



<u>Against the Proposition</u> Very few pediatric patients will clinically benefit from protons over photons (Does every Gy matter?)

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Main Arguments

1. We don't know that every Gy matters. Evidence-based medicine dictates that we prove that before assuming it.

- 2. Photon plans can and are being improved dramatically, narrowing or eliminating the dosimetric gap vs protons.
- 3. Second malignancies don't occur where the dose is low.





1. We don't know that every Gy matters

- Evidence-based medicine dictates that we prove that before assuming it.
- The majority of structures in the majority of photon plans are kept well below tolerance doses.
- We don't know if it is detrimental to the patient if given 50% of an organ dose tolerance (based on 5% risk) instead of 10%.
- Most of our organ tolerance doses are designed to result in less than 5% toxicity rate. We barely have sufficient data to establish that accurately, how many patients do you think it would take to distinguish 2% from 5% risk?
- RadOncs don't believe every Gy matters- We know this because they accept plans where OAR doses could have been lowered without much loss of PTV coverage.
- We treat curative patients with simplistic plans where large volumes of non-target tissue are needlessly irradiated (using APPA, 3-field or 4-field for example).



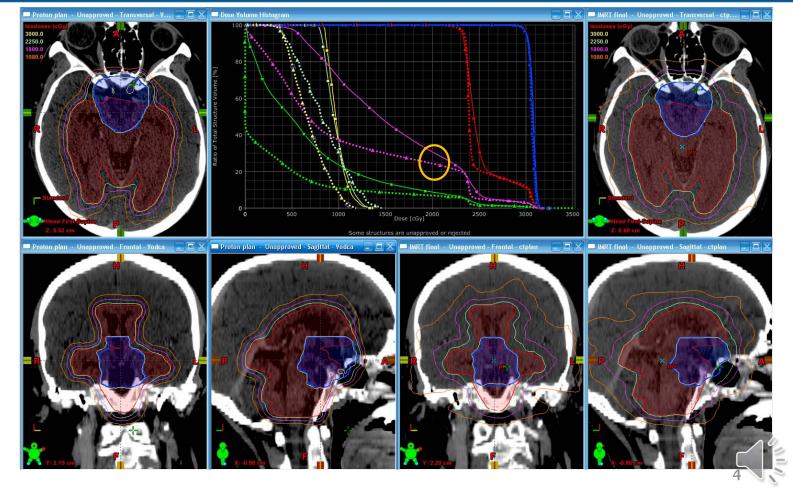


CNS Germinoma (30Gy Rx): Protons vs. IMRT

proton-dashed

L cochlea-yellow, R cochlea-grey, braintissuemagenta, body-green,

Greater brain sparing with protons below 20Gy where there is minimal risk.

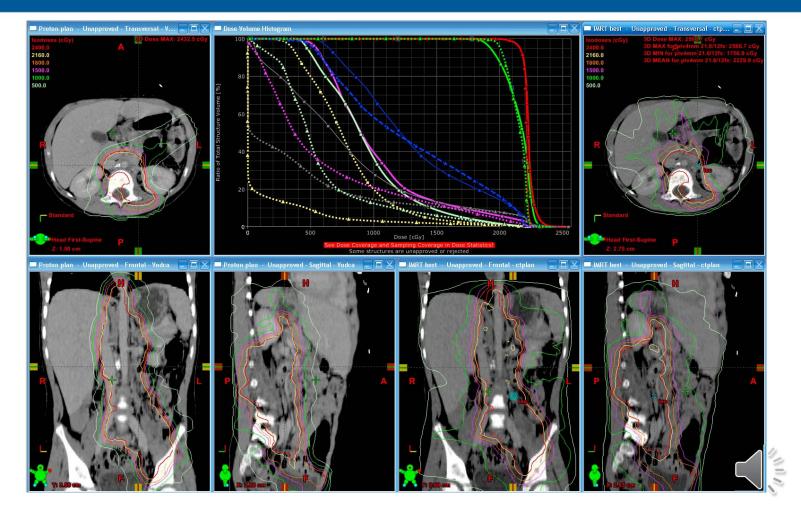




Neuroblastoma (21.6Gy): Protons vs. IMRT

proton-dashed

Body-grey, L kidney- magenta, R kidney-It green, liver-yellow, vertbody spareblue,





