The Role of Proton Therapy in Modern Radiation Oncology Practice

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Disclosures

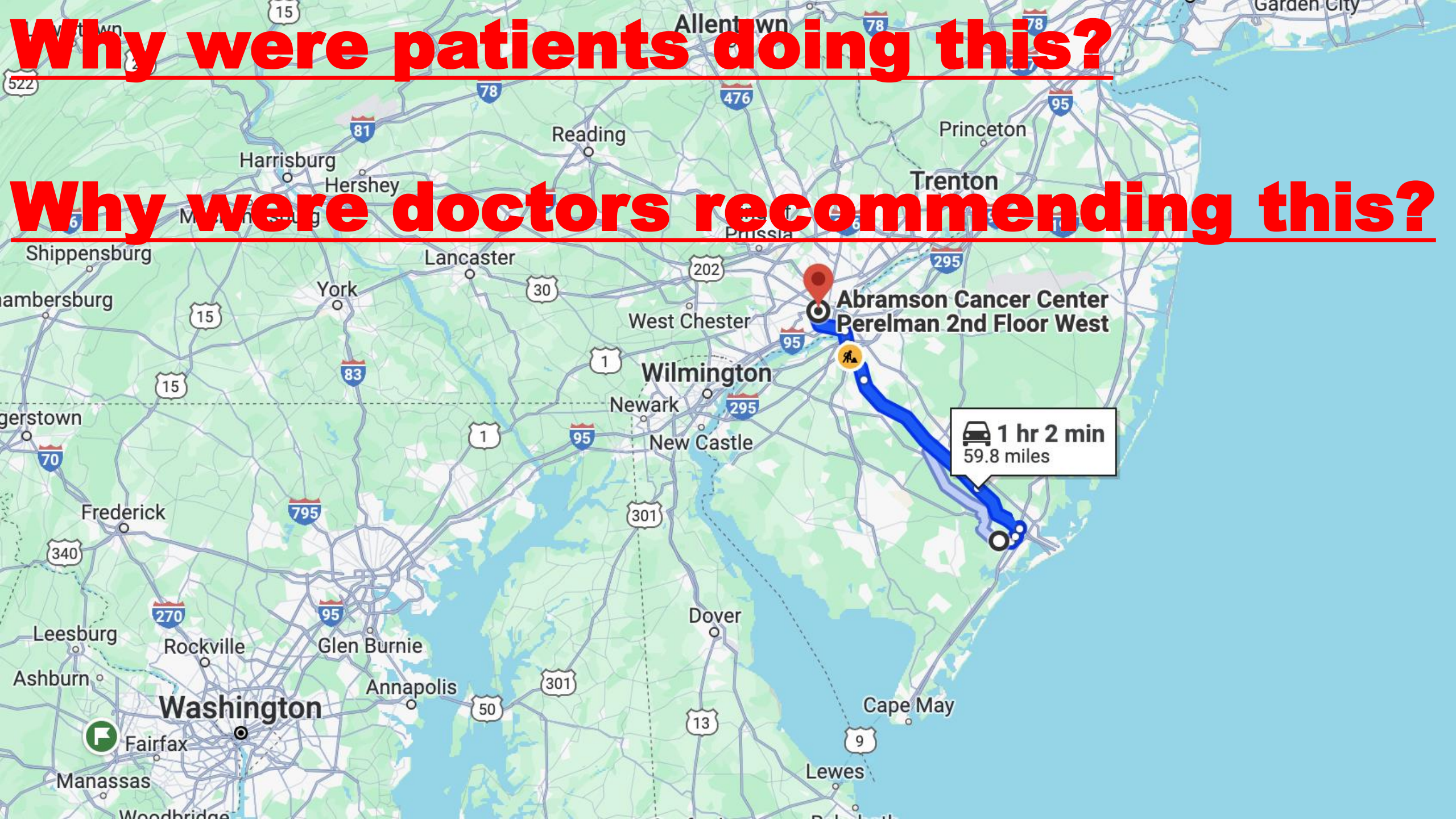
None

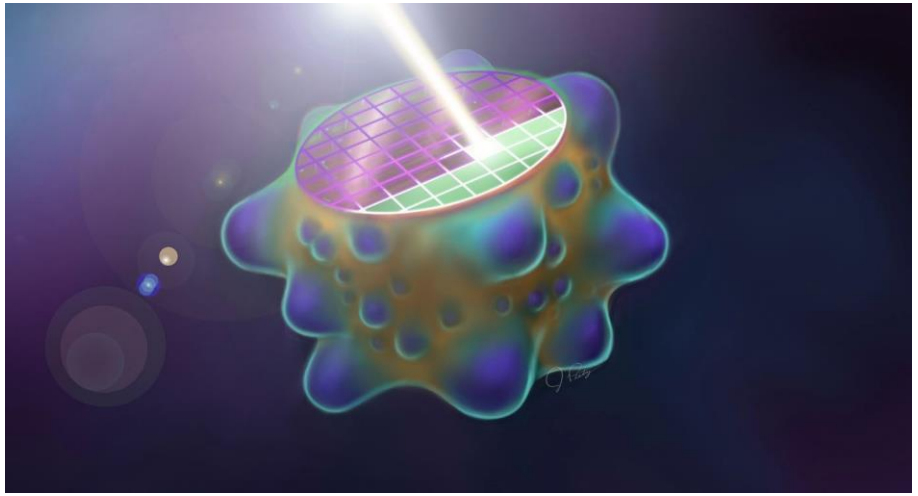
Overview

- Why Proton Therapy?
- Commonly accepted indications for Proton Therapy
  - Pediatric Cancers
  - Mediastinal Cancers
  - Spine / Base of Skull tumors
  - Brain tumors
  - Esophageal Cancer
  - Liver Cancer
- Special Considerations
  - Genetic Mutations
  - Re-Irradiation
- Patient Experience and QOL

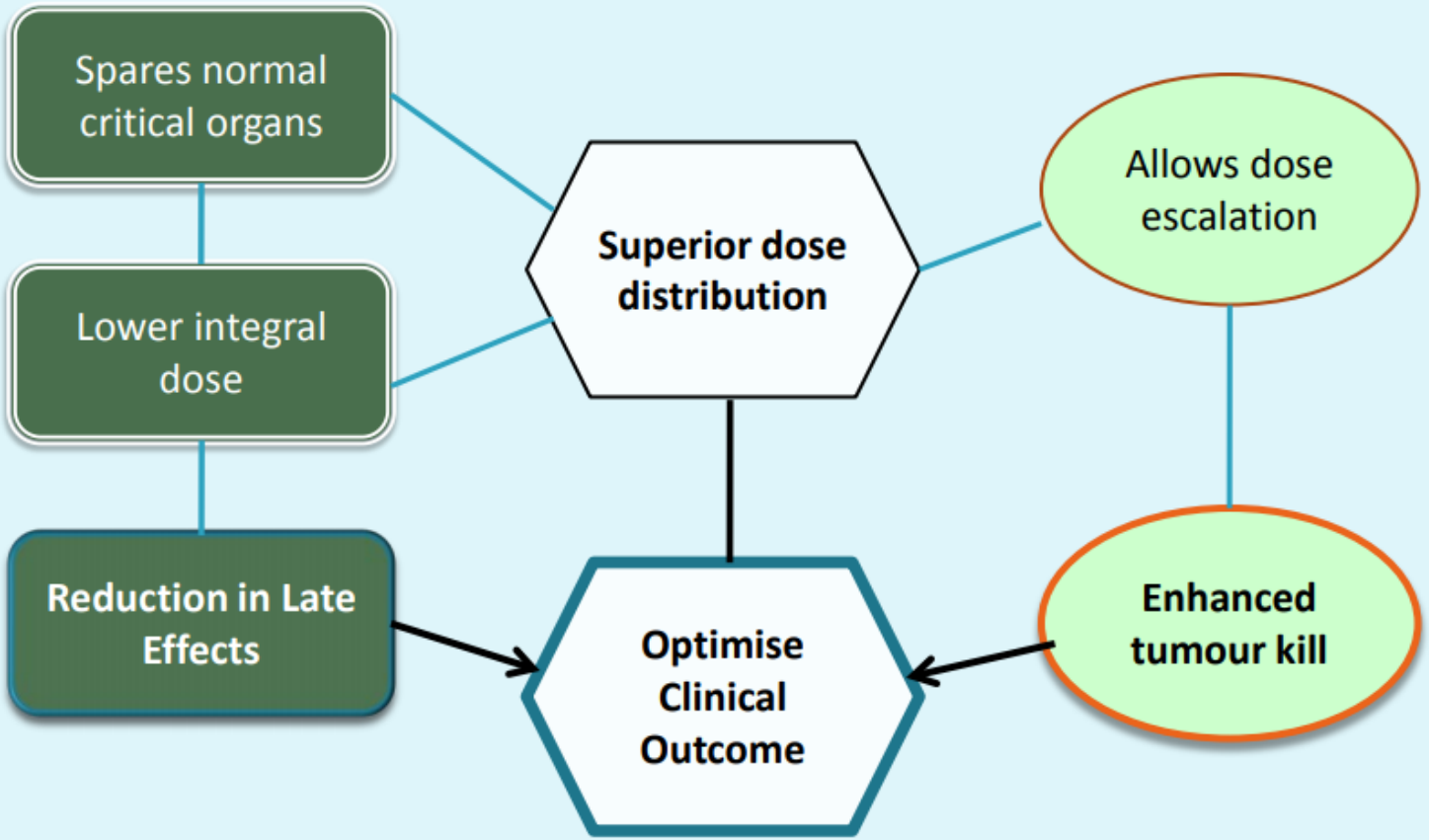
Why were patients doing this?

