

The Rise, Fall, and Rise Again of Proton Therapy

or

Never count out a well-financed therapy

Anthony Zietman MD
Shipley Professor of Radiation Oncology
Massachusetts General Hospital
Harvard Medical School

The rollercoaster ride of proton therapy and prostate cancer

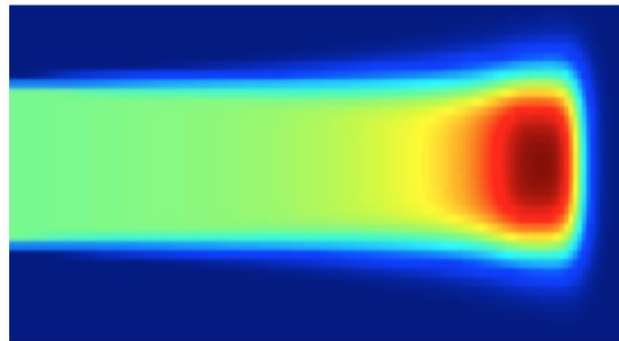
- **Hope**
- **Disappointment**
- **Shame**
- **Resurrection**

The rollercoaster ride of proton therapy and prostate cancer

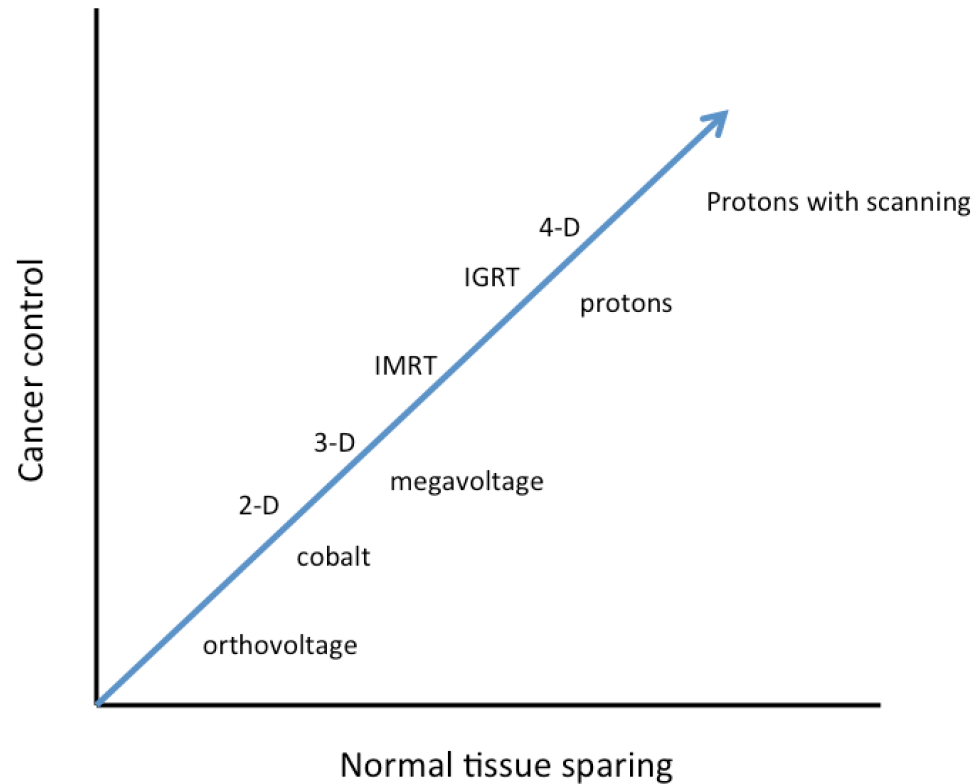
- **Hope**
- Disappointment
- Shame
- Resurrection



A century of “delivery tools” in radiation oncology

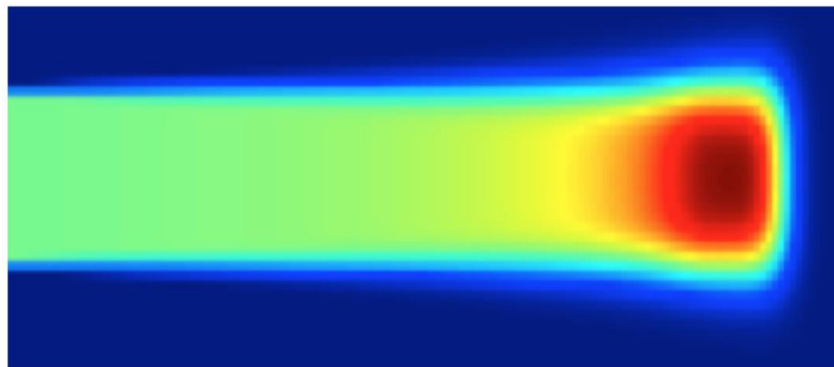
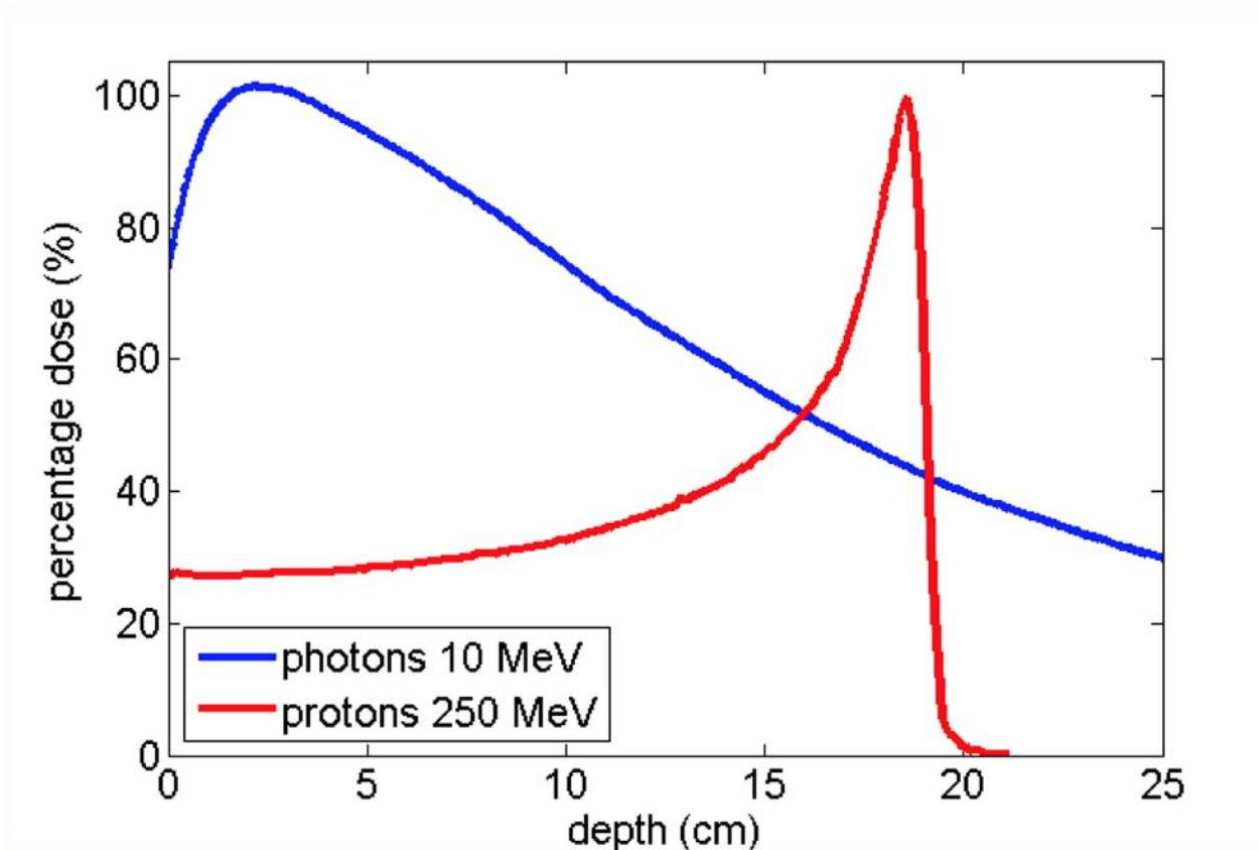


The “arrow of progress”



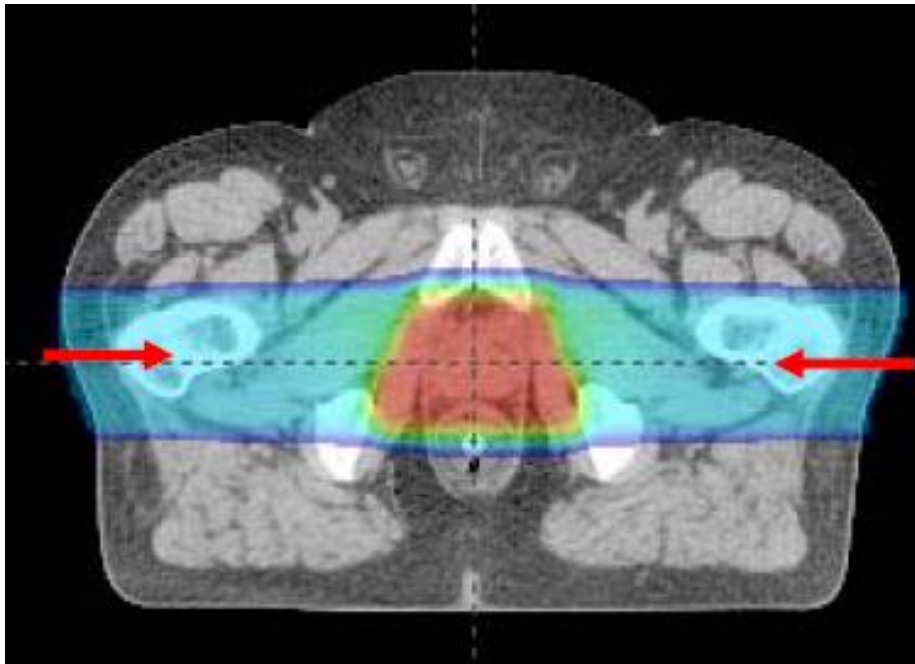
Protons – “The Point of the Arrow”

