Proton vs Photon Radiation Therapy in the Treatment of Central Nervous System Tumors

Zachary S. Buchwald, MD, PhD

Associate Professor of Radiation Oncology

Emory University School of Medicine

Why does it matter if we select protons vs photons?

Goal of CNS Radiation

- Maximize tumor control
- Minimize injury to critical structures in the brain (optic nerves, brain stem)

Challenges:

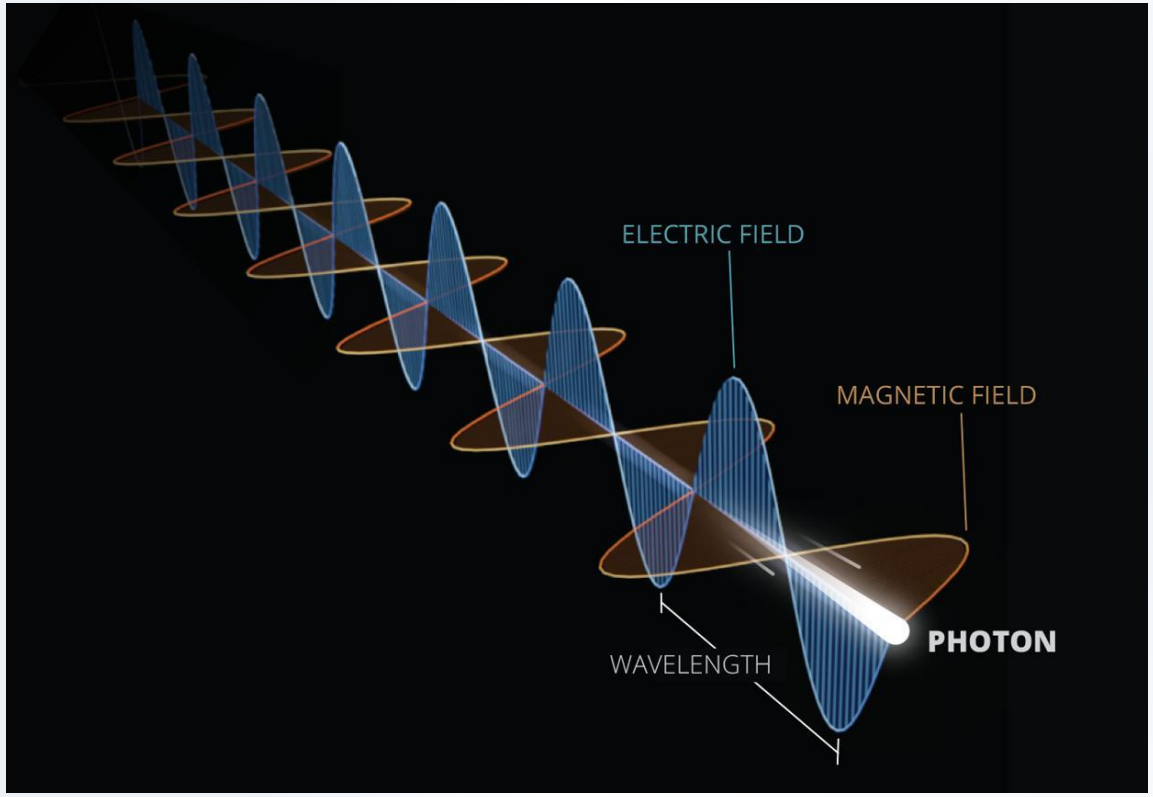
- Neurocognitive decline
- Endocrine dysfunction
- Hearing loss
- Radionecrosis
- Secondary malignancies

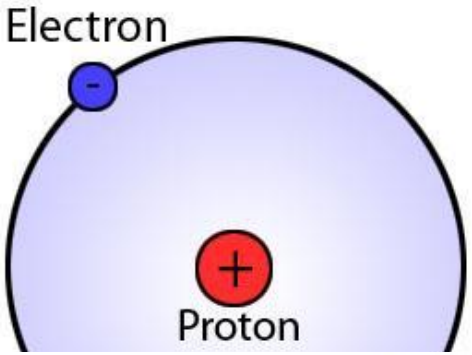
Central question: Does proton therapy improve outcomes beyond better dose distributions?

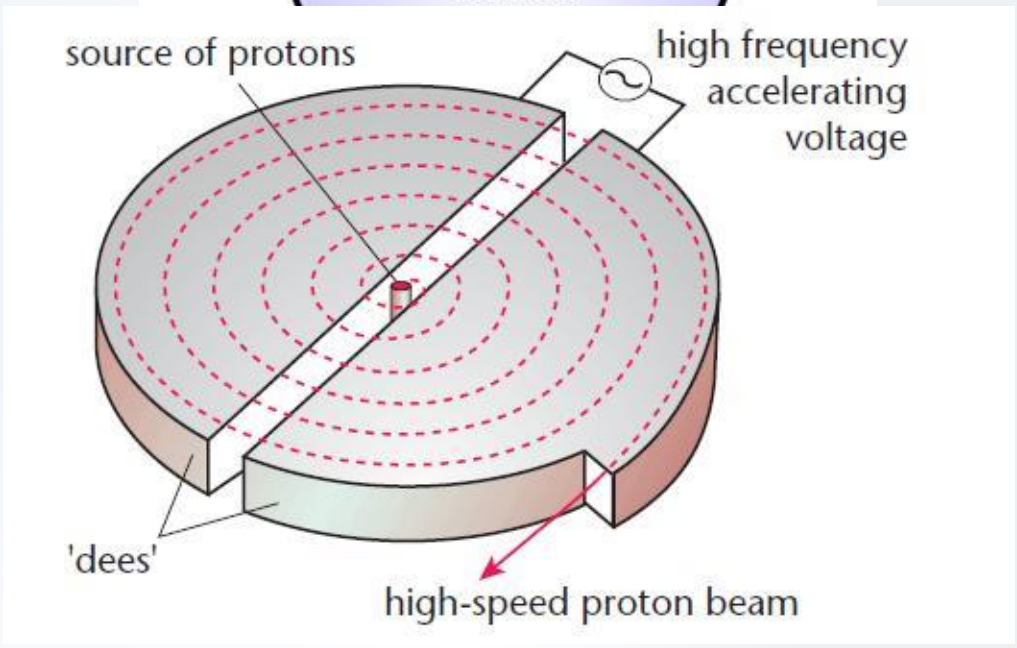
Outline

- Physics of Protons vs Photons
- Protons for leptomeningeal disease
- Protons for low grade glioma
- Protons for high grade glioma
- Protons for brain metastases

