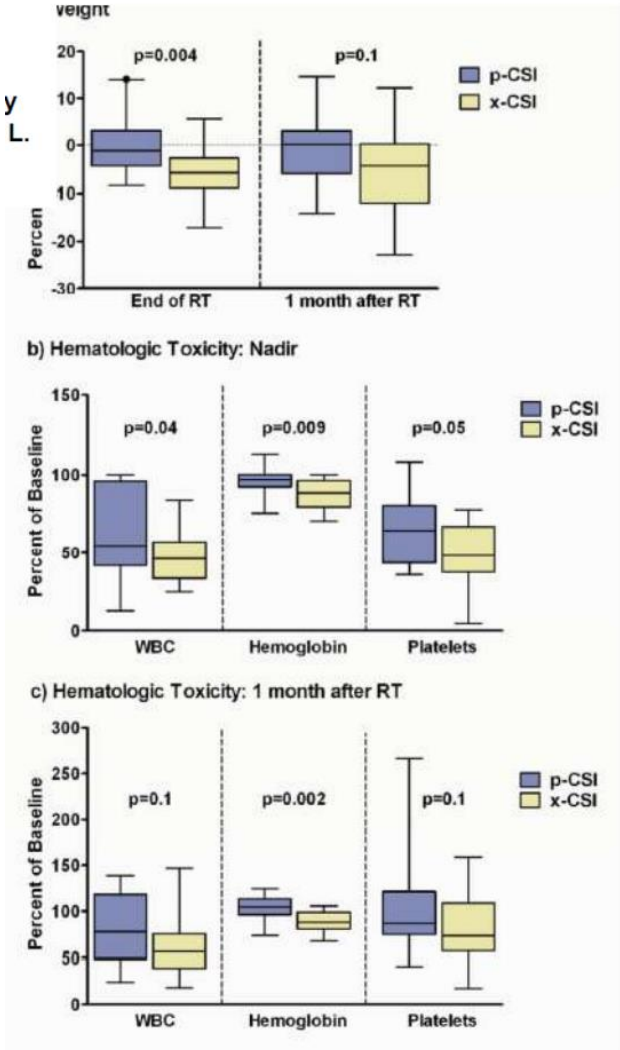
clinical outcome

Proton Beam Craniospinal Irradiation Reduces Acute Toxicity for Adults with Medulloblastoma

Aaron P. Brown, M.D.[a], Christian L. Barney, B.S.[e], David R. Grosshans, M.D., Ph.D.[a], Mary Frances McAleer, M.D., Ph.D.[a], John F. de Groot, M.D.[b], Vinay K. Puduvalli, M.D.[b], Susan L. Tucker, Ph.D.[d], Cody N. Crawford, C.M.D.[a], Meena Khan, C.M.D.[a], Soumen Khatua, M.D.[c], Mark R. Gilbert, M.D.[b], Paul D. Brown, M.D.[a], and Anita Mahajan, M.D.[a]



PT & Acute Toxicity



Int J Radiat Oncol Biol Phys. 2013 June 1; 86(2): 277–284. doi:10.1016/j.ijrobp.2013.01.014.

clinical outcome

Neuro-Oncology

Neuro-Oncology 18(6), 881–887, 2016
doi:10.1093/neuonc/nov302
Advance Access date 19 December 2015

Endocrine outcomes with proton and photon radiotherapy for standard risk medulloblastoma

Bree R. Eaton, Natia Esiashvili, Sungjin Kim, Briana Patterson, Elizabeth A. Weyman, Lauren T. Thornton, Claire Mazewski, Tobey J. MacDonald, David Ebb, Shannon M. MacDonald, Nancy J. Tarbell, and Torunn I

