Protons or Photons for Prostate Cancer: The Case for Equipoise

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Disclosures

- I have never used protons
- Duke is exploring protons
- I was trained in Gainesville

Proton beam is an
excellent treatment
for prostate cancer…

..as are active surveillance,
radical prostatectomy,
IMRT and brachytherapy.

Goitein and Cox

1) Depth dose superior; entrance and exit
2) All relevant differences are physical; biology doesn't matter
3) Severity of tissue injury increases with dose

"These points are not contested… they are demonstrated facts."

JCO 26:175, 2008

Goitein and Cox

"..the practitioners of proton beam therapy have found it ethically unacceptable to conduct RCTs comparing protons with x-rays."

They have lost equipoise.

JCO 26:175, 2008

Goitein and Cox

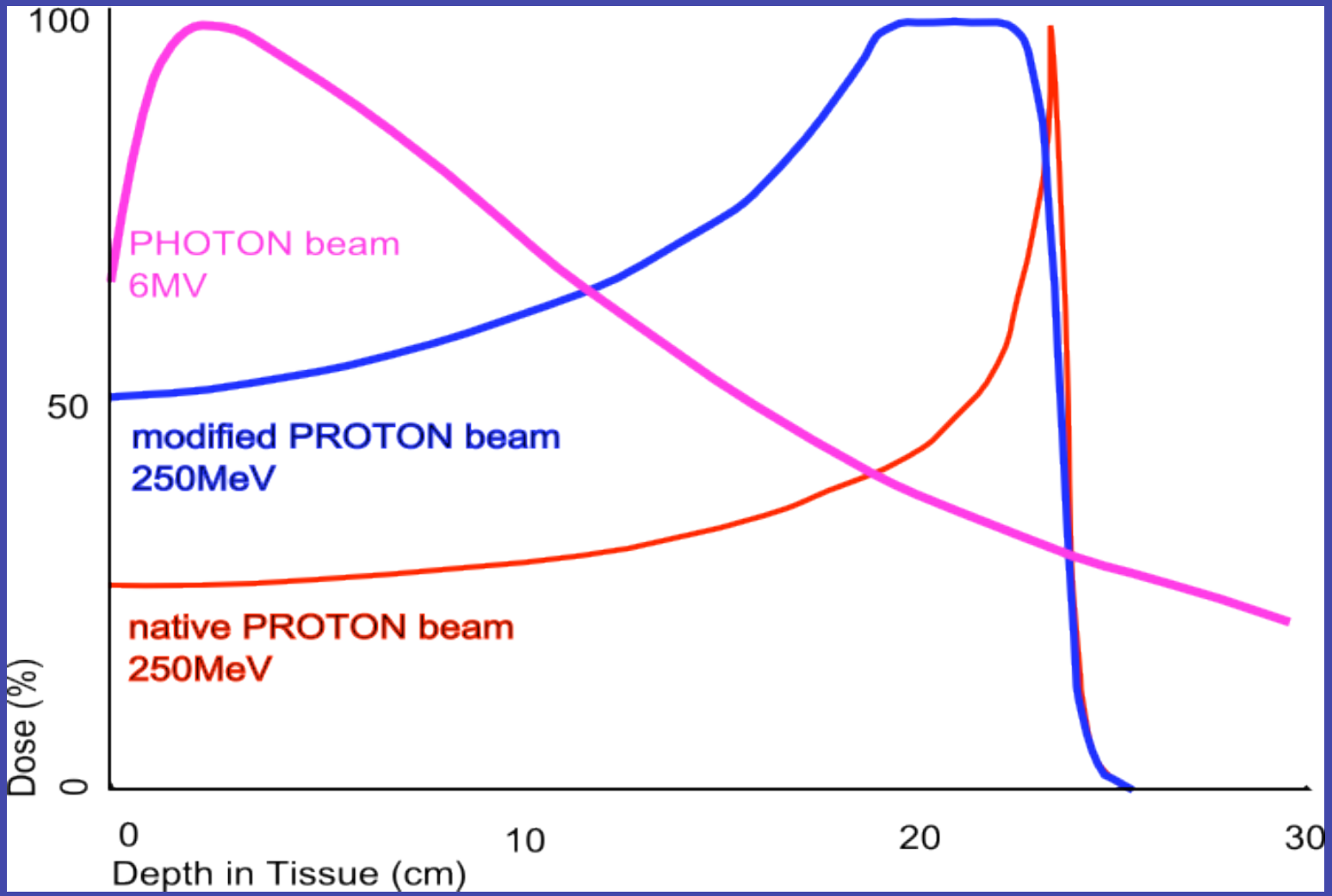
1) Depth dose superior; entrance and exit (Physics)
2) All relevant differences are physical; biology doesn't matter (Biology)
3) Severity of tissue injury increases with dose (Clinical Oncology)

Contesting the Uncontested!

