Protons: Basics and Controversies

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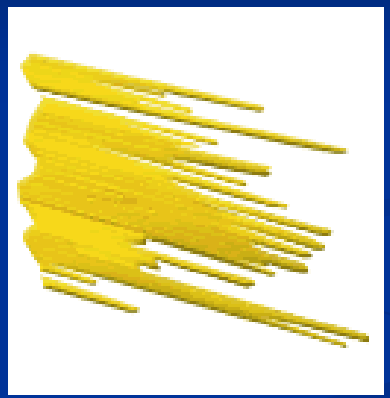
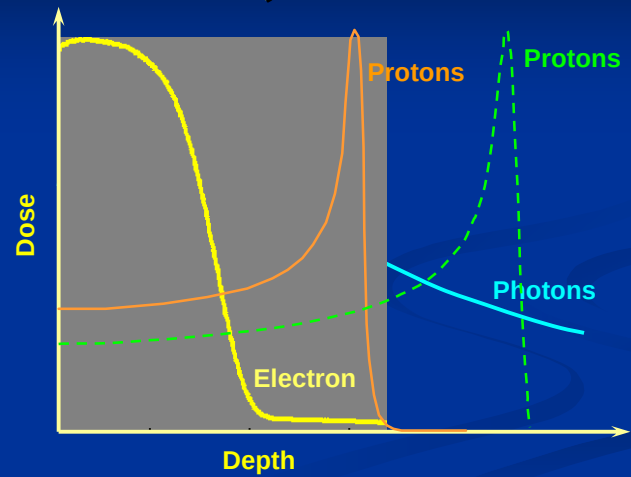
19 April 2008

Electron Tracks in Patient

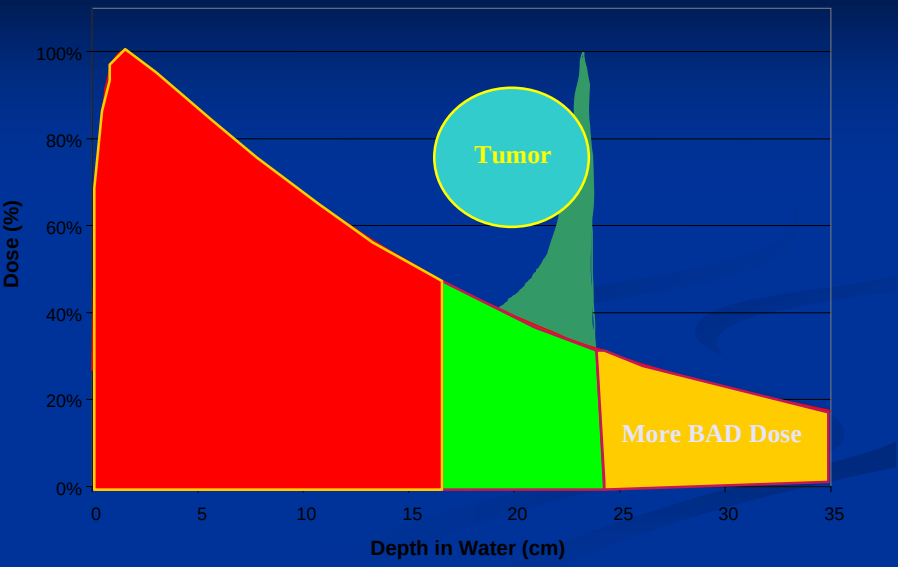
Proton Tracks in Patient



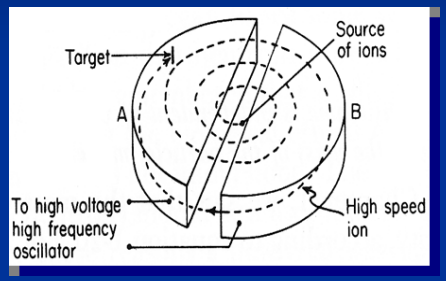
Percent Depth Dose for Photons, Electrons, and Protons

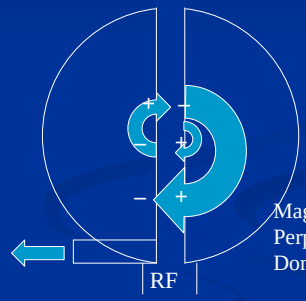


Good Dose/Bad Dose



Cyclotron

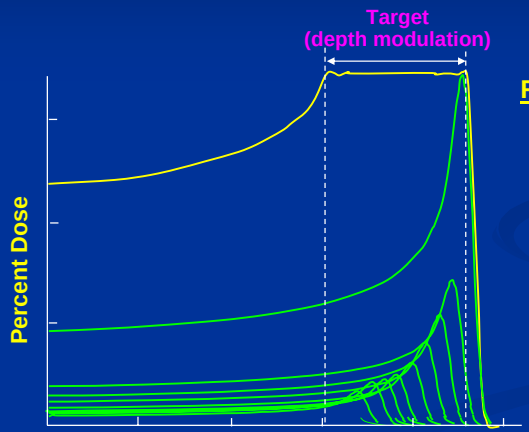




Magnetic Field Perpendicular t
Donuts.

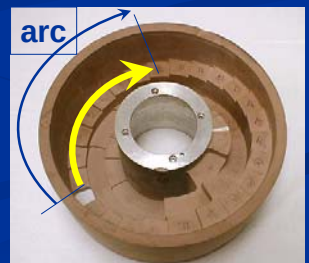
$$F = Bev$$
$$\frac{mv^2}{r} = Bev$$
$$t = \frac{\pi r}{v} = \frac{\pi m}{Be}$$

Clinical Proton Beam: The Spread-Out-Bragg-Peak (Passive Scattering)