The Physics of Protons vs Photons

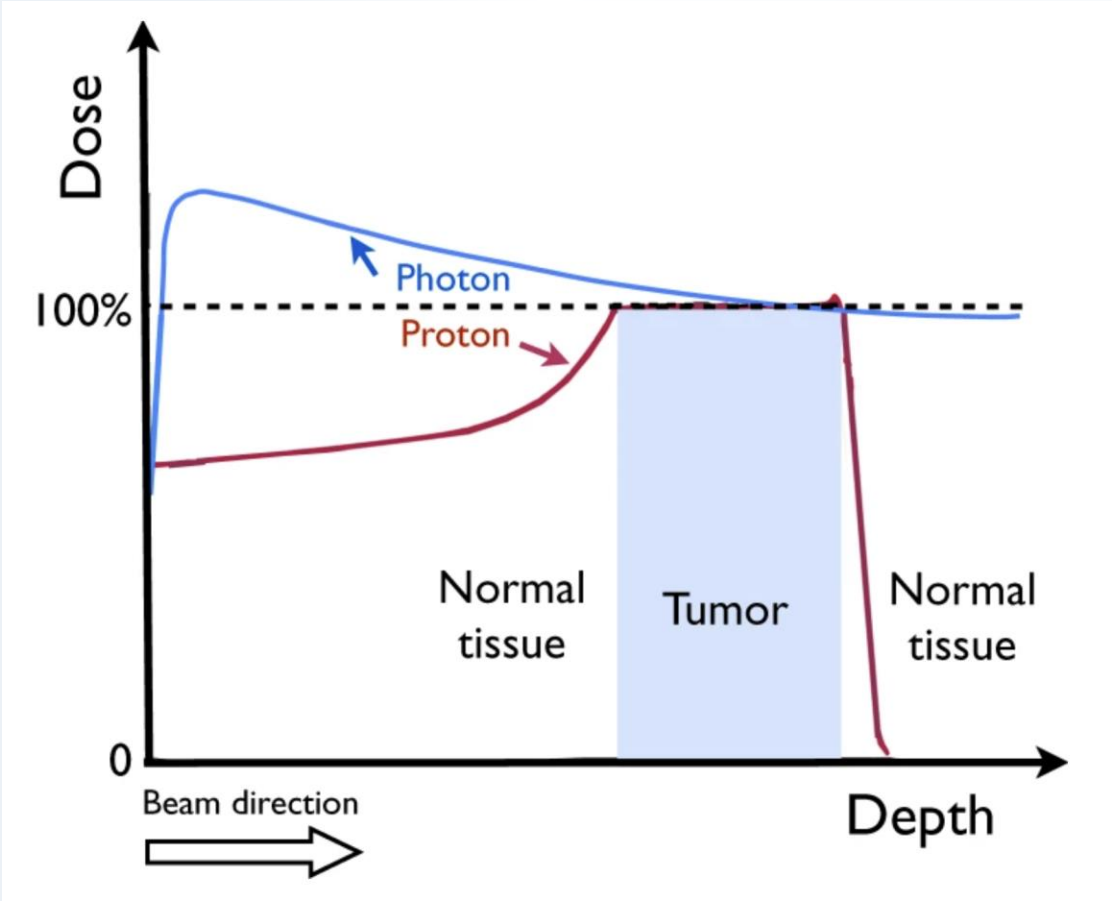


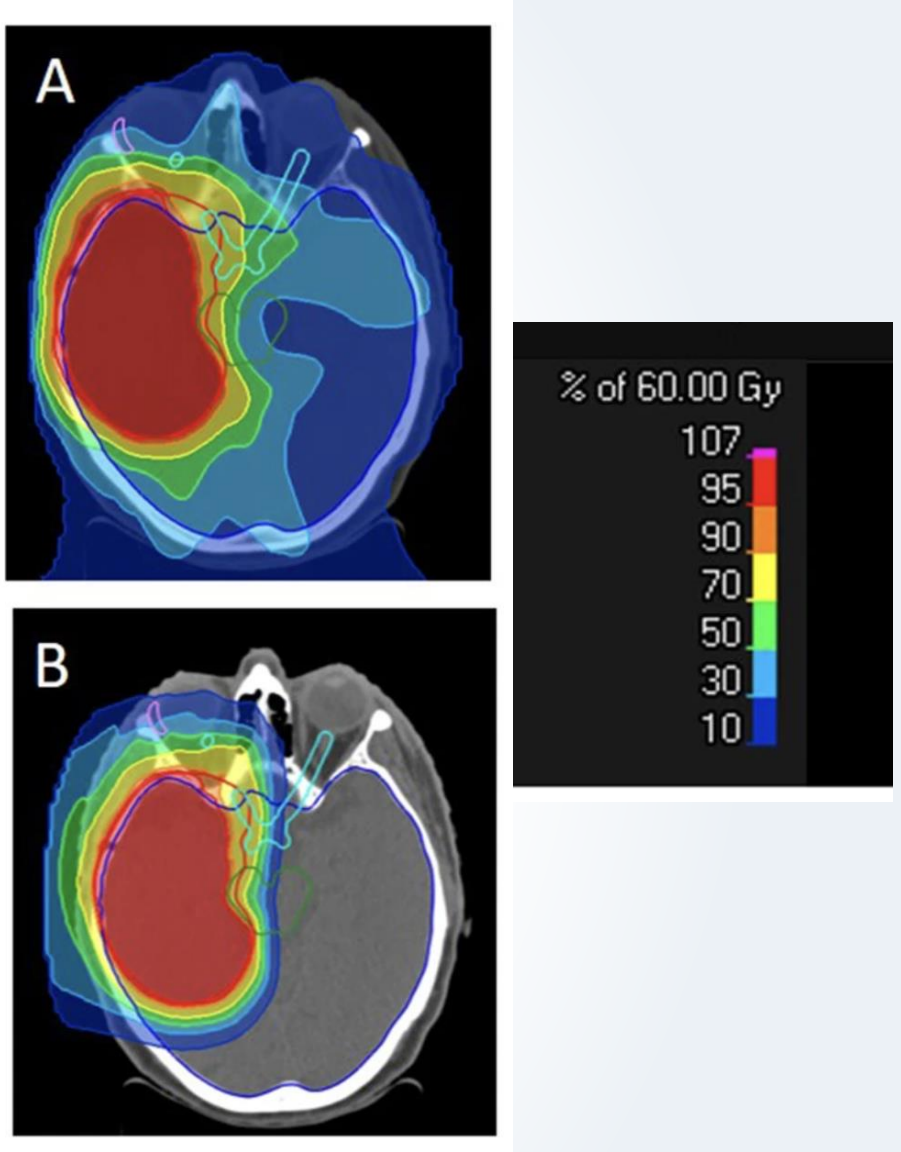




Kamran et al. Prostate Cancer and Prostatid Diseases;

The Physics of Protons vs Photons





Kamran et al. Prostate Cancer and Prostatid Diseases;