JCO 26:175, 2008

Ernest Rutherford

Physics of Protons



Is it really this simple?

Physics of Protons

Uncertainties:

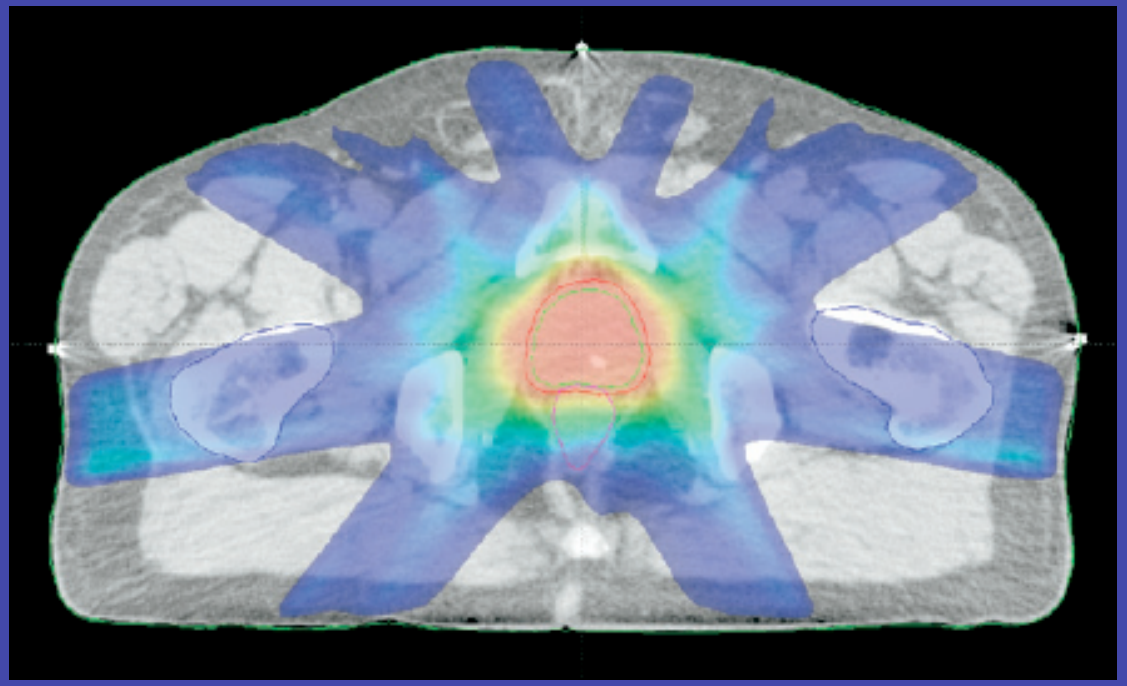
- CT approximation
- Tissue inhomogeneities
- Accelerator energy
- Scattering system
- Compensator density