Why were doctors recommending this?



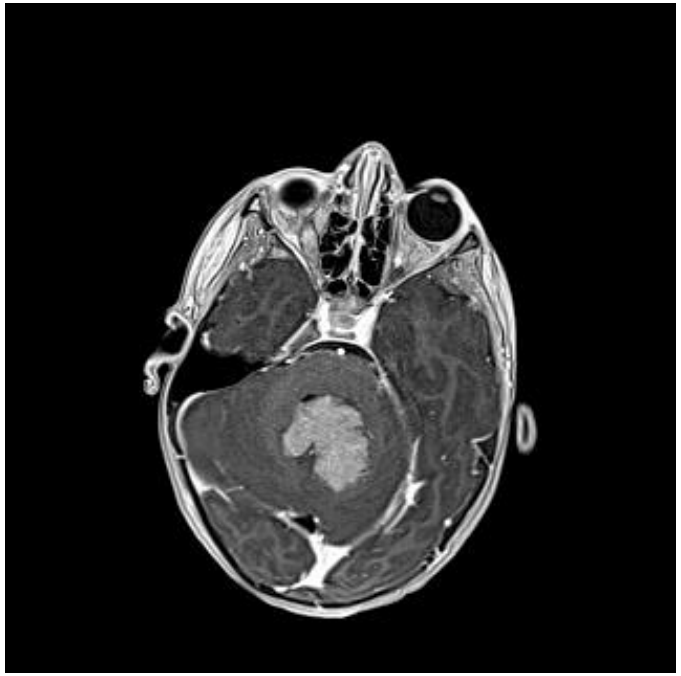


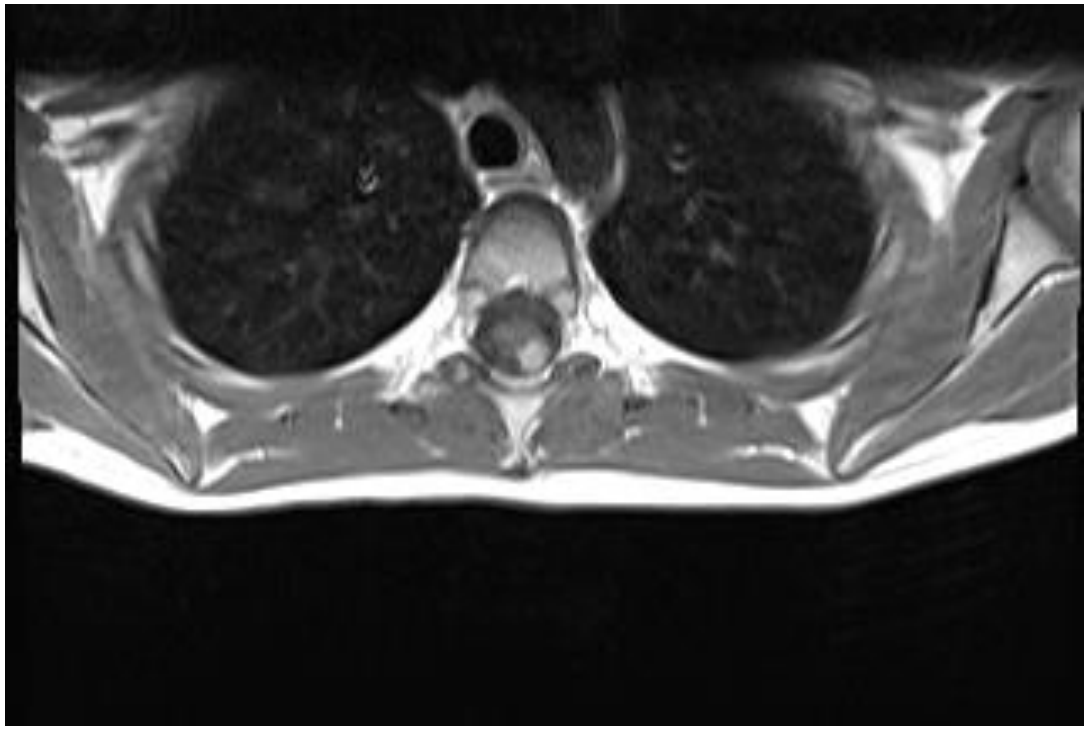
Potential Clinical Advantages of Protons



Pediatric Cancers

- 4 yo who presents with ataxia x 3 days accompanied by intermittent nausea and vomiting and headaches that have been ongoing for 1 month





Pediatric Cancers

- Patient underwent maximal safe resection

The pathology showed focal anaplastic features, including cell-cell wrapping and nuclear molding are noted, but the overall **histologic appearance is that of a classic medulloblastoma**. The neoplastic cells are strongly and diffusely positive for synaptophysin and negative for GFAP and EMA. GFAP highlights the surrounding brain parenchyma.

The patients LP was **positive** for neoplastic cells

History of Cranial Spinal Irradiation

- Concept of CSI was advanced by Dr. Edith Paterson (Wife of Ralston Paterson)

- Prior to CSI, patients with medulloblastoma were treated with posterior fossa or whole brain RT

- She advocated treating the entire neuraxis after autopsies showed metastatic deposits to brain and spinal cord

- CSI in 27 patients resulted in a 3-year OS of 65% (Acta Radiologica 1953)

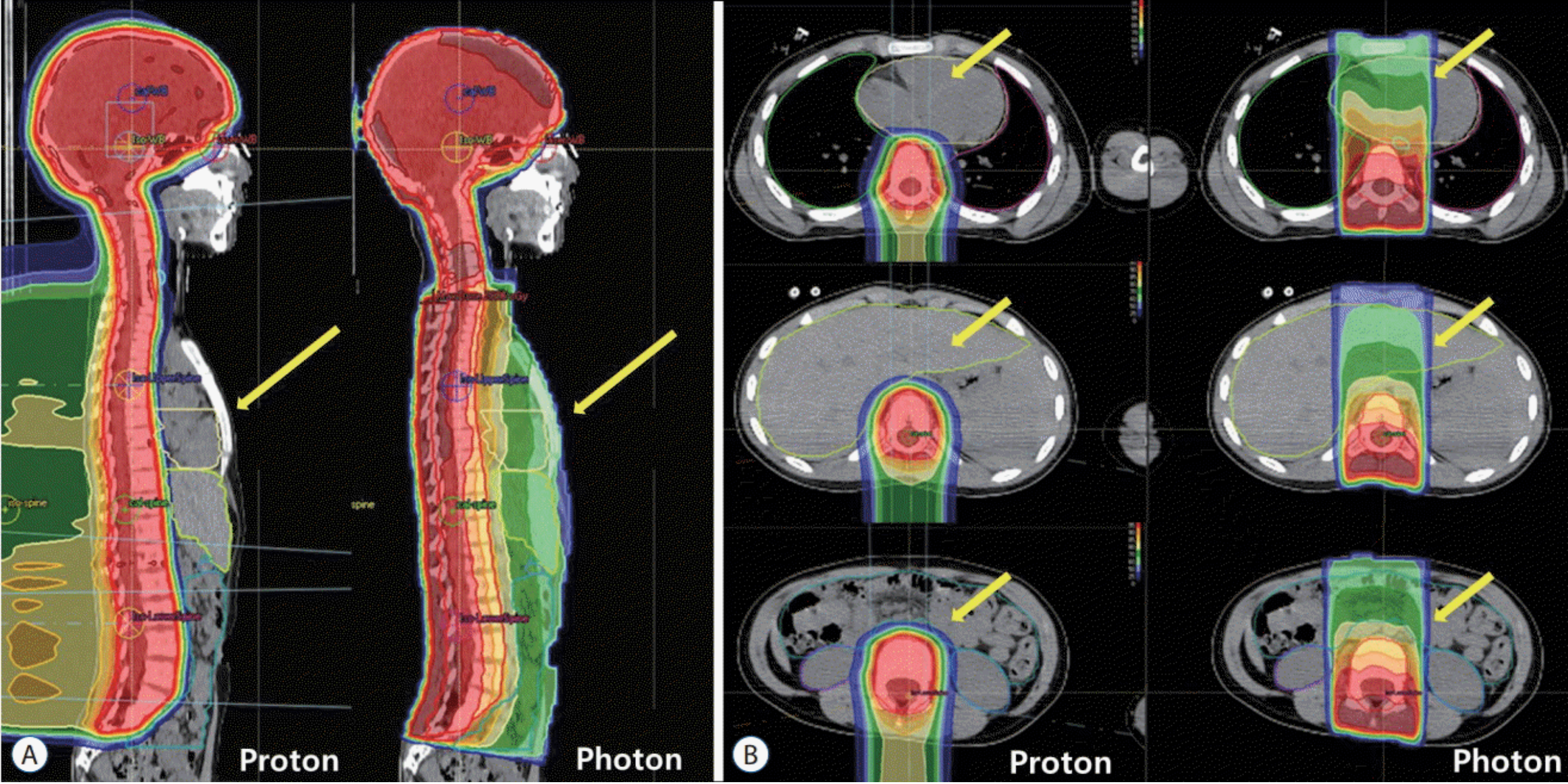
Inl. J Radialion OncologyBio/. Phys.. Vol. 13, pp. 1081-1091