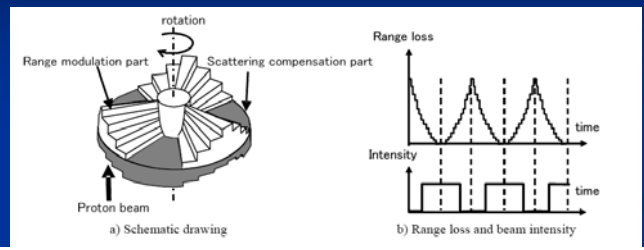
Range Modulator Wheel

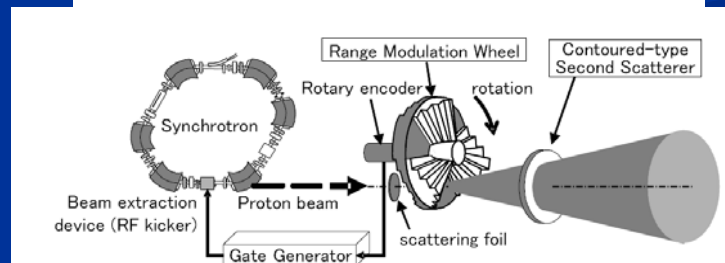
- rapidly spinning wheel
- arc = mod



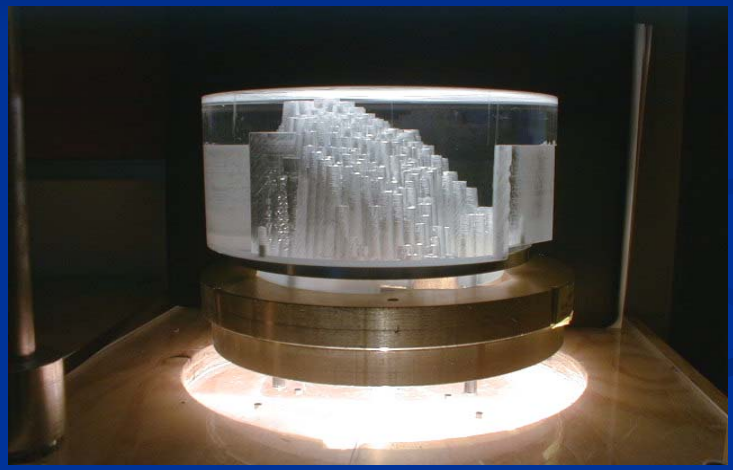
Range Modulation

Matsuda et al., Hitachi, Ltd. Power Systems

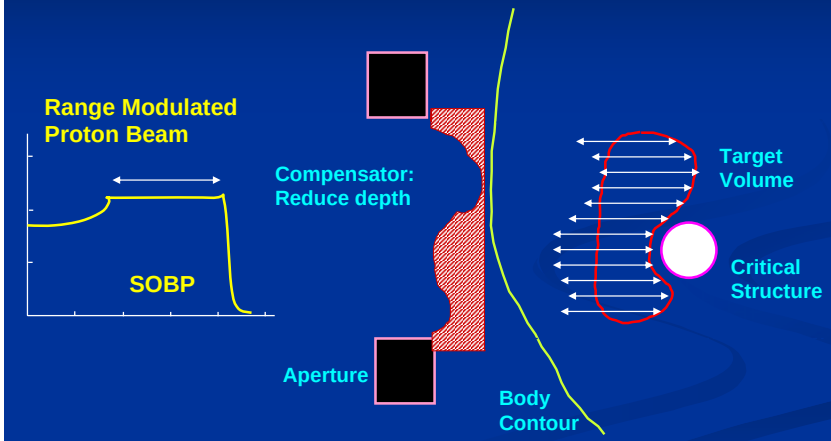


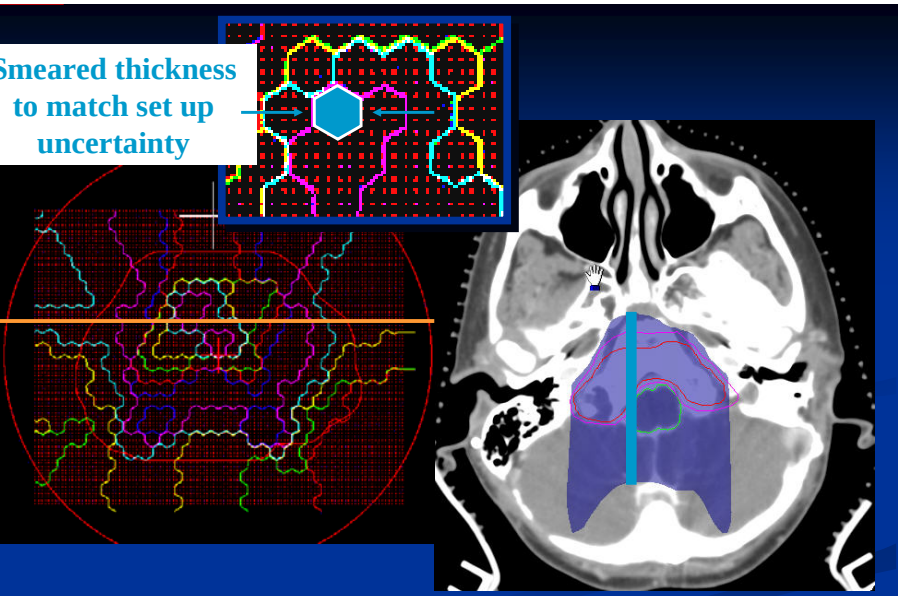


Lucite Range Compensator



Clinical Proton Beam: Distal Tracking





RC iso-thickness lines

Lucite Range Compensator

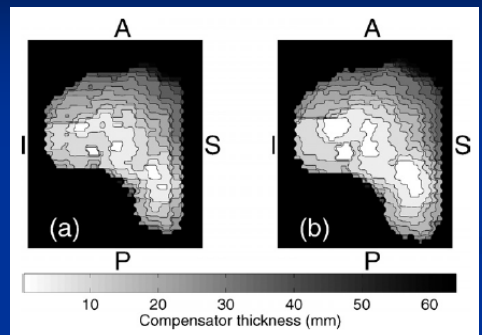
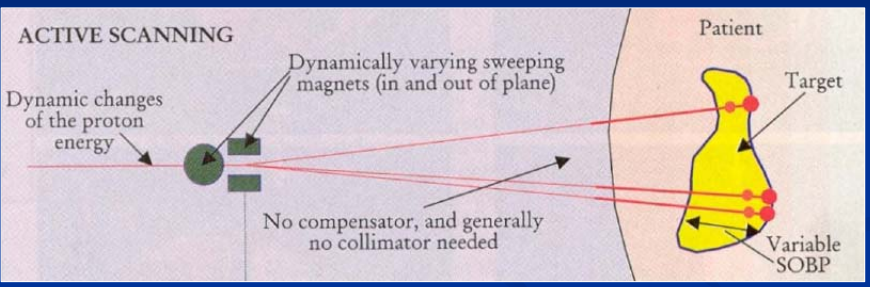


