Proton Therapy vs. IMRT

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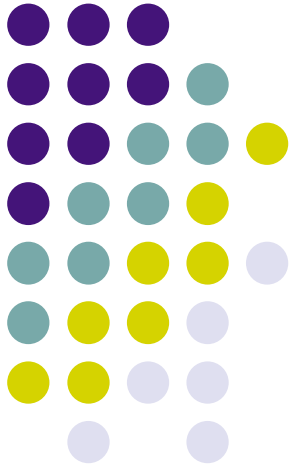
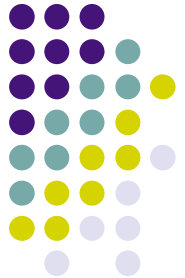
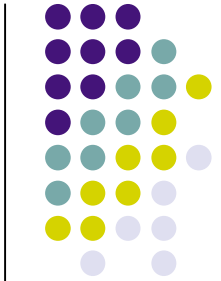


Disclosures



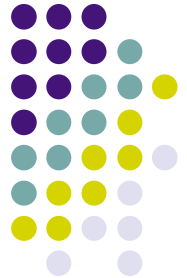
- ProCure Clinical advisory board.
- I was faculty at UF and the experience here presented is the current standard at UFPTI
- We are trying to bring proton therapy to South Florida.

Arguments against Protons?



- Minimal clinical data
  - Comparisons between non-randomized data is difficult.
  - Therapeutic Ratio: TCP/NTCP
  - The engineering paradigm, not the scientific paradigm applies to P+
- Not superior to IMRT
  - – Protons are superior to IMRT
    - proton therapy has a better dose distribution the question is the magnitude of the benefit not the superiority.
    - The optimal delivery to match the potential dosimetric benefit
    - Integration with systemic agents such as chemotherapy.
- Too expensive
  - Cost will come down as more competitive systems become available (IBA, Varian, Still rivers, home grown systmes – IU – LLUMC).
  - Patient toxicity will be shown to decrease, thus lowering societal costs
  - Hypofractionation can lower treatment costs and can be better done with P+ as smaller volumes are treated to lower.
  - My proposed trials are cheaper than IMRT to currently used doses. The open trial at UF is competitive with IMRT costs based on moderately hypofractionated regime.
- Neutrons → 2nd cancers
  - Even with DS P+, the available clinical data does not support the arguments/hypothesis generated by Hall and Brenner
  - Improved P+ design today has significantly decreased neutrons
  - Current DS systems produce comparable neutron contamination than IMRT.

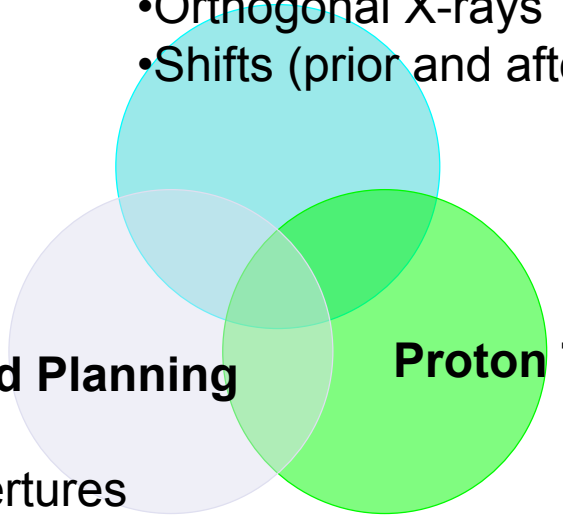
Comparing Proton Therapy and IMRT



I. Clinical results
II. Biologic end points
III. Dosimetric differences
IV. Uncertainties
V. Inter-fraction error
VI. Intra-fraction error
VII. Randomized trials

Image Guided Therapy

Delivery (IGRT)
- Visicoils (dose disturbances)
- Orthogonal X-rays
- Shifts (prior and after)

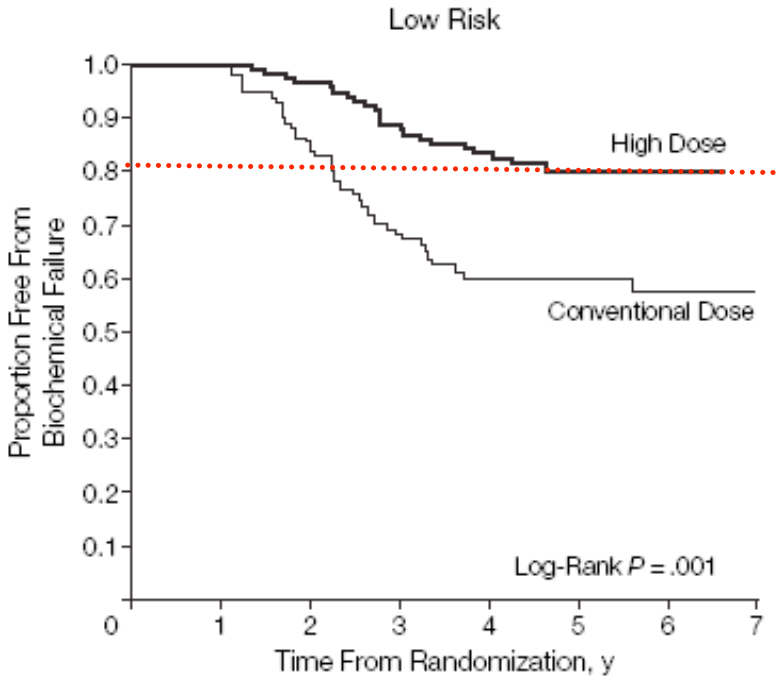


Simulation and Planning
- MRI based
- optimizing apertures
- beam angles
- smearing