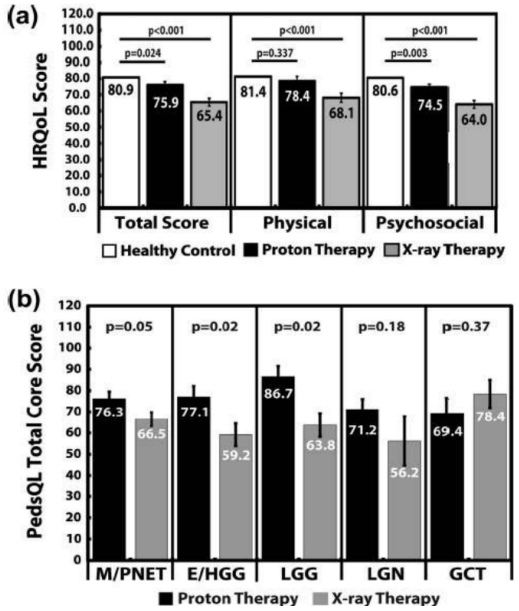
original reports

Superior Intellectual Outcomes After Proton Radiotherapy Compared With Photon Radiotherapy for Pediatric Medulloblastoma

Lisa S. Kahalley, PhD[1,2]; Rachel Peterson, PhD[3]; M. Douglas Ris, PhD[1,2]; Laura Janzen, PhD[3]; M. Fatih Okcu, MPH, MD[1,2]; David R. Grosshans, MD, PhD[4]; Vijay Ramaswamy, MD, PhD[3,5]; Arnold C. Paulino, MD[4]; David Hodgson, MD[6]; Anita Mahajan, MD[7]; Derek S. Tsang, MD, PhD[6]; Normand Laperriere, MD[6]; William E. Whitehead, MPH, MD[1,2]; Robert C. Dauser, MD[1,2]; Michael D. Taylor, MD, PhD[3,5]; Heather M. Conklin, PhD[8]; Murali Chintagumpala, MD[1,2]; Eric Bouffet, MD[3,5]; and Donald Mabbott, PhD[3,5]

Yock TI et al.
Quality of life outcomes in proton and photon treated pediatric brain tumor survivors.
Radiother Oncol. 2014 Oct; 113 (1):89-94

- **57 PT vs. 63 XRT**
- **Ped. Brain tumours**
- **PedsQL Tests after 3 years**



Clinical Investigation

Cognitive and Adaptive Outcomes After Proton Radiation for Pediatric Patients With Brain Tumors

Margaret B. Pulsifer, PhD,*,† Haley Duncanson, PhD,*,†
Julie Grieco, PsyD,*,† Casey Evans, MS,*
Irene Delgado Tseretopoulos, PhD,* Shannon MacDonald, MD,†,‡
Nancy J. Tarbell, MD,†,‡ and Torunn I. Yock, MD†,‡

Neurocognitive effects of proton radiation therapy in adults with low-grade glioma

