

Radiation for Gliomas : Where does proton therapy fit in?

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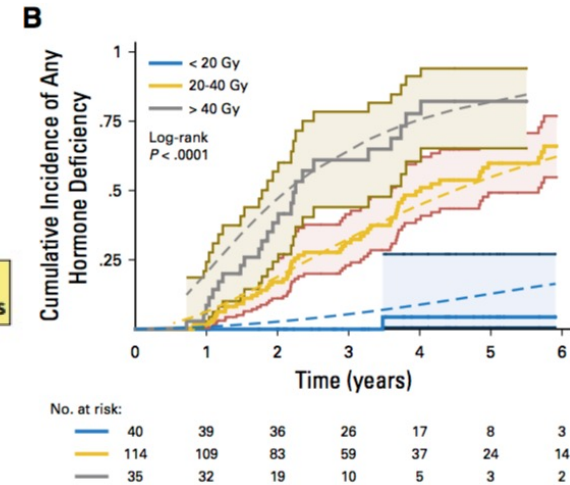
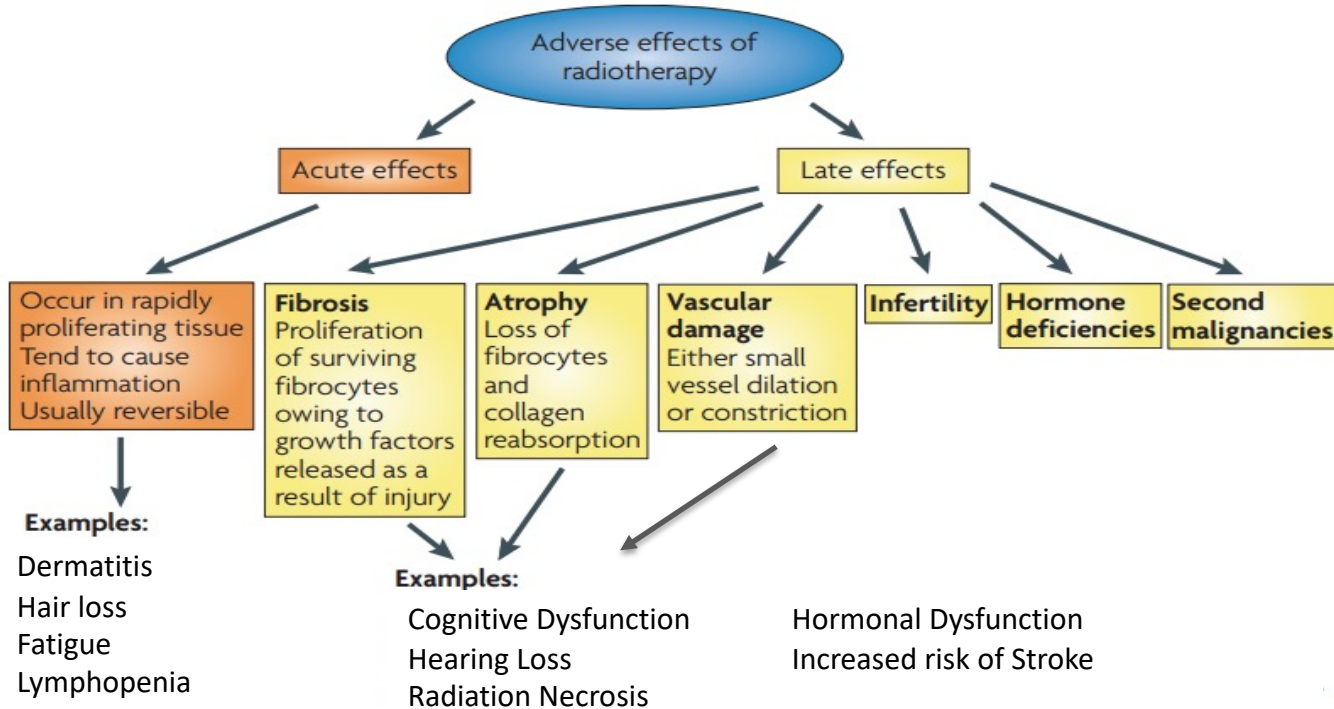
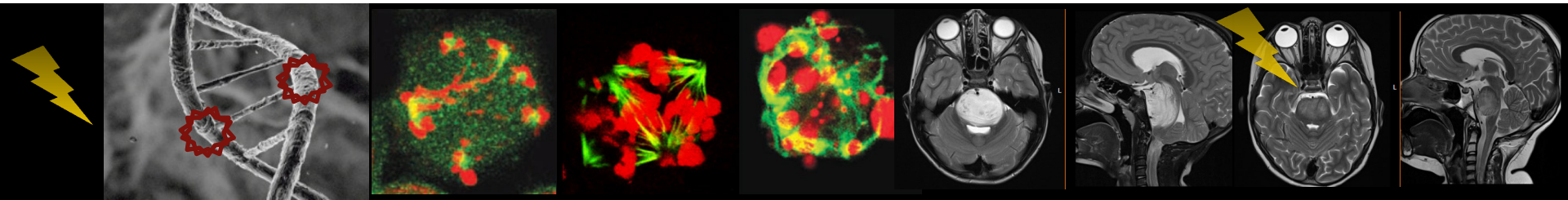


Radiation for Gliomas

- Radiation + Chemotherapy is standard of care for most gliomas
- Radiation with Photon Therapy (X-Rays) is an excellent treatment
 - Mature technology
 - Vast experience, widely available
 - Safety and efficacy well defined
 - Cost effective