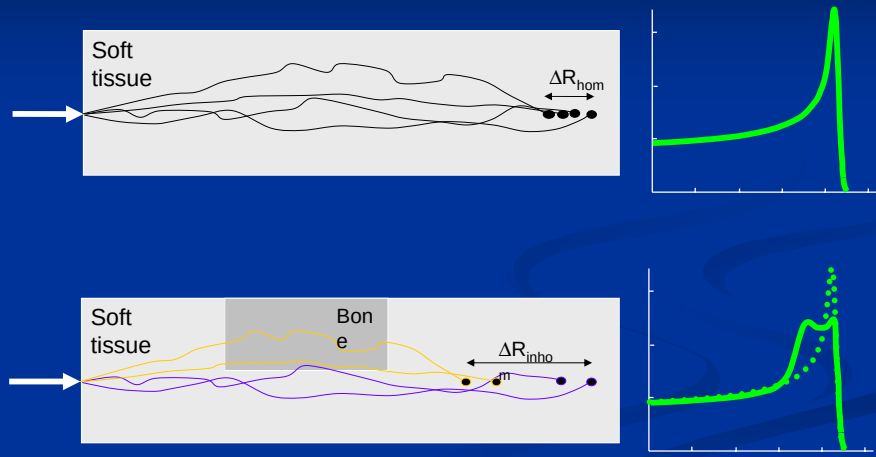
Fig. 1. A proton range compensator map: (a) designed based on the radiologic depth of the target's distal edge; and (b) smeared to counter the range uncertainties. The letters indicate anterior (A), posterior (P), inferior (I), and superior (S) directions.

Clinical proton tx: Passive Scattering vs. Active Scanning

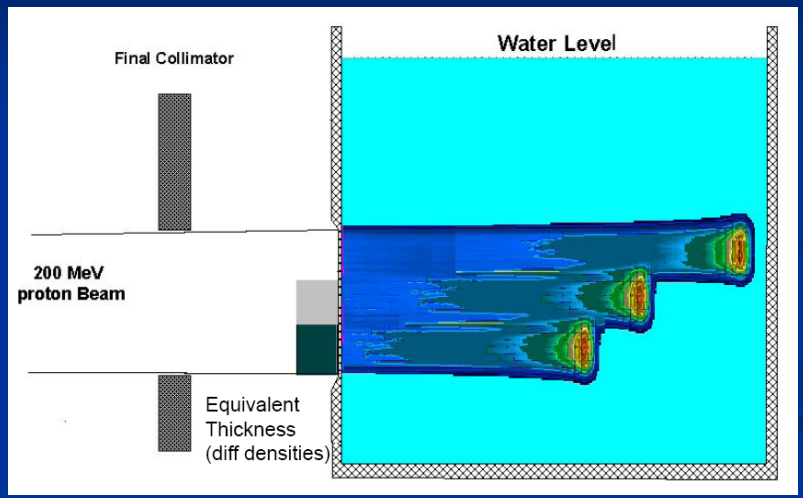


- Fewer neutron production than with passive scattering
- More sensitive to organ motion than scattering (paints layer by layer)
- Not the same as IMPT: Scanning can be used to deliver homogenous or heterogeneous dose distributions. With IMPT, heterogeneous proton fields combine to create a homogeneous dose distribution

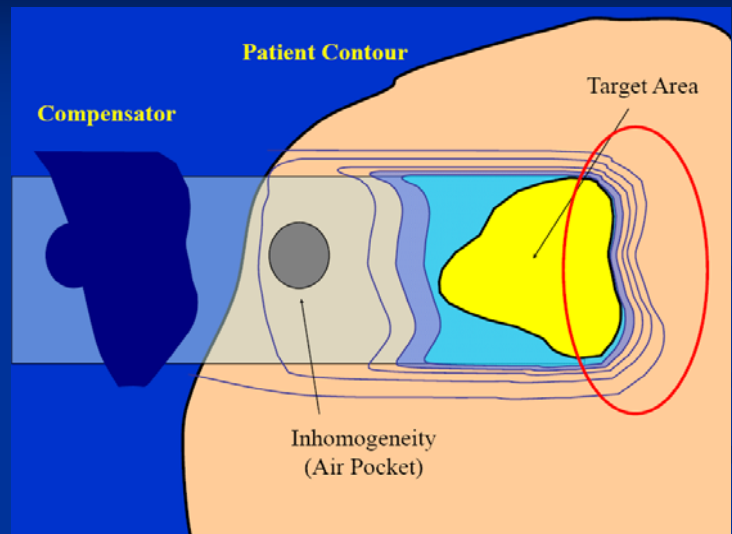
Proton Interactions: Tissue Inhomogeneity Effects



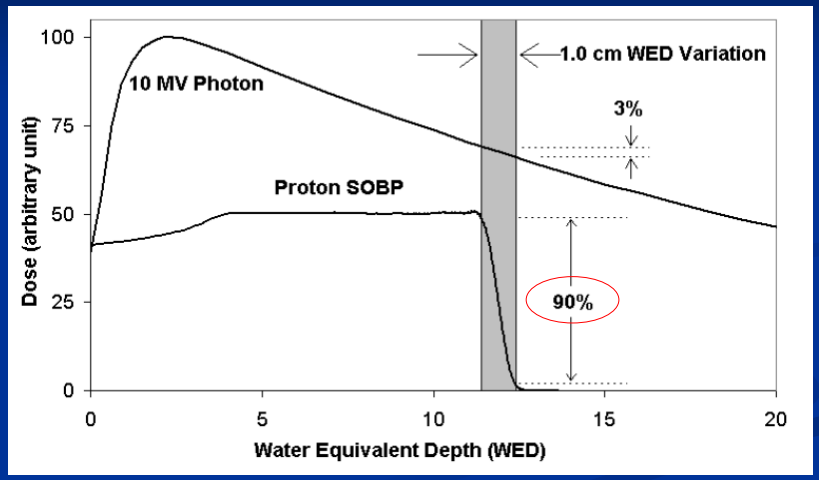
Tissue Heterogeneity



Tissue Heterogeneity



Setup Uncertainty and Motion: CAUTION



Remember the *distal* edge: Small amounts of tumor motion or setup uncertainty can drastically change dose distribution