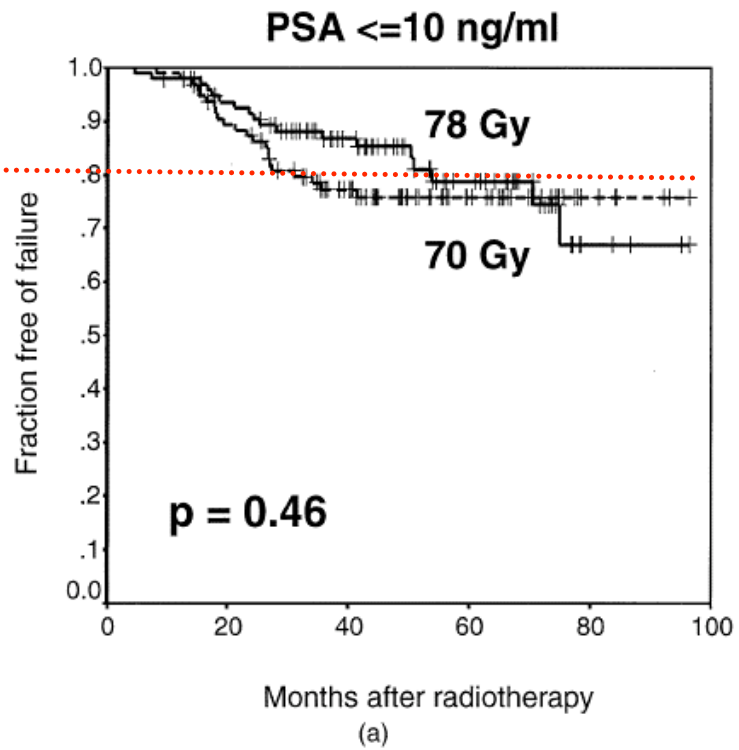
Proton Therapy

→ **Optimal Radiation Therapy**

I. Clinical Results



No. at Risk								
High Dose	111	111	92	74	64	38	14	4
Conventional Dose	116	116	111	99	88	56	24	12



Zietman et al JAMA. 2005;294:1233-1239 Pollack et al IJROBP 2002; 53:1097–1105

Toxicity

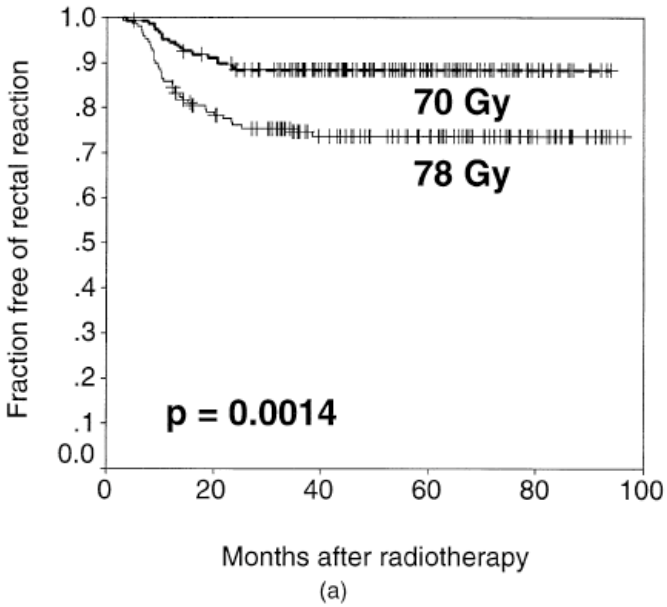
Table 2. Acute and Late Genitourinary and Gastrointestinal (Rectal) Morbidity, by Assigned Radiation Therapy Dose and Toxicity Grade

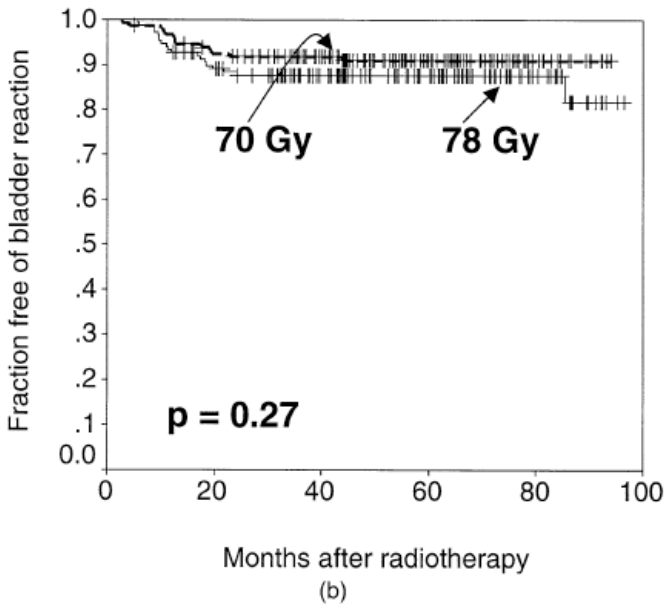
	No. (%)							
	70.2 GyE (n = 196*)				79.2 GyE (n = 195)			
Morbidity	Grade 1	Grade 2	Grade 3	Grade 4	Grade 1	Grade 2	Grade 3	Grade 4
Acute								
GU	79 (40)	82 (42)	2 (1)	0	69 (35)	95 (49)	2 (1)	1 (1)
GI	62 (31)	81 (41)†	2 (1)	0	48 (25)	112 (57)†	0	0
Late								
GU	85 (43)	35 (18)	3 (2)	0	84 (43)	39 (20)	1 (1)	0
GI	71 (36)	15 (8)‡	1 (1)	0	84 (43)	33 (17)‡	1 (1)	0

Abbreviations: GI, gastrointestinal; GU, genitourinary.
*One patient underwent radical prostatectomy rather than radiation therapy because the bowel was too close to the prostate for safe administration of radiation. This patient was excluded from analysis of morbidity.
†$P = .004$ by χ^2 test.
‡$P = .005$ by χ^2 test.

Zietman et al JAMA. 2005;294:1233-1239

Toxicity





Pollack et al IJROBP 2002; 53:1097–1105

IMRT results

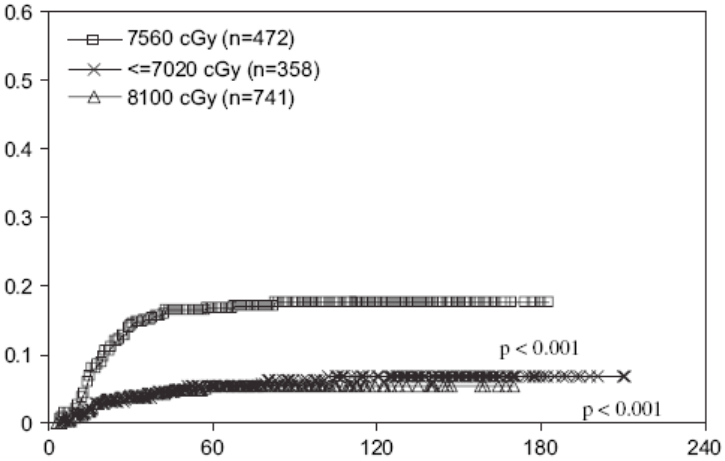


Fig. 1. The incidence of late Grade ≥2 rectal toxicities by prescription dose.