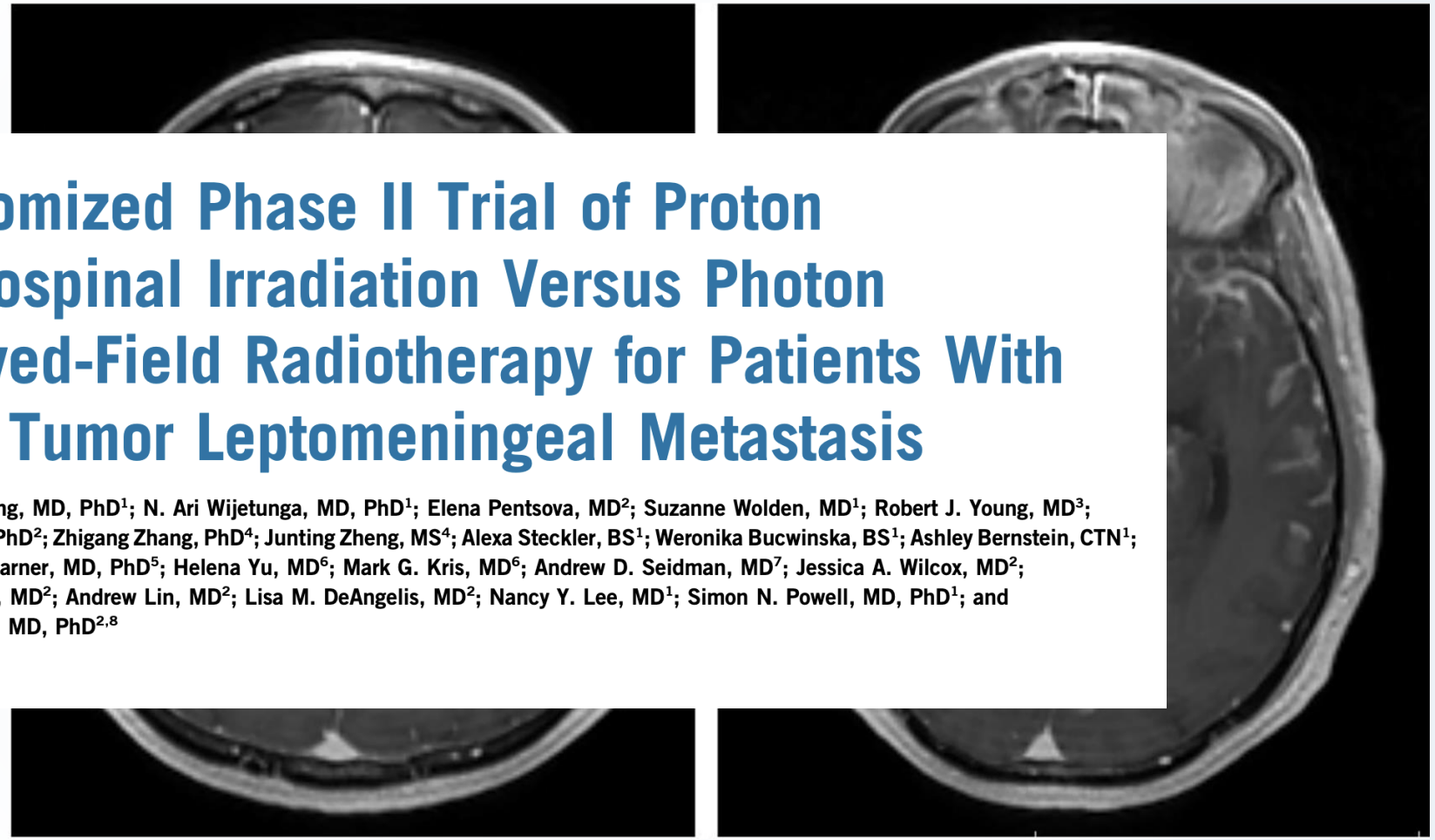
Solid Evidence for Craniospinal Radiation in LMD

Benefits:

- Dramatically lower ha
- Lower lung
- Lower bowe
- Lower thyro

Examples:

- Medulloblas
- Leptomenin
- Germ cell tumors

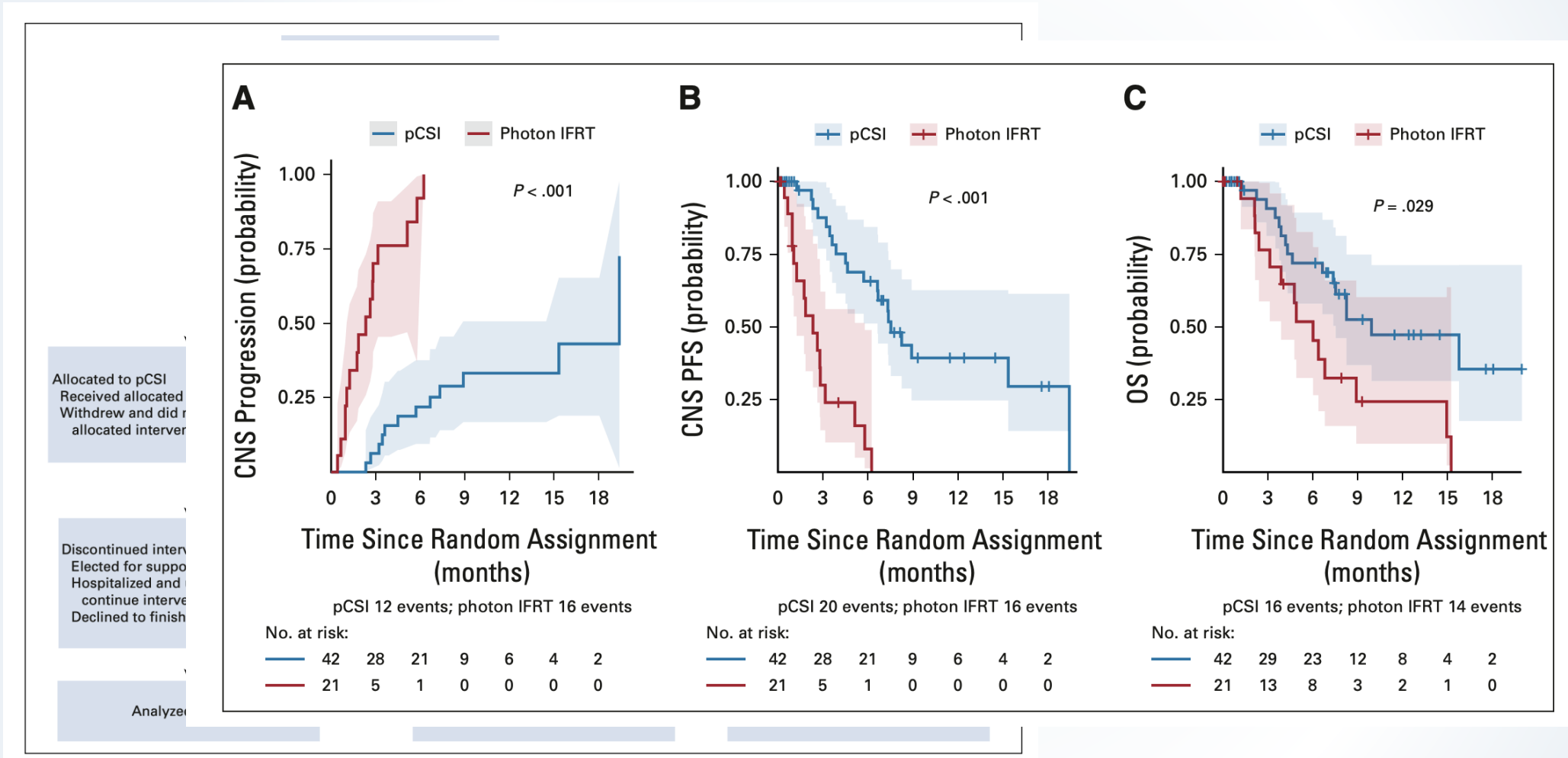


original reports

Randomized Phase II Trial of Proton Craniospinal Irradiation Versus Photon Involved-Field Radiotherapy for Patients With Solid Tumor Leptomeningeal Metastasis