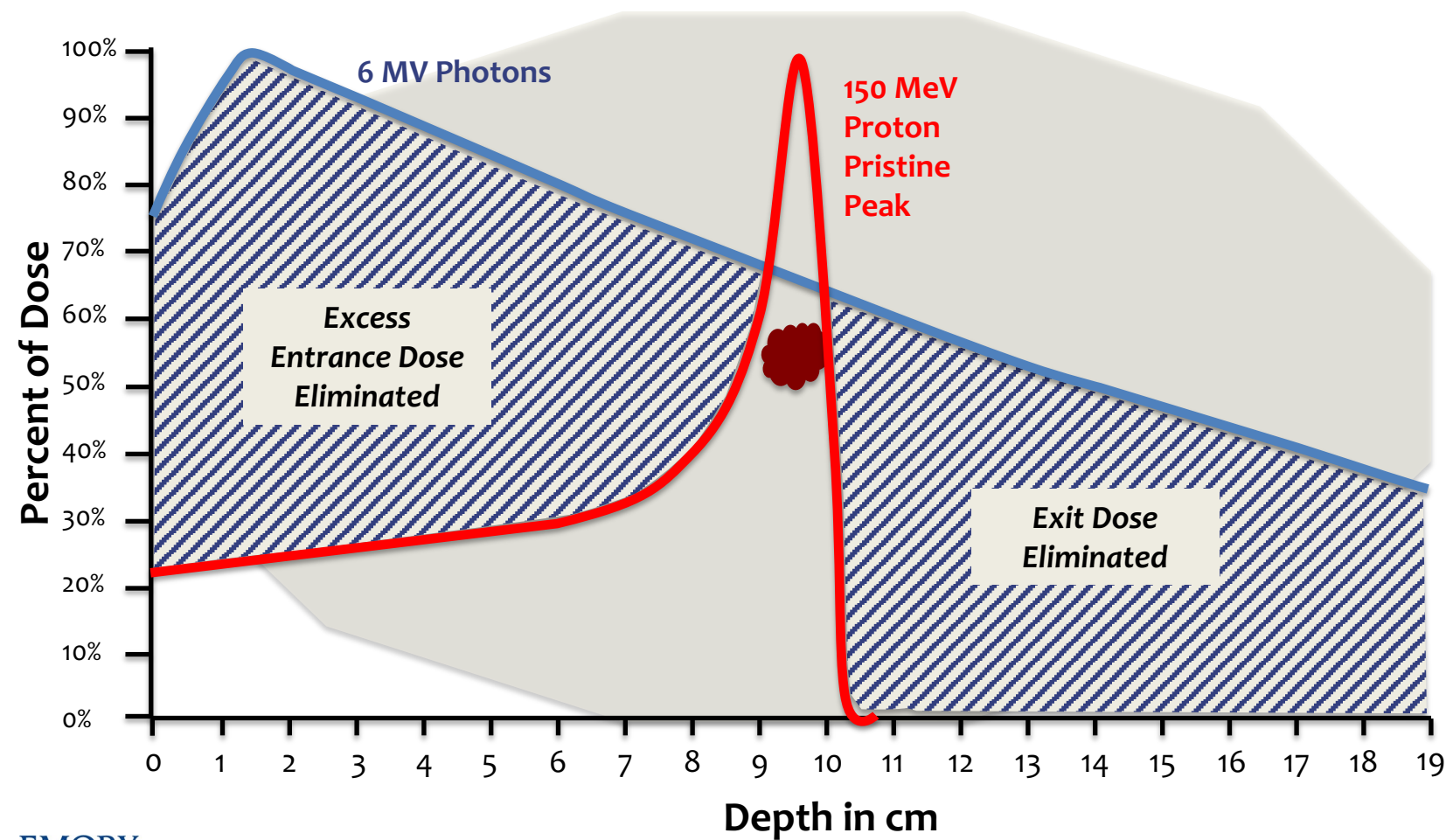
Radiation Therapy



Eriksson & Stigbrand. Tumor Biol 2010; 31:363-372
 Vatner et al. J Clin Oncol 2018; 36 (28):2854-62
 Barnett et al. Nature Rev Ca 2009;9:134-142