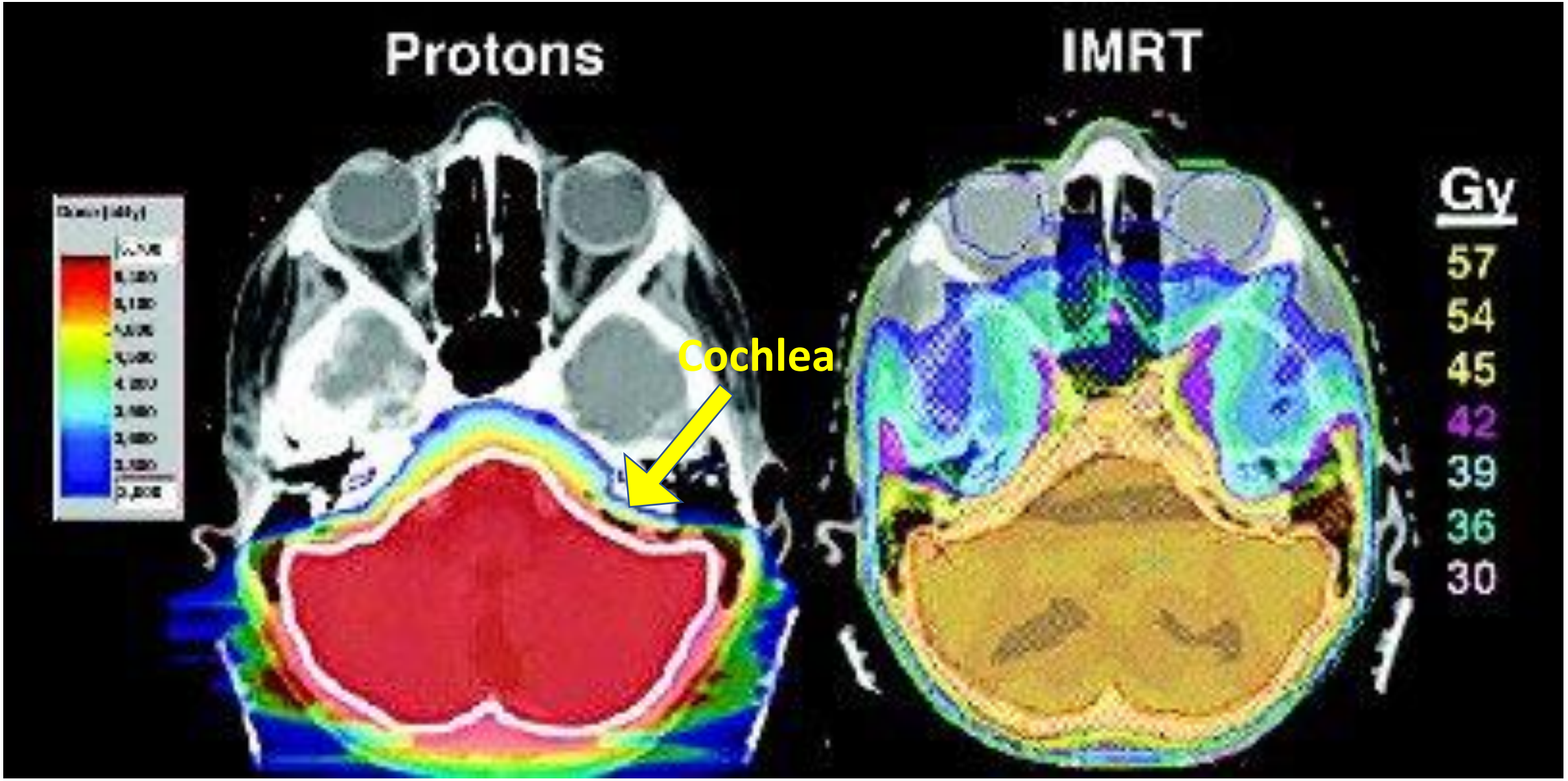
Late Effects

- Growth suppression
  - Vertebral growth stunted from CSI
  - Decreased GH production
- Endocrine
  - Hypopituitarism (GH, FSH/LH, TSH, and ACTH)
- Somnolence syndrome
- Cerebrovascular Accidents
- Ototoxicity
  - $\geq$ grade 3 in 50-60% if convention RT and cis
  - Cochlea V50<50%, max 35 Gy
- Secondary malignancies

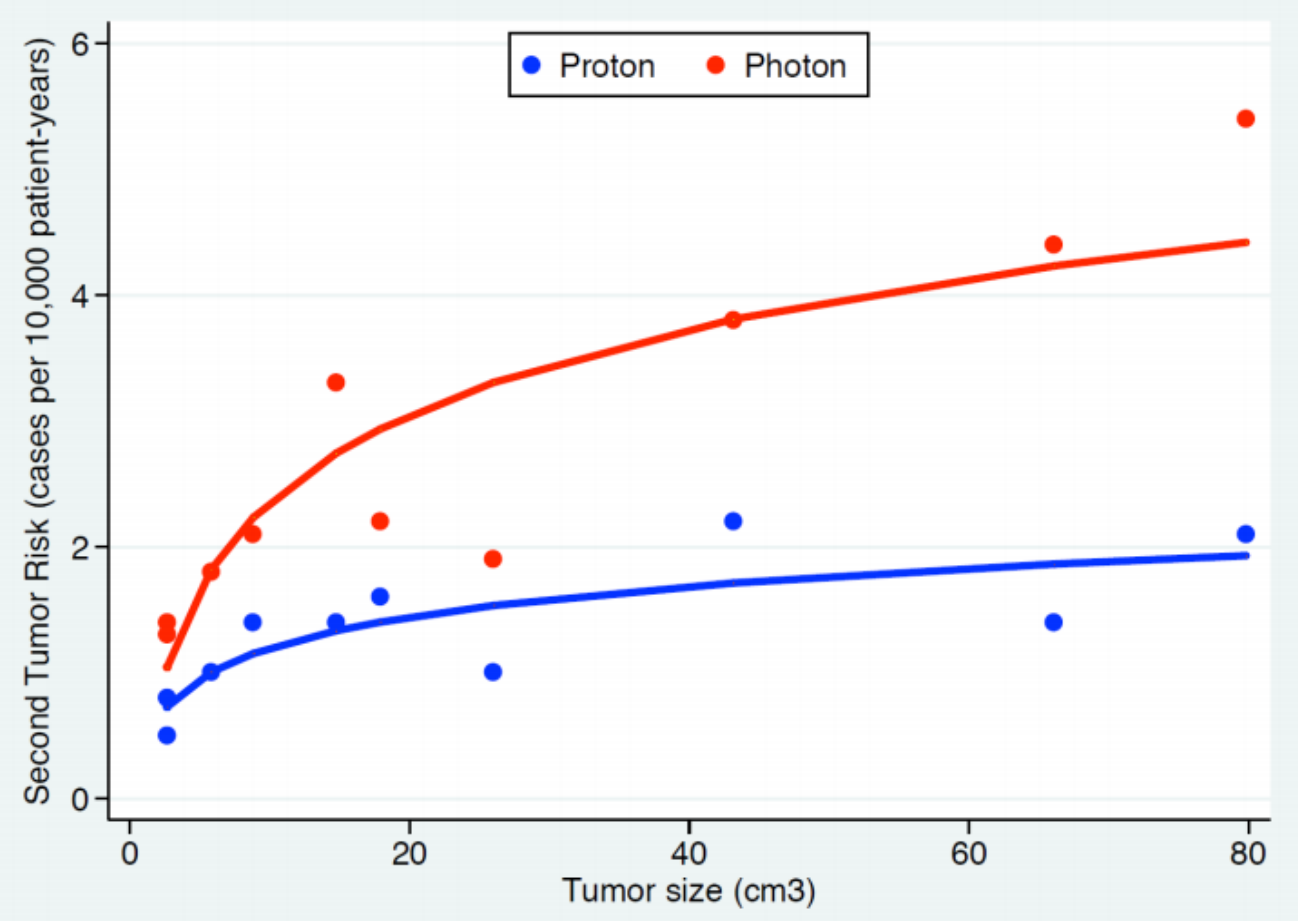
Protons for Medulloblastoma?

- Significant interest in protons for CSI to spare tissue anterior to the spinal cord
- <u>What is the data in support of protons?</u>
- Long-term results of an MGH phase II trial reported comparable survival to prior photon series and improved acute and late toxicities *(Yock, Lancet Oncol, 2016)*
- Emory/MGH matched-pair analysis of proton vs. photon patients (n=77) suggested that late endocrine abnormalities reduced in the proton group *(Eaton, Neuro-Oncology, 2015)*
- CSI with protons feasible for very young patients (median age 35 mo) after a median f/u of 39 mo *(Jimenez, IJROBP, 2013)*