Distal margin is uncertain

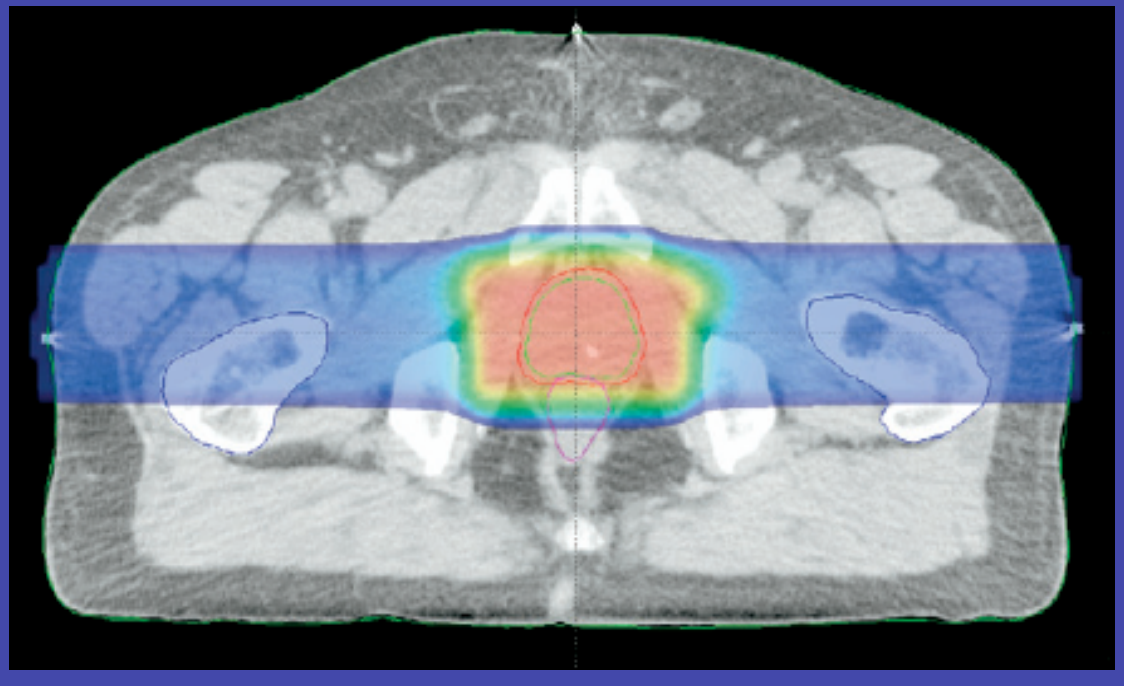
Physics of Protons

The inherent uncertainties of the proton beam dose **should** lead to an **increase** in PTV for proton therapy.

$$PTV_{prot} > PTV_{phot}$$



IMRT



Prot

Physics of Protons

"The great advantage that protons have of stopping at a well-defined depth within the patient is also a source of difficulty."

"…the perception that proton technology is mature is wrong."