Percent Depth Dose: Photons vs Protons

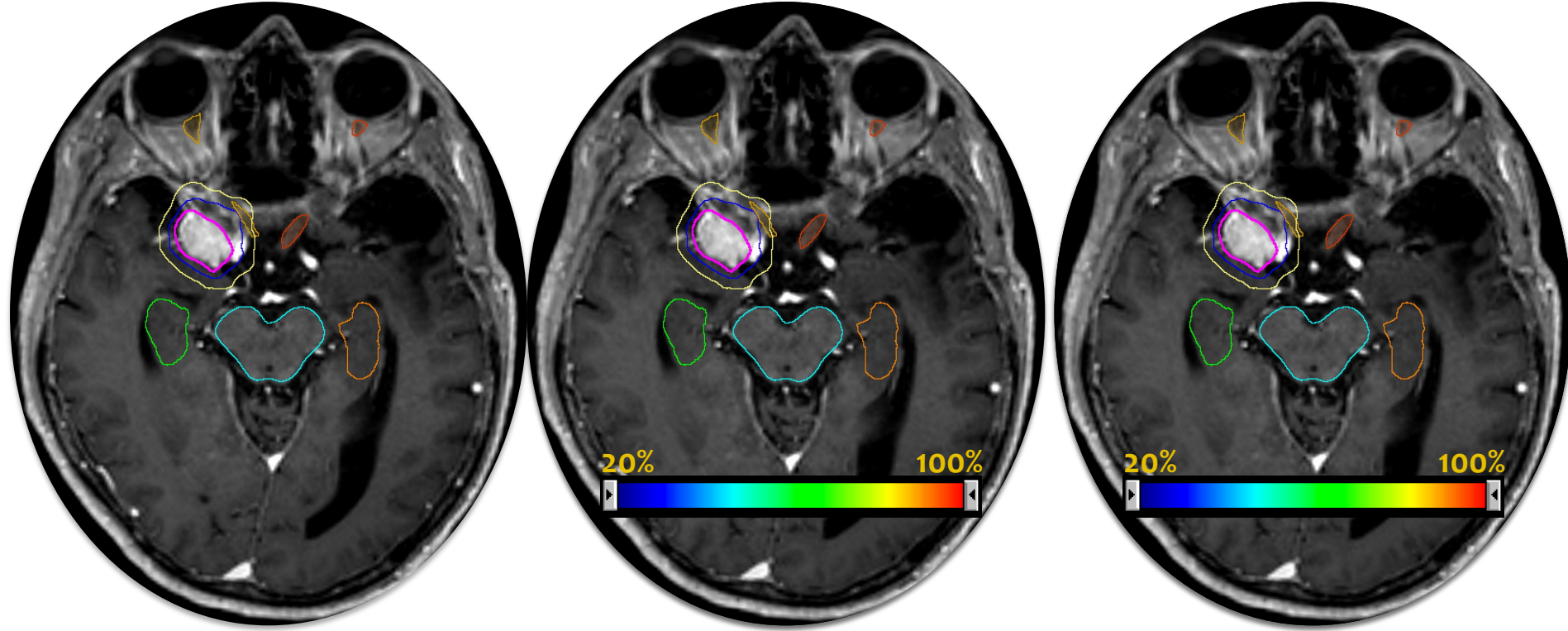


Proton versus X-ray Therapy

Sphenoid Wing Meningioma

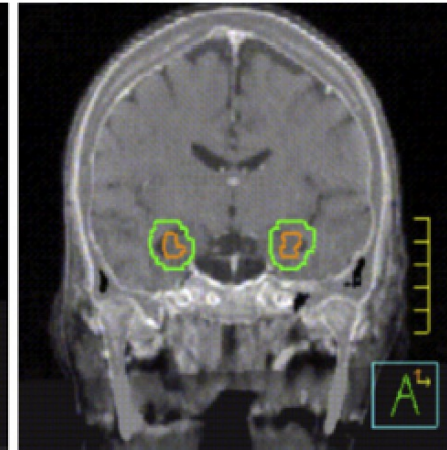
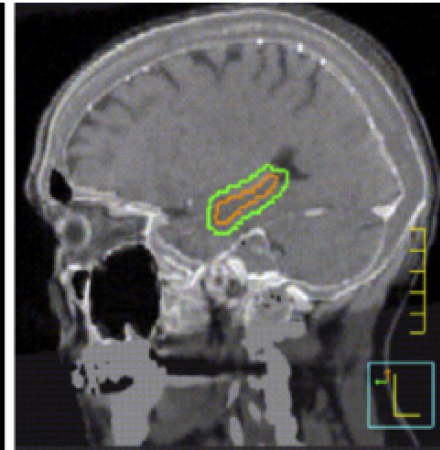
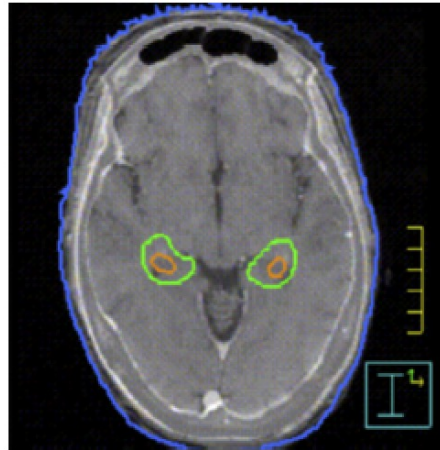
Lateral 6 MV X-ray Field

Lateral Proton Field



Hippocampus

- In temporal lobe of brain
- Learning and memory
- Spatial navigation
- Emotional behavior

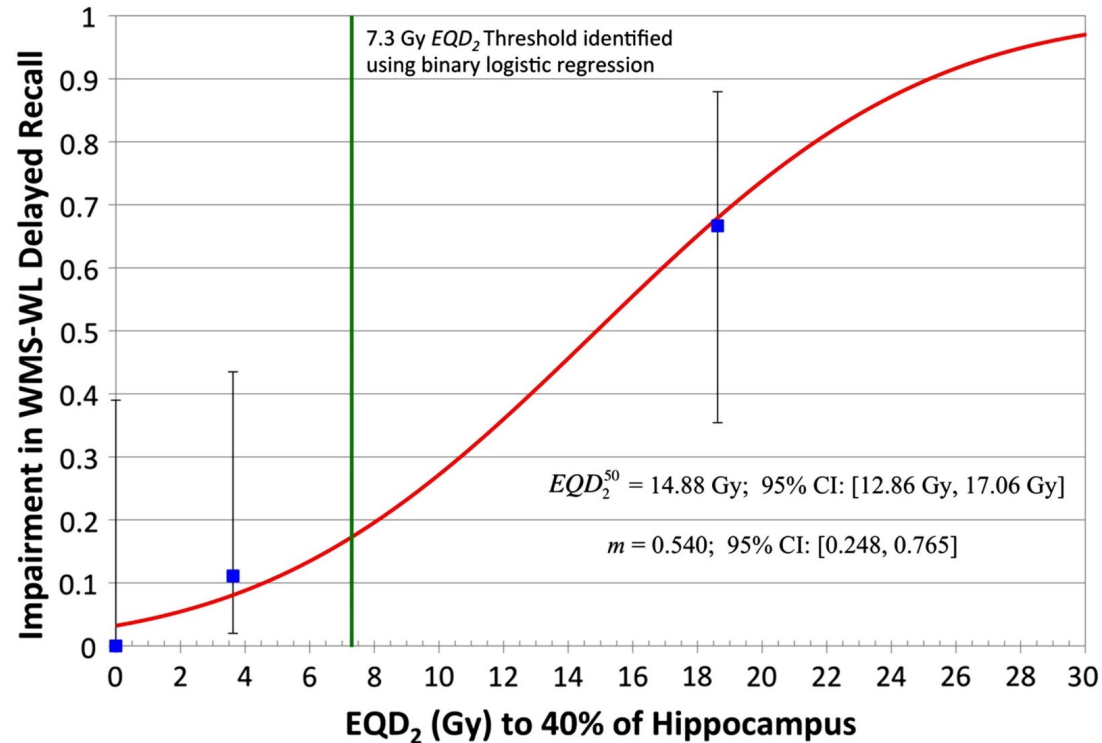


Gondi et al IJROBP 78(4):1244-1252, 2010



Hippocampal Dosimetry Predicts Neurocognitive Function Impairment

- Prospective evaluation
- Adult with benign tumors and **low-grade gliomas**
- 50.4 – 54 Gy
- **A relatively low dose of radiation to 40% of the bilateral hippocampus was associated with long-term list-learning delayed recall**