A
Proton
Photon
B
Proton
Photon


Protons
IMRT
Cochlea
Gy
57
54
45
42
39
36
30

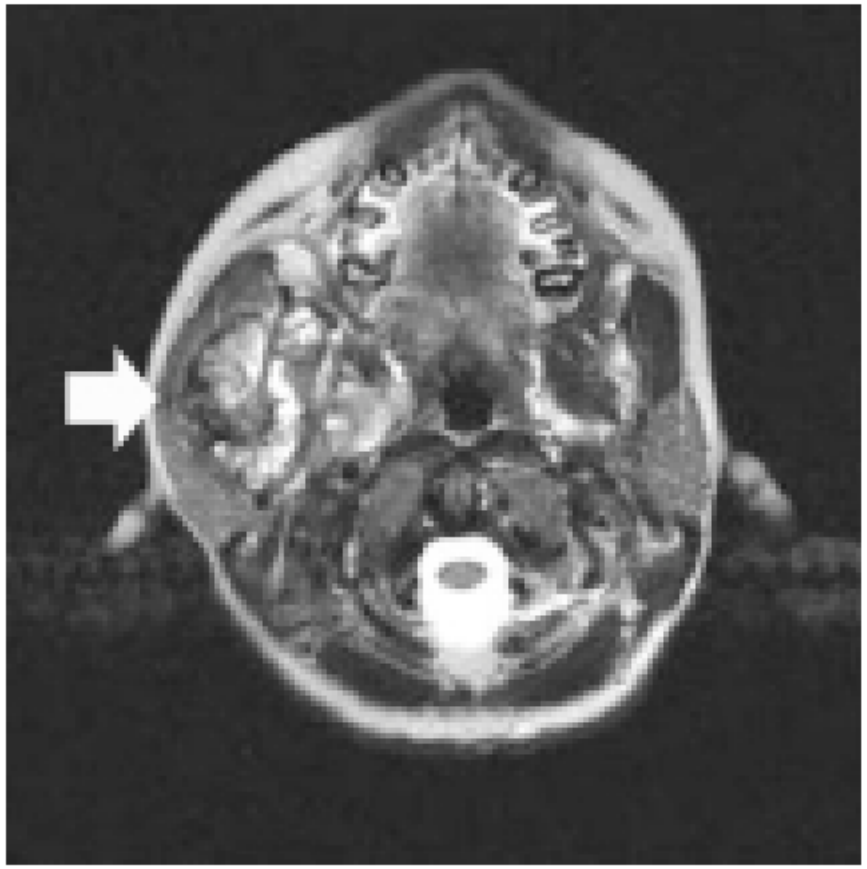
Second tumor risk after radiation therapy for meningioma

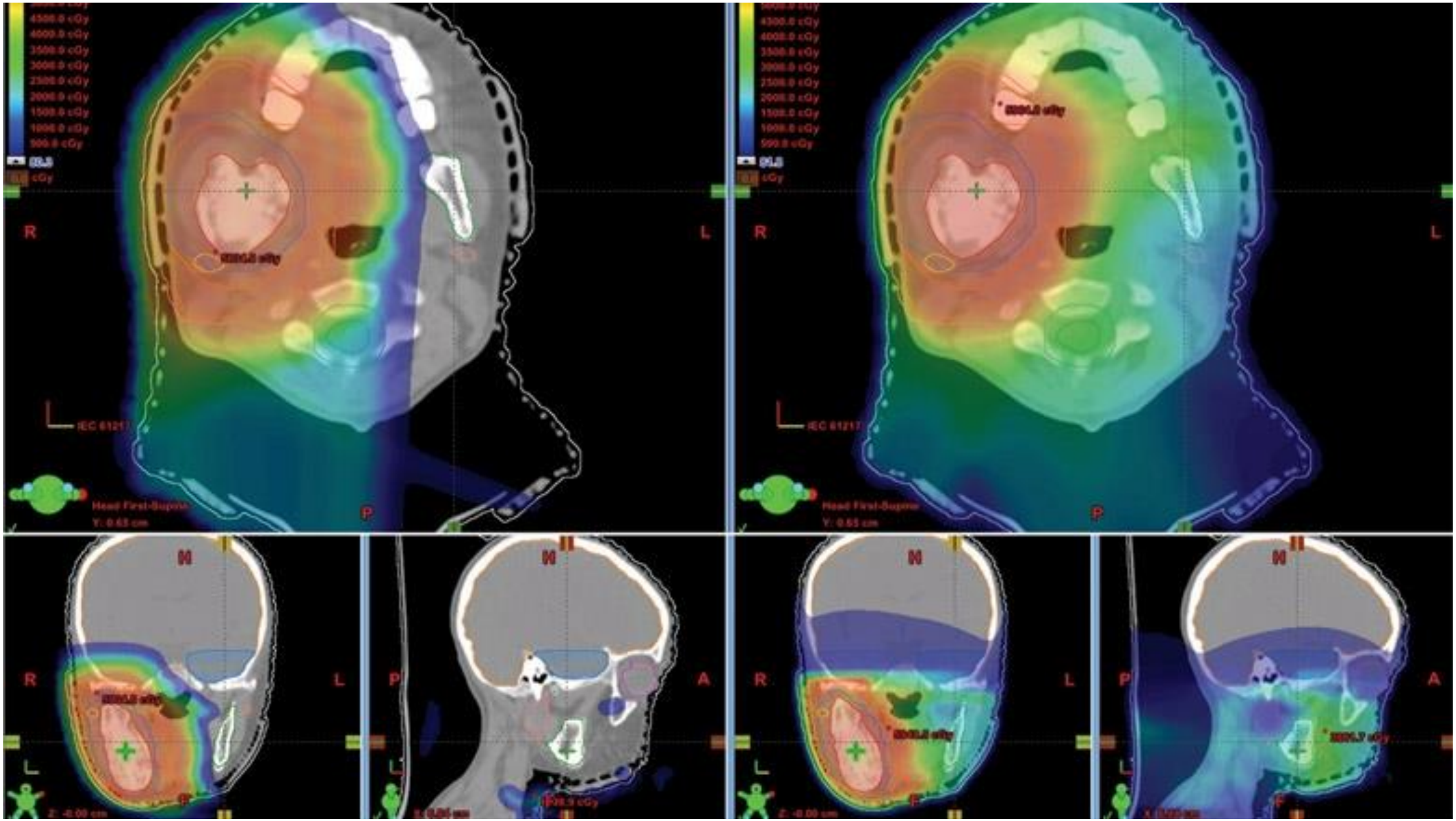


Arvold N et al. IJROBP 2011

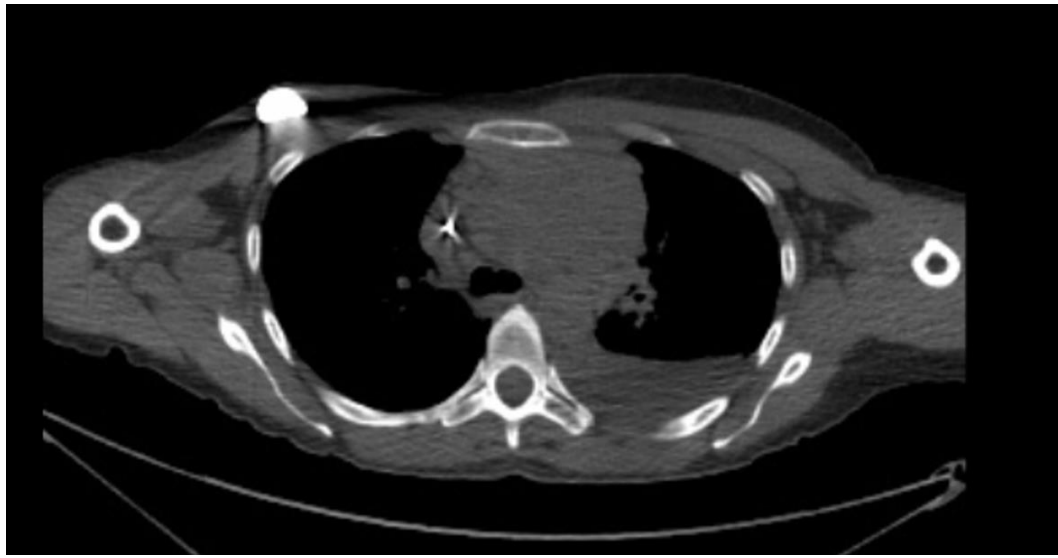
Sarcoma

- 10 year old girl with a tumor measuring 3.7 x 3.5 x 7.7cm in the right mandible
- Biopsy consistent with Ewing sarcoma
- Completed 6 cycles of multiagent chemotherapy
- Complete resection deemed to be challenging and disfiguring
- Patient referred to Radiation Oncology