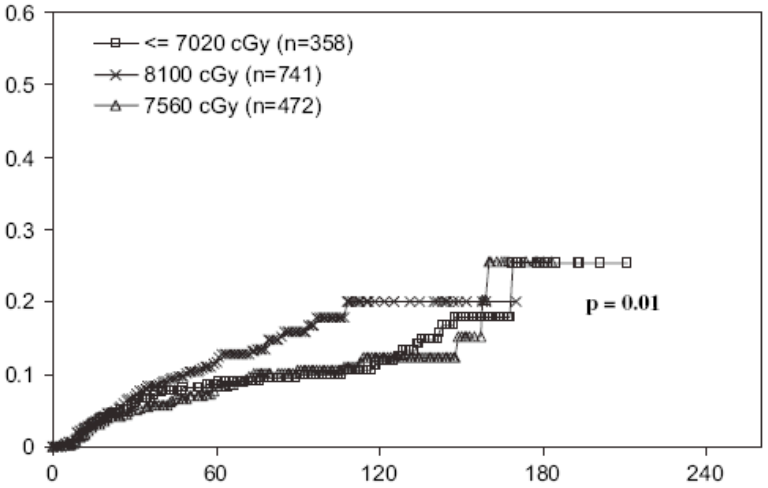
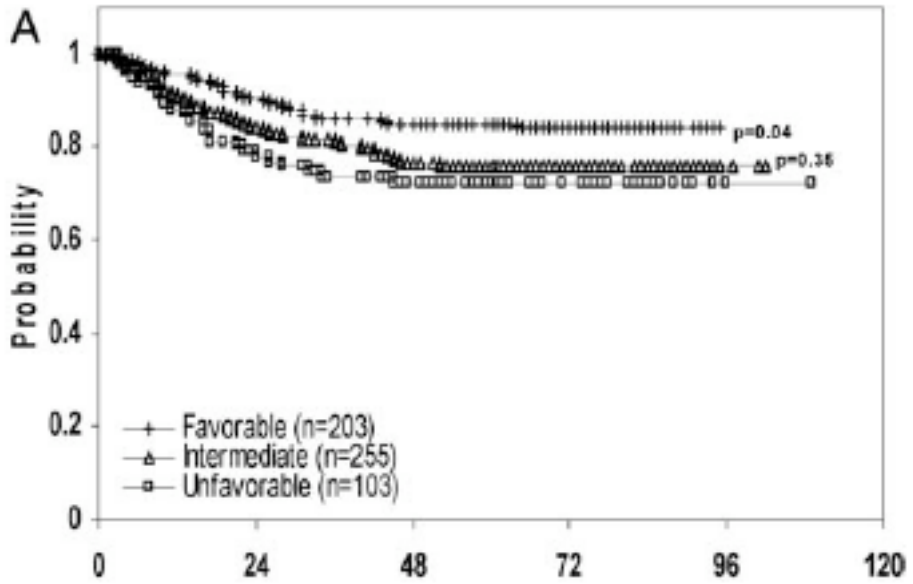


Fig. 3. The incidence of late Grade ≥2 urinary toxicities by prescription dose. A significant increase in Grade 2 toxicities was observed for patients treated to 81 Gy compared with lower doses ($p = 0.01$).

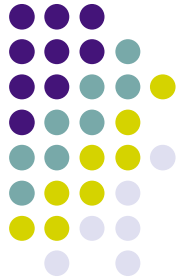
Zelefsky et al IJROBP 2008; (70):pp.1124–1129

IMRT results



Zelefsky et al. Urology 2006; (176): pp 1415-1419,

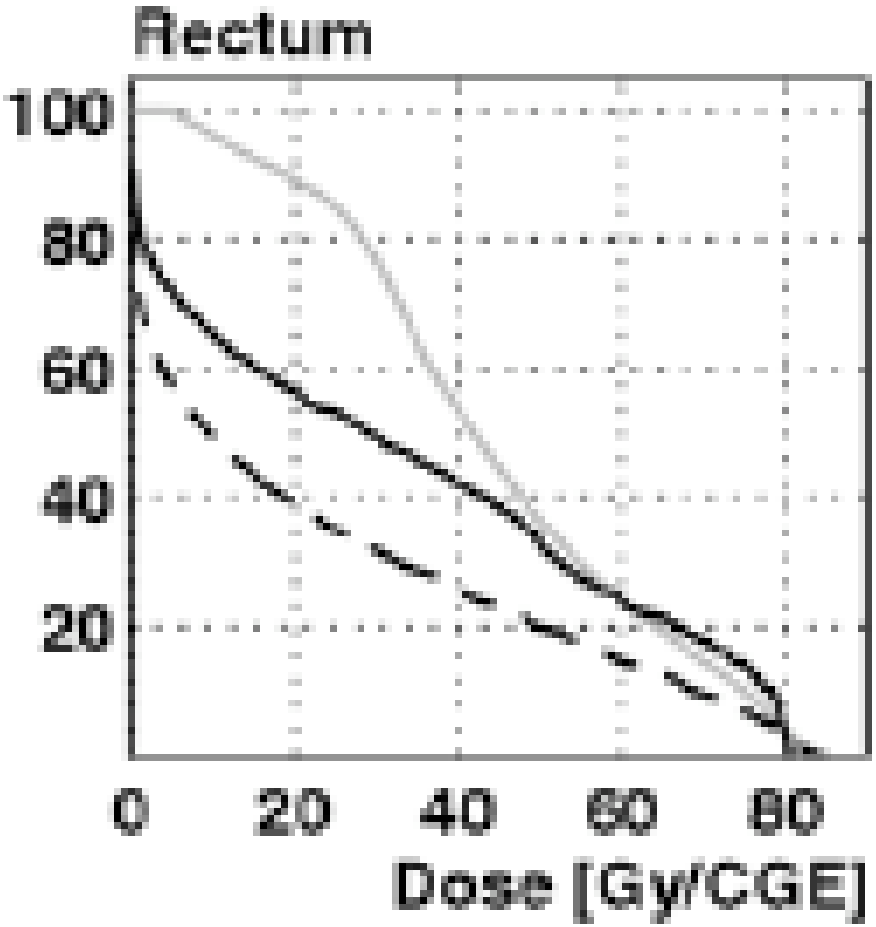
IMRT Results



- 5-year chronic ≥2 toxicity was 5% GI and 20 GU.
- 5-year BFS 85%.
- Single institution experience and results across the country are likely to be higher.