Protons – a substantial upgrade

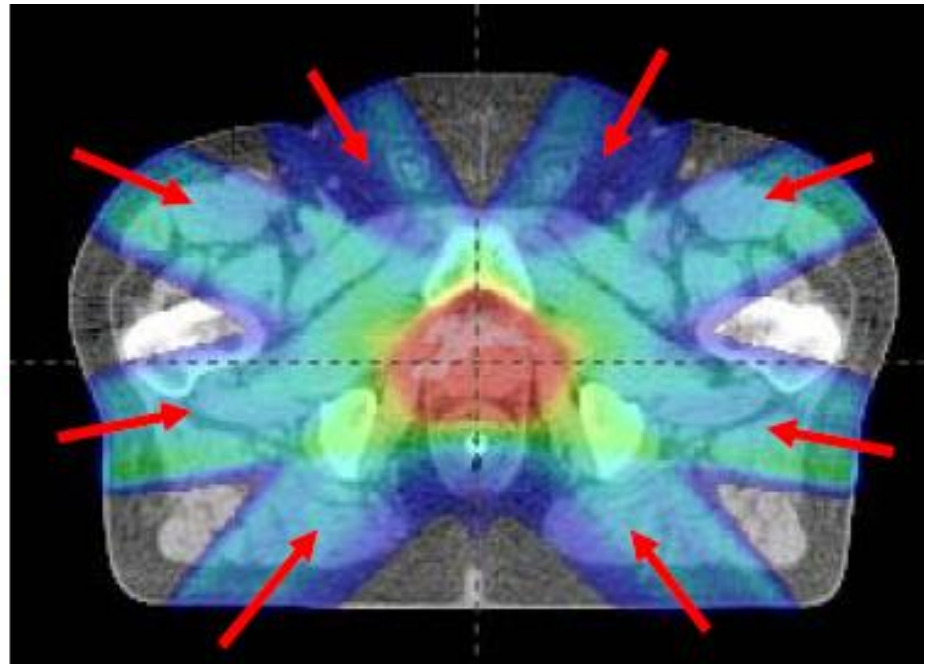


But let's discuss prostate cancer

Protons



IMRT

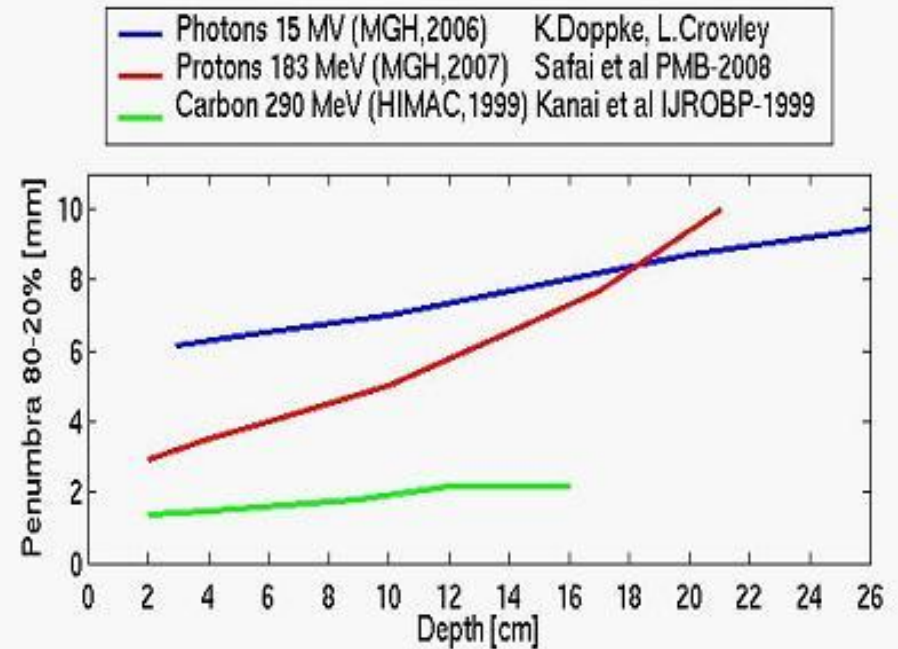
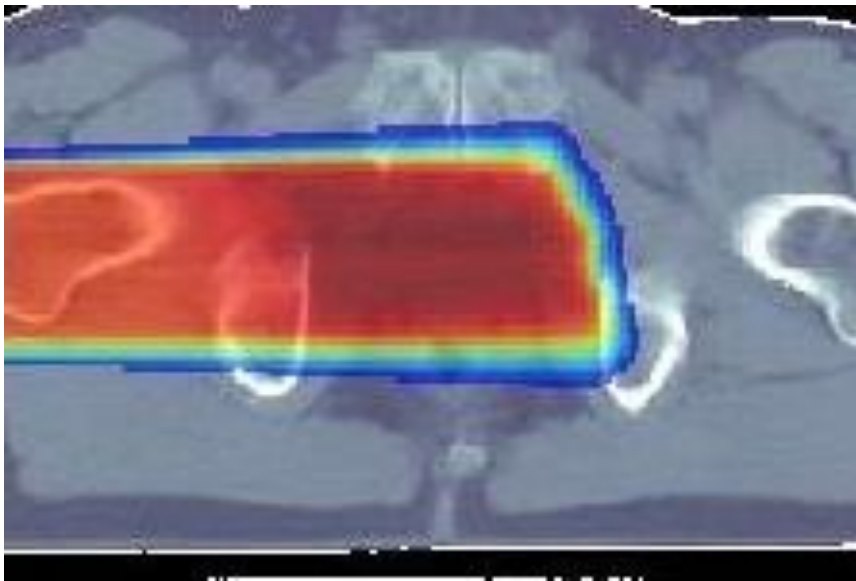


The rollercoaster ride of proton therapy and prostate cancer

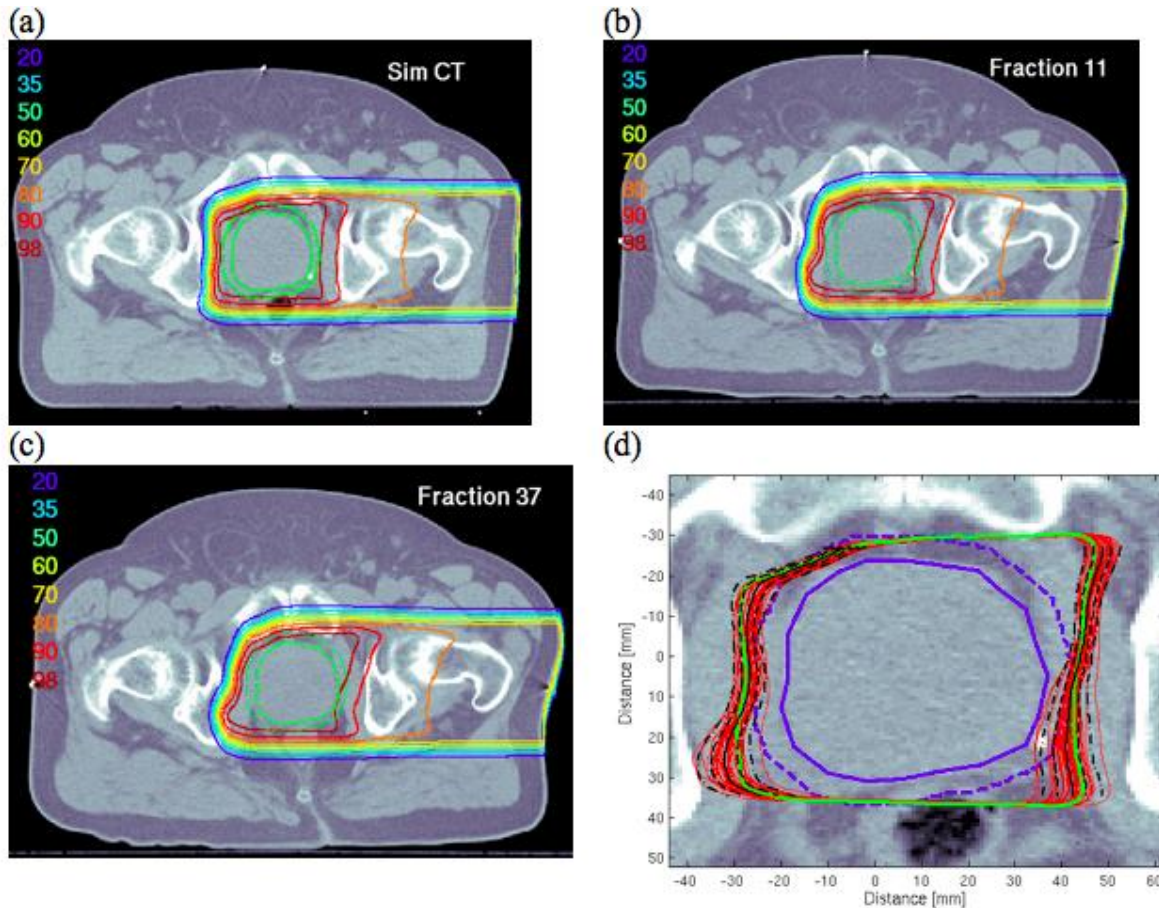
- Hope
- **Disappointment**
- Shame
- Resurrection