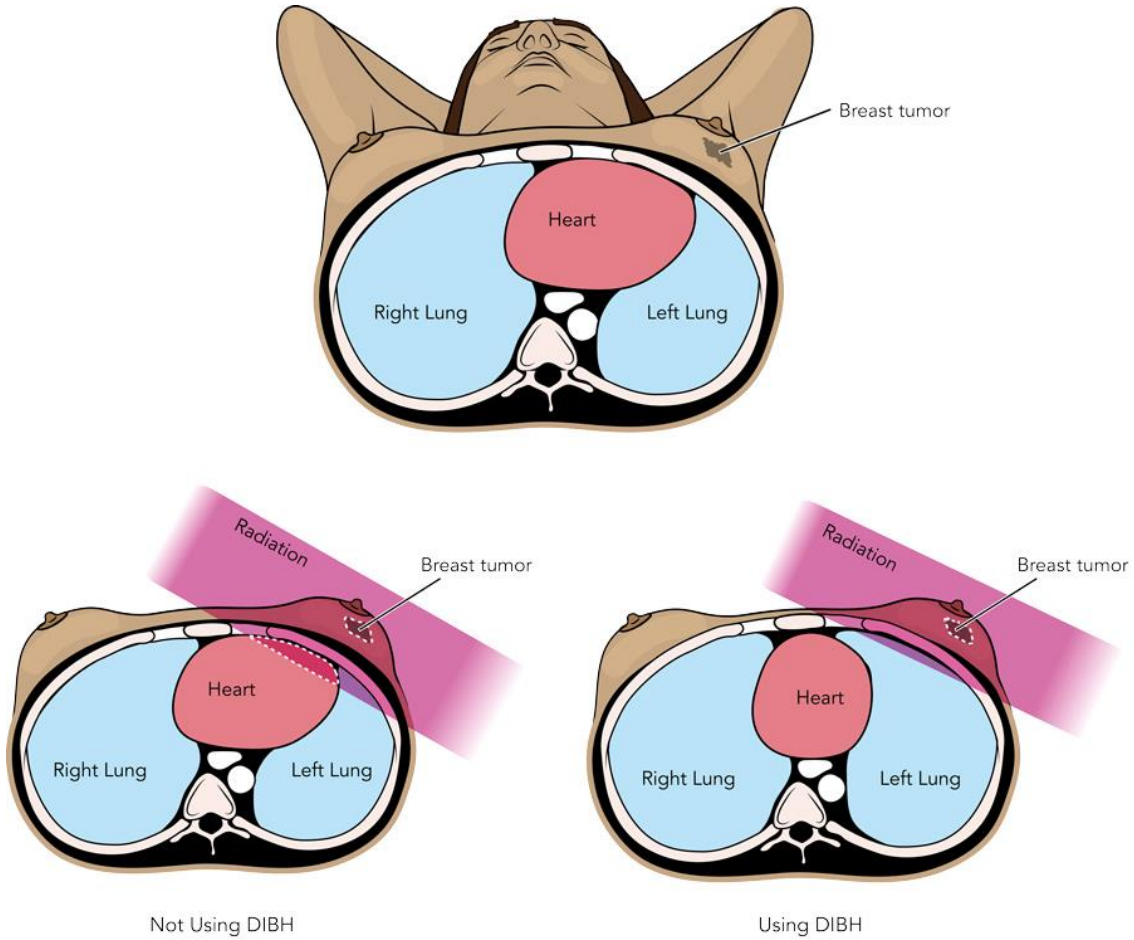

R
L
P
A
M
Head First-Supine

Mediastinal Tumors



- Hodgkin Lymphoma
  - Mediastinal involvement
  - Dose to breast
    - Association with future breast cancer development
  - Dose to heart and lung
    - Association with long term morbidity
- 27 y/o F with Stage IIA nodular sclerosing Hodgkin lymphoma with bulky mediastinal disease and axillary disease s/p 6 cycles of ABVD with complete response.

Deep Inspiration Breath Hold (DIBH)



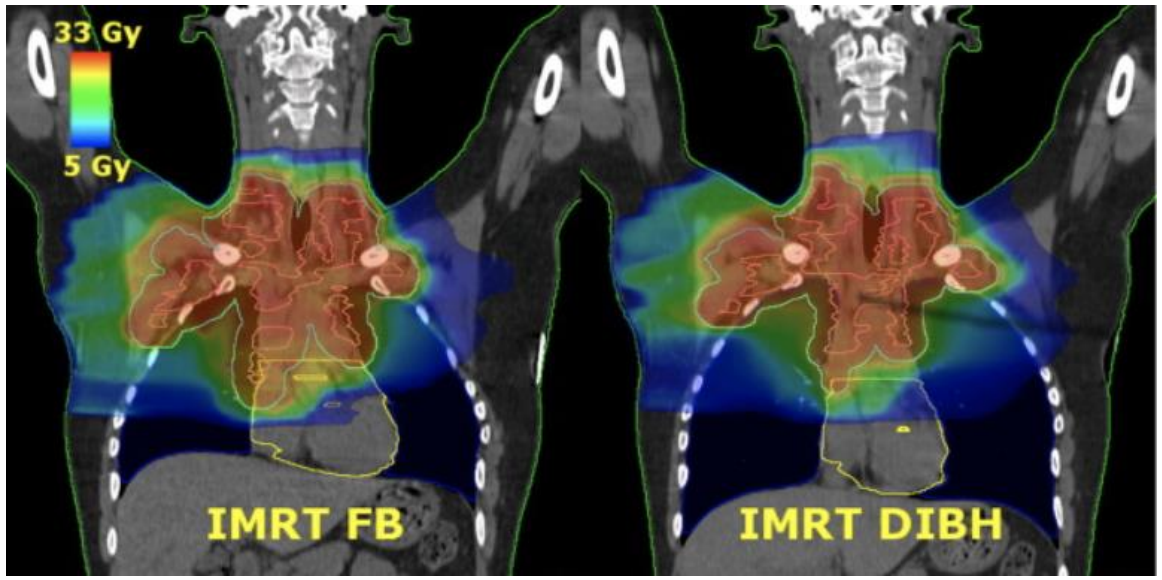
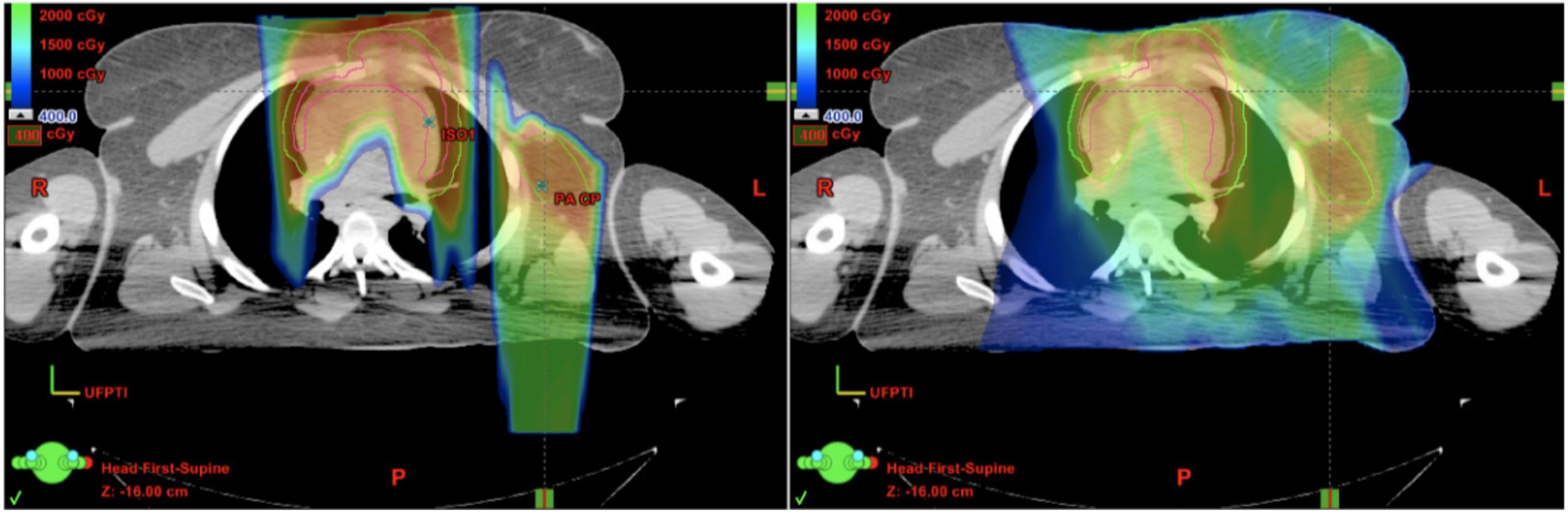


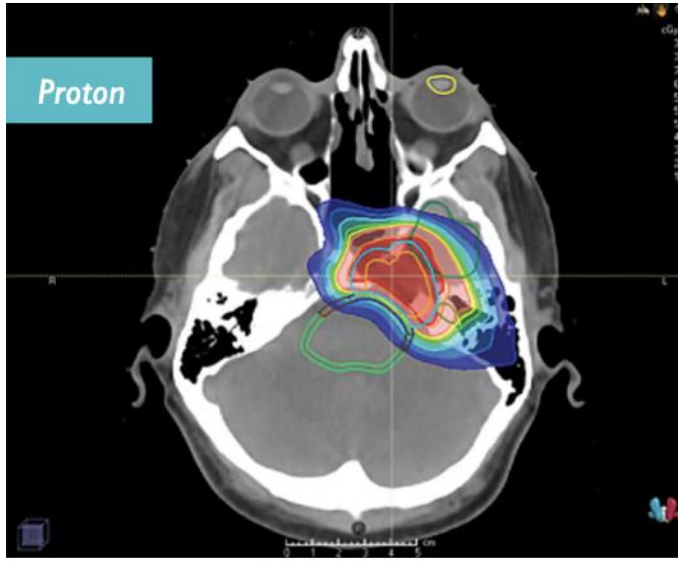
Image from: ResearchOutreach.org

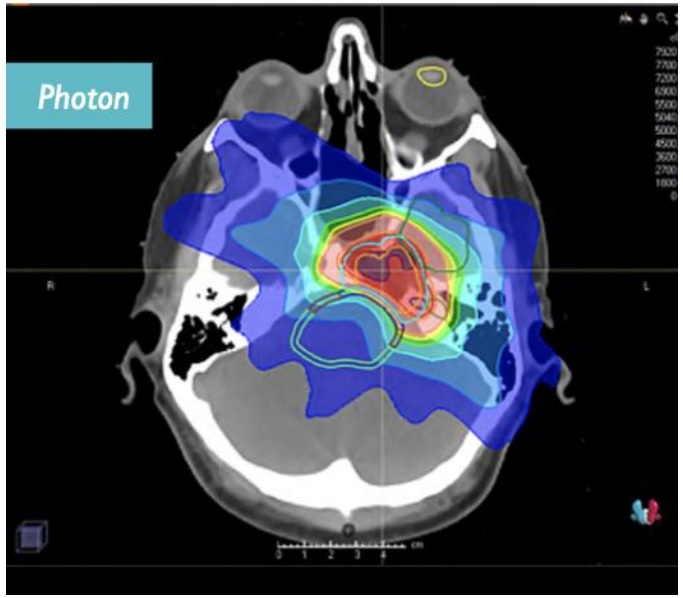
Breast dose reduction with Proton therapy and DIBH