20 adult patients with LGG, median f/u 5 years, 5-year OS 84%

Indication for PBT: age > 40 years, GTV > 6 cm, progression

54 Gy RBE in 30 fractions, CTV-margin 15 mm

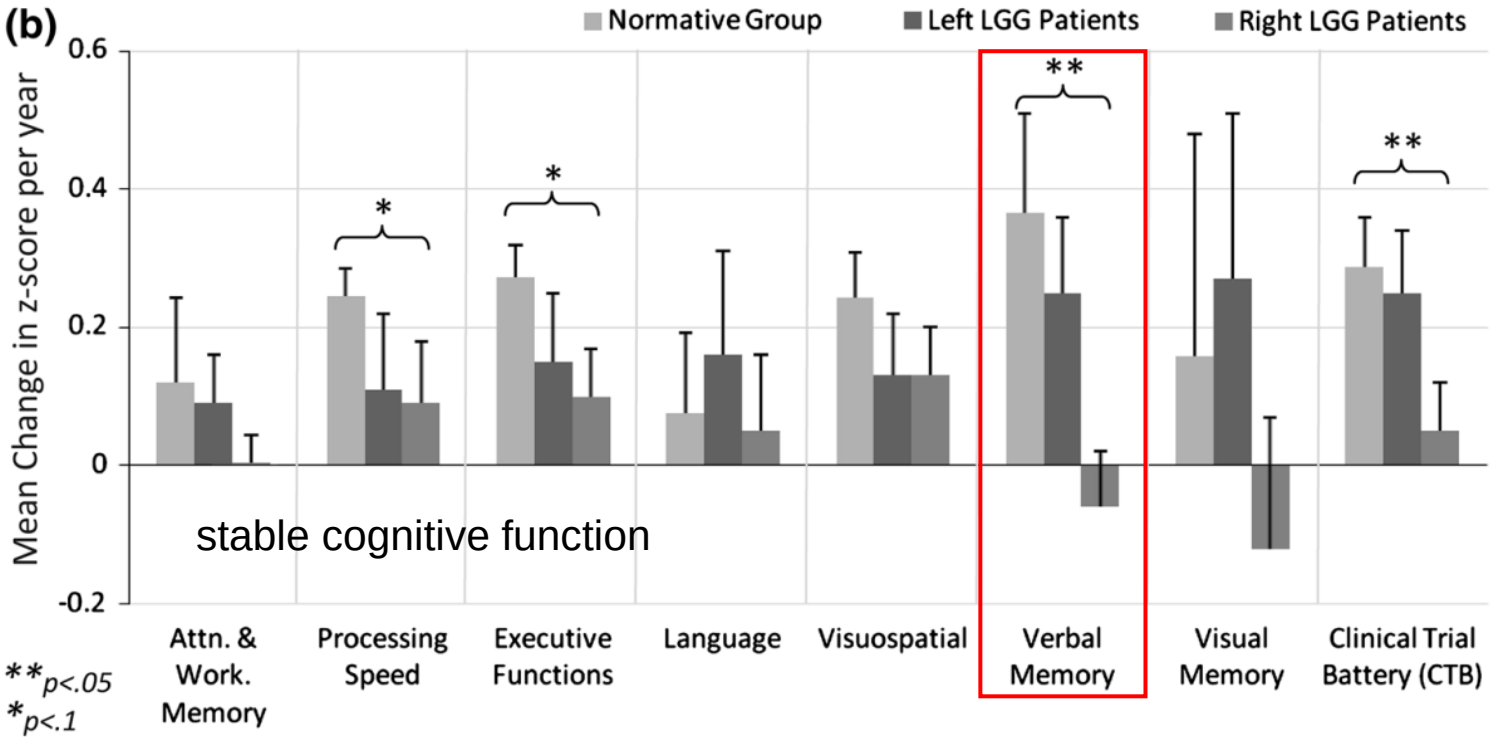


Table 1 Cognitive tests by domain

Domain	Test(s)
Intellectual	WAIS-III[a] Full Scale IQ
Visuospatial	WAIS-III[a] Perceptual Organization
Language	WAIS-III[a] Verbal Comprehension
	Boston Naming Test
	Auditory Naming Test
Attention/working memory	WAIS-III[a] Working Memory
	WMS-III[b] Spatial Span
	CPT-II[c] Inattention
	CPT-II[c] Vigilance
Processing speed	WAIS-III[a] Processing Speed
	Trail Making Test Part A
Executive function	Trail Making Test part B
	COWAT[d] F-A-S
	WCST[e] Errors
	CPT-II[c] Impulsivity
Verbal memory	HVLT-R[f] Total Recall
	HVLT-R[f] Delayed Recall
	HVLT-R[f] Retention
Visual memory	BVMT-R[g] Total Recall
	BVMT-R[g] Delayed Recall
Clinical trials battery	HVLT-R[f] Total Recall
	Trail Making Test Part A
	Trail Making Test Part B
	COWAT[d] F-A-S

[a] Wechsler adult intelligence scale—3rd edition
[b] Wechsler memory scale—3rd edition
[c] Conners' continuous performance test—2nd edition
[d] Controlled oral word association test
[e] Wisconsin card sorting test
[f] Hopkins verbal learning test—revised
[g] Brief visuospatial memory test—revised

Shermann 2016

clinical outcome

Cancer. 2020 Aug 1;126(15):3560-3568. doi: 10.1002/cncr.32938. Epub 2020 May 19.