Gondi et al IJROBP 85(2):348-354, 2013



Clinical Case: Oligodendroglioma

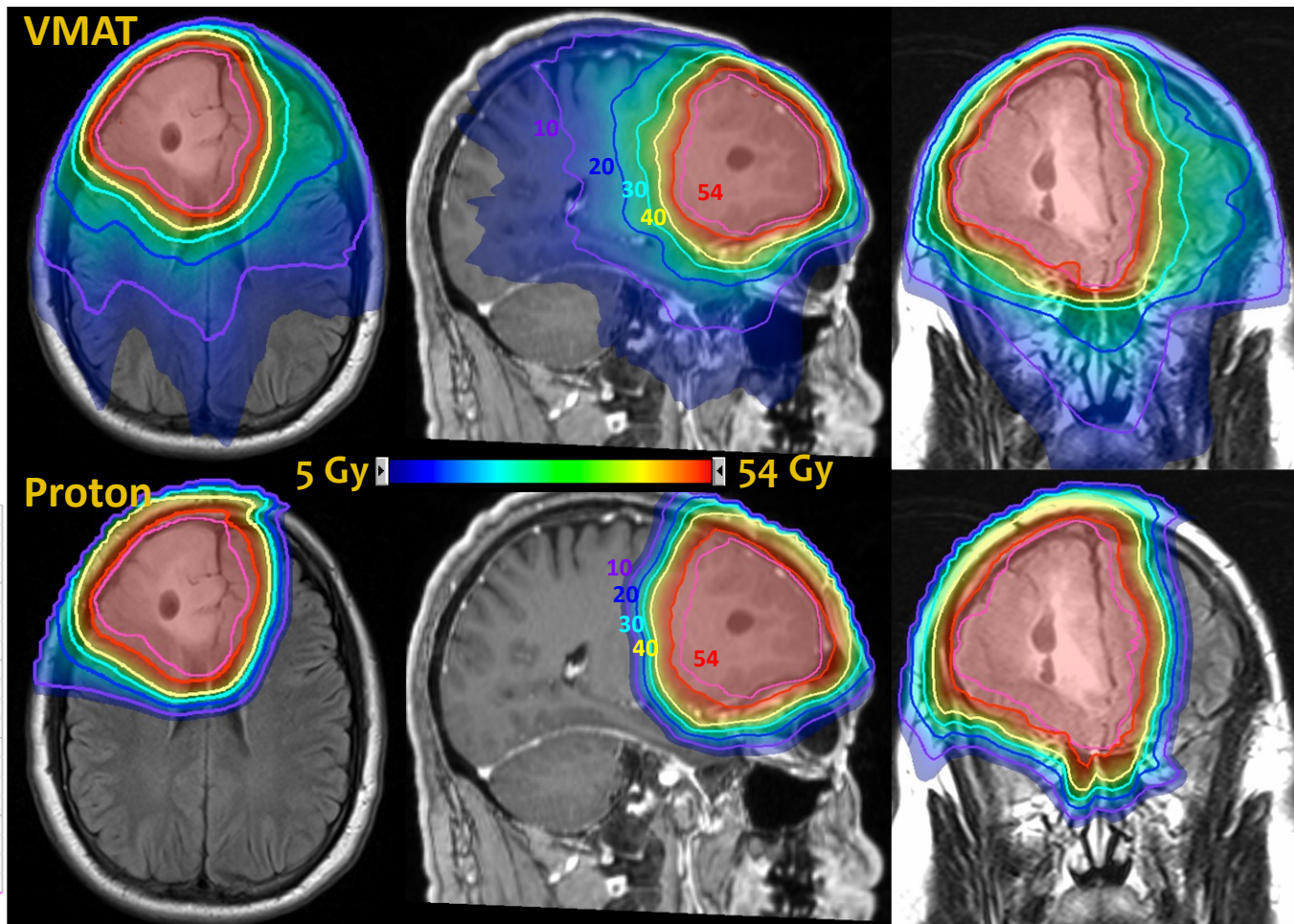
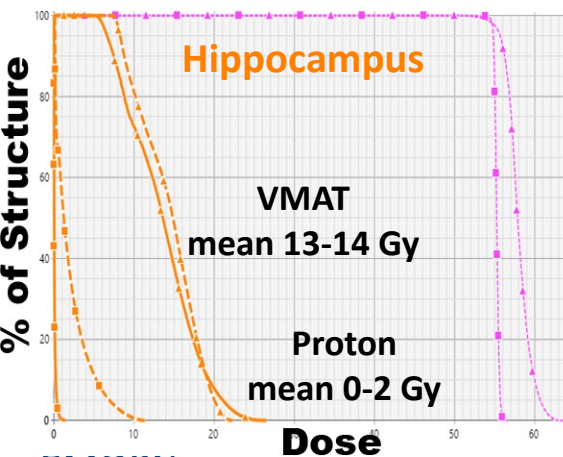
Diagnosis: oligodendroglioma
1p19q codeleted