Tumors or Spine and Base of Skull

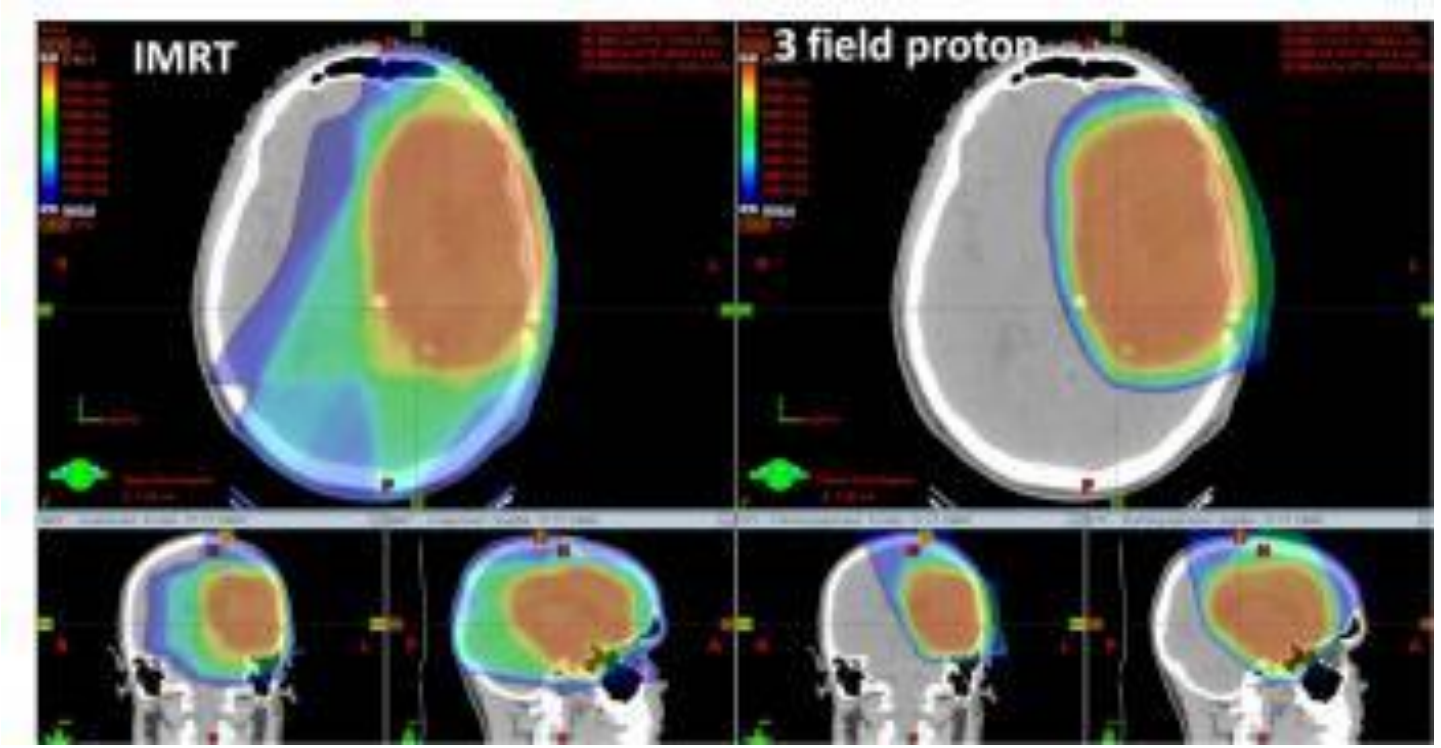
- Chordomas
  - Surgical resection is primary therapy, however, GTR is challenging
  - Radiation therapy given in adjuvant setting (Doses from 72-79Gy)
  - Critical structures area adjacent to the treatment volume
    - Brainstem
    - Optic apparatus
  - Proton therapy allows for rapid dose fall off near critical organs
- Tumors of the Spine
  - Proton therapy can spare the spinal cord



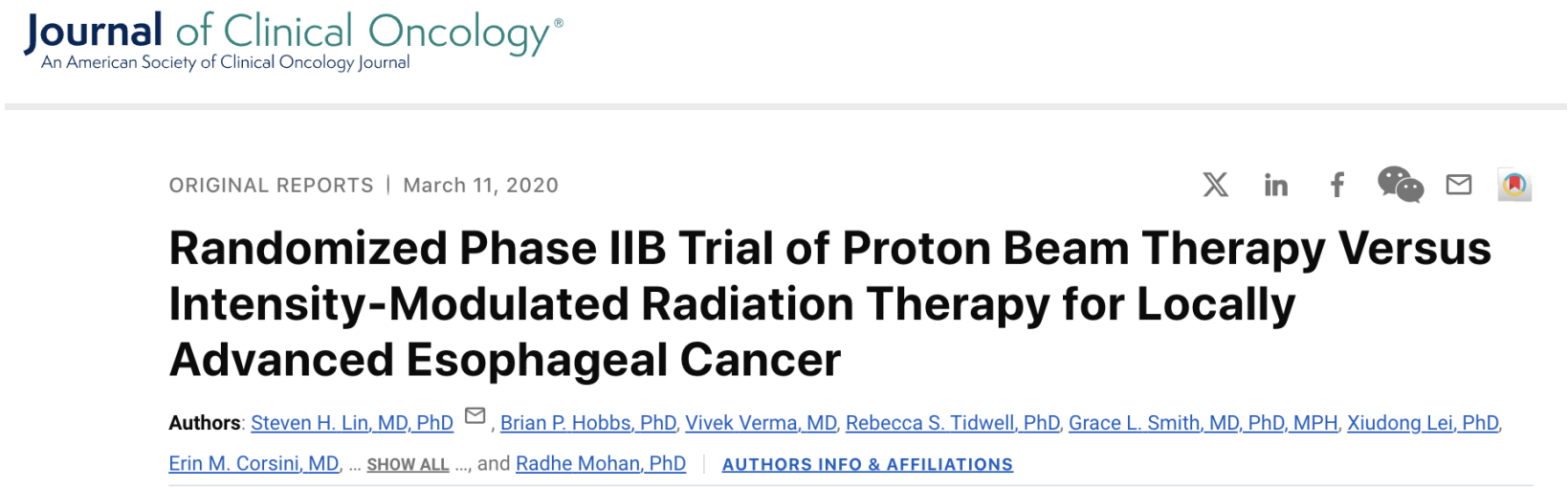


Brain Tumors

- Similar local control of tumors, but improved sparing of critical structures
- Low Grade Gliomas
- Meningiomas
- Critical Structures to avoid:
  - Cochlea
  - Optic nerve/chiasm
  - Brainstem
  - Spinal Cord
- Consideration of dose escalation

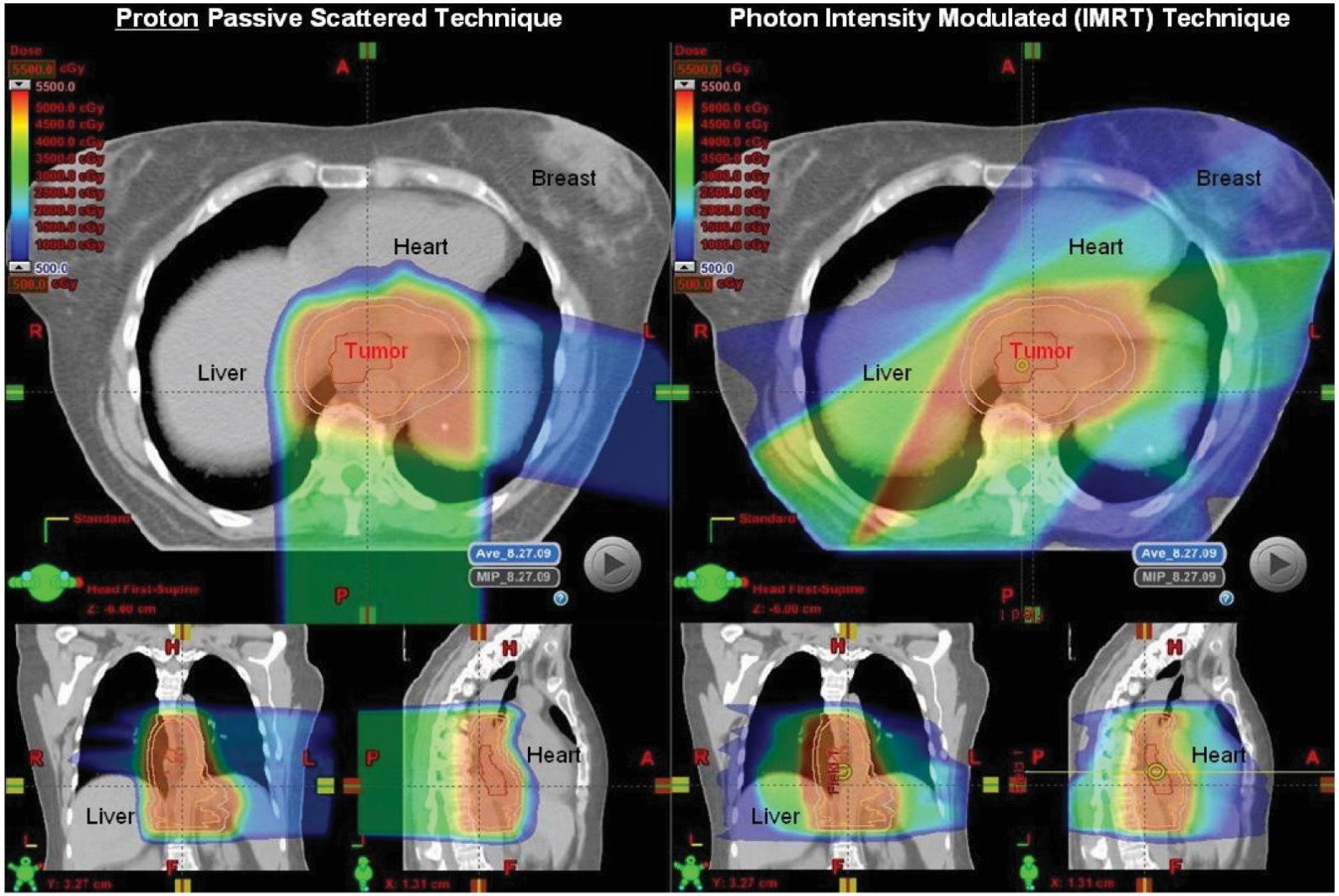


Esophageal Cancer



- Primary endpoint: total toxicity burden (TTB)
  - composite score of 11 distinct adverse events (AEs) over the duration of 1 year following treatment
  - TTB was 2.3 times higher for IMRT than PBT