Second cancer risk after primary cancer treatment with three-dimensional conformal, intensity-modulated, or proton beam radiation therapy

Michael Xiang [1,2], Daniel T Chang [1], Erqi L Pollom [1,2]

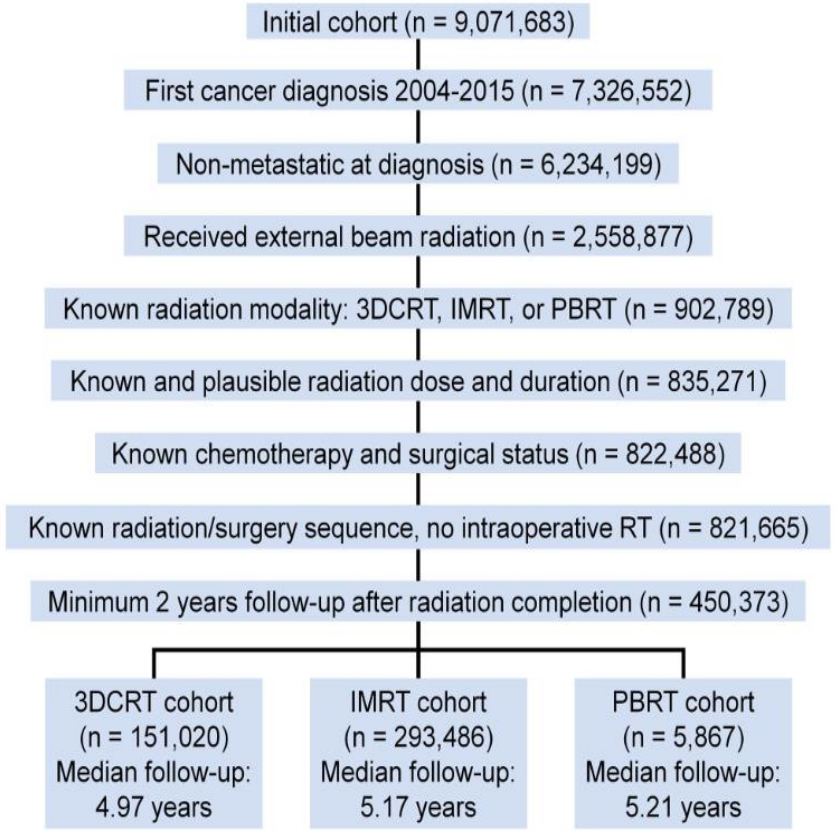


FIGURE 1. This is a Consolidated Standards for Reporting Trials (CONSORT)-style diagram for cohort identification. 3DCRT indicates 3-dimensional conformal radiation therapy; IMRT, intensity-modulated radiation therapy; PBRT, proton beam radiation therapy.

Evidence for less 2nd malignancies

TABLE 2. Overall Second Cancer Risk for Intensity-Modulated Radiation Relative to Three-Dimensional Conformal Radiation and Proton Beam Radiation Relative to Intensity-Modulated Radiation[a]

Cohort and Adjustment Method(s)	Adjusted OR (95% CI)	*P*
IMRT relative to 3DCRT		
Nonmatched, multivariable	1.00 (0.97-1.02)	.75
Matched, univariable	1.03 (1.00-1.06)	.04
Matched, multivariable	1.00 (0.98-1.03)	.75
PBRT relative to IMRT		
Nonmatched, multivariable	0.31 (0.26-0.36)	<.0001
Matched, univariable	0.30 (0.26-0.36)	<.0001
Matched, multivariable	0.29 (0.24-0.35)	<.0001

Abbreviations: 3DCRT, 3-dimensional conformal radiation, IMRT, intensity-modulated radiation; OR, odds ratio; PBRT, proton beam radiation; CI, confidence interval.

[a]Values were estimated using multivariable adjustment, matching, or both (with the same covariates used in Table 1).