Unique Issues: Gold Seeds

Phys. Med. Biol. **52** (2007) 2937–2952

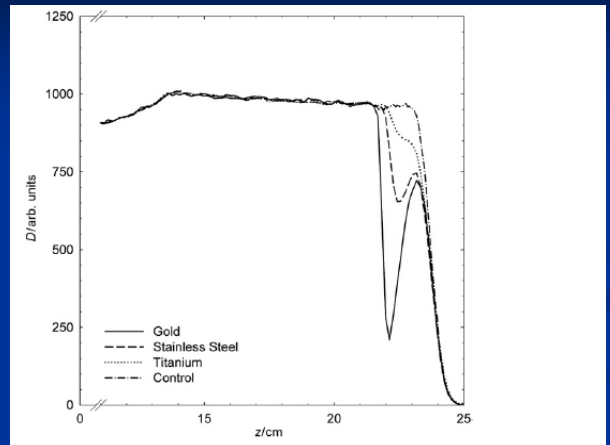
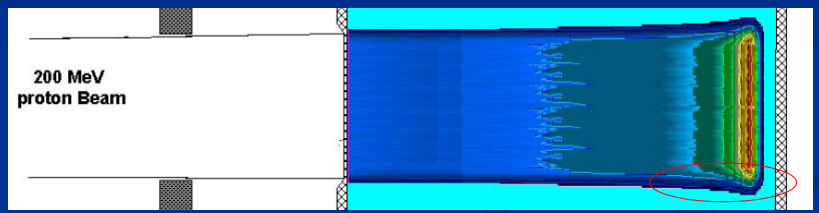


Figure 4. Simulated relative absorbed dose (D) as a function of depth (z) in the pelvic (slab) phantom revealing the dose perturbations caused by the *large* (1.25 mm in diameter and 3.0 mm long) fiducials made from gold, stainless steel and titanium. In these simulations, the fiducials were oriented *parallel* to the beam axis and located near the *distal* end of the high-dose region of the spread-out Bragg peak. For comparison, the unperturbed (control) depth dose profile is also shown.

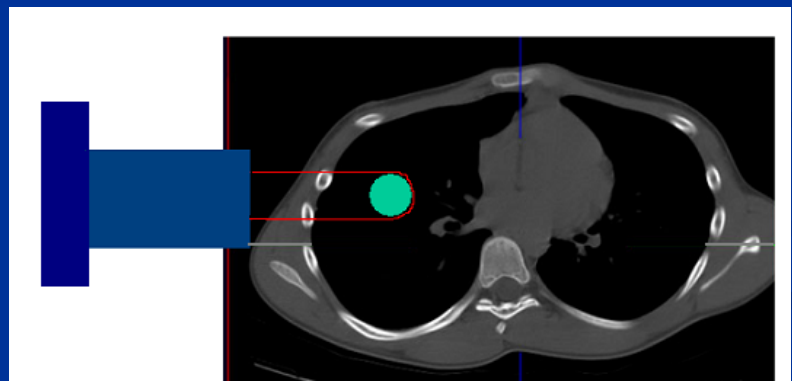
Setup Uncertainty and Motion: CAUTION

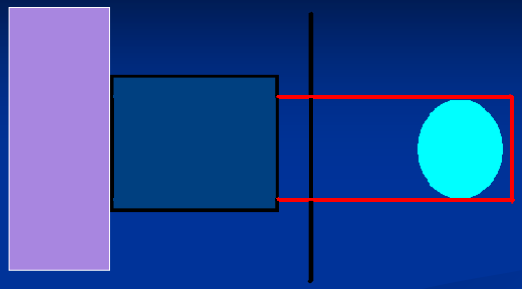


Sharp lateral falloff requires planning for edge uncertainty

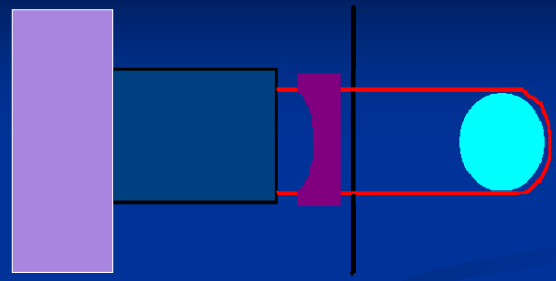
Reality Check of Moving Targets in Heterogeneous Media

The desired dose distribution conforms tightly to the medial margin of the target. In practice, this is harder to achieve than one might think.

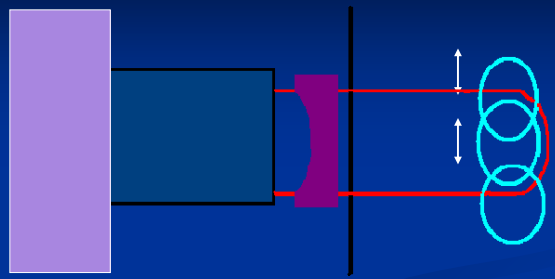




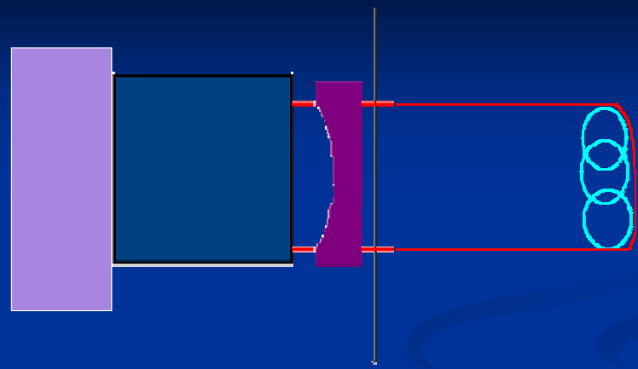
Assuming a perfectly flat interface and uniform density throughout the volume, the dose distribution around the target is easy conformed to the correct depth via the Bragg peak modulation.



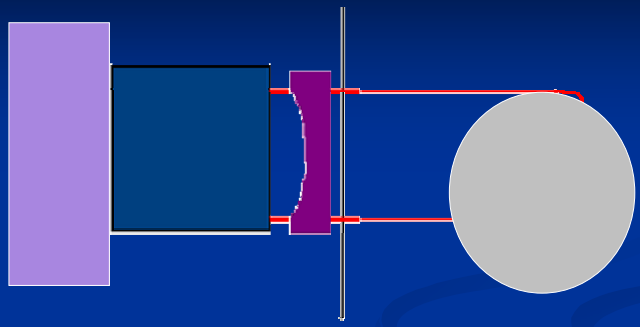
To conform the distal end of the distribution to the target, a RC is inserted.