Goitein, IJROBP 70:654, 2008

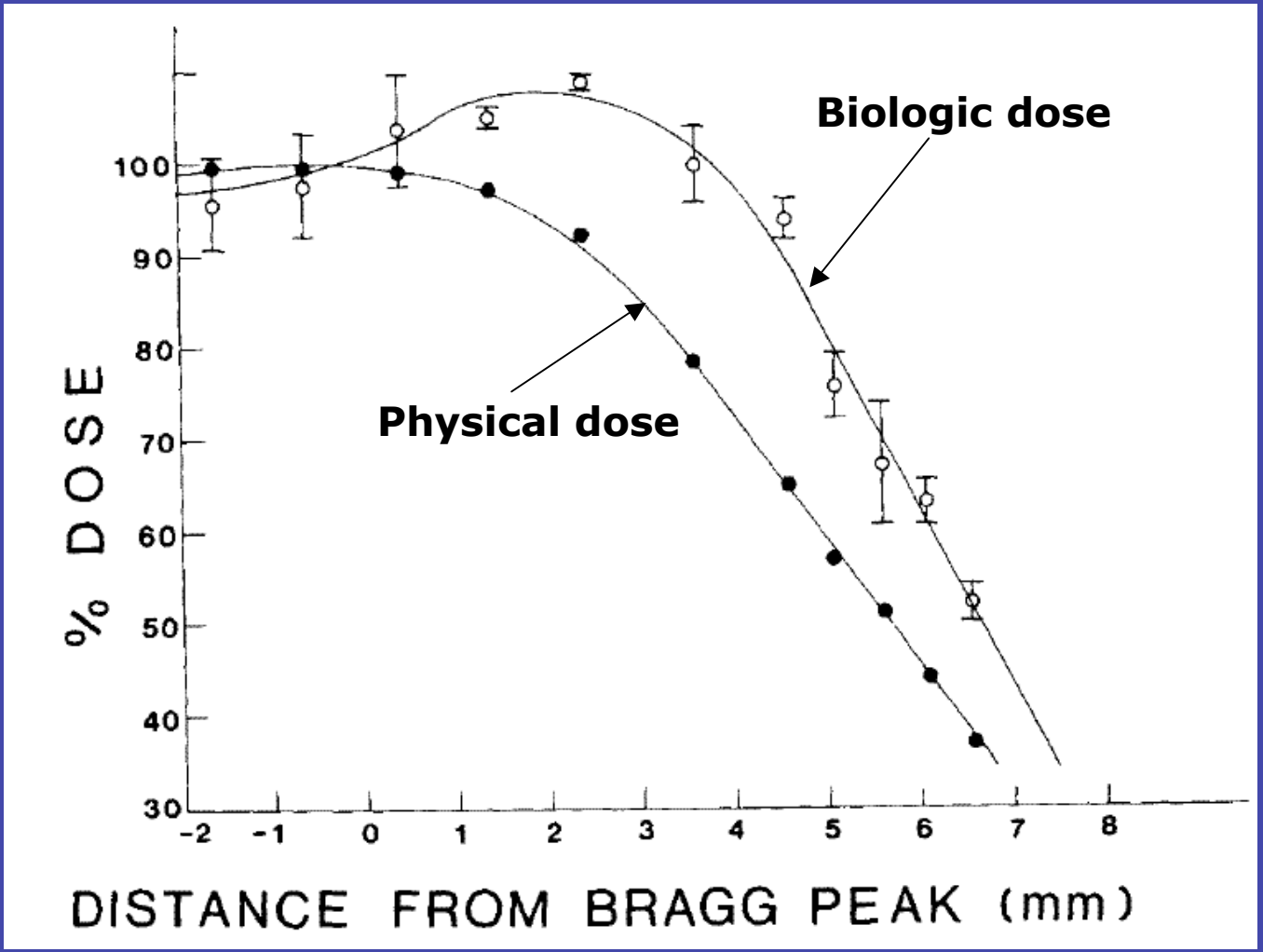
Physics of Protons

I reserve the right
to be skeptical of
any study/report if
these uncertainties
are not considered.

Protons are not photons!

Herman D. Suit

Biology of Protons



RBE increases beyond peak!

Robertson, Cancer 35: 1664, 1975

Biology of Protons

"..there is a local "hot region" over the terminal few millimeters of the SOBP and an extension of the biologically effective range. This needs to be considered in treatment planning, particularly for single field plans or for an end of range in or close to a critical structure."

Paganetti, IJROBP 53:407, 2002

Biology of Protons

"For SOBP proton beams, variations in RBE with dose, target characteristics, and position appear to be in the range of 10-15% or less. Effective dose (RBE times physical dose) **may** appreciably impact treatment outcome."

Gerweck and Paganetti
"Proton and Charged Particle Radiotherapy", 2008

Gilbert H. Fletcher

Clinical Oncology

Goitein and Cox:

"Radiation delivered to normal tissues causes damage to them, just as it does to tumors, and the severity of that damage increases with increasing dose."