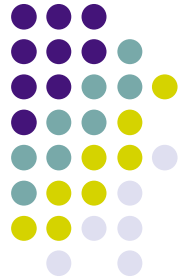
Zelefsky et al. Urology 2006; (176): pp 1415-1419,

MGH



Trofimov et al IJROBP 2007; 69:pp. 444–453,

II. Biology



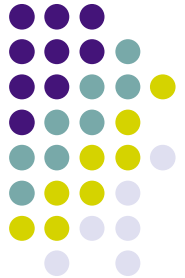
- Proton therapy has a low LET and the RBE has been found to be similar to photon therapy.
- Higher LET and RBE are seen at the distal part of the SOBP

Table A2. RBE values *in vivo* obtained in clinical beams

Biological system	Endpoint	Beam (MeV)	SOBP (cm)	γ-Dose/Fract (Gy)	RBE plateau	RBE SOBP prox	RBE SOBP mid	RBE SOBP distal	RBE distal fall-off	Reference	Ref.
Lung tolerance in mice	LD_{50} (180–270 d)	200	7	2.3–3.7			0.86; 0.96; 1.05; 1.02			^{60}Co	(36)
				4.4–8.8			1.09; 1.07; 1.02; 1.06				
				7.4–18.6			1.04; 1.2; 1.33; 1.55				
Normal mouse lung	LD_{50} / 180 d	160	10	12.6			0.73			^{60}Co	(37)
				13.0			1.08				
				15.2			1.04				
Mouse lens	MCD_{50}/7 mo			9.9			1.02				
Mouse tail vertebrae	70% growth/8 wk			12.0			1.21				
				13.6			1.23				
Mouse testes weight loss	50% contr. weight			0.7			1.13				
				2.5			1.15				
Mice leg	Skin contradiction	250	9	5.3			1.02			^{60}Co	(35)
				6.0			1.03				
Mouse jejunal crypt	Inactivation	160	10	1.4–2.1	1.09		1.15			^{60}Co	(31)
				11–18	1.06		1.11				
Intest. crypt reg. In mice	Inactivation	85	3	10–17			1.08			^{60}Co	(23)
Intest. crypt reg. in mice	Inactivation	200	7	10–17			1.14			^{60}Co	(36)
Intest. crypt reg. in mice	Inactivation	200	7	13.6	1.14; 1.18	1.23	1.15	1.26		^{60}Co	(32)
				14.4	1.1; 1.16	1.18	1.12	1.23			
				15.1	1.07; 1.14	1.14	1.09	1.21			
Intest. crypt reg. in mice	Inactivation	200	7	1.5			1.14	1.29		^{60}Co	(33)
				4.2			1.15				
				8.7			1.15				
Intest. crypt reg. in mice	Inactivation	235	10	14.22	0.94		0.98			6 MV	(20)
C3H/He mice	Acute skin reaction	250	3	21.5			0.77			180 kVp	(69)
				28			0.79				
				36			0.87				
Mouse thigh	Acute skin reaction	160	10	3.1–4.5			1.07			^{60}Co	(31)
Mouse foot	Acute skin reaction	80	1.8	8.5			1.2			^{60}Co	(34)
				13.0			1.15				
				20.7			1.24				
				33.7			1.15				
Mouse legs	Acute skin reaction	—	—	21.9			0.89			290 kVp	(71)
		250	6				0.74				
Mouse legs	Acute skin reaction	250	6	10.9			0.75			300 kVp	(72)
				22.3			0.74				
	Late skin contradiction			11.8			0.85				
				23.1			0.97				

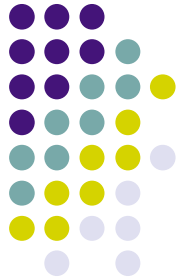
Paginate IJROBP 2002: 53; 407– 421.

RBE differences



- RBE differences can be potentially exploited or beam modulation to match RBE differences.
- Single beam treatments stopping close to a normal structure may not be preferred.
- Relatively, of no clinical significance for prostate cancer therapy due to the currently used beam arrangements.

Second malignancies

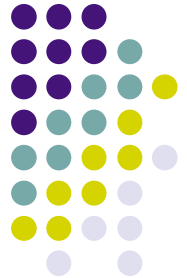


“Intensity-modulated radiation therapy may double the incidence of solid cancers in long-term survivors”

“An alternative strategy is to replace X-rays with protons. However, this change is only an advantage if the proton machine employs a pencil scanning beam”

Hall et al. IJROBP 2006; 65: 1-7.

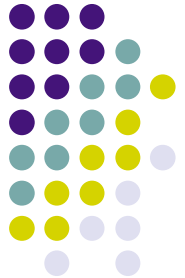
Wayne State University



- Second malignancy rates were significantly lower with neutron therapy or surgery compared to conventional radiation.
- For surgery 4.2% neutron/photon therapy was 6.0%, for photon therapy alone 10.3% at 5-years. With no difference between neutrons and surgery (p=0.3) and both significantly lower than photon (p=0.005).