Physical uncertainties – the penumbra



Physical uncertainties: Inhomogeneity and end-range-uncertainty

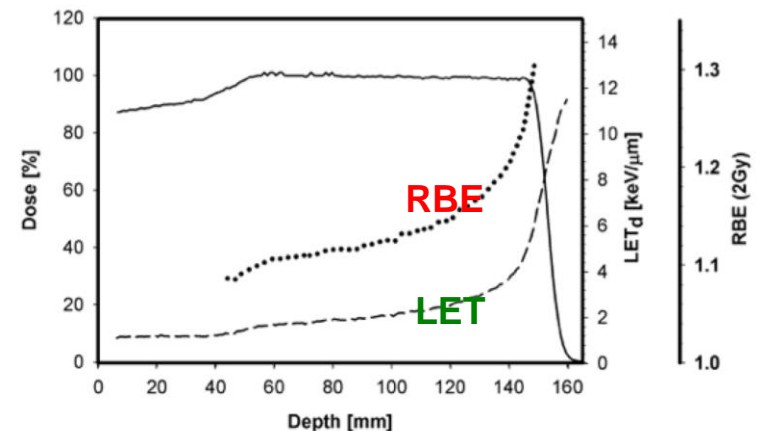


Biological uncertainties

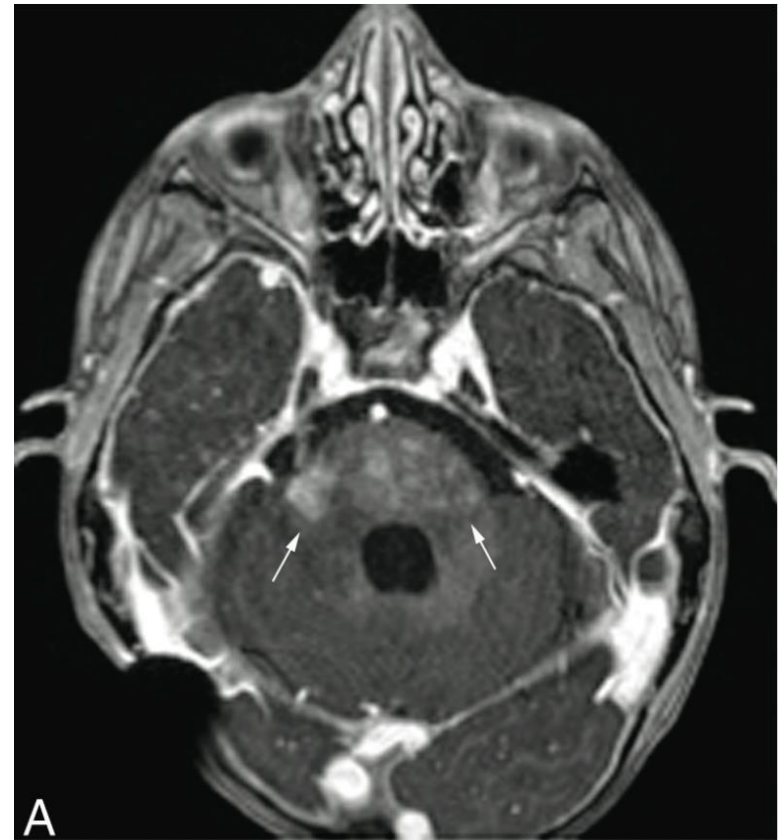
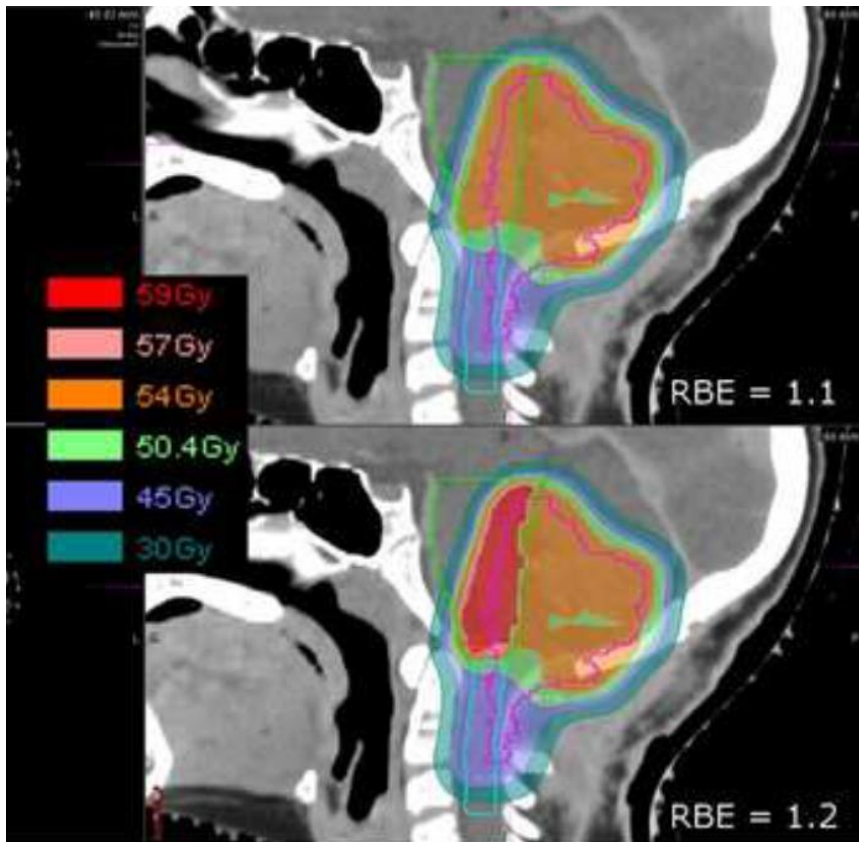
The RBE of a proton beam is approximated at 1.1

But.....

- It changes with LET
- It changes across the SOBP
- It is highest just beyond the Bragg peak
- It changes with fraction size
- It changes with A/B ratio of tissue