Surgery: biopsy
Chemotherapy: TMZ
Radiation: 54 Gy to T2

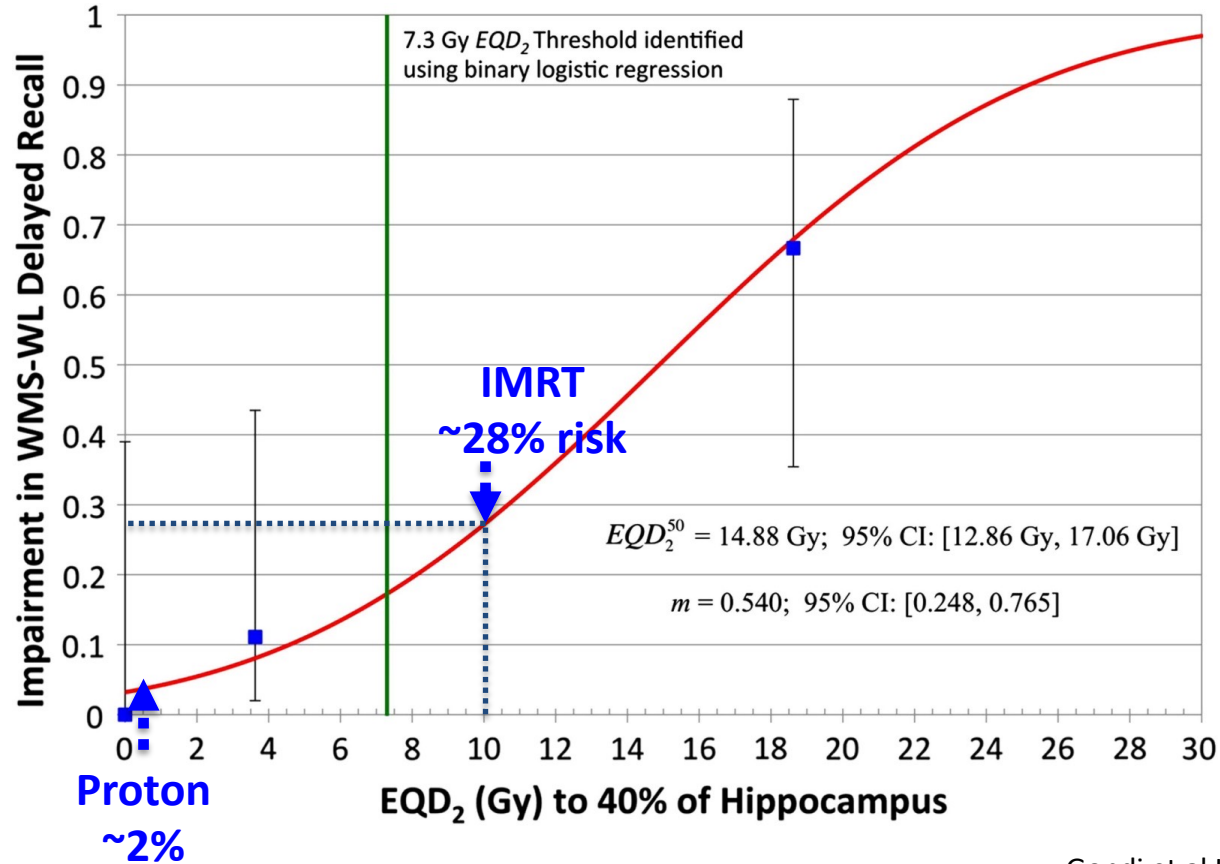
Hippocampal sparing

VMAT EQD₂ = 10 Gy₂ to 40%

Proton EQD₂ < 1 Gy₂ to 40%

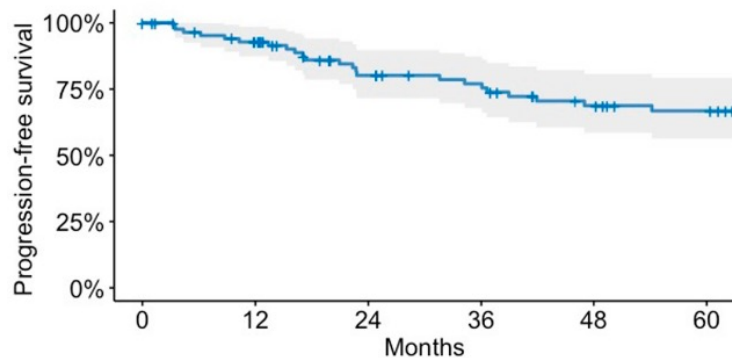
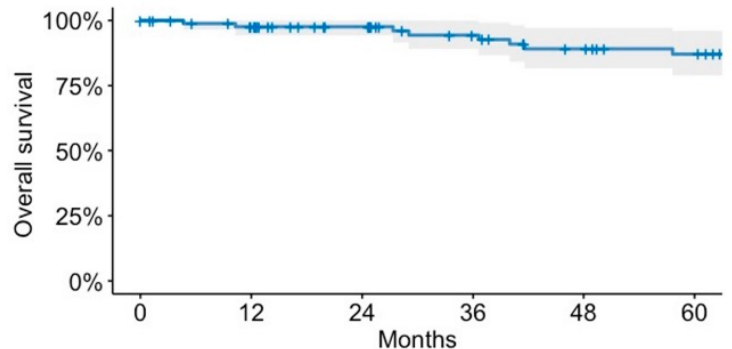


Proton therapy reduces risk of long-term memory impairment

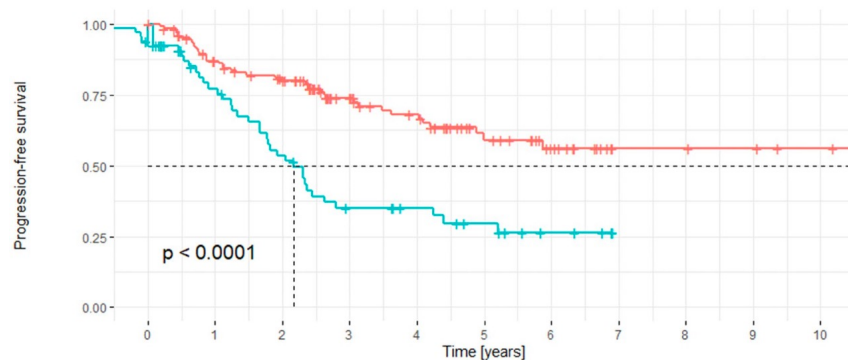
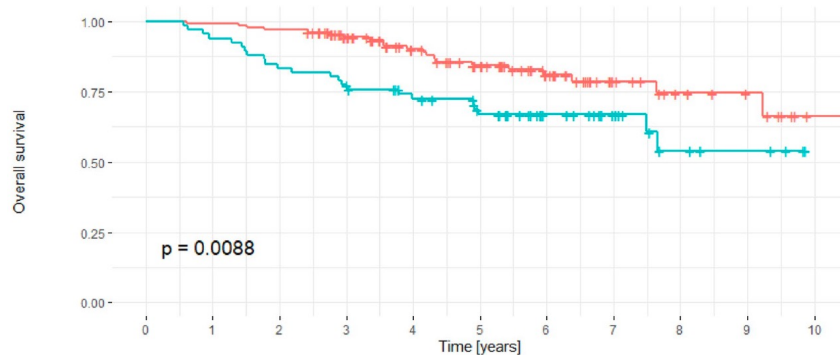