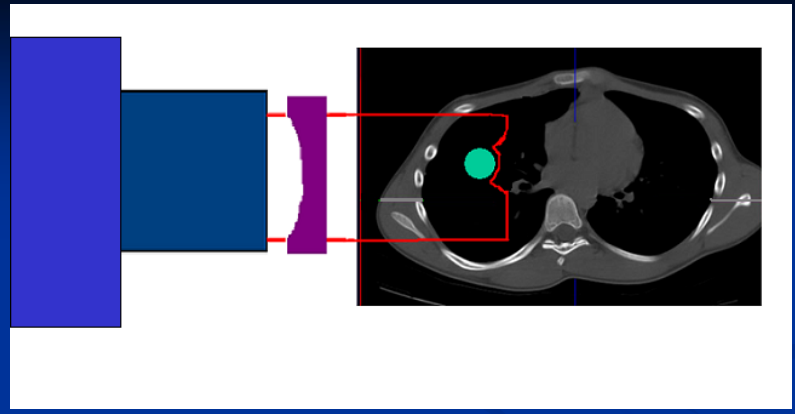
In the case of a moving target, one might imagine that margins as tight as this one would not work.



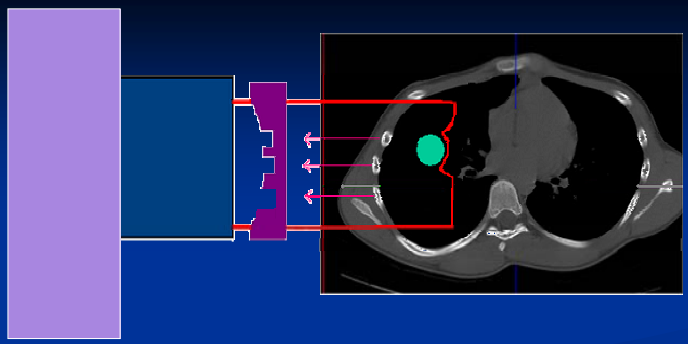
Consequently the RC and beam must incorporate the ITV. For a homogeneous media, this works well.



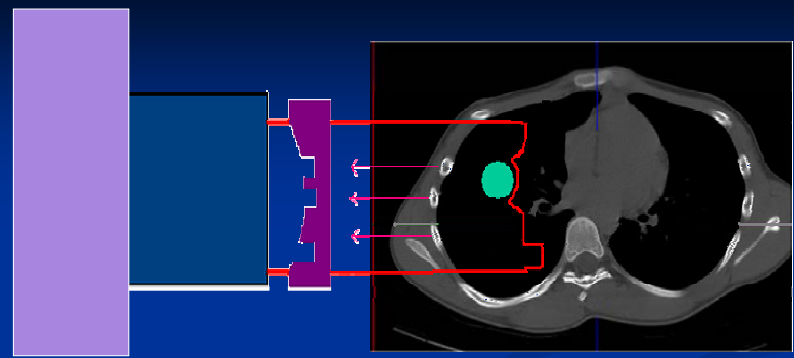
However, if the tumor happens to be in lung, the dose distribution must be modified to account for lack of attenuation.



Additional dose is given beyond the tumor in the margin area. We have not even considered the oblique incidence of the skin surface.



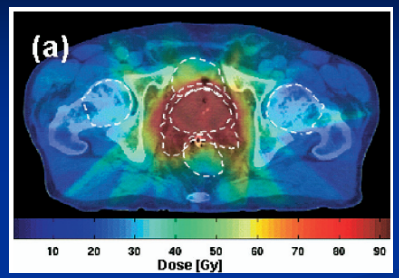
Additionally, you have a target that moves, and other variable density structures that do not – for example the ribs shown here. The ribs must also have a set up margin in the RC. If for some reason the ribs or RC are misaligned….



Final distribution and RC

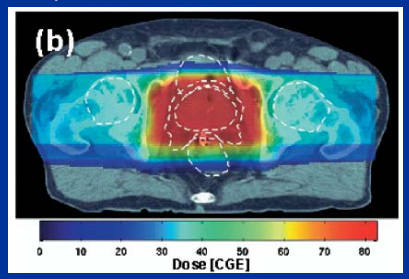
Harvard Prostate Planning Study

Int. J. Radiation Oncology Biol. Phys., Vol. 69, No. 2, pp. 444–453, 2007

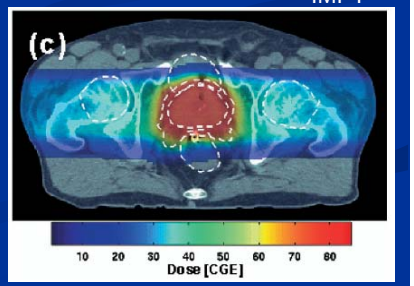


IMRT

3D protons



IMPT



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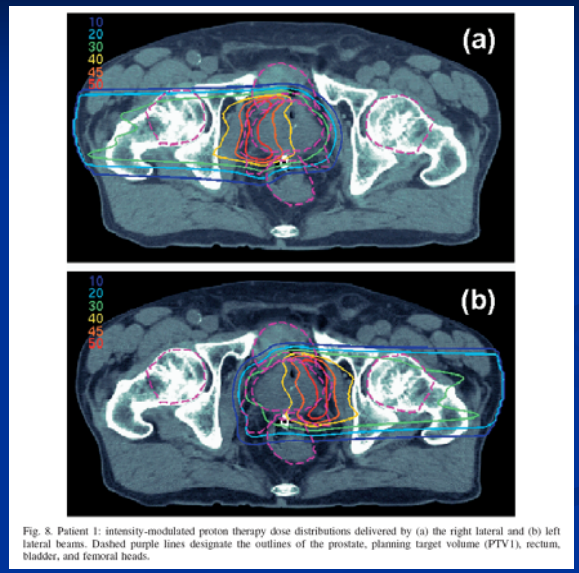
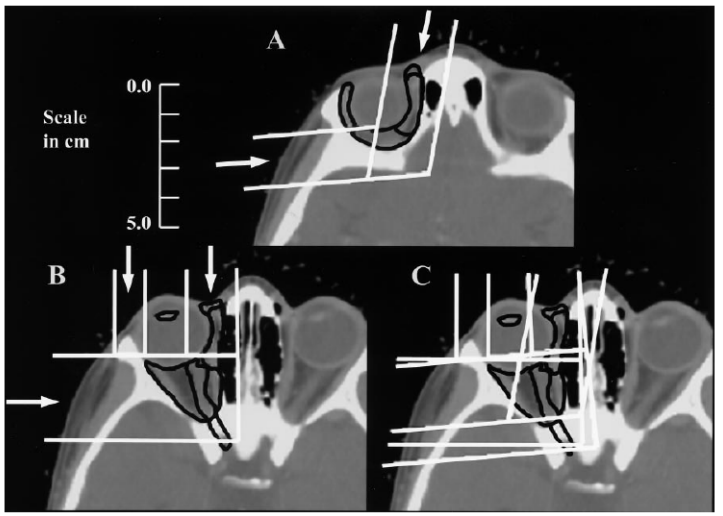