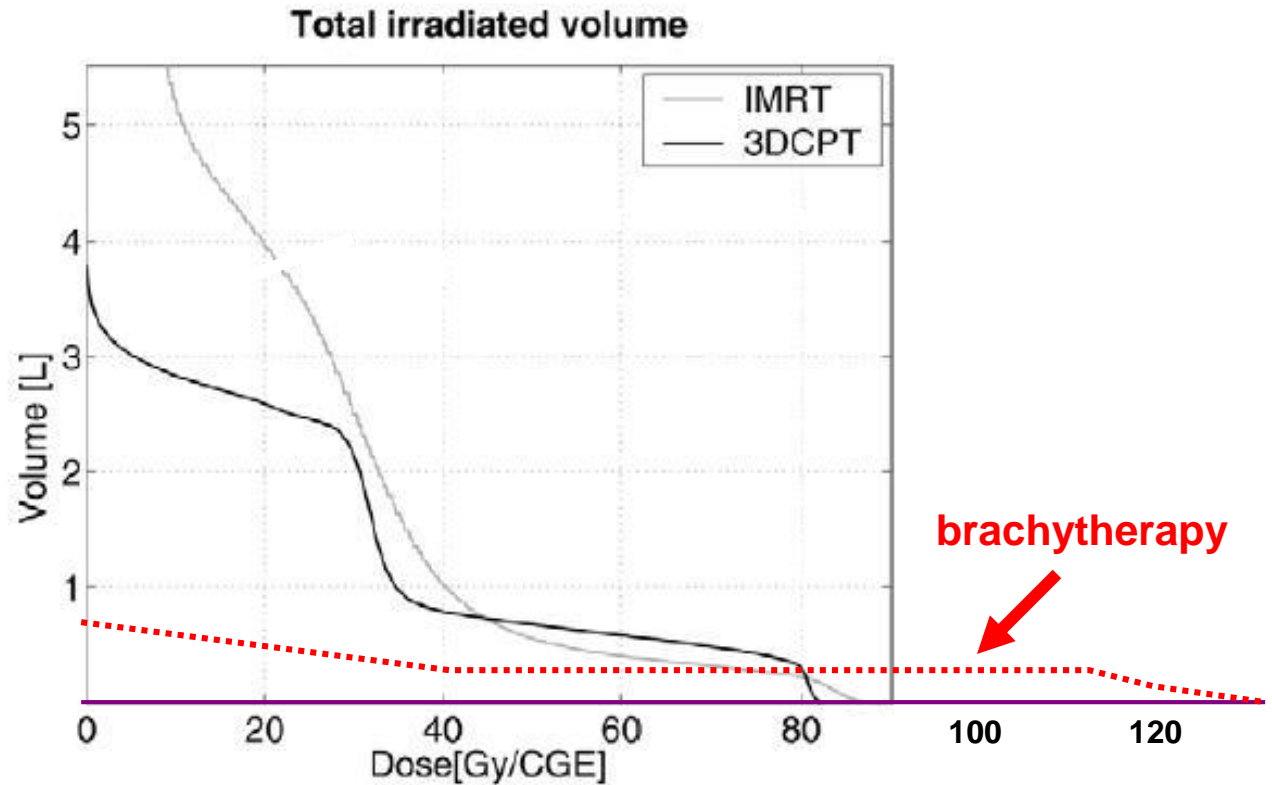
Biological uncertainties



Foe and Friend

Whole body radiation dose

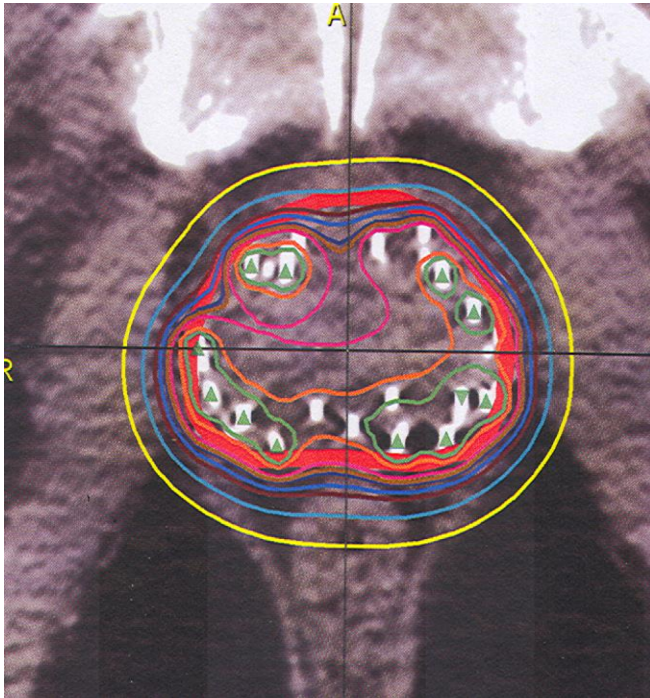
Prostate
plan



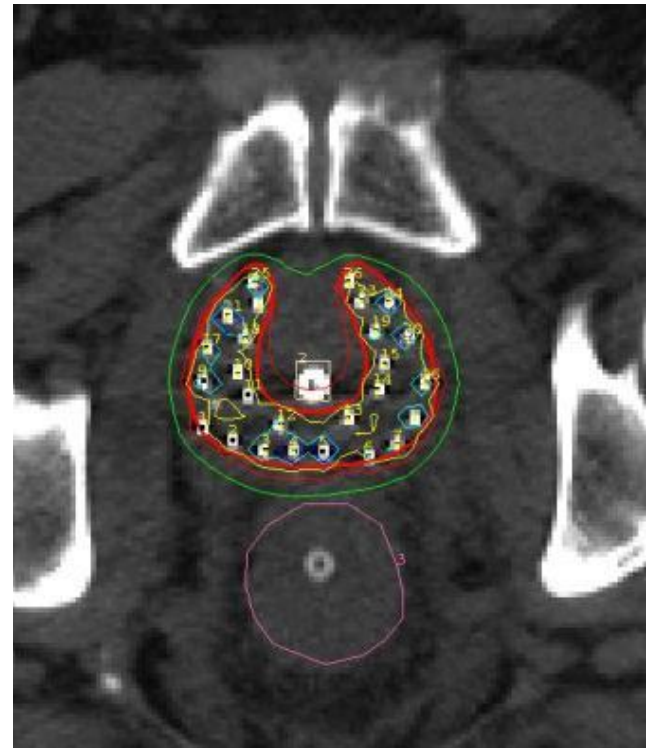
Trofimov et al IJROBP 2007

If comparing treatment plans.....

LDR



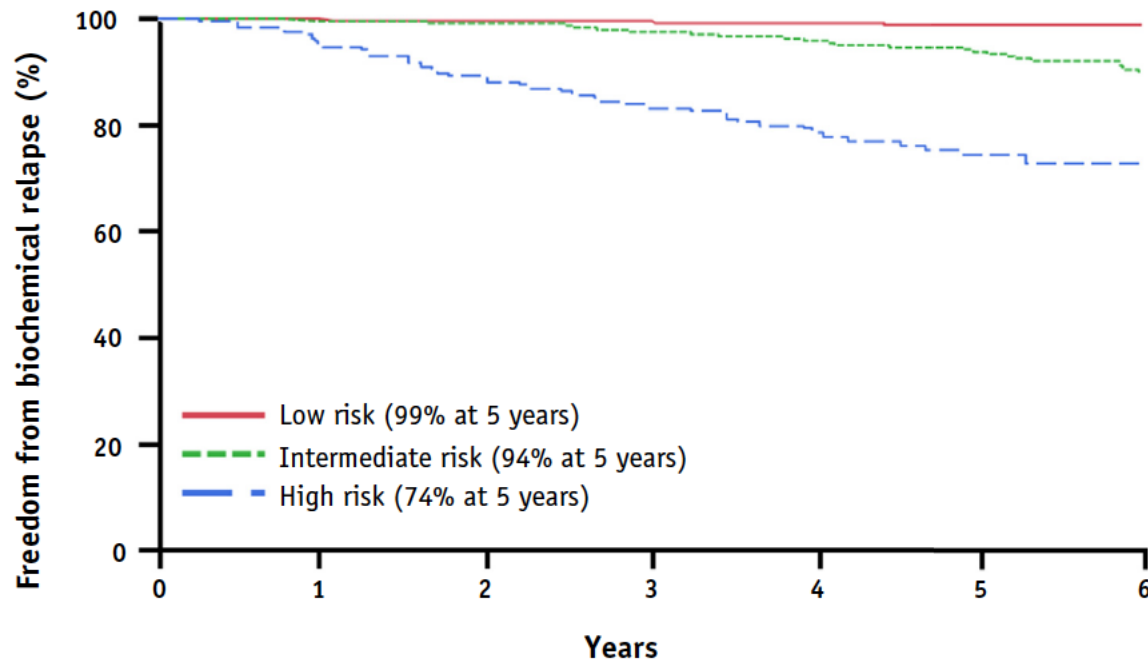
HDR



Brachytherapy always wins!!

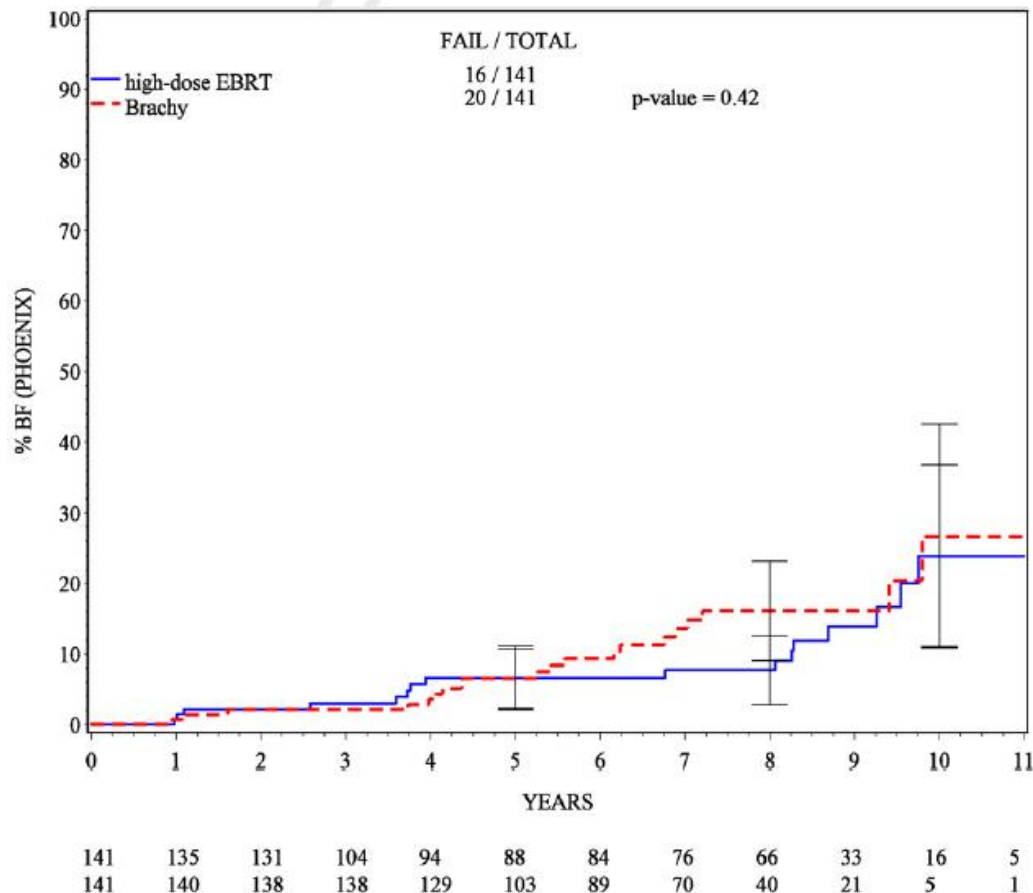
Does it cure patients ?