McGee et al Proceedings of ASTRO 2006 #2197

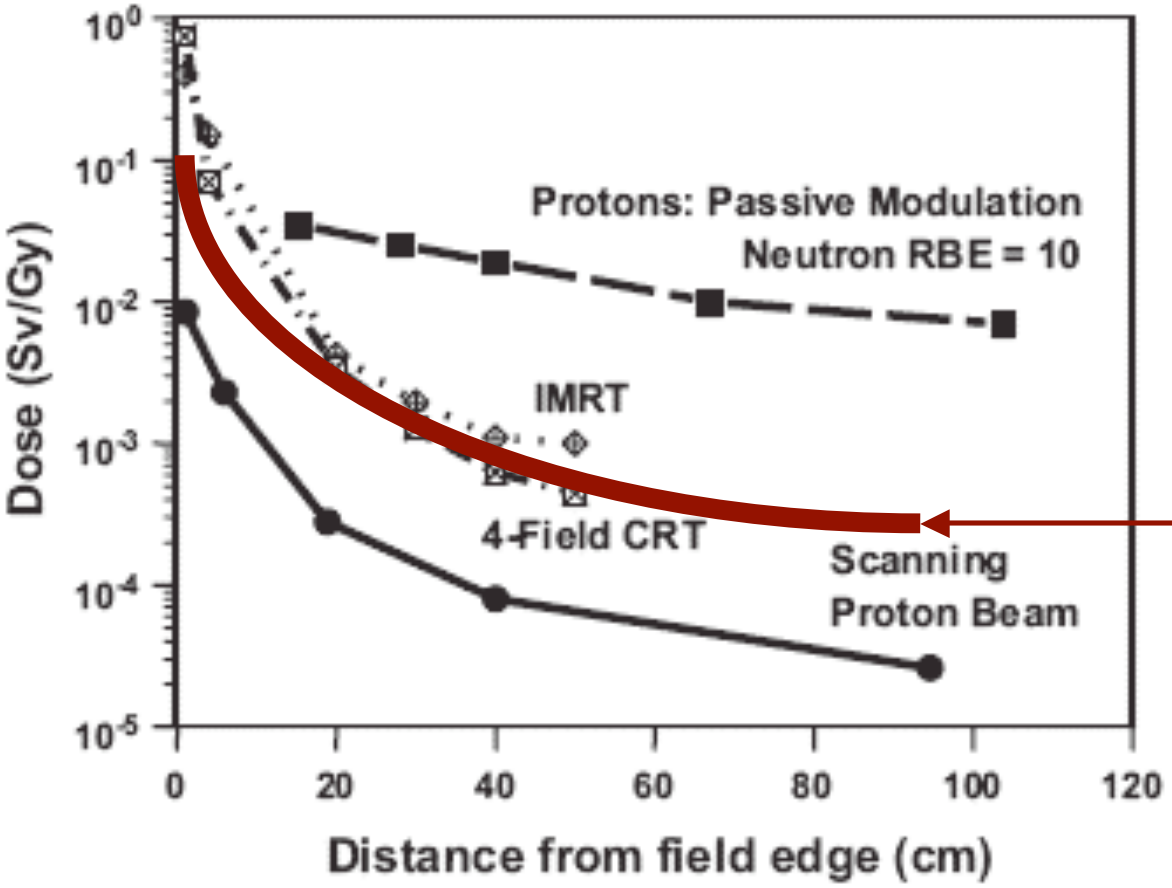
MGH



- Second malignancies after proton therapy for prostate cancer were low
  - 82 cases per 10,000 person year for prostate cancer patients
  - For an average of 7.2% at 5-years for all sites treated including H & N, CNS, and prostate.

Chung et al Proceedings ASTRO 2007 #1075

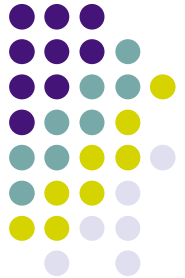
Dose outside the field



Current DS systems

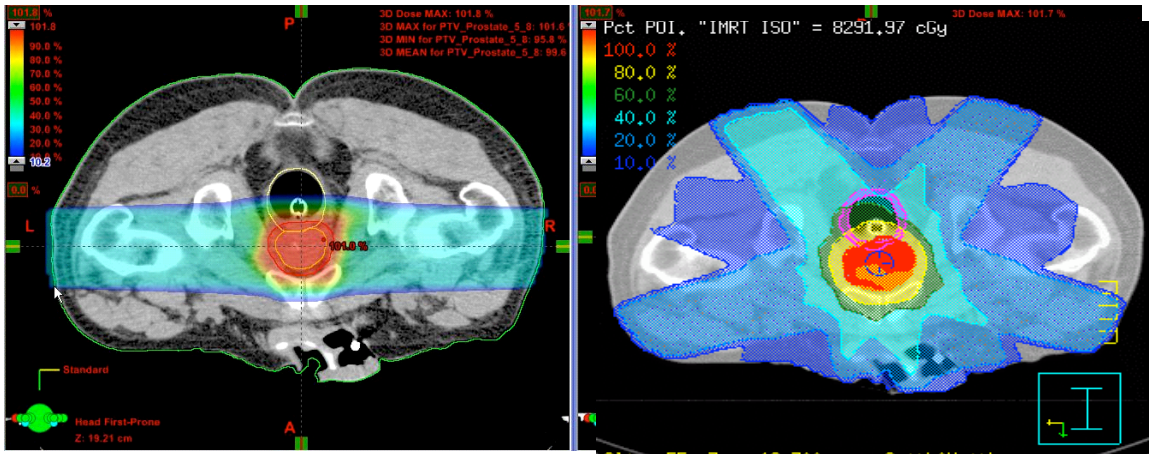
Hall et al. IJROBP 2006; 65: 1-7.

Summary



- Lower neutron doses are possible with scanned beam proton therapy compared to IMRT
- The higher RBE area can be placed safely away from normal dose limiting structures for prostate proton therapy.