Quality of life outcomes in proton and photon treated pediatric brain tumor survivors

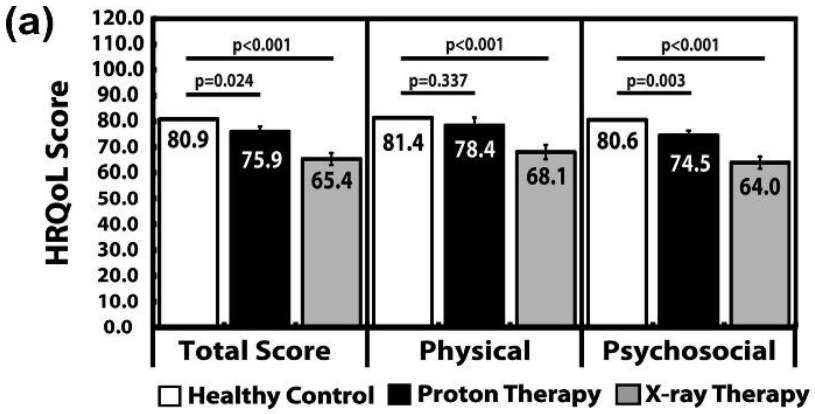
120 patients, PRT or XRT, median age 7 years, HRQoL after 3 years

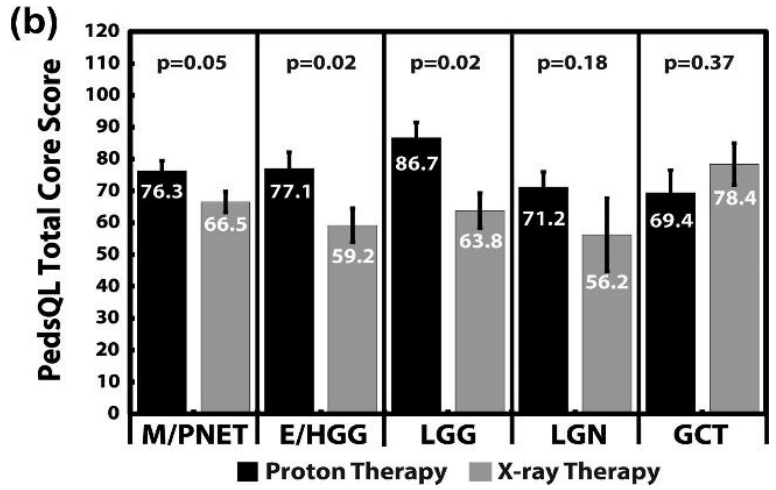
>50% MDB and HGG, RT dose 50–54Gy, 53–70% CHT

Table 2
Mean parent-reported PedsQL Core scores in the MGH proton and LPCH photon cohort.

Mean (SD) QOL scores	MGH protons ($N = 57$)	LPCH photons ($N = 63$)	p-Value	Data from normative child population*	p-Value for difference between MGH and normative child data	p-Value for difference between LPCH and normative child data
Total core score	75.9 (16.3)	65.4 (18.4) $N = 62$	0.002	80.9 (16.7)	0.024	<0.001
Physical summary score	78.4 (23.4)	68.1 (22.0) $N = 62$	0.015	81.4 (23.2)	0.337	<0.001
Psychosocial summary score	74.5 (14.9)	64.0 (18.7) $N = 62$	0.001	80.6 (16.52)	0.003	<0.001
Emotional functioning score	76.0 (16.1)	65.8 (22.0)	0.004	77.9 (20.7)	0.377	<0.001
Social functioning score	79.7 (19.4)	63.6 (23.7) $N = 62$	<0.001	85.4 (19.2)	0.031	<0.001
School functioning score	67.8 (20.6)	62.5 (22.3) $N = 53$	0.197	77.8 (22.0)	<0.001	<0.001

Note: N's for the specific category are given because not all patients filled out every sub category of the survey.
* *Source:* Varni JW, Seid M, Kurtin PS. PedsQLTM: reliability and validity of the pediatric quality of life inventory TM Version 4.0 generic core scales in healthy and patient populations. Med Care 2001; 39: 800–12.