University of Florida



Does it cure more patients than brachytherapy ?

Case-matched analysis: $n = 141 + 141$



Can we dose-escalate further ?

MGH-LLUMC prospective protocol

82Gy Passively scattered opposed lateral beams

Median follow-up 32 months

	Late morbidity	
	GU	GI
Grade 2+	30%	12%
Grade 3+	8%	1%

Does it reduce morbidity?

Two contemporaneous cohorts:

- **PROG 9509** **9.4 years**
- **Boston survey** **5.9 years**

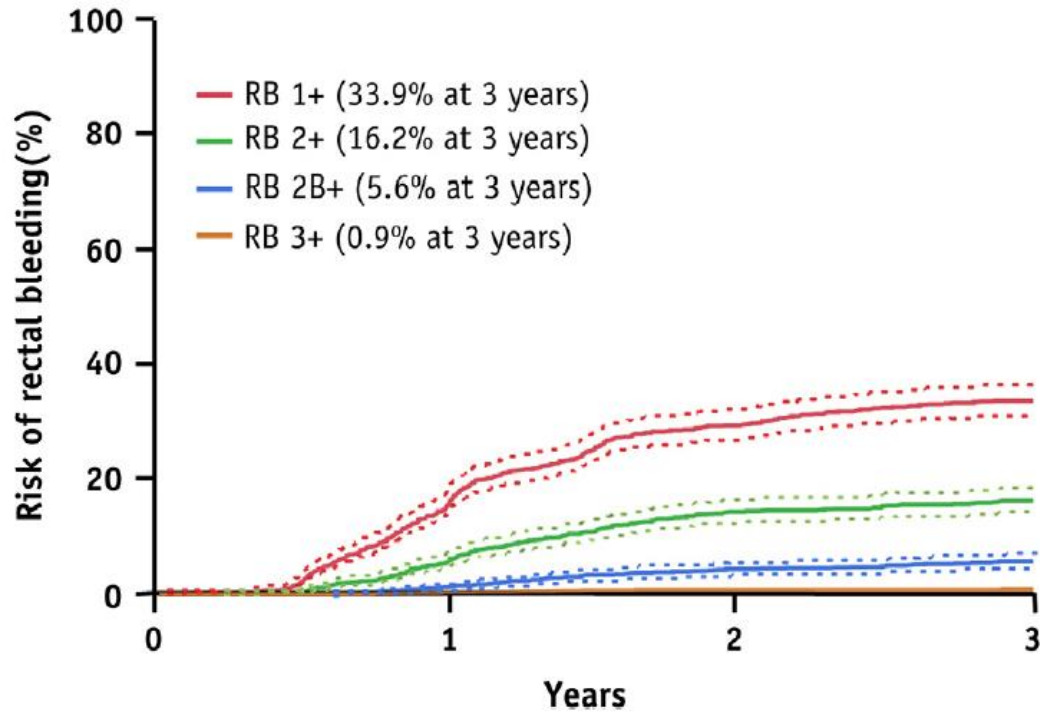
	PROG 9509	Boston survey
Number	280	97
Age at survey	76	75
Urinary obst/irr	24.0	21.8
Incontinence	10.2	11.2
Bowel problems	7.8	10.6
Sexual problems	67.1	76.3

Talcott et JAMA 2010

Does it reduce morbidity?

U Florida

1285 patients with median FU 3.5 years

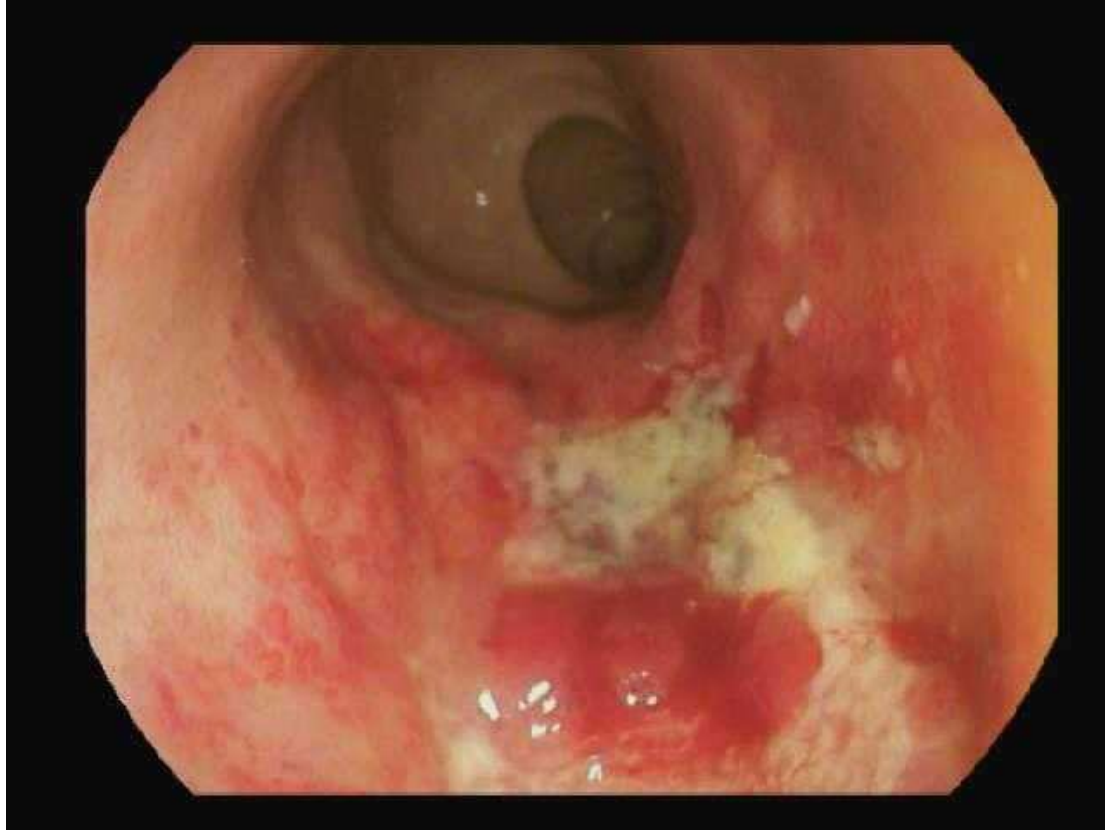


Colaco et al IJROBP 2014

Does it increase morbidity ?

IMRT vs Protons	HR
GI diagnoses	0.66
Hip fractures	NS
ED	NS
Urinary incontinence:	NS
(diagnoses, and procedures)	

**Physics looks better but could the
biology be worse ?**



**Proton beam appears to be
a reasonable treatment
for prostate cancer...**

**....as are radical prostatectomy,
IMRT, VMAT, brachytherapy, SBRT,
and active surveillance.**

The rollercoaster ride of proton therapy and prostate cancer

- Hope
- Disappointment
- **Shame**
- Resurrection



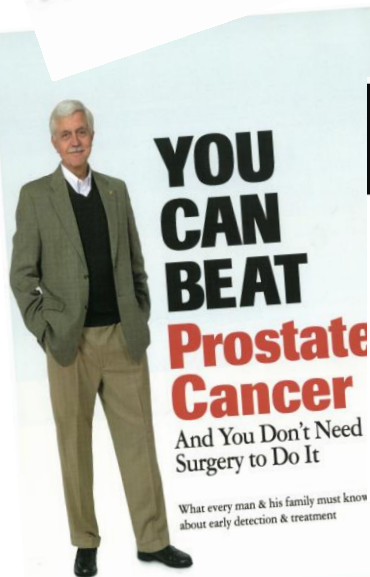
Prostate cancer was the economic driver for for the “Great Proton Expansion”

- **PSA screening and a huge “need”**
- **Good results relative to 1990s alternatives**
- **Patient and industry advocacy**
- **The Internet**
- **Competition and the need for prestige projects**
- **Novel financing and minimal FDA scrutiny**

Powerful influences

ProCure
TREATMENT CENTERS, INC.

CBS EVENING NEWS
with Katie Couric



This is the book the author wishes had been available when he was diagnosed with prostate cancer.

By
Prostate Cancer Survivor,
Robert J. Marckini



U.S. Edition ▾

News Video TV Opinions More...

U.S. World Politics Tech Health Entertainment Living Travel **Money** Sports

New York City, NY 37° Sign in

Search CNN

Is proton therapy the 'magic bullet' for cancer?

By Peter Shadbolt, for CNN

Updated 8:33 AM ET, Thu January 22, 2015



U.S. News & WORLD REPORT

HITACHI
Inspire the Next

Societies that allow medical advertising regularly see “arms races”

da Vinci Surgery Specialists

LESS INVASIVE.
MORE PRECISE.
FASTER RECOVERY.