Jonathan T. Yang, MD, PhD[1]; N. Ari Wijetunga, MD, PhD[1]; Elena Pentsova, MD[2]; Suzanne Wolden, MD[1]; Robert J. Young, MD[3]; Denise Correa, PhD[2]; Zhigang Zhang, PhD[4]; Junting Zheng, MS[4]; Alexa Steckler, BS[1]; Weronika Bucwinska, BS[1]; Ashley Bernstein, CTN[1]; Allison Betof Warner, MD, PhD[5]; Helena Yu, MD[6]; Mark G. Kris, MD[6]; Andrew D. Seidman, MD[7]; Jessica A. Wilcox, MD[2]; Rachna Malani, MD[2]; Andrew Lin, MD[2]; Lisa M. DeAngelis, MD[2]; Nancy Y. Lee, MD[1]; Simon N. Powell, MD, PhD[1]; and Adrienne Boire, MD, PhD[2,8]

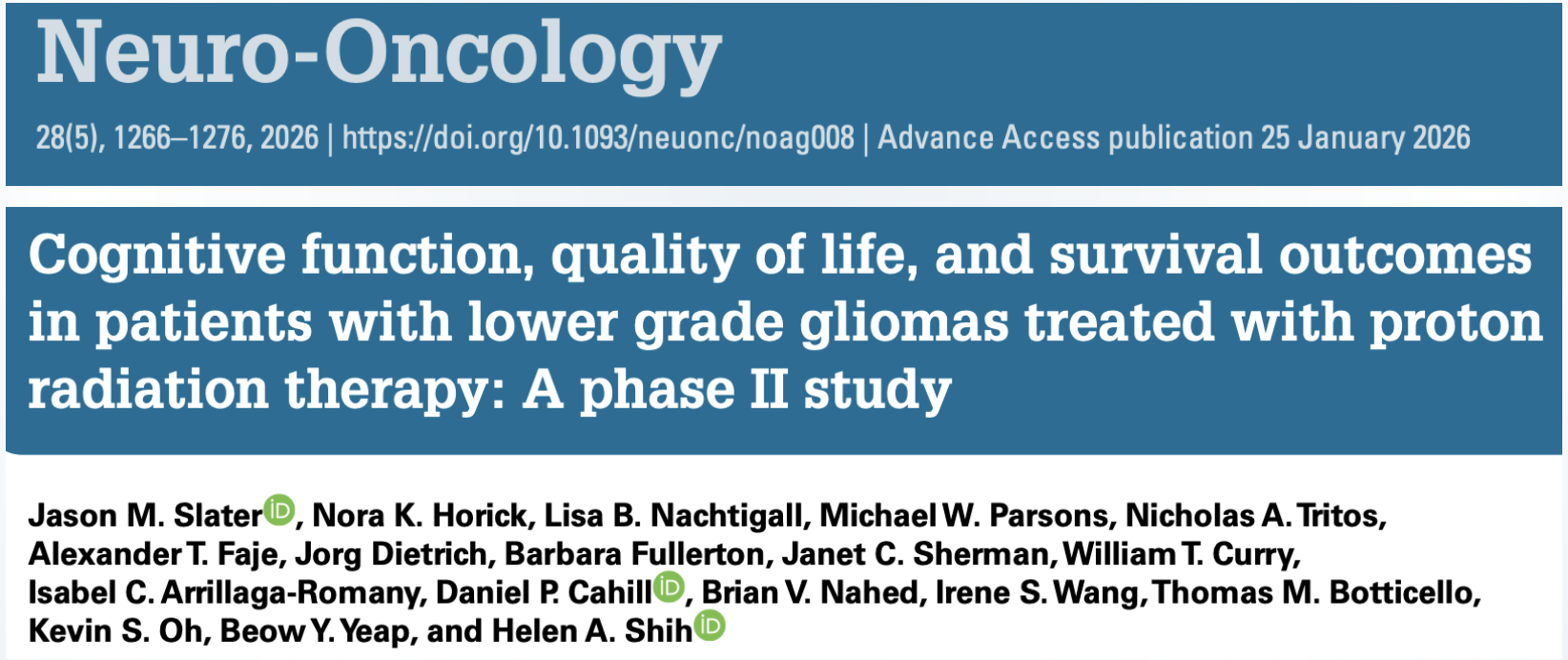
Phase II Randomized Study of Photons vs Protons for LMD



What about for Low Grade Gliomas?

Patients can survive often >10 years therefore critical to reduce treatment related toxicities:

- Neurocognitive
- Neuroend



Neuro-Oncology

28(5), 1266–1276, 2026 | https://doi.org/10.1093/neuonc/noag008 | Advance Access publication 25 January 2026

Cognitive function, quality of life, and survival outcomes in patients with lower grade gliomas treated with proton radiation therapy: A phase II study

Jason M. Slater, Nora K. Horick, Lisa B. Nachtigall, Michael W. Parsons, Nicholas A. Tritos, Alexander T. Faje, Jorg Dietrich, Barbara Fullerton, Janet C. Sherman, William T. Curry, Isabel C. Arrillaga-Romany, Daniel P. Cahill, Brian V. Nahed, Irene S. Wang, Thomas M. Botticello, Kevin S. Oh, Beow Y. Yeap, and Helen A. Shih