III. Dosimetric Differences



Dose distribution for Proton Therapy

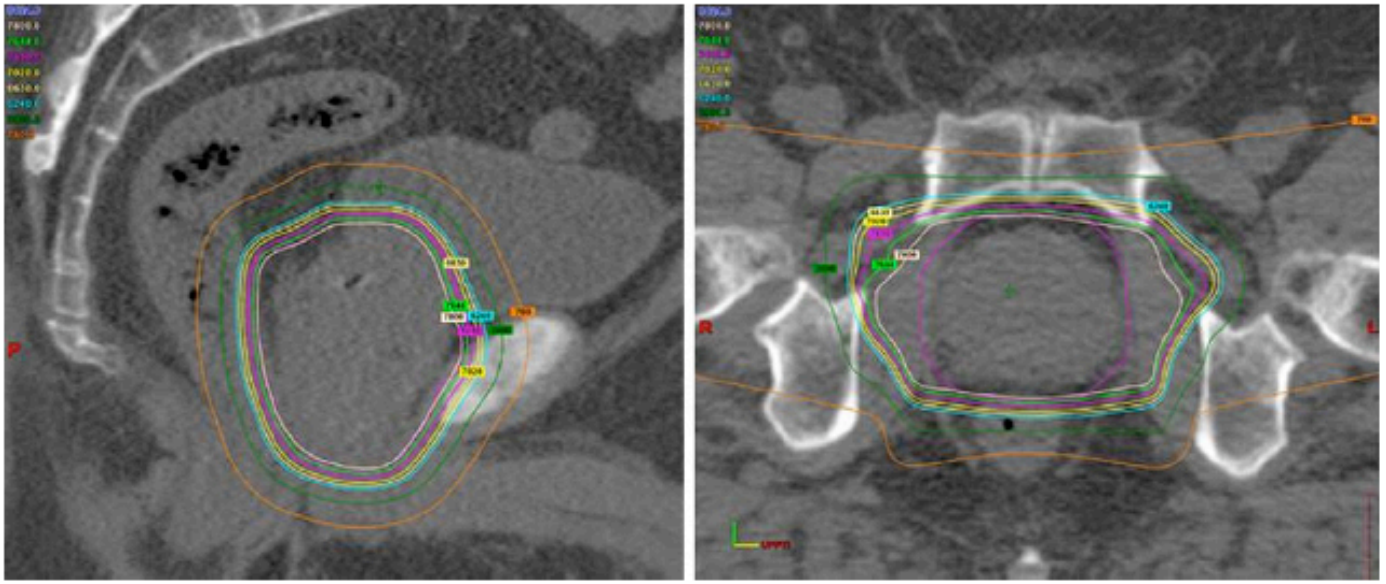


Fig. 4. Sagittal (left) and axial (right) projection for the same patient as in Fig. 1, including isodose lines with water alone. The green line represents the 50% isodose line that includes less than half the rectal circumference.

Penumbra differences

	Dose fall off per mm			
	95%-80% IDL		80%-20% IDL	
	Protons	**IMRT**	**Protons**	**IMRT**
Posterior direction	4.1%	2.0%	6.2%	1.5%
Superior direction	4.1%	7.5%	6.2%	5.8%

Keole et al. Proceedings ASTRO 2008

Penumbra for prostate proton therapy

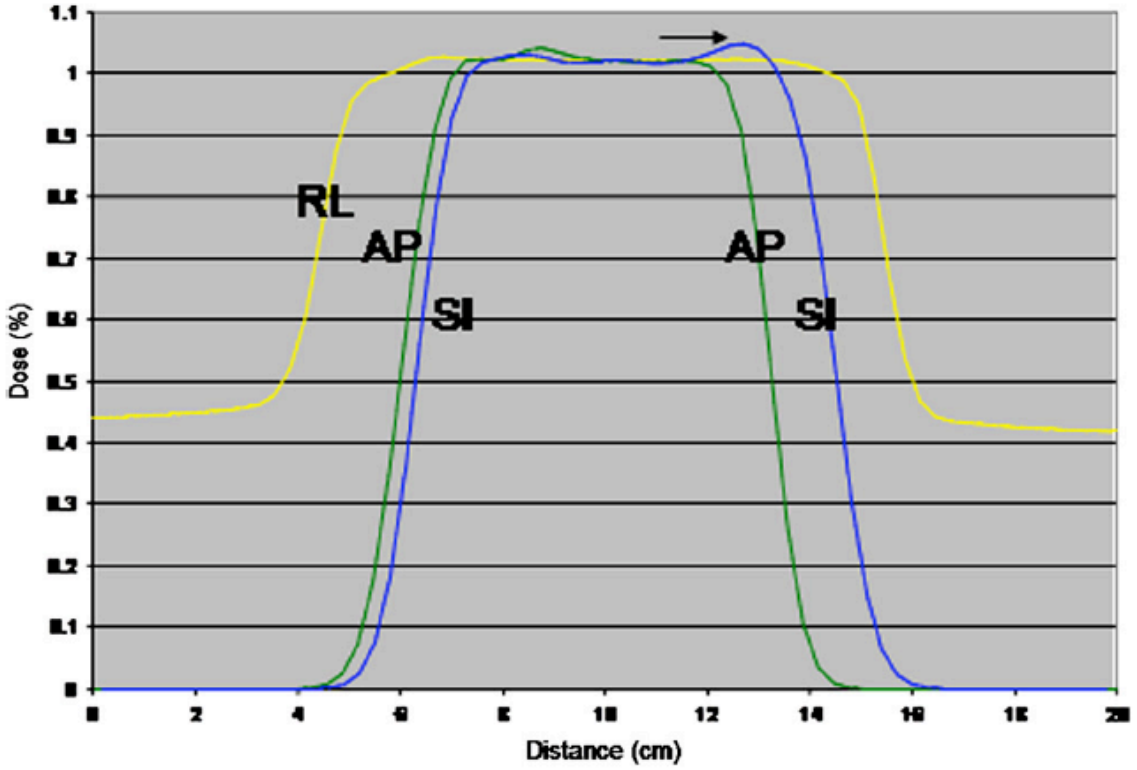


Fig. 7. Dose profiles in different beam directions at beam isocenter: 1, superoinferior (SI); 2, anteroposterior (AP); and 3, right–left (RL).