Yock 2014

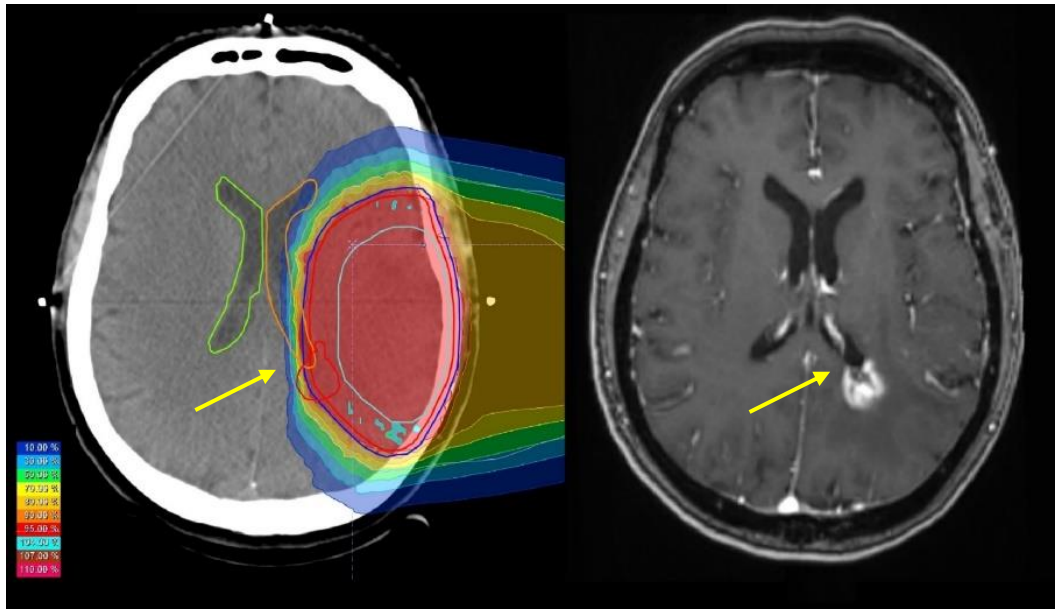
Radiation induced contrast enhancement after proton beam therapy in patients with LGG – How safe are protons?

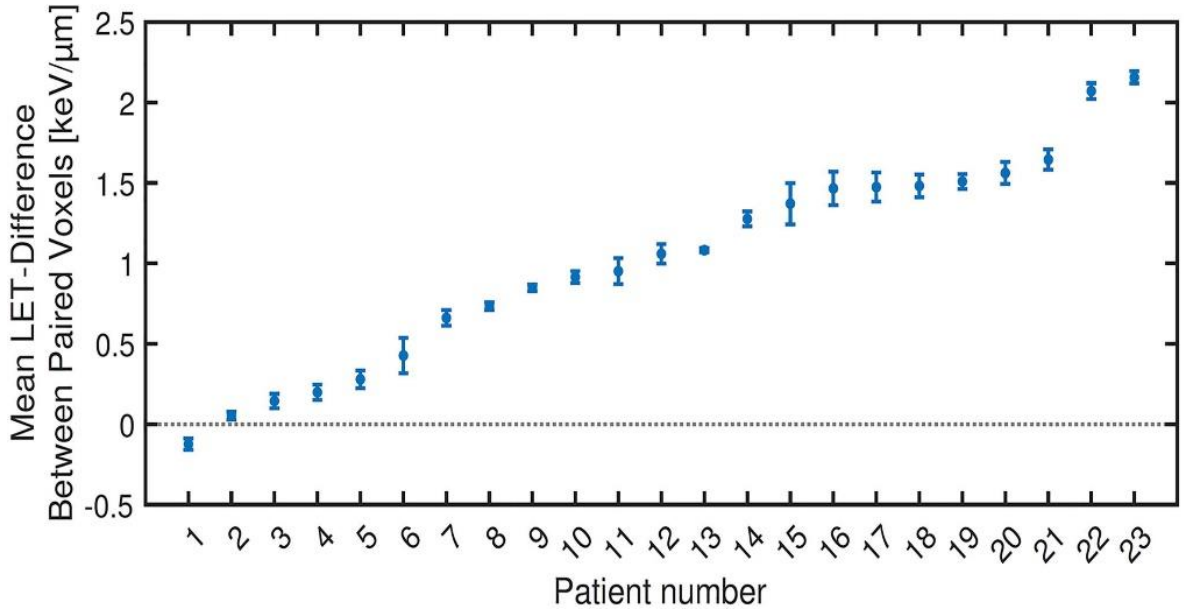
110 patients with LGG treated with PBT, >1200 MRIs, median f/u 39 months, 7-year-OS 90%