Protons i

Single Arm for LGG

- Grade 1-
- 60 patie
- 5-year PF

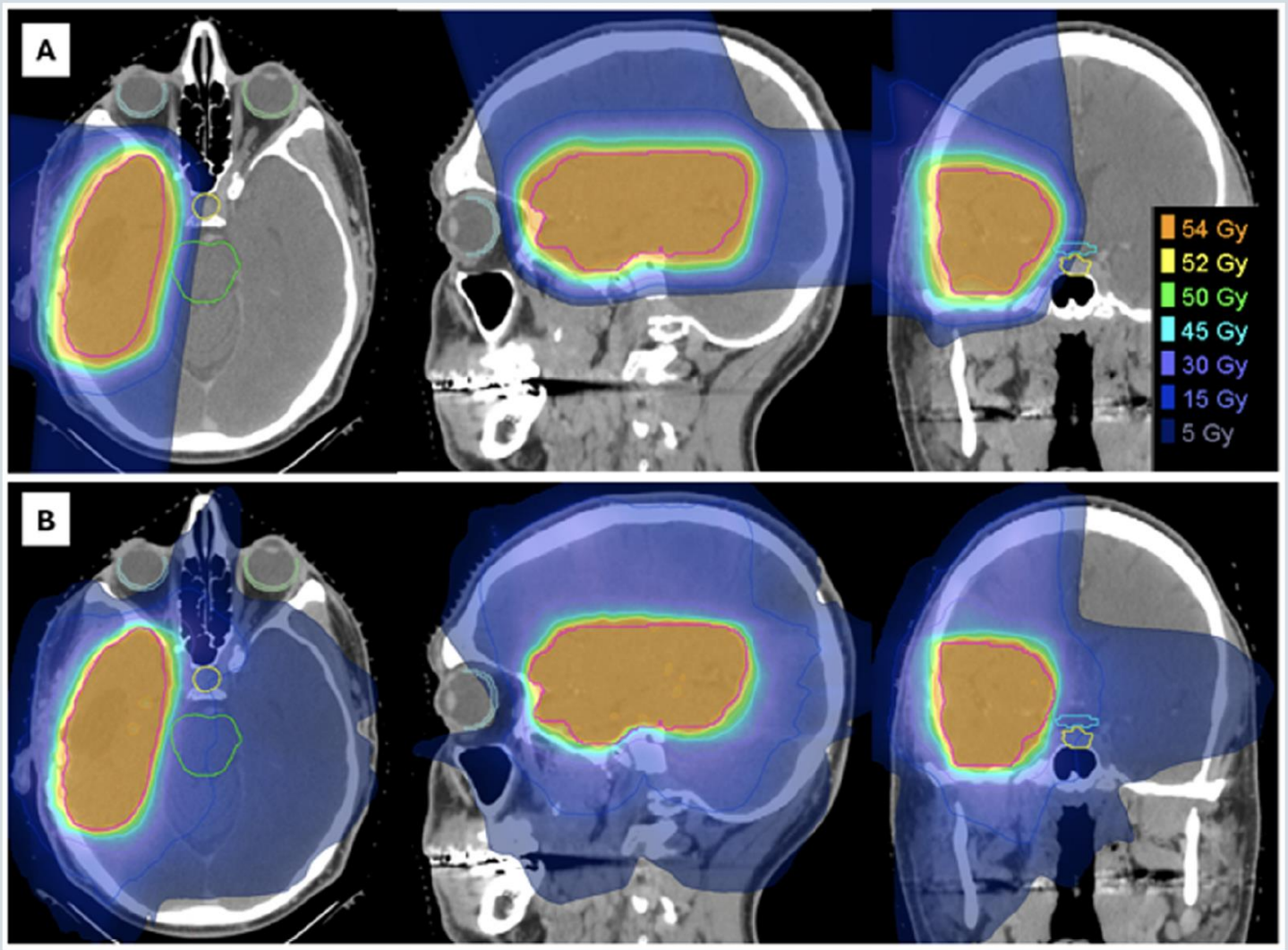


Figure 1. Comparison treatment plan of proton (A) and intensity-modulated radiotherapy (B). Whereas equitable dose is delivered to the tumor, proton therapy can significantly reduce collateral radiation dose to radiation sensitive structures of the optic nerve, optic chiasm, pituitary, and overall brain which may help to reduce radiation associated adverse effects.

Protons in Low Grade Glioma

Table 3. Neuroendocrine data

	All patients			Patients with at-risk pituitary (D50>1 Gy(RBE))	
Axis	Baseline central deficits	New deficits	Total deficits	New deficits	Pituitary D50 for new deficits (Gy(RBE))
Thyrotropic	0/59[#] (0%)	1/59[#] (2%)	1/59[#] (2%)	0/26[#] (0%)	0
Corticotropic	0/60 (0%)	0/60 (0%)	0/60 (0%)	0/27 (0%)	-
Growth hormone	0/60 (0%)	0/60 (0%)	0/60 (0%)	0/27 (0%)	-
Gonadotropic, male	3/28 (11%)	2/25 (8%)	5/28 (18%)	1/18 (6%)	17.8
Gonadotropic, female	0/30* (0%)	0/30[§] (0%)	0/30 (0%)	0/8[†] (0%)	-
Total	3/60 (5%)	3/57 (5%)[#§]	6/60 (10%)	1/27 (4%)	

*Two excluded for oral contraceptive use at baseline.
[#]One excluded for baseline primary hypothyroidism.
[§]Two excluded for oral contraceptive use at last follow up.
[†]One excluded for oral contraceptive use at last follow up.

Neurocognitive Deficits:

- 34% at baseline
- 19/43 (44%) at 3 years
- 15/45 (43%) at 5 years

What about protons for High Grade Gliomas?

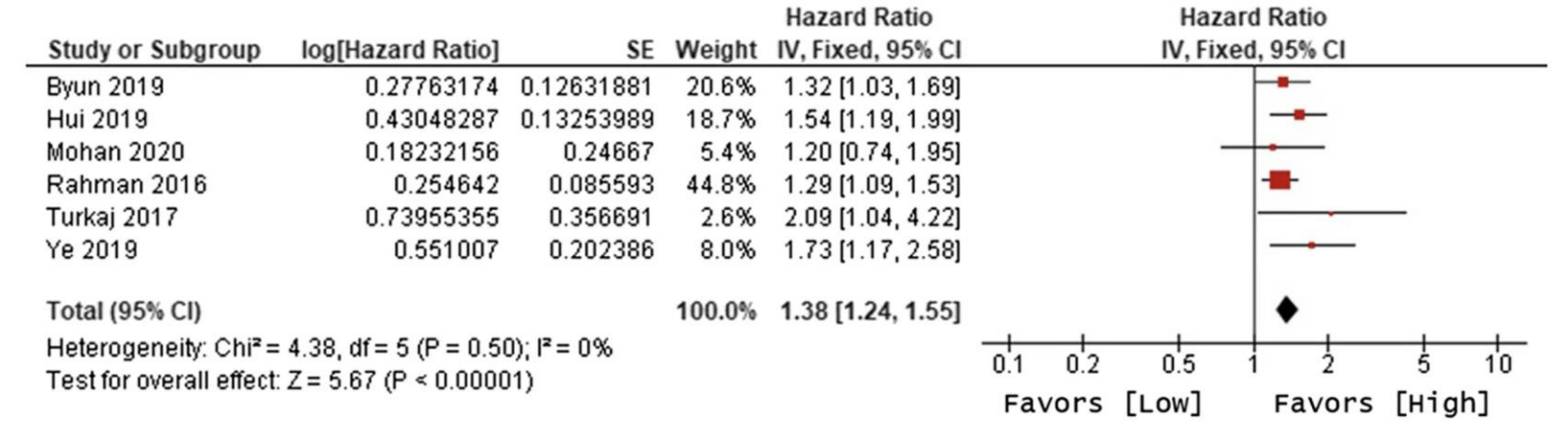
Bottom Line:

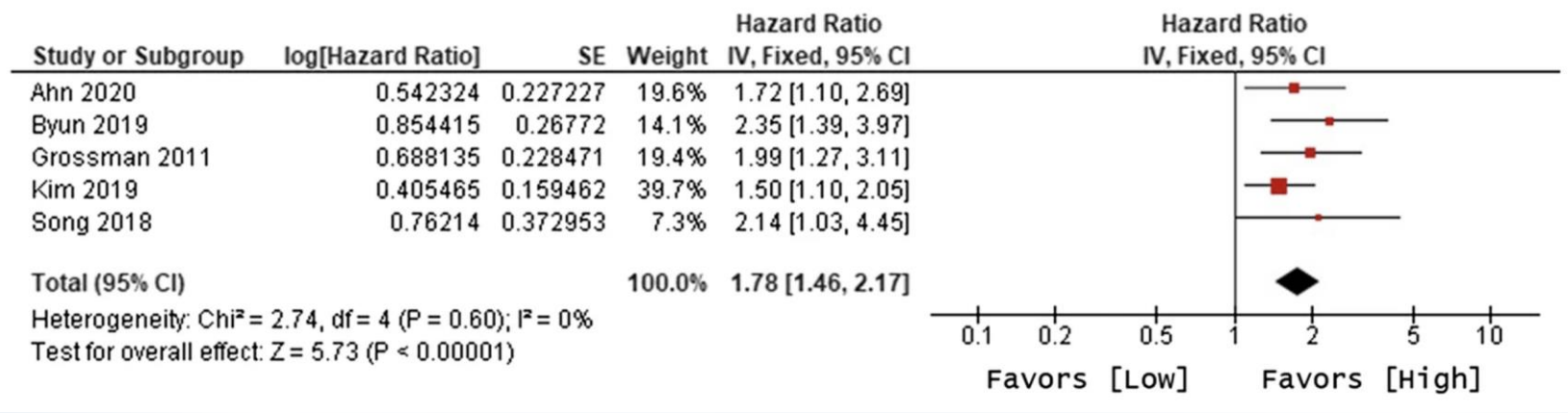
- Does not improve neurocognitive outcomes
- Reduces lymphopenia (level I evidence)
- Does it improve survival – to be determined

What about protons for High Grade Gliomas?