Vargas et al IJROBP 2008; 70: pp. 1492–1501,

Dosimetric differences

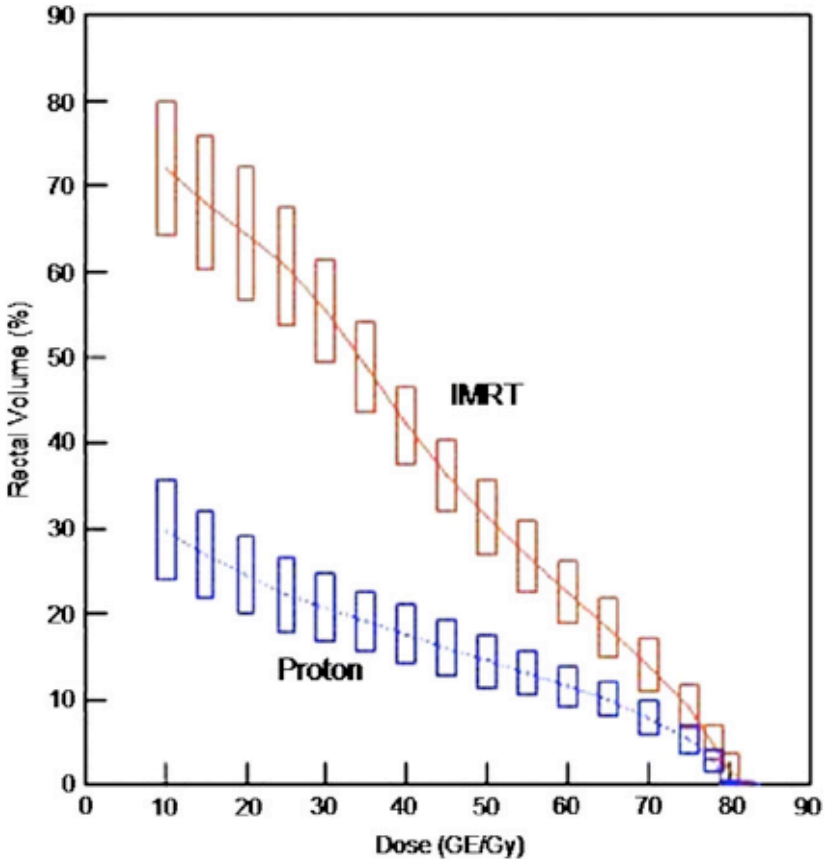
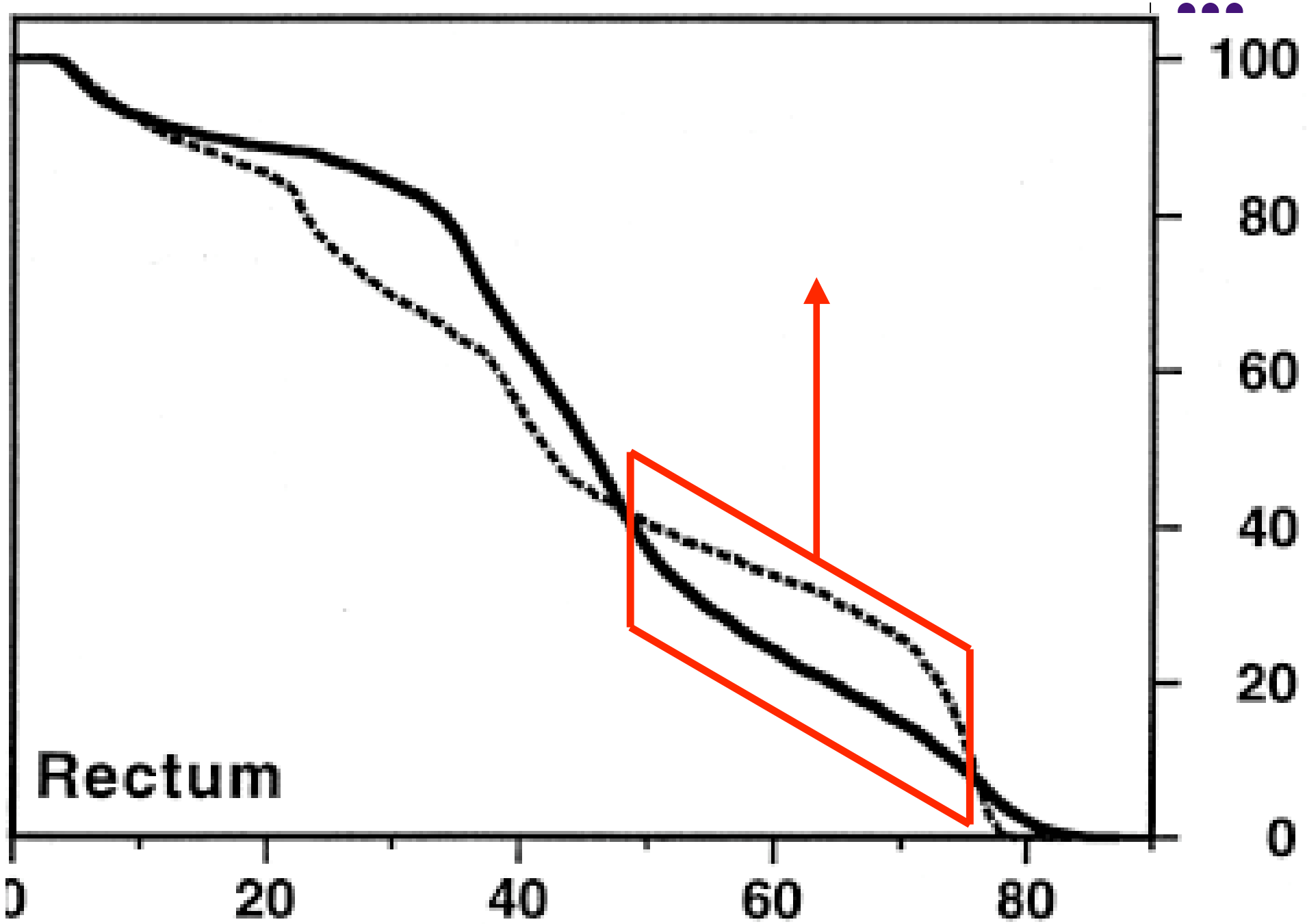
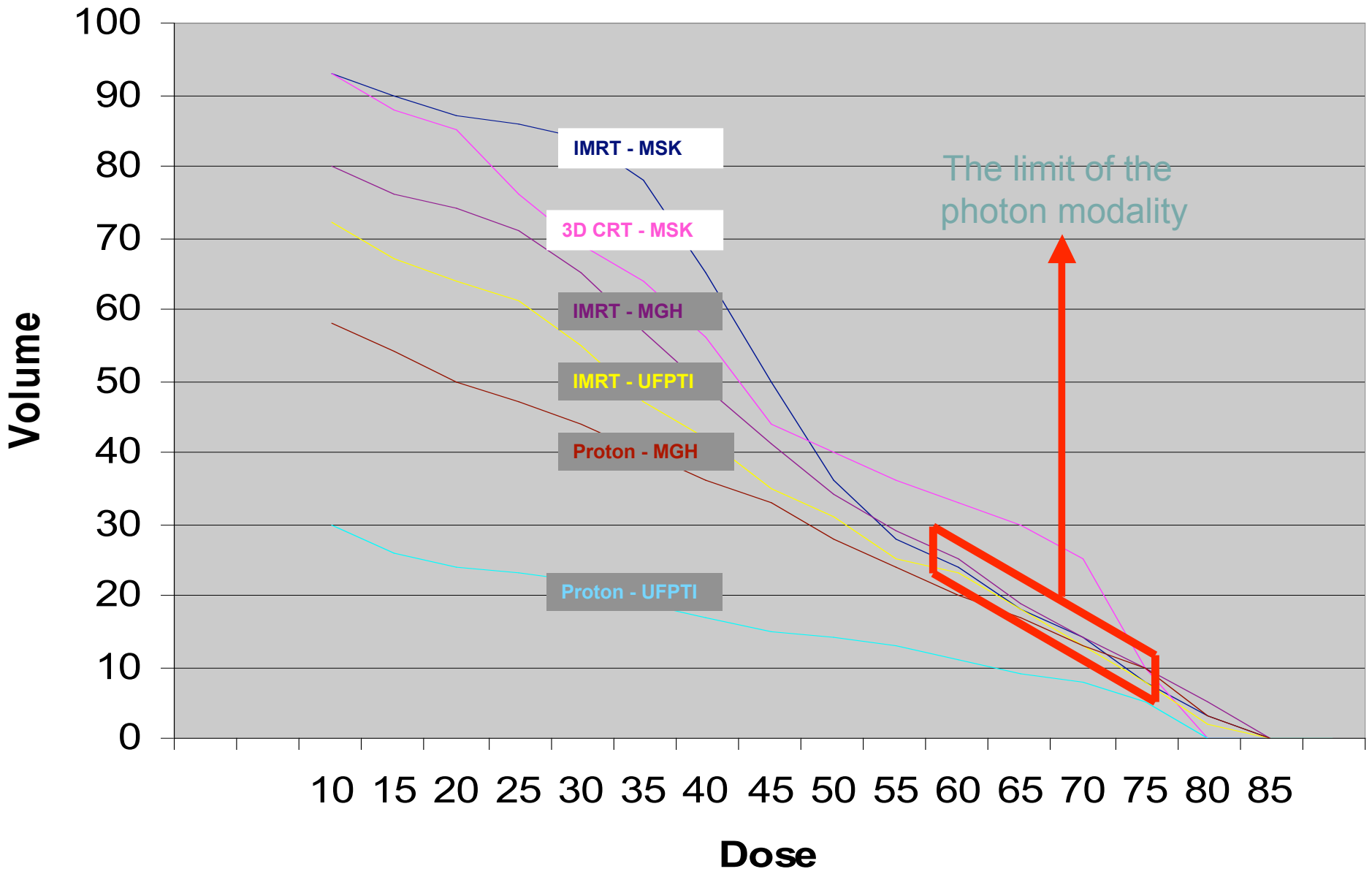