2. Photon plans could be improved dramatically, narrowing or eliminating the dosimetric gap vs protons.

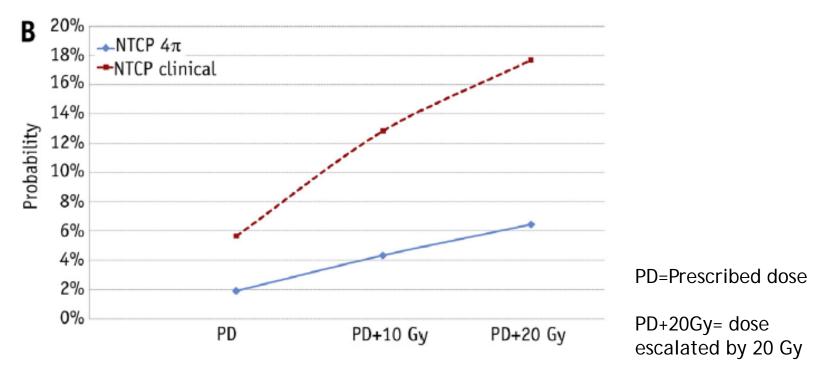
- For many of the publications comparing clinical outcomes of protons vs. photons, the quality of the photon plans are suspect. For example, in one paper, the photon IMRT brain tumor plan used 6 coplanar beams. Do you think we would have better DVHs with 10 noncoplanar beams? We could use 20 noncoplanar beams and do even better. It wouldn't cost us tens of millions of dollars either, anyone with a modern linac can reasonably do that.
- Here is another reason why we know RadOncs don't believe every Gy matters, or they would insist on the use of more noncoplanar beams and other more technically complex plans.





4Pi with 20 Beams Allows Safe Dose Escalation

 4π SBRT for head-and-neck cancer 407



Int J Radiation Oncol Biol Phys, Vol. 91, No. 2, pp. 401-409, 2015





- One of the major selling points of protons is the promise of reduced secondary malignancy (SM).
- But, where proton plans remove dose is in the low and medium dose region. The majority of SM occur in the high dose region. We know that by studying patients who actually got SM. We also know that the risk for SM is linear with dose, not bell-shaped.
- Therefore, the chance of reducing SM with protons is minimal.
- Are there any clinical trials comparing SM with protons to photons? YES





MGH Case Control Study of SMN: Proton vs Photon Irradiation-

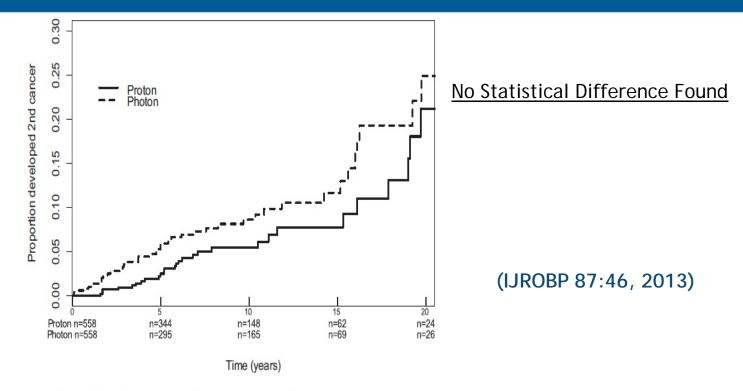
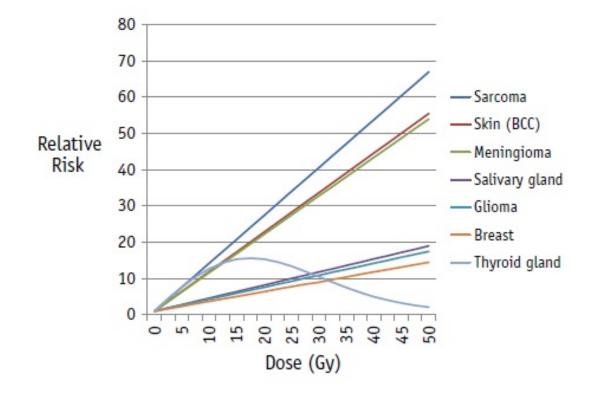


Fig. 1. Cumulative incidence curves for second cancer after radiation therapy for proton patients (solid line) and photon patients (dotted line) (log-rank P = .085).





CCSS SMN study



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Conclusions

- The vast majority of children needing radiotherapy are equally well served by a high quality photon plan as with a proton plan.
- Although it may be logical to think that every Gy matters, we have little evidence that it does.
- There is little evidence that the risk of SM is lower with protons than photons, and based on what we know about SMs, that they occur predominantly in the high dose volume and risk increases with dose, there is little reason to think the risk will be substantially lower with protons.





 For all these reasons, it is my belief that very few children will benefit from a proton plan over a high quality photon plan.