Protons for Gliomas: Clinical Outcomes

89 Patients with Low-Grade Gliomas
PSI, Switzerland



194 Patients Grade 2-3 IDH+ Gliomas
Heidelberg, Germany

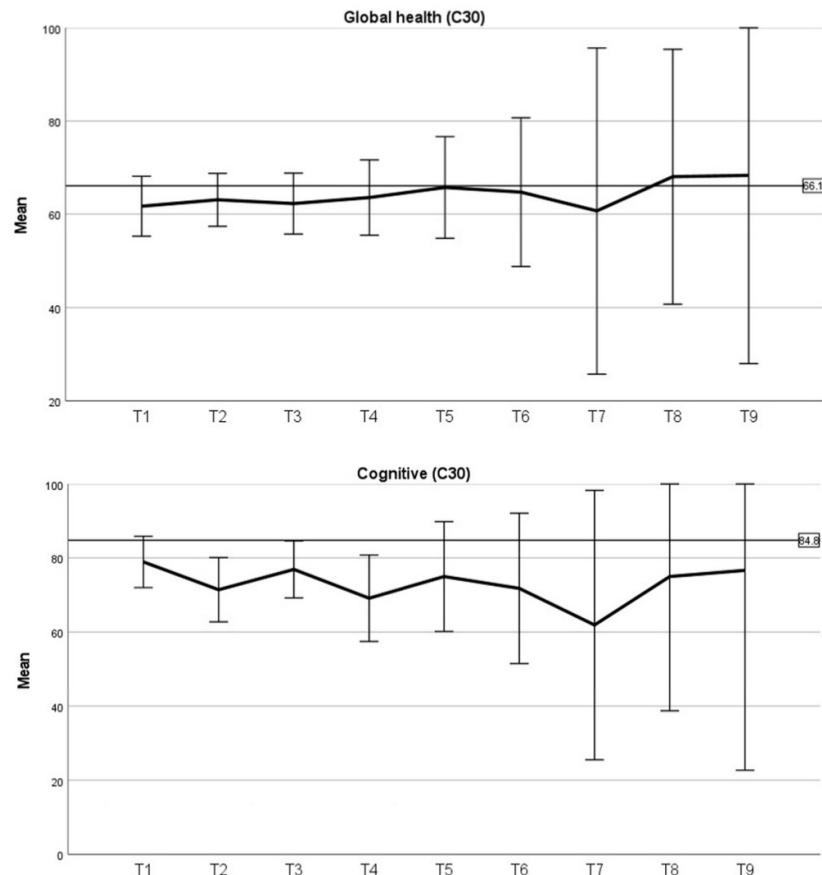


Strata —+— WHO grade 2 —+— WHO grade 3

Stable Neurocognitive Function and QOL after Proton Therapy

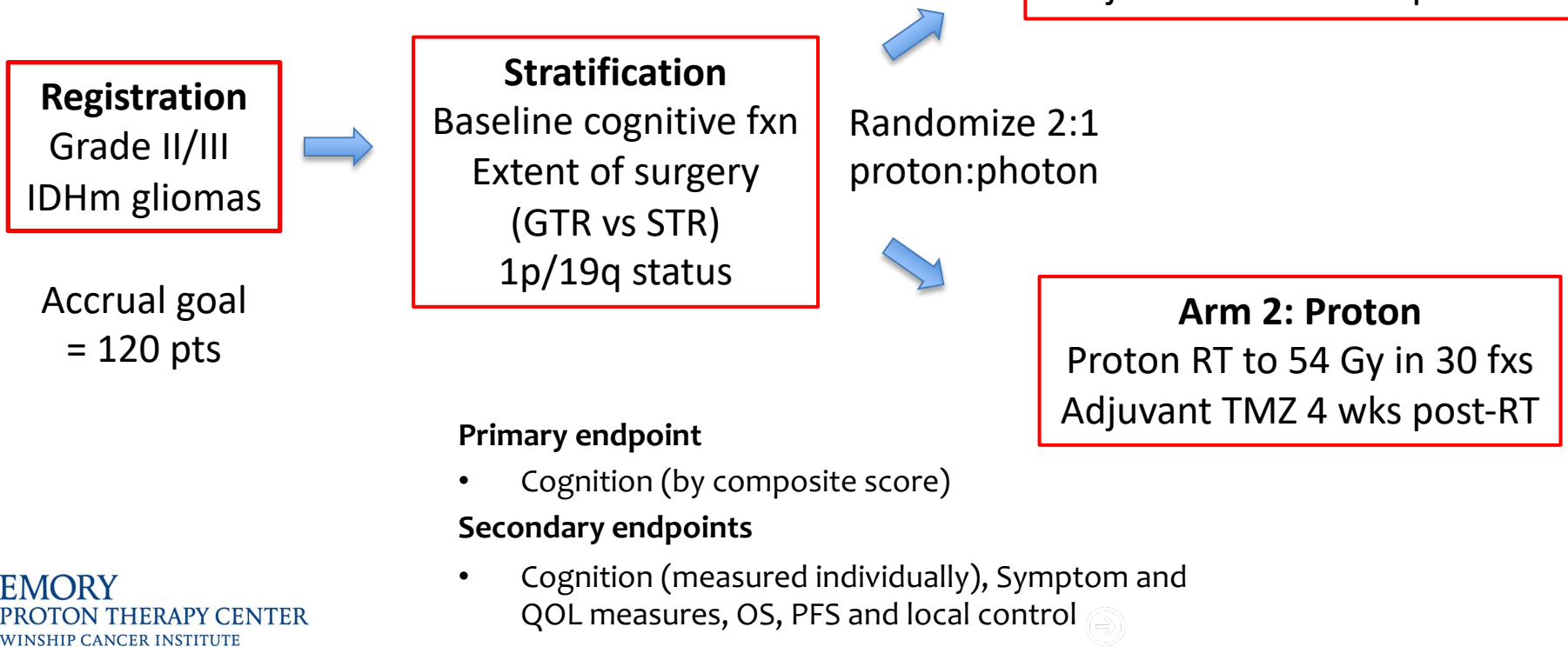
Neurocognitive performance following PRT.

	Baseline \pm SD	Mean change per year \pm SE	P
Intellectual	0.47 \pm 0.56	0.08 \pm 0.04	0.044
Visuospatial	0.54 \pm 0.69	0.14 \pm 0.04	0.003
Language	-0.50 \pm 2.19	0.05 \pm 0.09	0.549
Attention & working memory	0.24 \pm 0.49	0.03 \pm 0.04	0.502
Processing speed	0.06 \pm 0.83	0.10 \pm 0.05	0.076
Executive function	-0.18 \pm 0.62	0.13 \pm 0.06	0.059
Verbal memory	-0.72 \pm 1.19	0.06 \pm 0.06	0.364
Visual memory	-0.81 \pm 1.41	0.02 \pm 0.17	0.921
Clinical Trial Battery	-0.35 \pm 0.78	0.13 \pm 0.05	0.025
<i>Emotional</i>			
Beck anxiety	8.9 \pm 8.0	-0.55 \pm 0.33	0.105
Beck depression	12.7 \pm 9.9	-0.10 \pm 0.50	0.846
<i>Quality of life</i>			
FACT-G	77.0 \pm 18.4	1.70 \pm 0.96	0.093
FACT-fatigue	32.7 \pm 14.8	1.03 \pm 0.42	0.017
FACT-Br	131.0 \pm 28.5	1.64 \pm 1.03	0.133



Low-grade glioma: NRG-BN005

Will there be less toxicity with proton therapy in treatment of patients with lower grade gliomas?

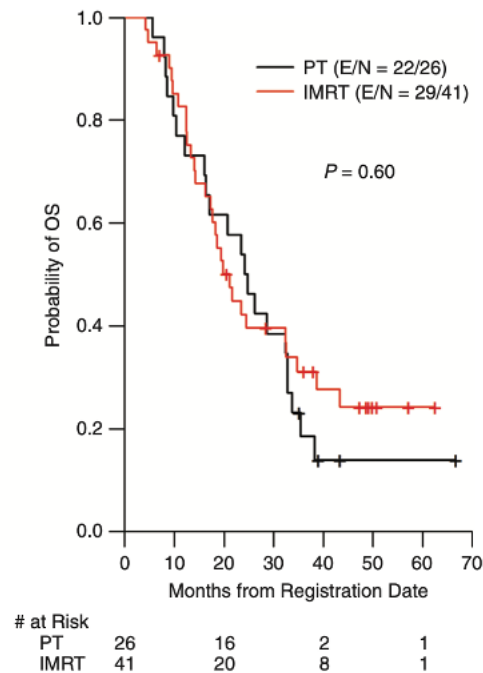
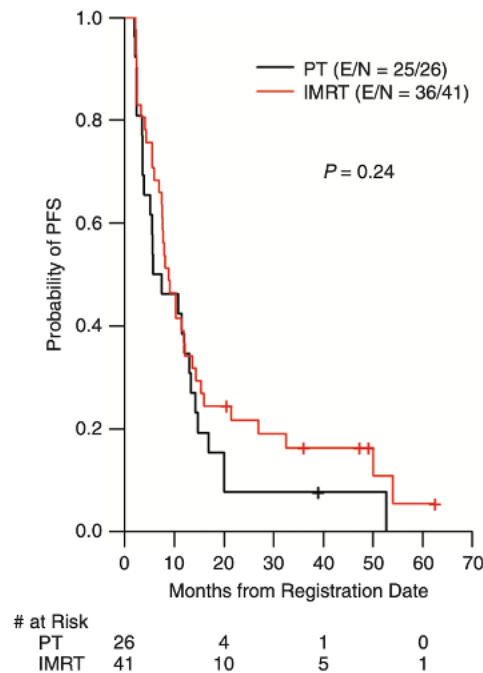