Bottom Li

- Does n
- **Reduce**
- Does it

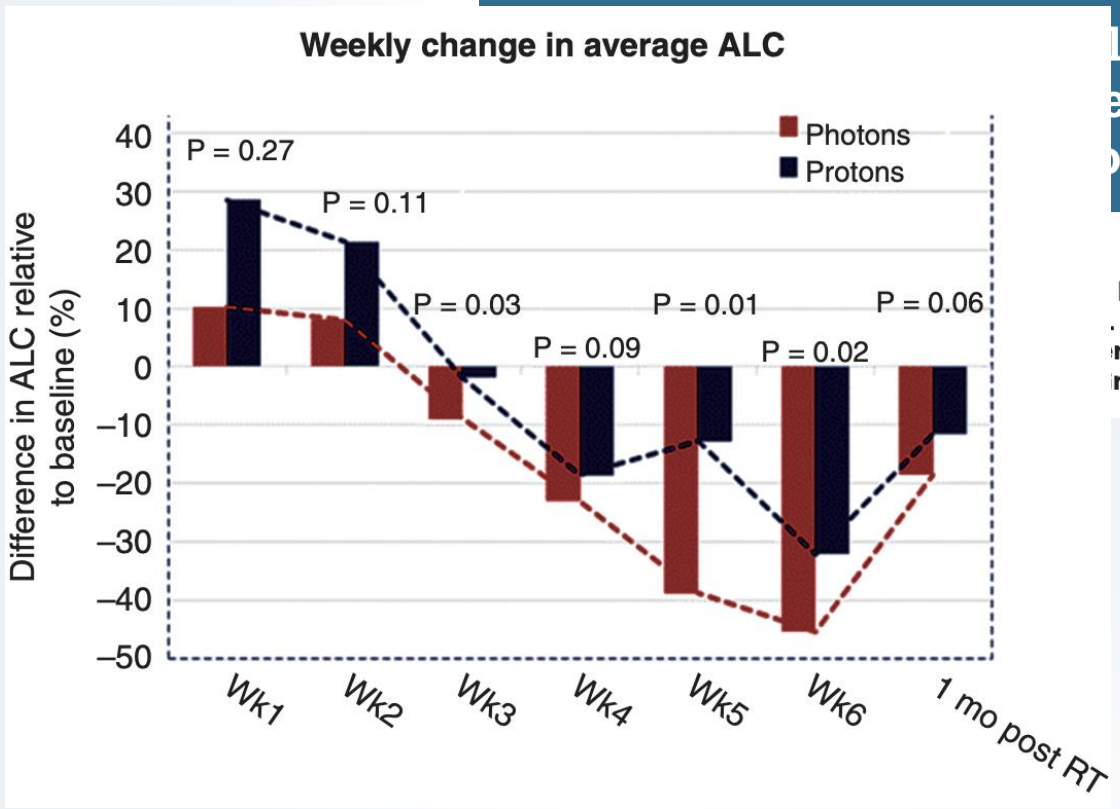


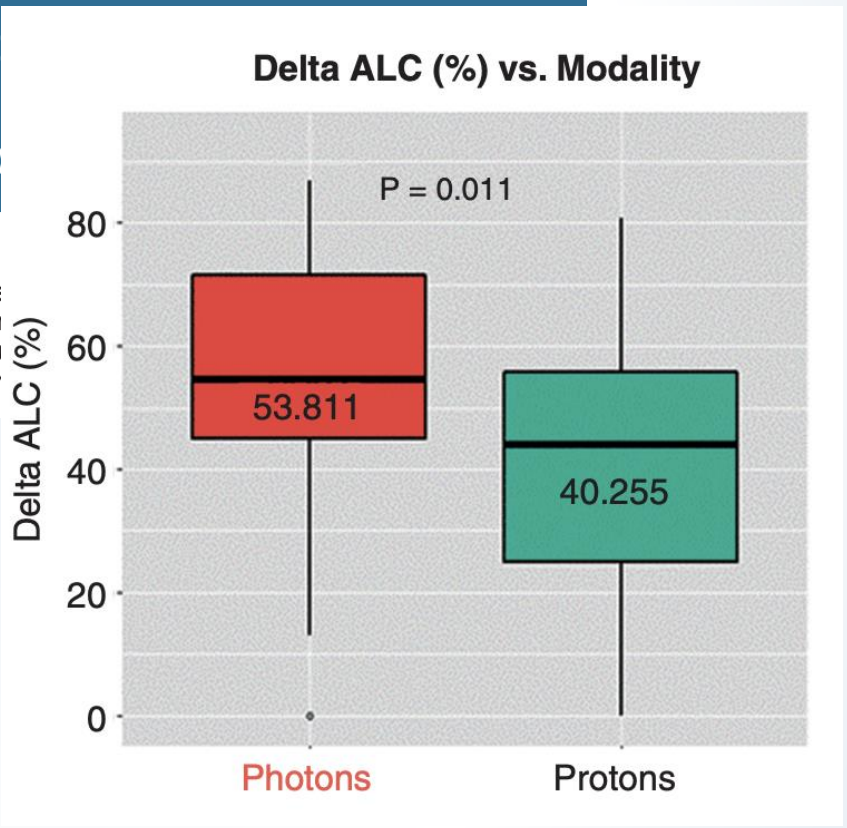


Saeed et al. Radiation Oncology 2024

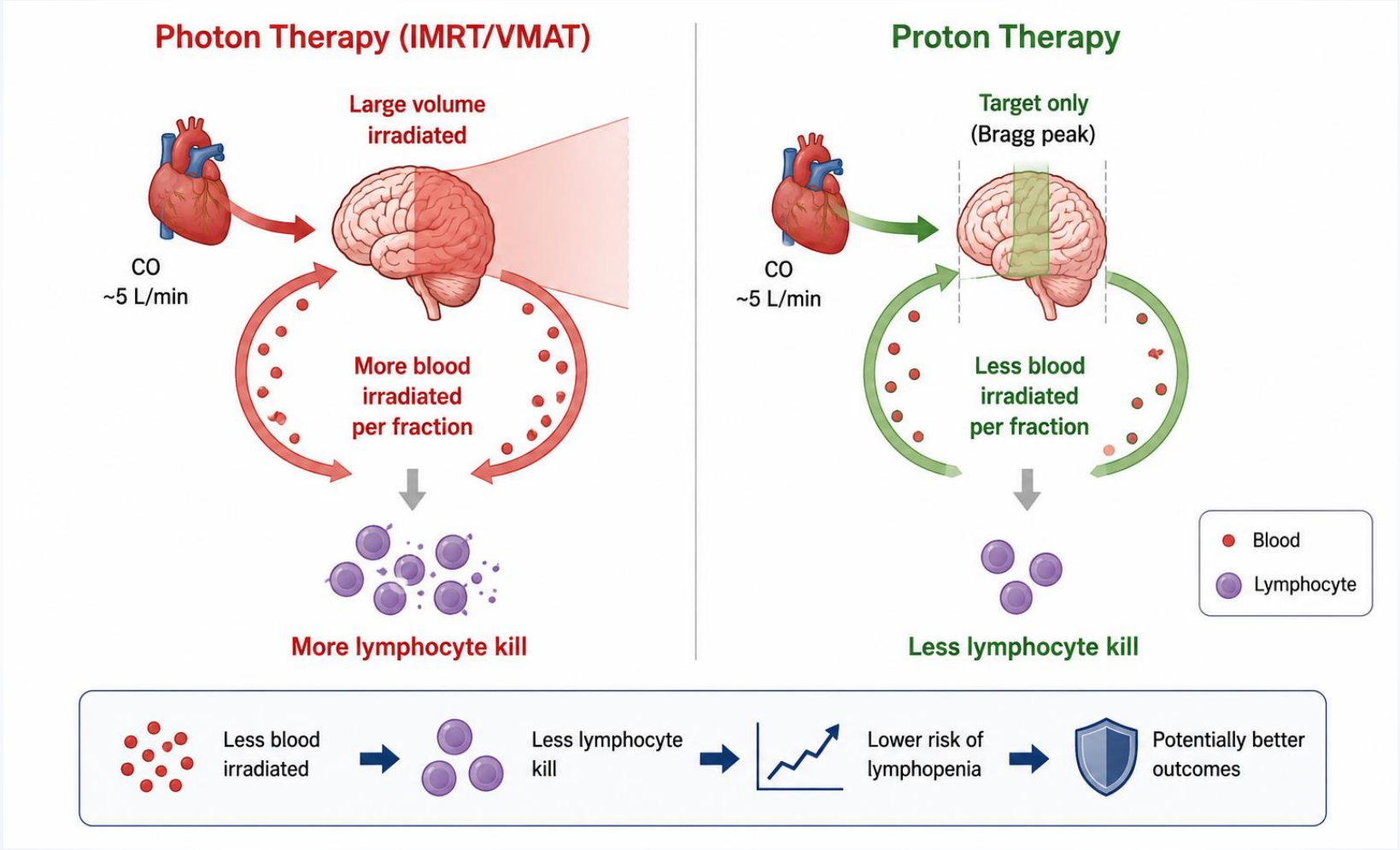
What about protons for High Grade Gliomas?

Neuro-Oncology
23(2), 284–294, 2021 | doi:10.1093/neuonc/noaa182 | Advance Access date 5 August 2020