Distinct spatiotemporal pattern of RICE suggests intrinsic radiation sensitivity of ventricular border

Voxel-level based analysis revealed correlation between **increased LET** and origin of RICE

Findings provide clinical evidence that protons have variable RBE and a **fixed factor of 1.1 is inappropriate**





Harrabi 2022

International Journal of Radiation Oncology*Biology*Physics
Volume 108, Issue 3, Supplement, 1 November 2020, Pages S67-S68

Oral Scientific Session

Back to the Future: Helium Ion Therapy 2020

A. Mairani [1], S. Mein [1], B. Kopp [1], J. Besuglow [1], I. Dokic [1], J. Naumann [2], S. Harrabi [3], A. Abdollahi [4], T. Haberer [5], J. Debus [1]

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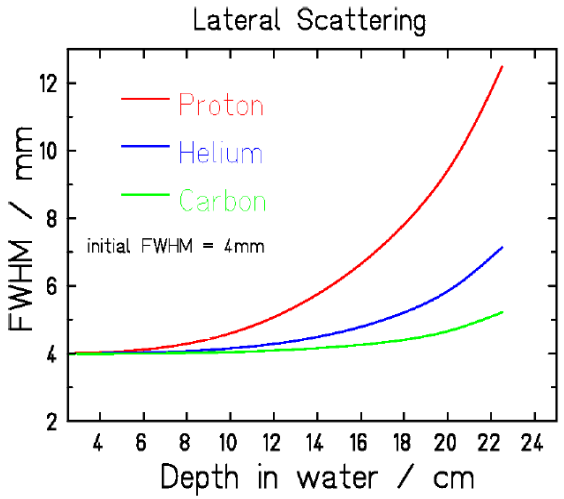
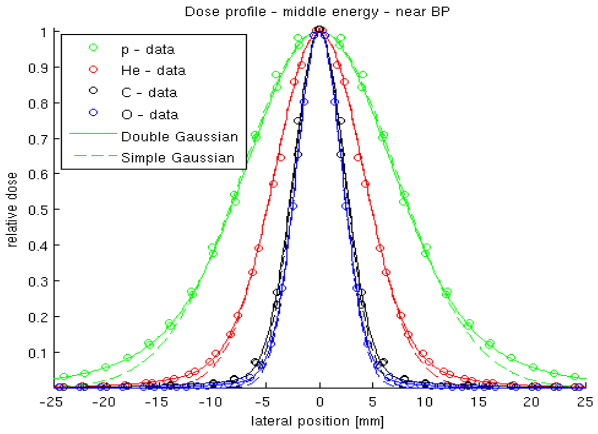