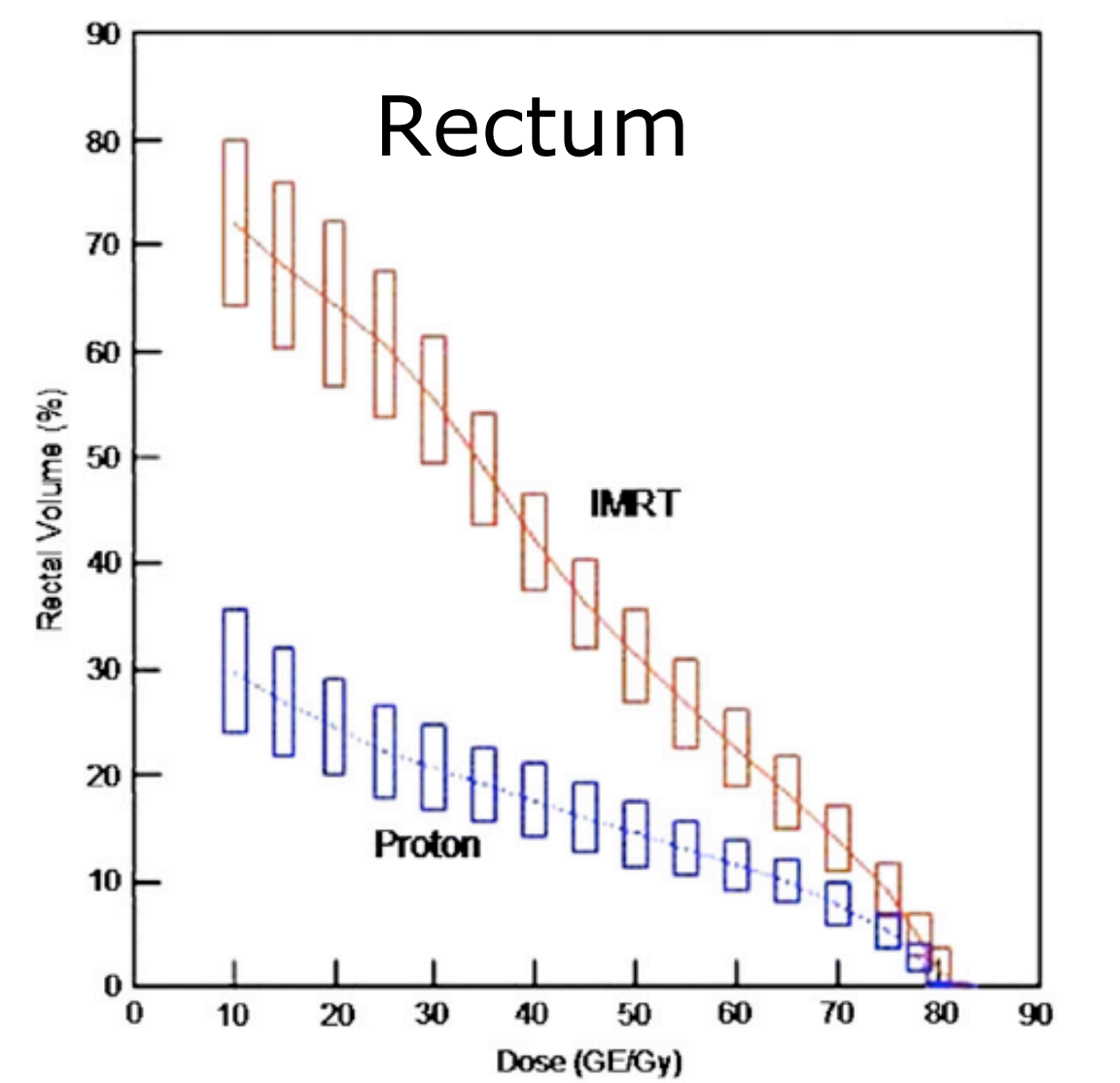
JCO 26:175, 2008

Clinical Oncology

DVH comparisons:

- Dependent on planner
- Dependent on TPS
- ? $PTV_{prot} > PTV_{phot}$
- ? RBE increase beyond peak

DVH comparisons



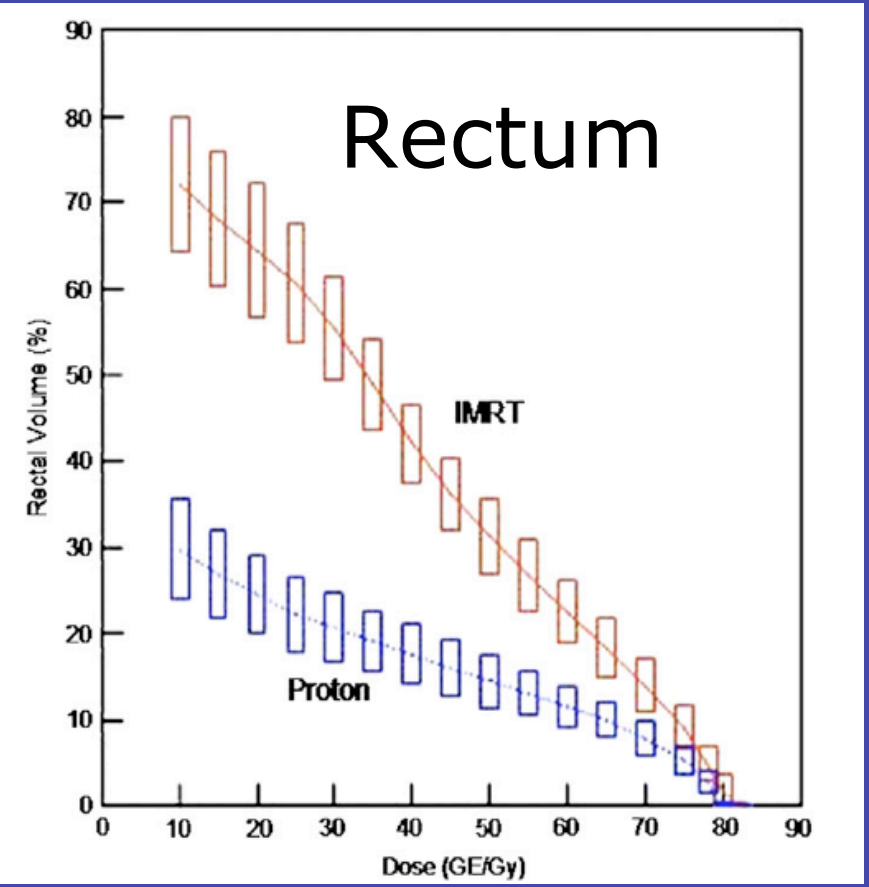
IMRT can do better; push the constraints!