Fig. 8. Patient 1: intensity-modulated proton therapy dose distributions delivered by (a) the right lateral and (b) left lateral beams. Dashed purple lines designate the outlines of the prostate, planning target volume (PTV1), rectum, bladder, and femoral heads.

Novel Techniques: "Patch"

Int. J. Radiation Oncology Biol. Phys., Vol. 47, No. 4, pp. 979–984, 2000



Novel Techniques: "Patch"

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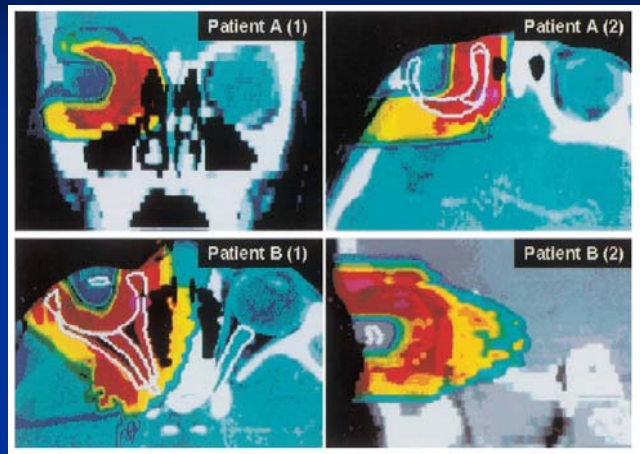


Fig. 2. Patient A. Planning CT scan in coronal (1) and transverse (2) section with clinical target volume (CTV, medial and retrobulbar), gross tumor volume (GTV, medial structure) and nontarget lacrimal gland (lateral) contoured. Color display of dose distribution starting at 10 CGE (blue) with prescribed dose levels of 40 and 50 CGE to the CTV and GTV, respectively. Patient B. Planning CT scan in transverse (1) and sagittal (2) section with clinical target volume (CTV) and nontarget lens and optic nerves contoured. Gross tumor volume (GTV) is located superiorly and is not present on these representative sections. Color display of dose distribution starting at 10 CGE (blue) with prescribed

Features Added for Proton Planning

A snout id must be selected from the snouts defined

"Alignment DRRs" can be created for beams with DRR setup parameters

The air gap from the face of aperture to the skin is specified

Sample & Average CT Values

Patch Beam Targets
Structure drawing tools must be available with beams displayed

The fabrication tool diameter must be specified

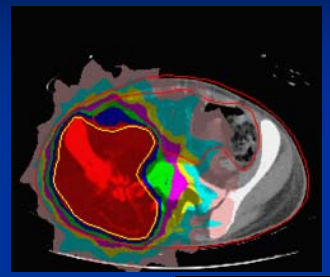
Isothickness line display of smeared, unsmeared, or double-smeared RC

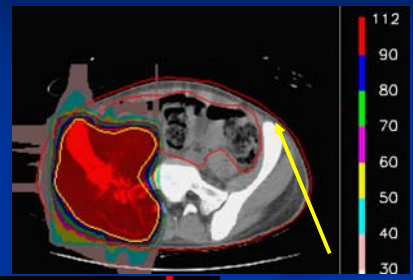
The prescribed range specified by user and validated to machine

IMPT vs. IMRT: Ewing's Sarcoma

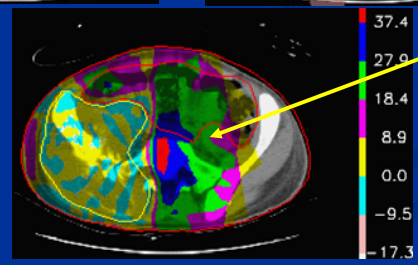
6 MV X-RAYS IMRT

PROTONS IMPT





DIFFERENCE
(IMXT - IMPT)