Esophageal Cancer



(A)

Liver Cancer

- Dose to tumors limited by the adjacent healthy liver parenchyma, and concern for radiation induced liver disease (RILD)
- Occurs 4-8 weeks after radiation therapy completed
- Patients with classical RILD usually present with fatigue, abdominal pain, increased abdominal girth, hepatomegaly, anicteric ascites and elevation of Alk Phos out of proportion to ALT/AST
- Risk of RILD increases as dose to healthy parenchyma increases

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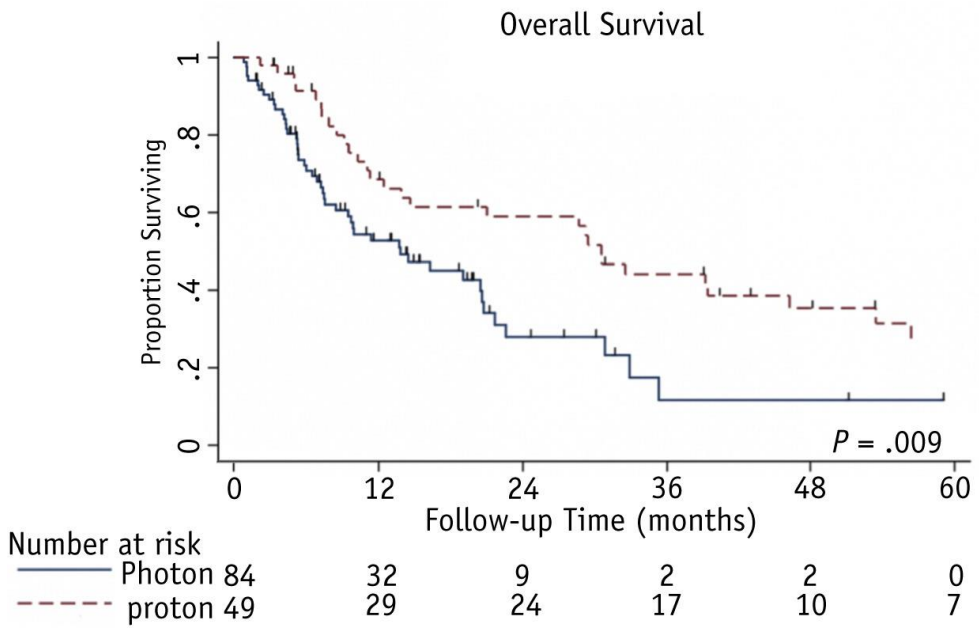
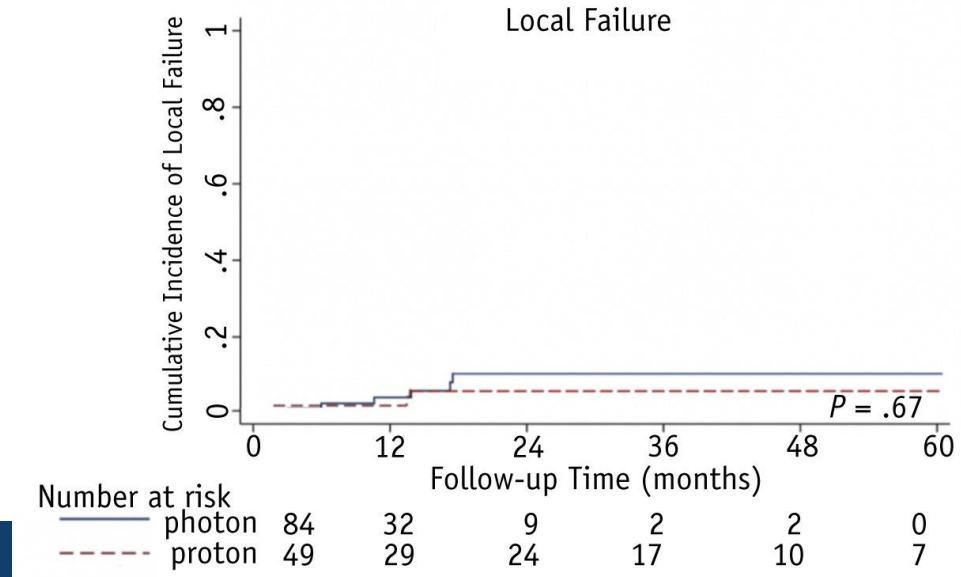
Clinical Investigation

Protons versus Photons for Unresectable Hepatocellular Carcinoma: Liver Decompensation and Overall Survival

- Retrospective study of patients with nonmetastatic, unresectable HCC w/o previous liver-directed therapy treated with ablative RT from 2008-2017
- Objective: To compare clinical outcomes of proton vs. photon ablative RT
- Included:
  - 133 patients: 84 (63%) received IMRT and 49 (37%) received PBT
- Main Outcome Measures
  - Overall survival
  - Incidence of non-classic RT induced liver disease

Sanford et al (MGH), IJROBP, 2019





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Clinical Investigation

Protons versus Photons for Unresectable Hepatocellular Carcinoma: Liver Decompensation and Overall Survival

- PBT and IMRT achieved equivalent local and locoregional tumor control
- PBT resulted in median survival of 31 months vs. 14 months for IMRT
- Patients treated with PBT were 4x less likely to develop RT induced liver disease

Conclusion: PBT was associated with improved survival compared to IMRT, which may be driven by decreased incidence of posttreatment liver decompensation