PTVprot = PTVphot

Vargas, IJROBP 70:744, 2008

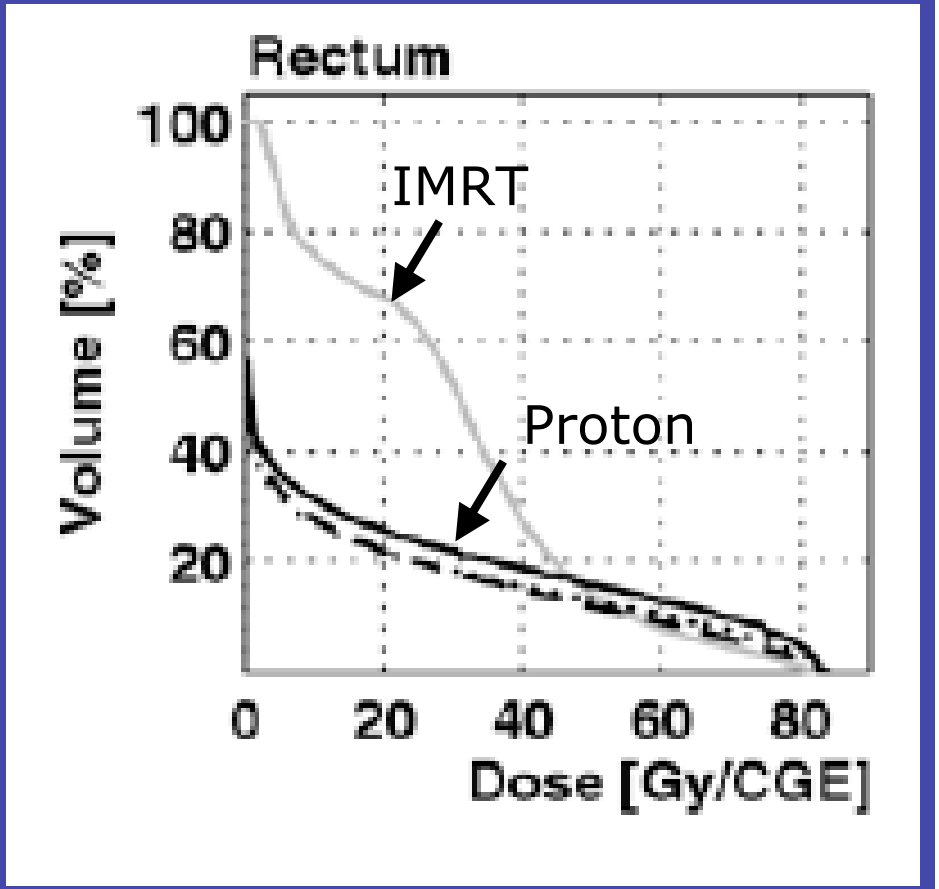
DVH comparisons

UF



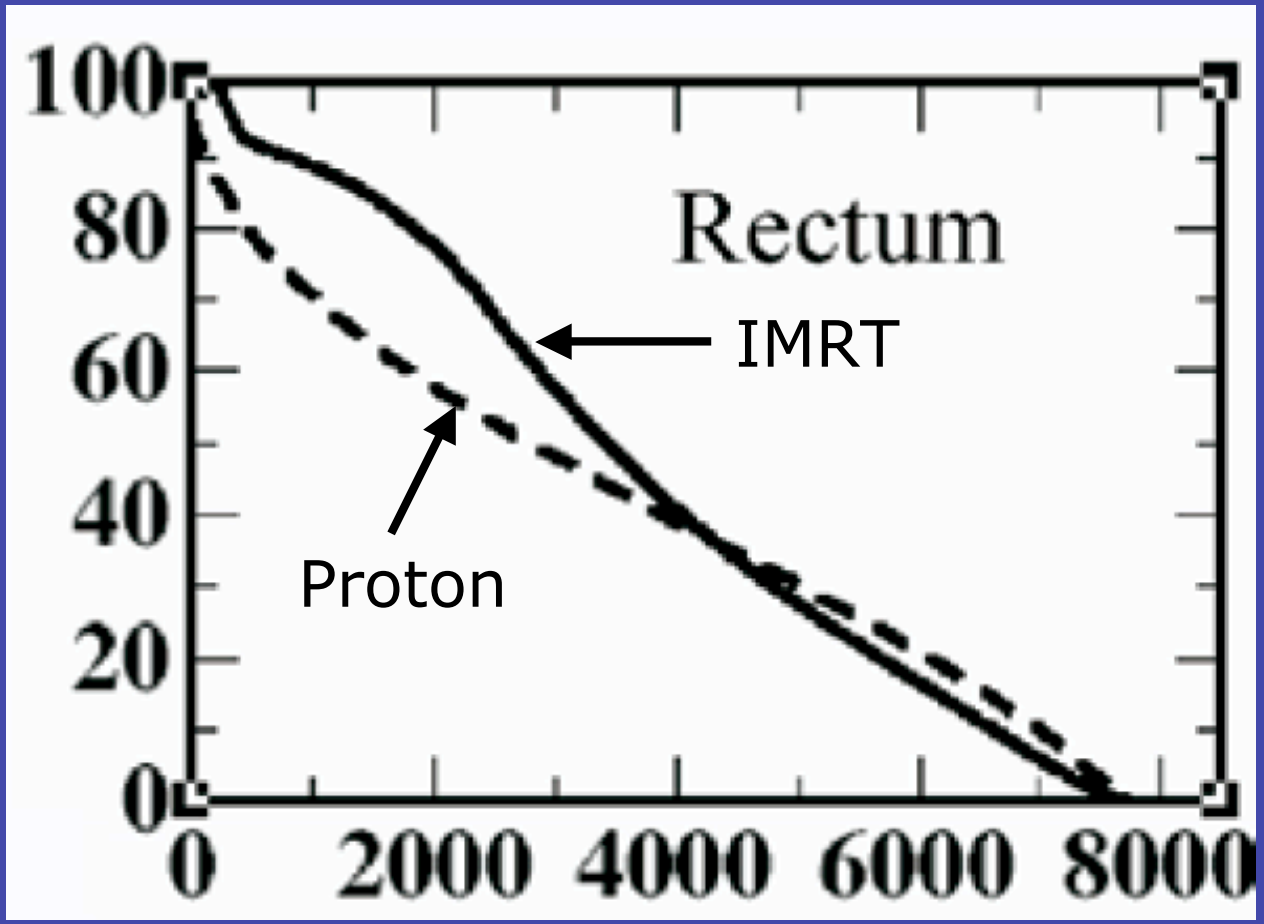
Vargas, IJROBP 70:744, 2008

MGH



Trofimov, IJROBP 69:444, 2007