Dr. Sherri Levin
Sherri S. Levin, M.D. & Associates
SERVING HOUSTON AREA WOMEN SINCE 1989

Robotic Surgery • Gynecology • Fertility • Obstetrics
Office Based Procedures • Medical Cosmetic Services

Danielle Wiest, da Vinci® Surgery Hysterectomy Patient



I'M A DA VINCI® BELIEVER
BECAUSE I GOT BACK TO MY LIFE QUICKLY

Since 2000, more than 1.5 million minimally invasive surgeries have been performed worldwide using the da Vinci Surgical System. This advanced technology provides surgeons with enhanced visualization, precision and control. In fact, 100% of the top 50 cancer hospitals in the United States use the da Vinci Surgical System.

Patients like Danielle Wiest are believers because results matter.

da Vinci Surgery
Results Matter.
See facts and clinical data
at www.davincisurgery.com/facts

Patients can typically maintain
intimacy during treatment.

Proton therapy

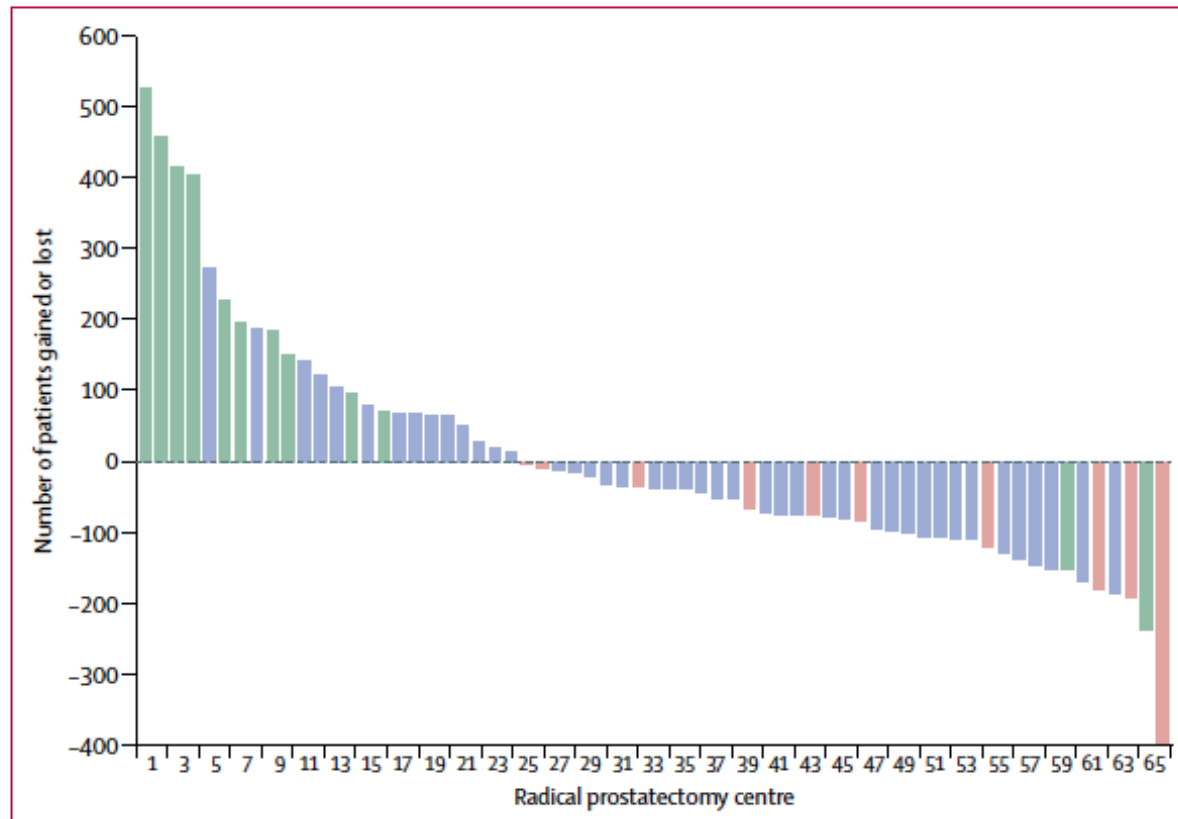
Fighting cancer

Not treatment side effects

ProCure
Proton Therapy Center



65 UK Radical Prostatectomy centers 2010-2014 during an era of patient choice



Green – robotic centers

Red – centers that closed

Blue – non-robotic centers

Competition and the Prestige Project

Patients and hospital CEOs alike want:

- **Robotic surgery**
- **PET scanners**
- **Proton therapy centers**

Competition and the Prestige Project

How is a prestige project funded?

- **Federal or state grants**
- **Deep pockets**
- **Philanthropy**
- **Loans**

Proton facility economics: the importance of prostate treatment

- **“Simple” prostate treatments have 70% of reimbursement of “complex” (pediatric, skull base)**
- **But 3-5 prostate cases can be treated for every “complex”: case**

Johnstone et al JACR 2012

**Market forces can overwhelm
a weak evidence base**

**Patterns of “care” become
disconnected from evidence**

VOLUME 25 • NUMBER 24 • AUGUST 20 2007

JOURNAL OF CLINICAL ONCOLOGY

E D I T O R I A L

The *Titanic* and the Iceberg: Prostate Proton Therapy and Health Care Economics

Anthony L. Zietman, *Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA*

Problem identified at highest level



Ezekiel Emanuel – New York Times Dec 2011

“The practice of no value medicine”

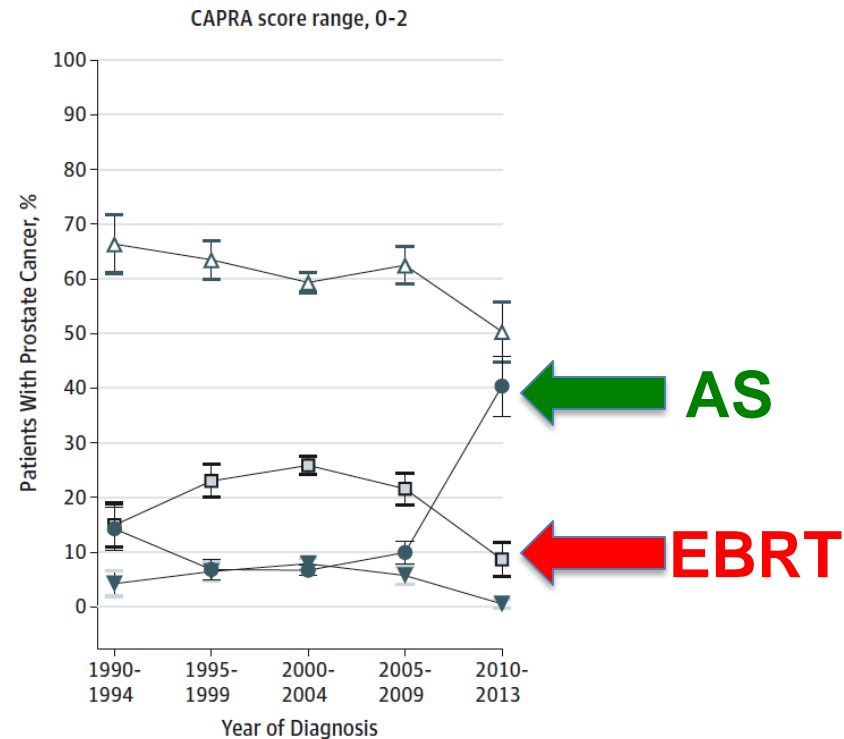
Payers revolt



**BlueCross
BlueShield**

Bottom drops out of the prostate “market”

- Rise of active surveillance
- Rise of the robot



Indiana public media

PROGRAMS ▾

PODCASTS ▾

VIDEO ▾

home

radio

tv

news

arts & music

kids & families

events

News



Business

Education

Environment

Justice

Politics

Health

Science

IU Proton Therapy Center And Cyclotron Facilities To Close

By CASEY KUHN

Posted August 22, 2014



67 people like this. [Sign Up](#) to see what your friends like.

The IU Health Proton Therapy Center and Cyclotron facilities will close in January 2015.

Proton therapy center files for bankruptcy



Scripps Proton Therapy Center opened in 2014 with five treatment bays and a 90-ton cyclotron that used magnets to accelerate

THE WALL STREET JOURNAL.

Big Bets on Proton Therapy Face Uncertain Future

Insurers balk at expensive radiation treatment; can smaller machines turn the tide?

Proton Therapy – At the “Tipping Point”

- **Payers revolt**
- **Lack of evidence base**
- **Alternative therapies**
- **Size and cost**

Can anything stop the bubble bursting?

The rollercoaster ride of proton therapy and prostate cancer

- Hope
- Disappointment
- Shame
- **Resurrection**

Can anything stop the bubble bursting?