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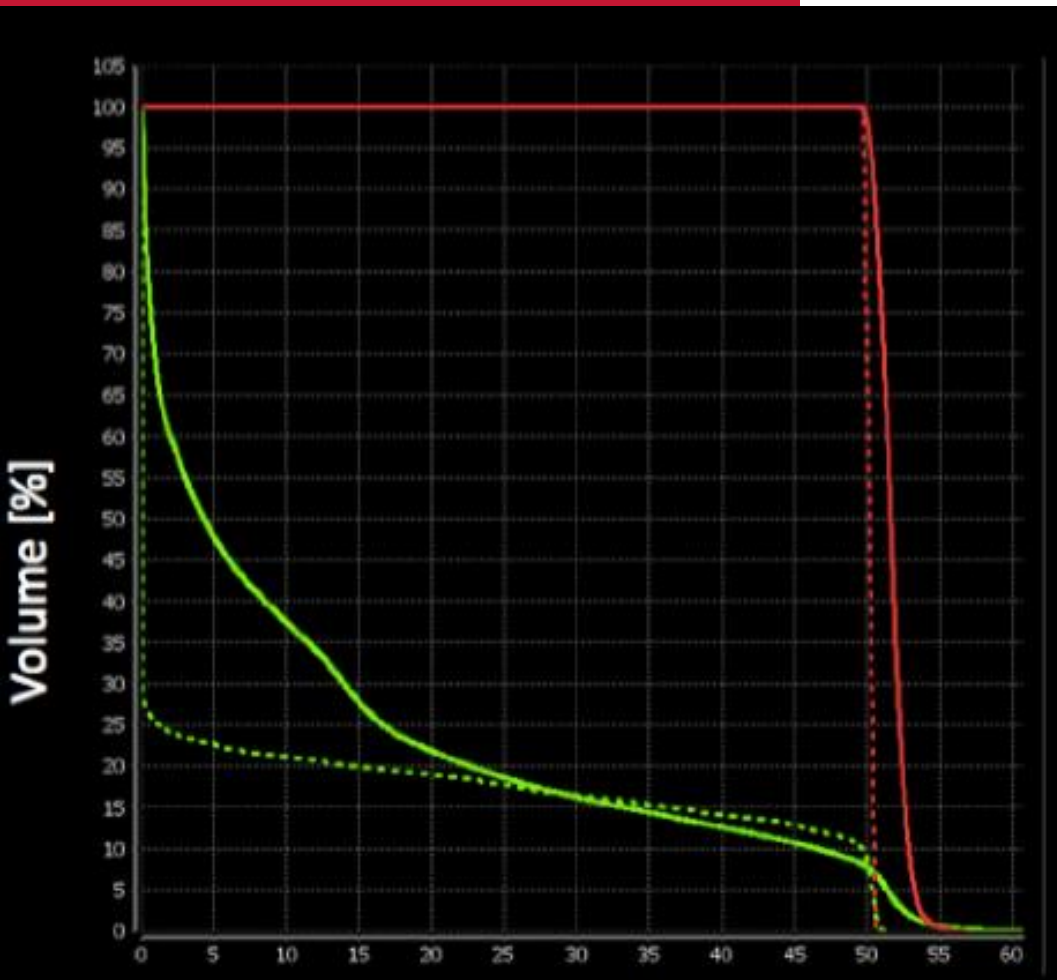
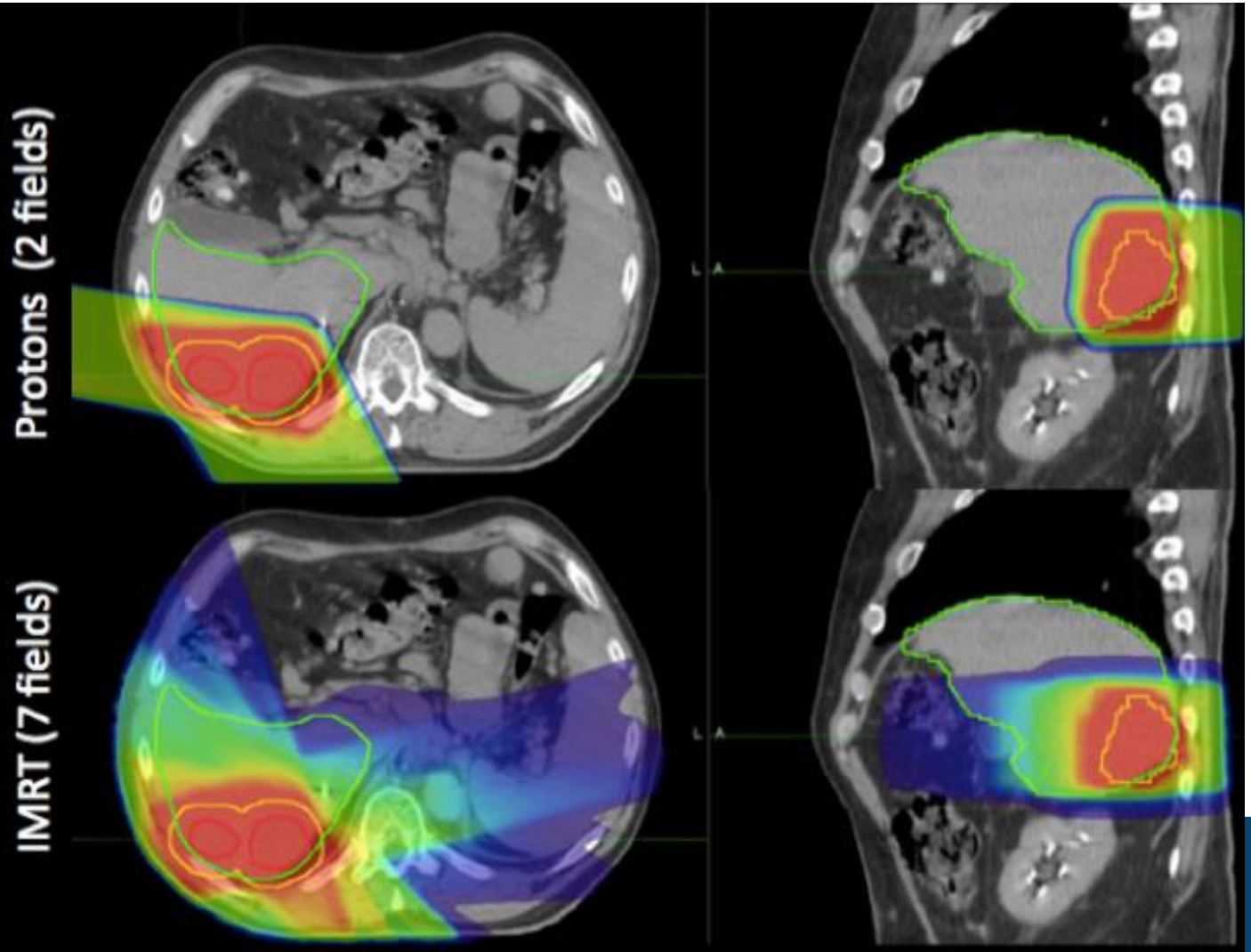
Clinical Investigation

Protons versus Photons for Unresectable Hepatocellular Carcinoma: Liver Decompensation and Overall Survival

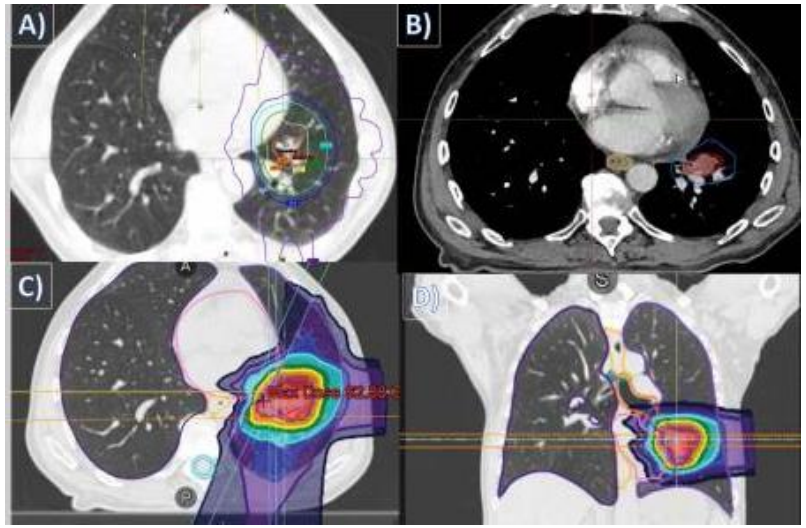




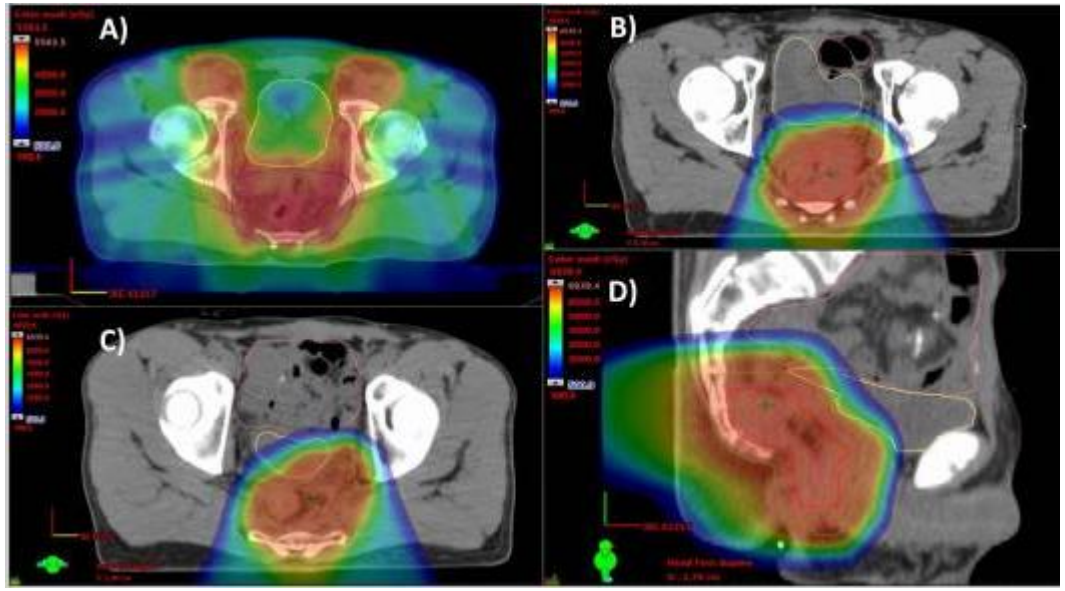
Sanford et al (MGH), IJROBP, 2019

Re-Irradiation & Genetic Mutations

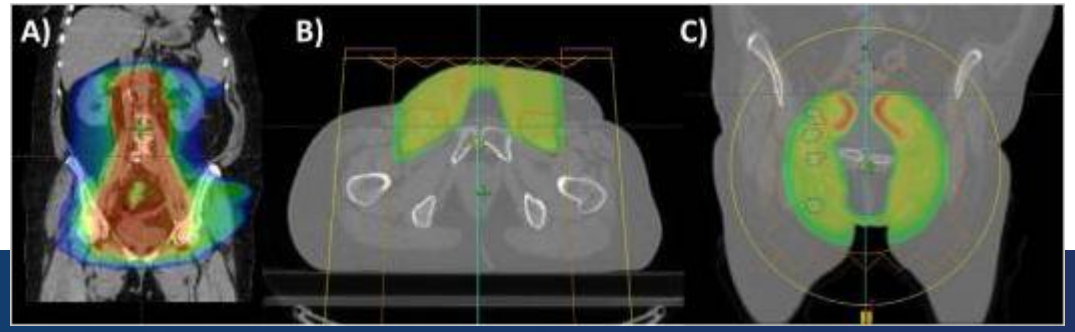
- Limit dose to uninvolved healthy tissue to prevent toxicity and secondary malignancy risk



Lung Cancer



Rectal Cancer



Endometrial Cancer

Proton Re-Irradiation. Simone et al, 2020 Semin Radiat Oncol

Patient Experience with Proton therapy

Original Investigation

FREE

December 26, 2019

Comparative Effectiveness of Proton vs Photon Therapy as Part of Concurrent Chemoradiotherapy for Locally Advanced Cancer

Brian C. Baumann, MD[1,2,3]; Nandita Mitra, PhD[3,4]; Joanna G. Harton, MS[4]; et al

» Author Affiliations | Article Information

JAMA Oncol. 2020;6(2):237-246. doi:10.1001/jamaoncol.2019.4889

- Protons associated with less grade 3+ CTCAE toxicity (Fewer unplanned hospitalizations)
- Less decline in QOL with proton therapy
- No difference in DFS or OS

Thank you!

Please reach out with any questions!

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