DVH comparisons



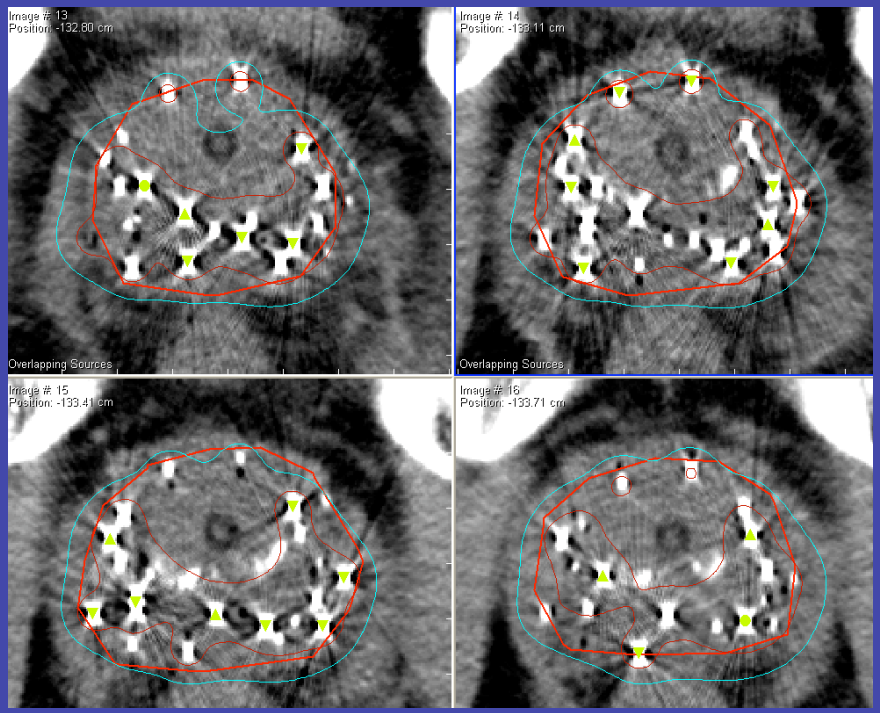
"The proton therapy plan was better at sparing the rectum at doses of less than 50 Gy. However, above 50 Gy, IMRT was better at sparing the rectum."