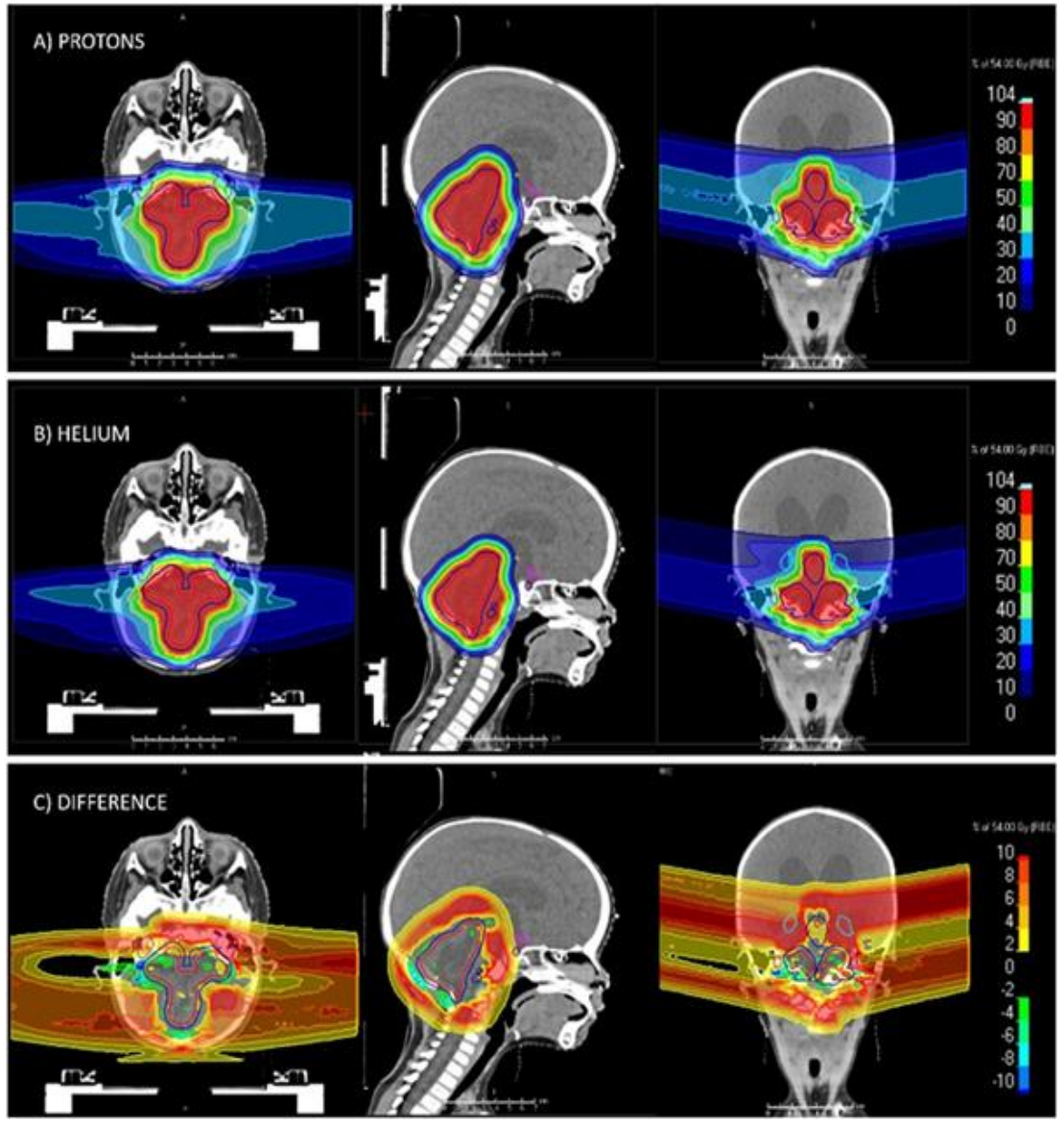


Image: Weber 2005

summary

hadron therapy is very important not only for the treatment of pediatric cancer

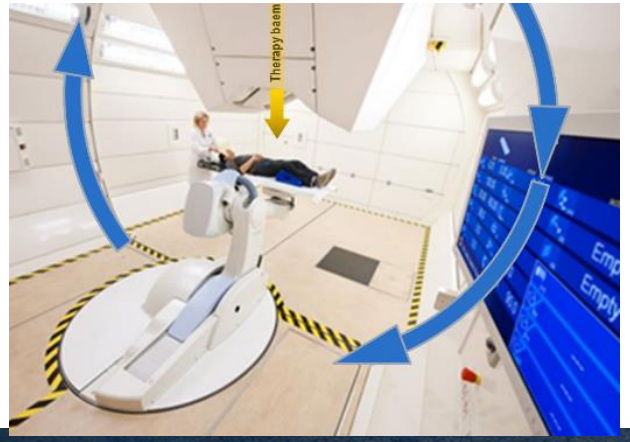
- **different physical properties:**
  - Steep dose gradient
  - Less entry dose
  - No or less exit dose

→ **sparing of normal tissue -> less acute and long term toxicity**

→ **treatment of otherwise untreatable tumors**

→ **dose escalation possible -> improved local control and survival**

- **accepted as standard alternative to photons**
- **growing evidence of clinical benefit**
- **increasing availability & use (Europe/worldwide)**



NCT
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Medical Faculty Heidelberg

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