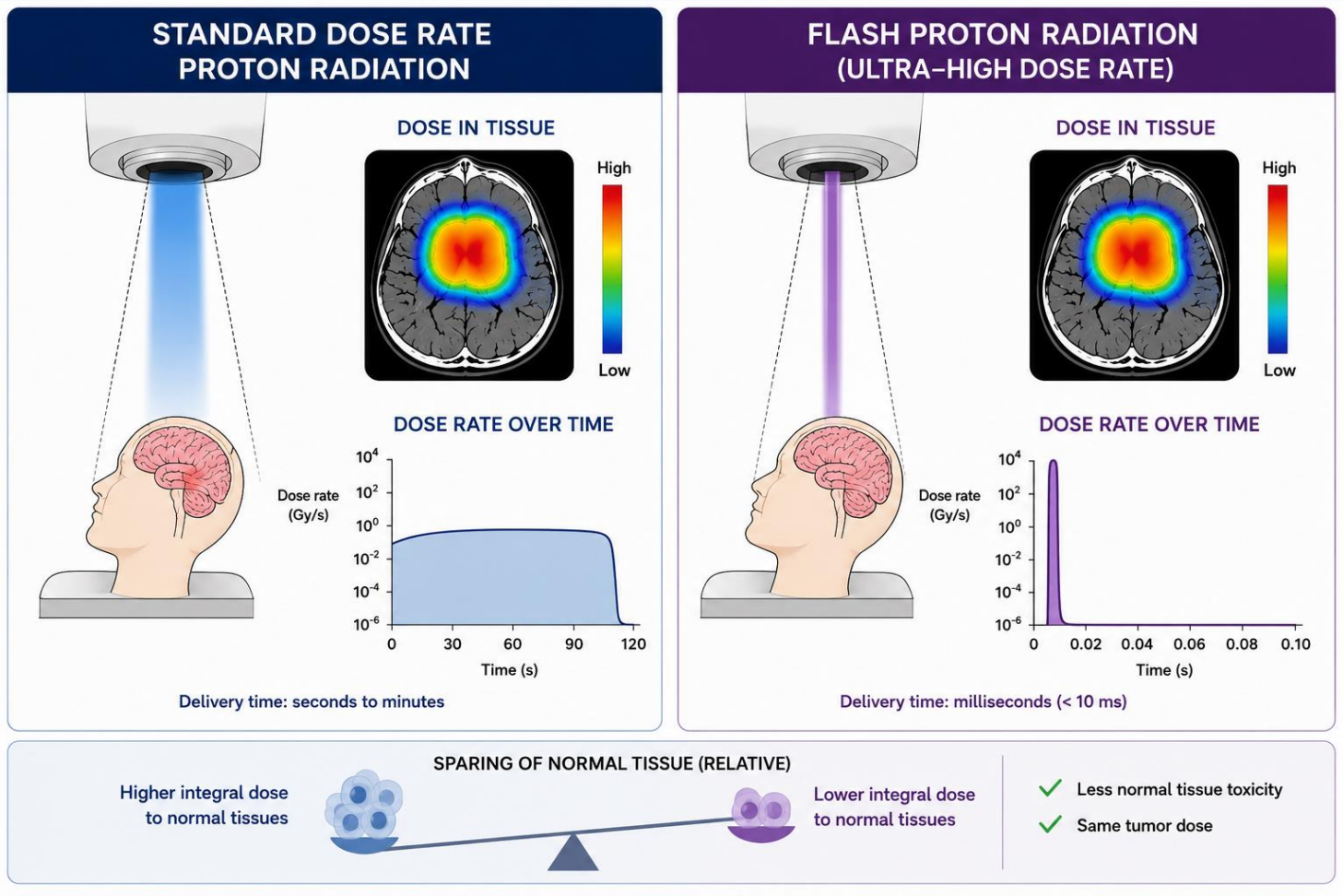




What do protons reduce lymphopenia?



What about FLASH?



What about protons for High Grade Gliomas?

Bottom Line:

- Does not improve neurocognitive outcomes
- Reduces lymphopenia (level I evidence)
- **Does it improve survival – to be determined**

What about protons for High Grade Gliomas?

NRG BN-001

Photon Dose Escalation arm 60 Gy vs 75 Gy -> no difference in OS

Proton Dose Escalation arm ->

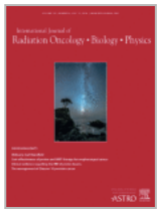
- 2 years absolute OS **6.8%** favoring the 75-Gy arm over the 60-Gy arm (49.9% vs 43.1%)
- 3 years OS difference of **4.6%** (30% vs 25.4%)

What about for brain metastases?

Bottom Line:

- Excellent l th no clear adva
- Potential f

International Journal of Radiation Oncology*Biology*Physics
Volume 101, Issue 4, 15 July 2018, Pages 820-829



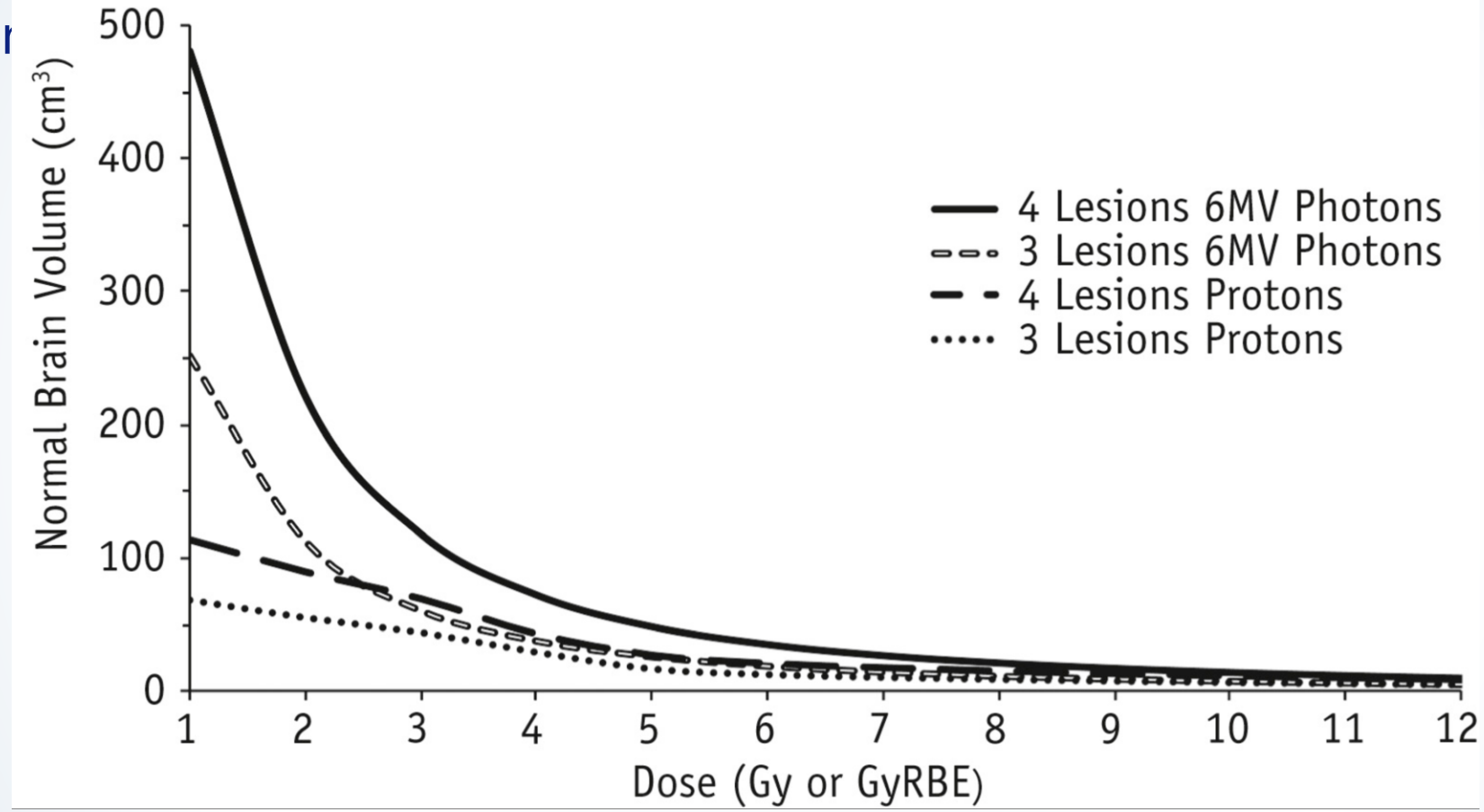
Clinical Investigation

Proton Stereotactic Radiosurgery for Brain Metastases: A Single-Institution Analysis of 370 Patients

Katelyn M. Atkins MD, PhD *, Itai M. Pashtan MD †, Marc R. Bussière MSc ‡, Kylie H. Kang BS §, Andrzej Niemierko PhD ‖, Jillian E. Daly BS ‡, Thomas M. Botticello BS ‡, Molly C. Hurd ¶, Paul H. Chapman MD #, Kevin Oh MD ‡, Jay S. Loeffler MD ‡, Helen A. Shih MD, MS, MPH ‡

What about for brain metastases?

- 12-mo



Conclusions

- Protons have a clear indication for leptomeningeal disease
- Serious consideration given for younger patients with LGG
- Possible treatment option for HGG