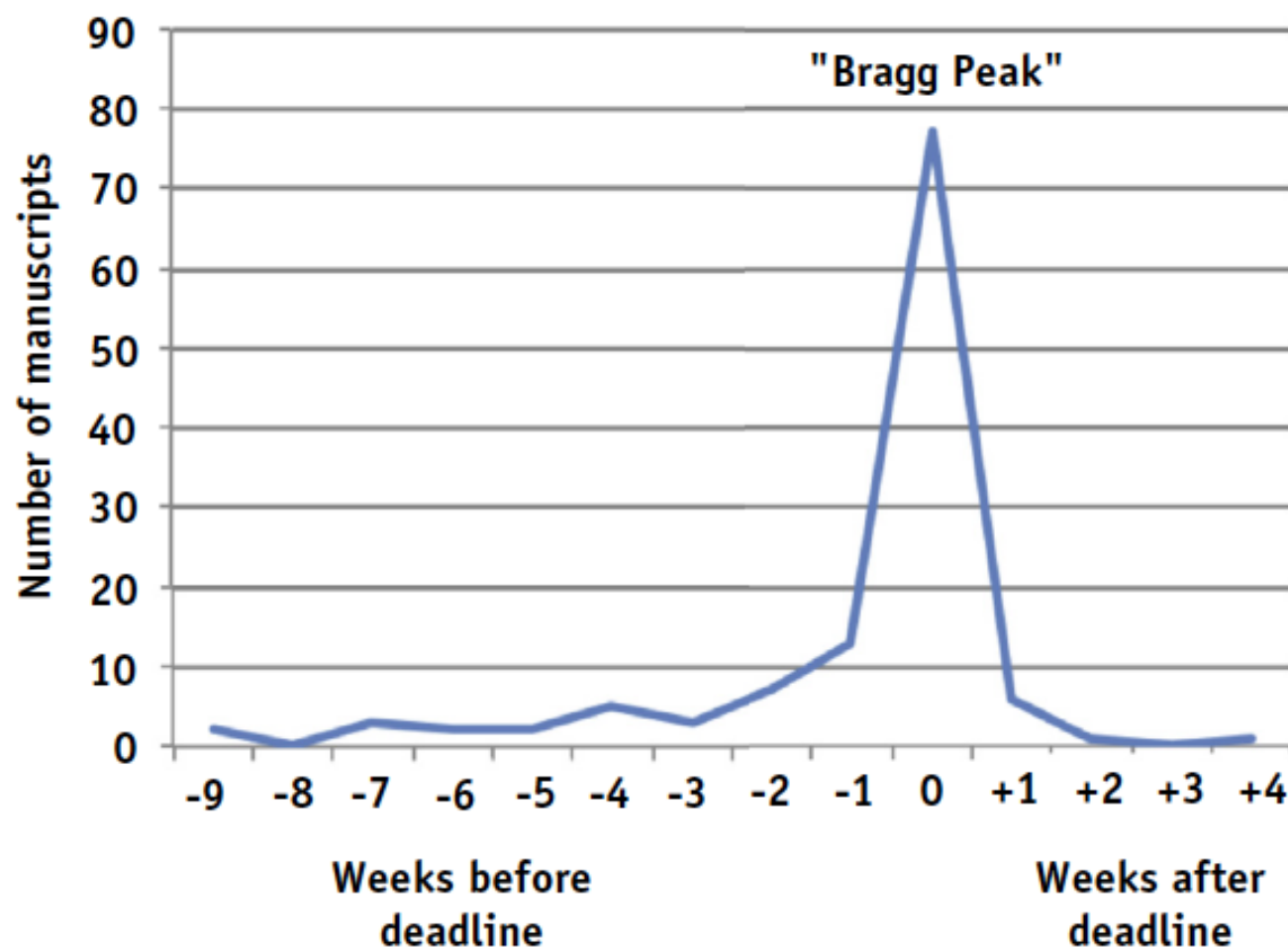
- **Rapid development of evidence**
- **Advances: IMPT, miniaturization, cost reduction**
- **New use model**
- **New payment model**

Can anything stop the bubble bursting?

Rapid development of evidence:

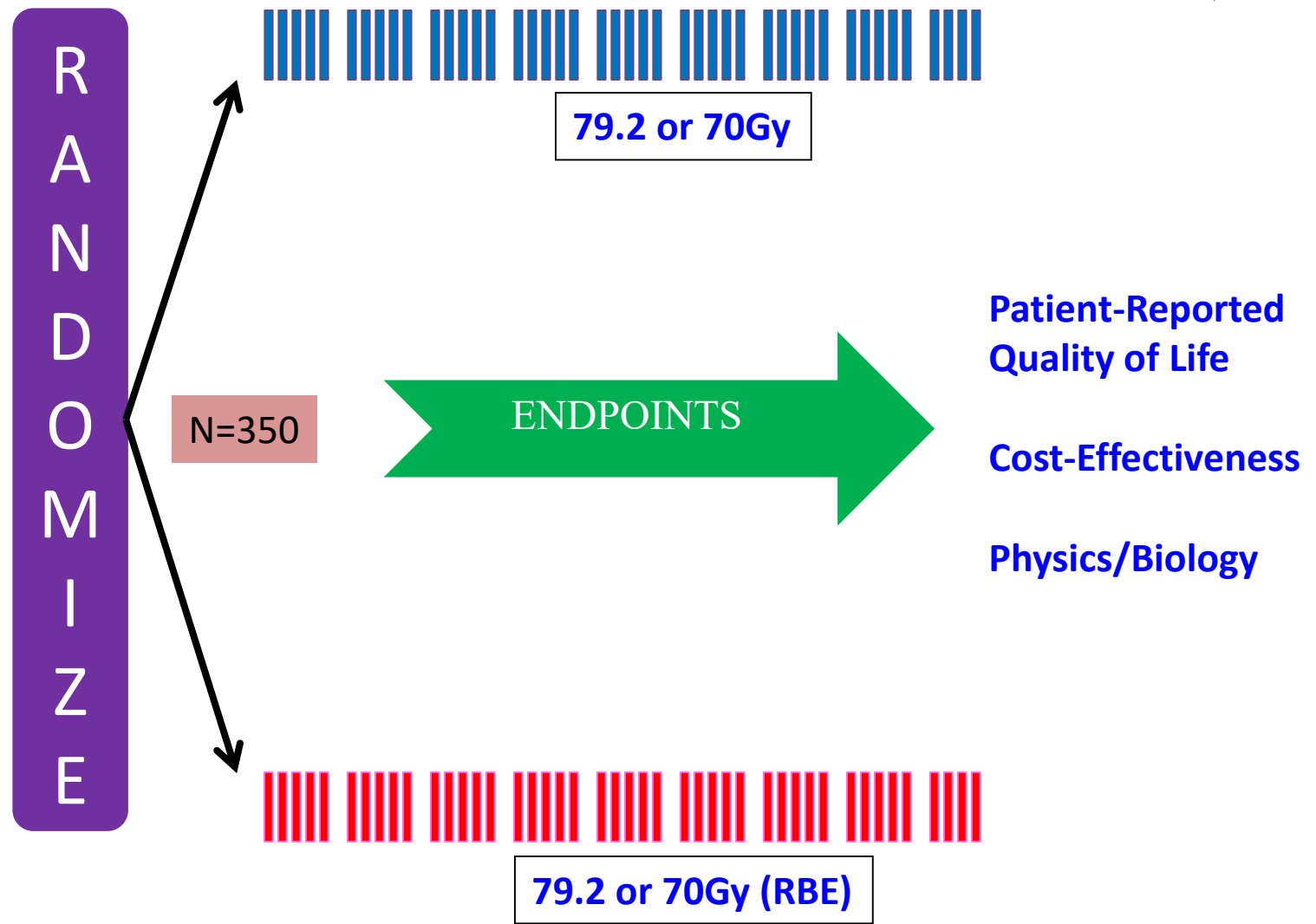
- **Multiple sites**
- **Collaborative grants and groups**
- **National trials of comparative effectiveness**

Particle Therapy submissions to the Red Journal in the weeks preceding and following the deadline for the Special Edition





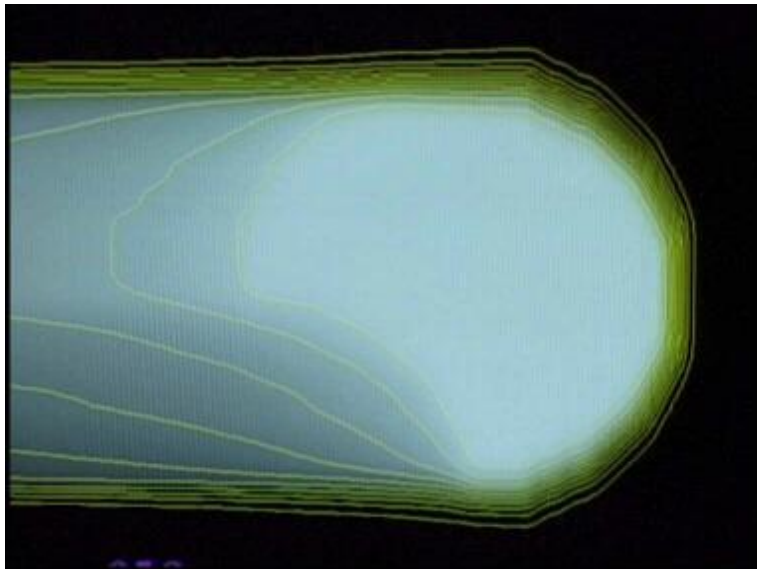
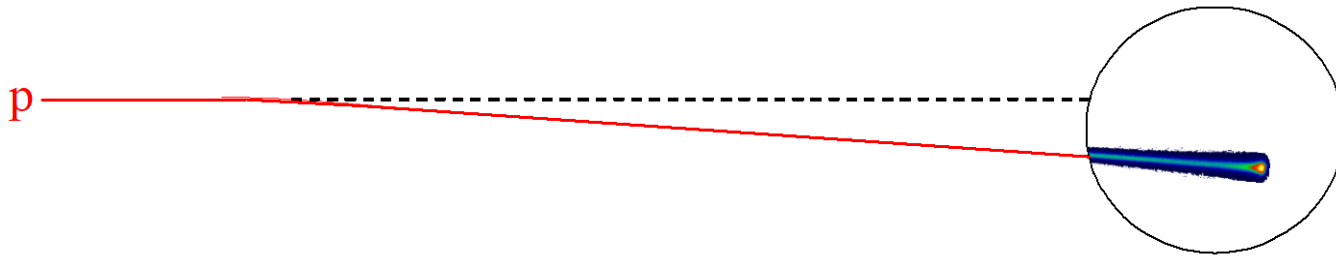
Low-Intermediate Risk Prostate Cancer