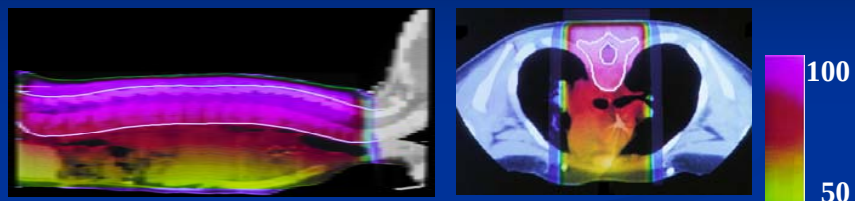


Dose Bath

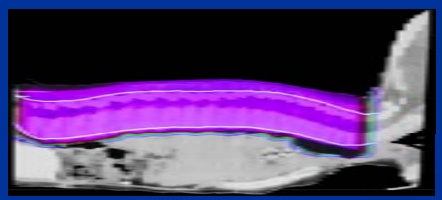
Clinical Benefit

Pediatric Medulloblastoma

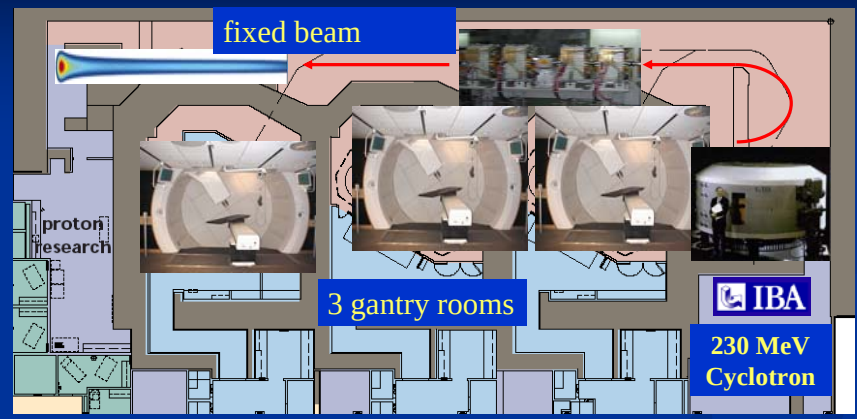
X-RAYS



PROTONS



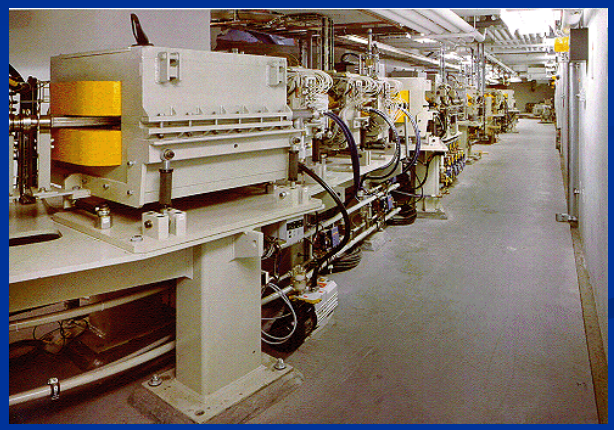
UFPTI Proton Area



- Integrated Facility Management
- Treatment Planning
- Patient Scheduling

Proton Beam Transport

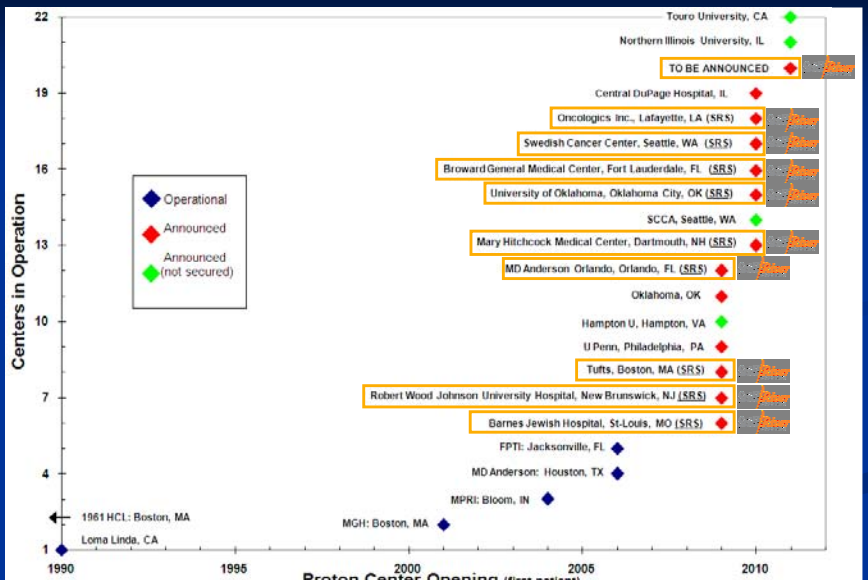
- Vacuum tubes to guide beam to its destination
- Maintains beam energy homogeneity and focusing



Proton Gantry

- Isocentric gantry with better than 1 mm isocenter radius
- 100 ton weight
- Rotation speed up to 1 RPM

Rapid US expansion of Proton Centers



Debate of Clinical Trials

Proton Therapy in Clinical Practice: Current Clinical Evidence (M. Brada, JOURNAL OF CLINICAL ONCOLOGY, 2007)

As is the case for any innovative technology, proton therapy requires considerable expertise, effort, and investment, and the introduction into clinical practice is initially without grade 1 and high-level grade 2 evidence.

Before rolling out proton therapy into daily practice, *it is necessary to establish its real additional value. This requires well-designed phase II trials and adequately powered phase III trials to provide objective information on the efficacy and toxicity compared with best conventional therapy.*

Debate of Clinical Trials

Proton Therapy in Clinical Practice: Current Clinical Evidence

The ***promising sites where protons may offer the potential advantage of more localized treatment are similar to the tumor sites where IMRT is being explored***.

However, ***prospective outcome data from appropriately designed studies in children should be available before protons become an accepted alternative to conventional therapy in pediatric tumors***.

An uncontrolled expansion of clinical units offering as yet unproven and expensive proton therapy is unlikely to advance the field of radiation oncology or be of benefit to cancer patients.

Debate of Clinical Trials

Should positive phase III clinical trial data be required before proton beam therapy is more widely adopted?

No

Herman Suit et al.

Massachusetts General Hospital,
Midwest Proton Radiotherapy Institute

Radiotherapy and Oncology (2008)

Debate of Clinical Trials

Should positive phase III clinical trial data be required before proton beam therapy is more widely adopted? No

Our assessment is that there is ***no medical rationale for clinical trials of protons*** as they deliver lower biologically effective doses to non-target tissue than do photons for a specified dose and dose distribution to the target.

Were proton therapy less expensive than X-ray therapy, there would be no interest in conducting phase III trails. The ***talent, effort and funds required to conduct phase III clinical trials of protons vs. photons would surely be more productive*** in the advancement of radiation oncology if employed to investigate real problems, e.g. the most effective total dose, dose fractionation, definition of CTV and GTV, means for reduction of PTV and the gains and risks of combined modality therapy.

Debate of Clinical Trials

Should Randomized Clinical Trials Be Required for Proton Radiotherapy? (Goitein and Cox, JOURNAL OF CLINICAL ONCOLOGY, 2008)

In our lives, we have lived to see almost identical arguments made regarding new technologies, including the introduction of cobalt-60 teletherapy, use of treatment simulators, the use of high-energy accelerators, the use of computed tomography, and so forth.

We look back now on those arguments and wonder at the poor judgment that was evidenced then, and feel sure that history will

Debate of Clinical Trials

The New York Times

By ANDREW POLLACK
Published: December 26, 2007

Cancer Fight Goes Nuclear, With Heavy Price Tag

Debate of Clinical Trials

The New York Times

By ANDREW POLLACK
Published: December 26, 2007

Proponents say that more than 800,000 Americans — representing nearly two-thirds of new cancer cases — undergo radiation therapy each year. If only 250,000 of them could benefit from protons, they would fill more than 100 centers.