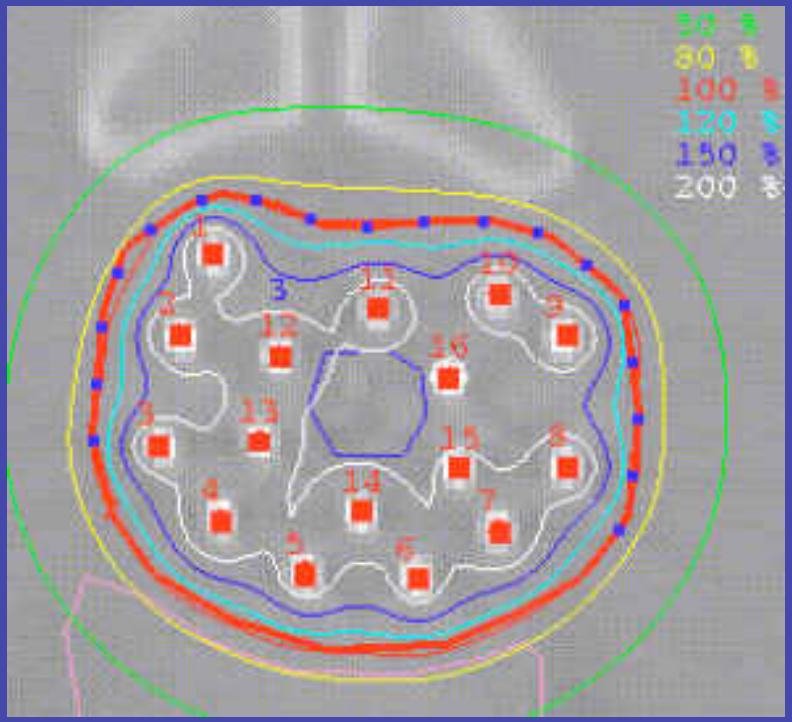
Zhang IJROBP 67:620, 2007

DVH Idolatry

We must be very careful
about the use of DVH
to argue for superiority;
clinical results in patients
should always matter
more than any surrogate.

DVH comparisons





Brachytherapy always wins!!

Goitein and Cox

1) Depth dose superior; entrance and exit
2) All relevant differences are physical; biology doesn't matter
3) Severity of tissue injury increases with dose

"These points are not contested… they are demonstrated facts."

It's not that simple…..

JCO 26:175, 2008

Protons or Photons for Prostate Cancer: Do We Need a Randomized Trial?

Proton Propaganda

A randomized trial has demonstrated that the higher total dose **made possible by protons** results in a higher biochemical disease-survival rate, with **no increase in radiation-related complications**.

Loma Linda Website, accessed 3/19/08

This unique characteristic gives proton therapy the ability to deposit a radiation dose in a **precise** manner and thus minimize damage to the surrounding normal tissue. This leads to **better cancer control with fewer side effects.**

MD Anderson website, accessed 3/19/08

"We have patients who **get treated in the morning** and **play golf in the afternoon**."

Jim Cox, The Economist 3/8/08

Superiority?

- Postmenopausal HRT
- Bare-metal coronary stents
- Megadose anti-oxidants
- BMT in breast cancer
- Swan-Ganz catheters
- Gabapentin in bipolar
- Erythropoietin
- Rofecoxib

Emanuel, JAMA 297:2131, 2007

A Possible Way Out

- Registry study
- HRQOL endpoint
- Patient-reported

Clinicians don’t gather data!

The Last Word

"…given that protons are a limited and expensive resource, it is important to identify the indications for which protons would probably have the greatest advantage—presumably largely for situations in which current therapies are inadequate."

Goitein and Cox JCO, 2008 epub 4/28/08