Proton Therapy for GBM

90 Patients
Newly Diagnosed GBM
MD Anderson
60 Gy

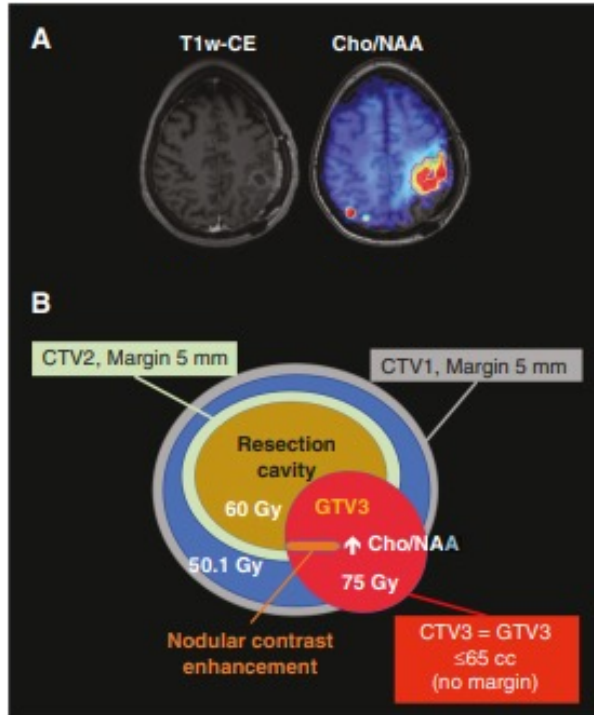
Proton (n=42)
27 treated per
study

X-ray (n=48)
40 treated per
study

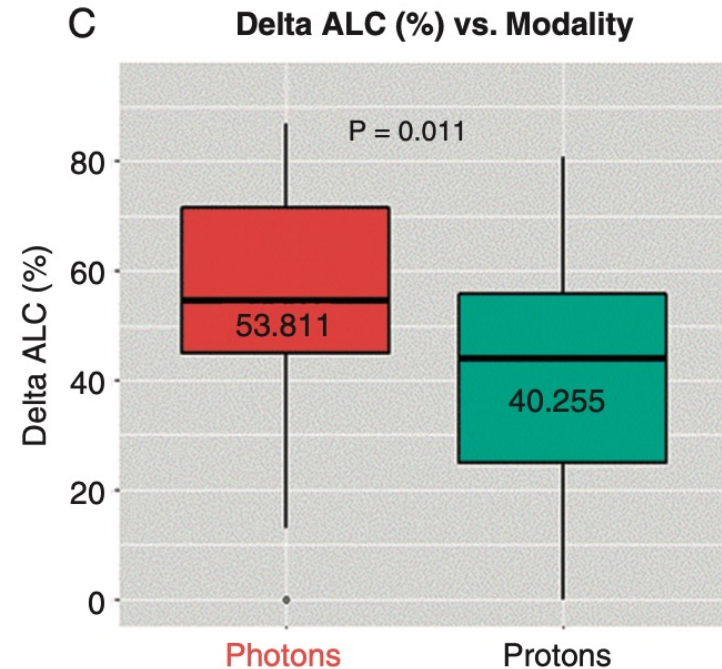


Proton Therapy for GBM: New Opportunities

Dose Escalation



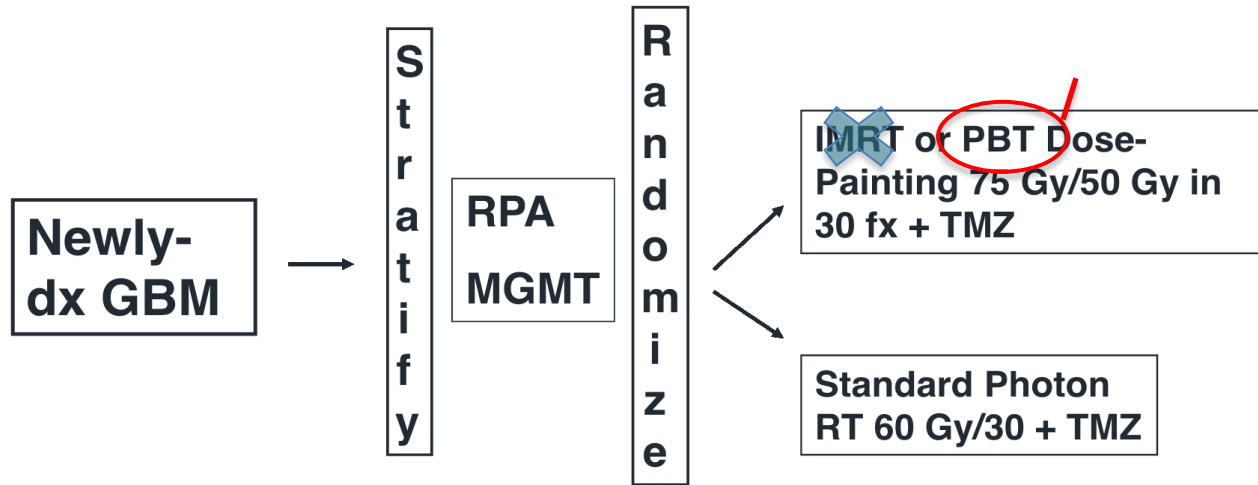
Reduced Lymphopenia



GBM: NRG-BN001

NRG-BN001: Phase IIR Trial HypoFx Dose-Esc IMRT or proton therapy vs. conventional photon RT with TMZ in newly diagnosed glioblastoma

Basic Eligibility: Newly dxed GBM; Residual tumor/postop cavity $\leq 5\text{cm}$; KPS ≥ 70