"**If they built one across the street I wouldn't worry about it," said James D. Cox**, chief of radiation oncology at the M. D. Anderson Cancer Center in Houston, which opened a $125 million proton center last year.

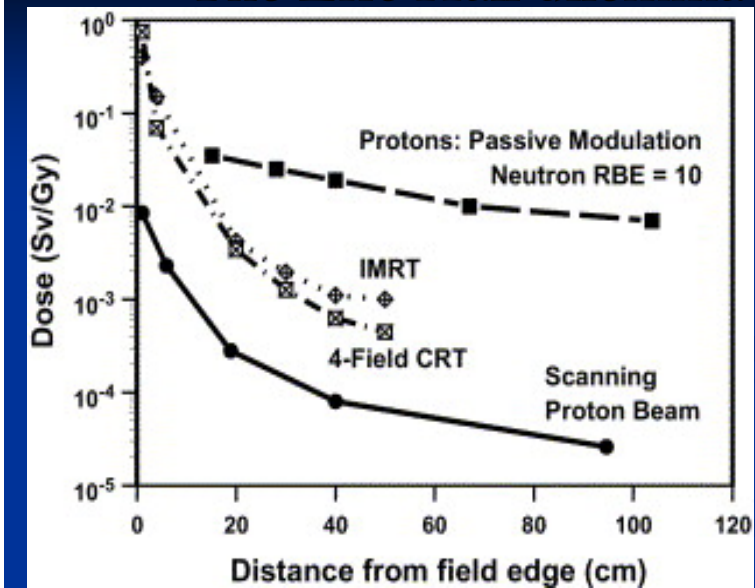
"**There are no solid clinical data that protons are better**," said Dr. **Theodore S. Lawrence**, the chairman of radiation oncology at the University of Michigan. "If you are going to spend a lot more money, you want to make sure the patient can detect an improvement, not just a theoretical improvement."

Debate of Clinical Trials

Whether or not you agree that Clinical Trials are Necessary for Protons, consider what Clinical Trials would bring to the community;

- **Standardization of Prescriptions/Limits**
  - **RBE Question: Is it 1.10, 1.20, or 1.00**
  - **PTV Prescriptions**
  - **Margin (Distal, Proximal and PTV-aperture)**
  - **OAR margins and Tolerances (RBE)**
- **Quality Assurance**
  - **RPC Involvement for Dosimetry**
  - **Plan Validation (Rx, Margins)**
  - **Field Verification Methods**
- **Quality of Life Issues**

The Eric Hall dilemma



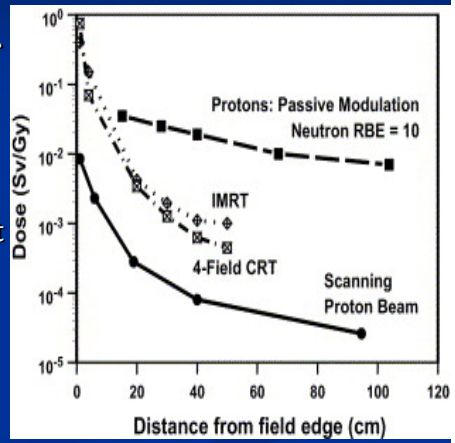
Intensity-modulated radiation therapy, protons, and the risk of second cancers. IJORBP 2006 May 1;65(1):1-

The Eric Hall dilemma

Dr. Hall's Fig. 10 (1) is incorrect by a factor ≥9 to the detriment of scattered vs. scanned protons.

The correct factor, the quality factor ratio is at most 0.9, rather than 3.5,

The estimation of # of protons was high by a factor of 2.5, etc.) p.q. FS used

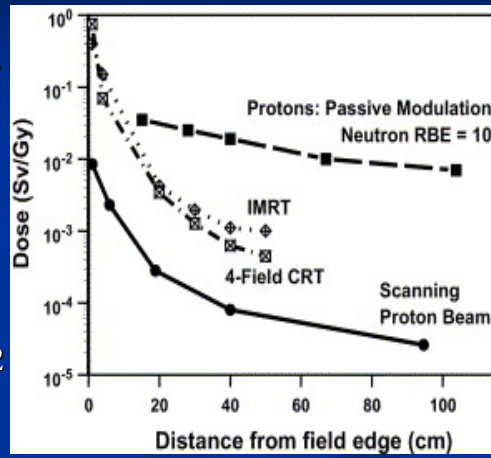


Gottschalk B.
nt J Radiat Oncol Biol Phys. 2006 Dec 1;66(5):1594

The Eric Hall dilemma

INCORRECT

- Experimental data on scattered p+ show neutron doses 2 orders of magnitude lower than shown, i.e., < photons
- The volume of non-target tissue treated at or above 30% of the prescribed dose is generally reduced by more than a factor of 2 with protons, compared to IMRT.)



H. Paganetti, T. Bortfeld, T. Delaney
IJORBP, Volume 66, Issue 5, Pages 1594-1595

Swiss 2nd Cancer study: Results

Table 3. Estimated absolute yearly rate (%) of secondary cancer incidence after treating a medulloblastoma case with either conventional X-ray, IM X-ray, or proton beams

Tumor site	X-rays (%)	IM X-rays (%)	Protons (%)
Stomach and esophagus	0.15	0.11	0.00
Colon	0.15	0.07	0.00
Breast	0.00	0.00	0.00
Lung	0.07	0.07	0.01
Thyroid	0.18	0.06	0.00
Bone and connective tissue	0.03	0.02	0.01
Leukemia	0.07	0.05	0.03
All secondary cancers	0.75	0.43	0.05
Relative risk compared to standard X-ray plan	1	0.6	0.07

Abbreviation: IM = intensity-modulated.

Table 2. Estimated absolute yearly rate (%) of secondary cancer incidence after treating a parameningeal rhabdomyosarcoma with either X-rays, IM X-rays, protons, or IM protons

	X-rays	IM X-rays	Protons	IM protons
early rate (%)	0.06	0.05	0.04	0.02
elative risk compared to standard				

Int. J. Radiation Oncology Biol. Phys., Vol. 54, No. 3, pp. 824–829, 20