PIs Jason Efstathiou and Justin Bekelman
Current accrual 270 patients – completes 2019

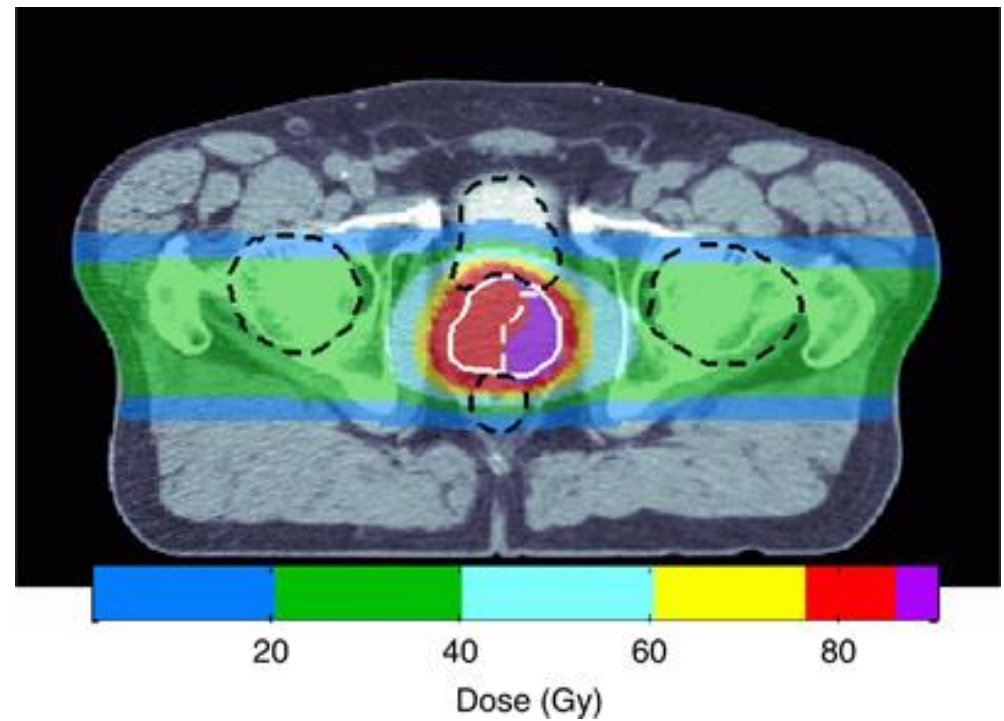
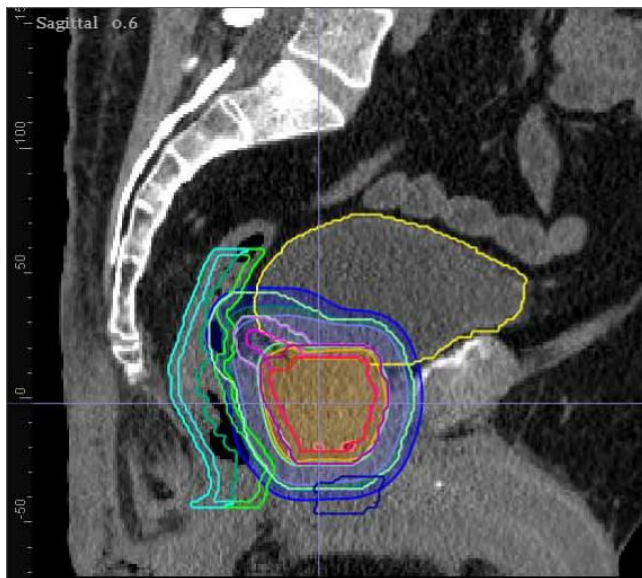
“Spot scanned” beams – the new wave

The dynamic application of scanned and modulated proton pencil beams



Images courtesy of Eros Pedroni

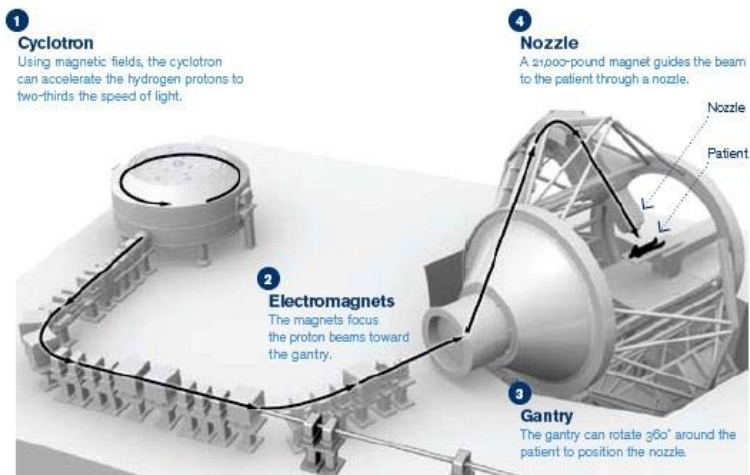
Planning with intensity modulation



Can anything stop the bubble bursting?

“Miniaturization”:

- Single gantry systems
- Gantry-less machines
- More efficient proton production



Can anything stop the bubble bursting?

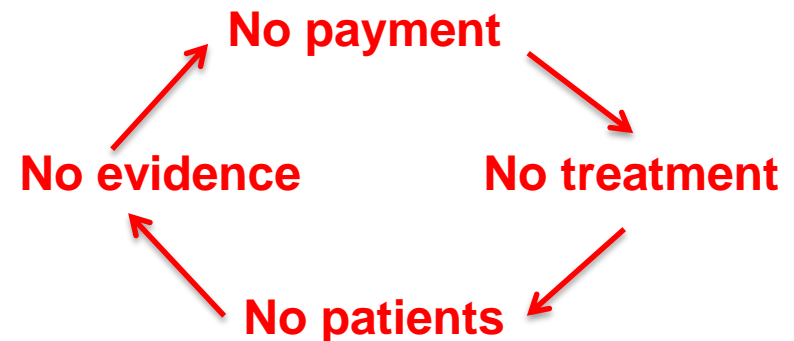
- **New use model**

Consortia: Michigan and NYC

- **New payment model**

Payment on protocols

Reference pricing



Protons in the age of Hypofractionation

Study	“Longer” Arm	“Shorter” Arm	Efficacy at 5 years	Late Toxicity	PROs
CHHiP	37fx/2.0Gy	20fx/3.0Gy	Similar	Similar	Similar
PROFIT	39fx/2.0Gy	20fx/3.0Gy	Similar	Similar	Similar
NRG 0415	41fx/1.8Gy	28fx/2.5Gy	Similar	Small ↑ GU/GI	Reporting tomorrow
HYPRO	39fx/2.0 Gy	19fx/ <u>3.4Gy</u>	Similar	↑GU	Not reported

Proton beam therapy – US treatment centers

2004



Proton beam therapy – US treatment centers

2017



Proton beam therapy – UK treatment centers



Government Commission:

1 multi-gantry facility per 30m population

Specific indications (no prostate)

Research mandate

Proton beam therapy – UK treatment centers



Private centers:

- **Risk generating unquenchable demand**
- **Risk undermining evidence-based indications**

Proton beam therapy – Holland



4 facilities for 13 million people

Consortia

Decisions based upon comparative planning

Proton beam therapy – Norway



4 facilities for 5 million people
Everyone will get protons for everything

Protons in the Age of Trump

- **Protons are here and will not go away**

Protons in the Age of Trump

- **Protons are here and will not go away**
- **Profit motive less but prestige motive high**

Protons in the Age of Trump

- **Protons are here and will not go away**
- **Profit motive less but prestige motive high**
- **Proton delivery will improve**

Protons in the Age of Trump

- **Protons are here and will not go away**
- **Profit motive less but prestige motive high**
- **Proton delivery will improve**
- **Proton biology will be worked out**

Protons in the Age of Trump

- **Protons are here and will not go away**
- **Profit motive less but prestige motive high**
- **Proton delivery will improve**
- **Proton biology will be worked out**
- **Proton delivery will become less expensive**

Protons in the Age of Trump

- **Protons are here and will not go away**
- **Profit motive less but prestige motive high**
- **Proton delivery will improve**
- **Proton biology will be worked out**
- **Proton delivery will become less expensive**
- **Proton delivery will be more evidence based**

Protons in the Age of Trump

- **Protons are here and will not go away**
- **Profit motive less but prestige motive high**
- **Proton delivery will improve**
- **Proton biology will be worked out**
- **Proton delivery will become less expensive**
- **Proton delivery will be more evidence based**
- **Protons will compete in the prostate “market”
whether there is evidence or not**