Sample Size: 576 patients

Primary endpoint: Overall survival

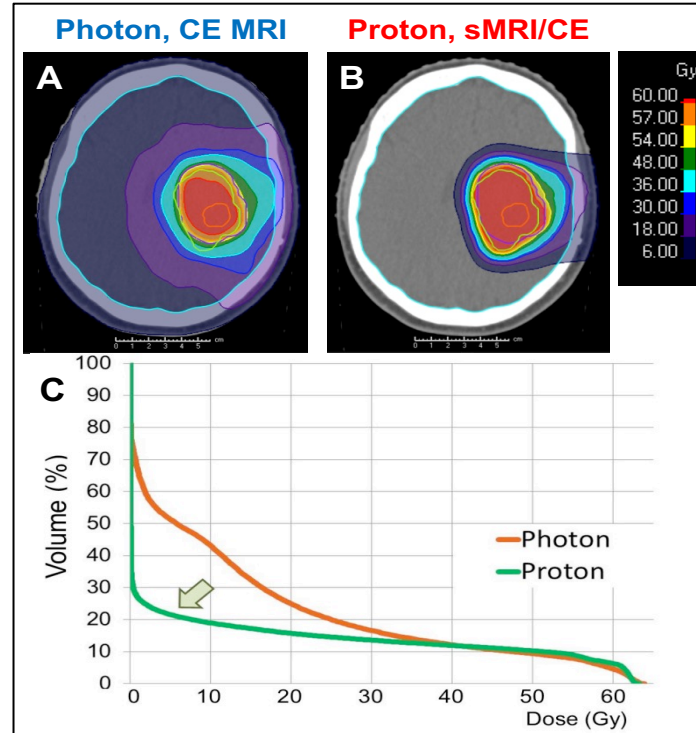
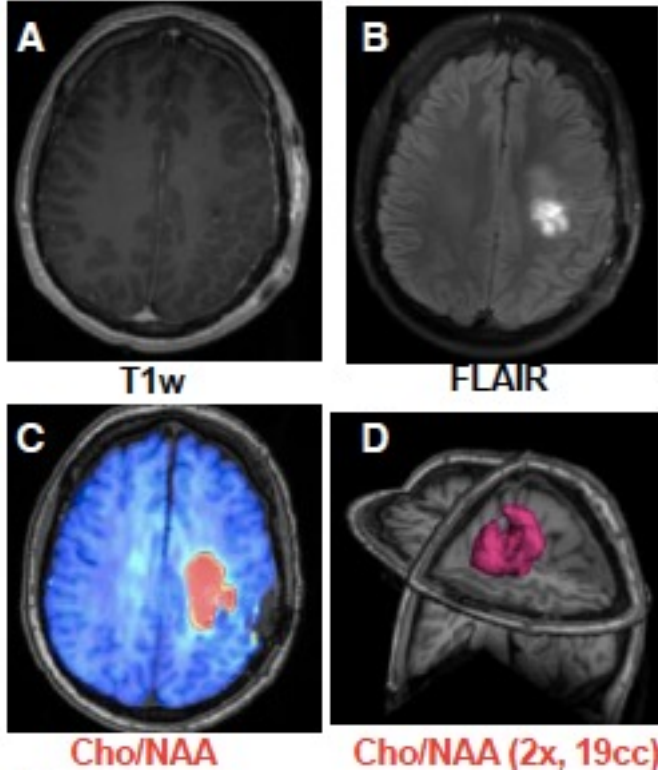
NRG
ONCOLOGY™

Basic Statistical Design:

Median survival 16 months with standard photon RT vs. 22.2 months with dose-esc IMRT or PBT



Pediatrics: sMRI guided proton therapy for pediatric HGG



Endpoints:

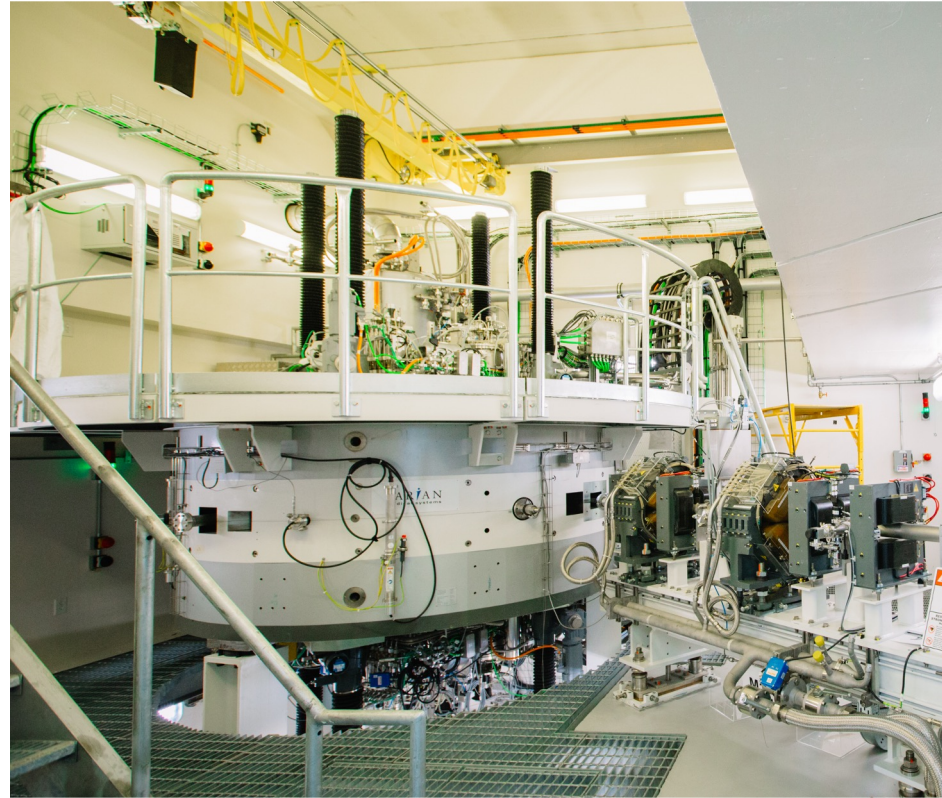
- PFS
- Failure Pattern
- OS
- Toxicity
- HRQOL
- Imaging correlates

Eligibility:

- HGG
- Age <22 years

Proton Therapy for Gliomas

- Ideal radiation modality for younger patients with favorable prognosis to minimize side effects
- May provide opportunity for RT dose escalation in GBM
- Safer option for re-irradiation in many cases
- Clinical trials and data collection are ongoing





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Thank you!
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