Fig. 3. Combined rectal dose–volume curves for proton therapy and intensity-modulated radiotherapy (IMRT) (n = 20 plans); error box shows 95% standard error.

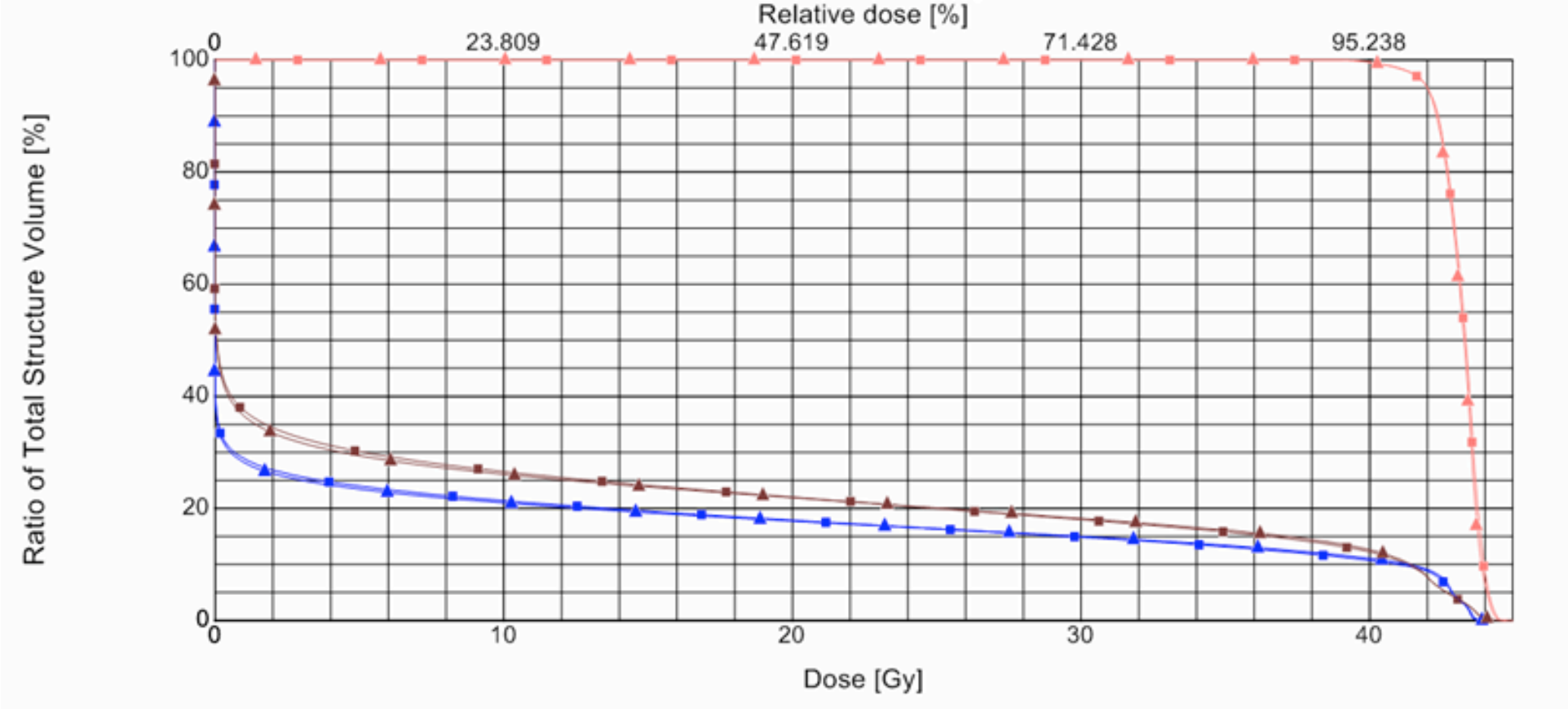
Vargas et al IJROBP 2008; 70: pp. 744–751


100
80
60
40
20
0
Rectum
0
20
40
60
80

Rectum

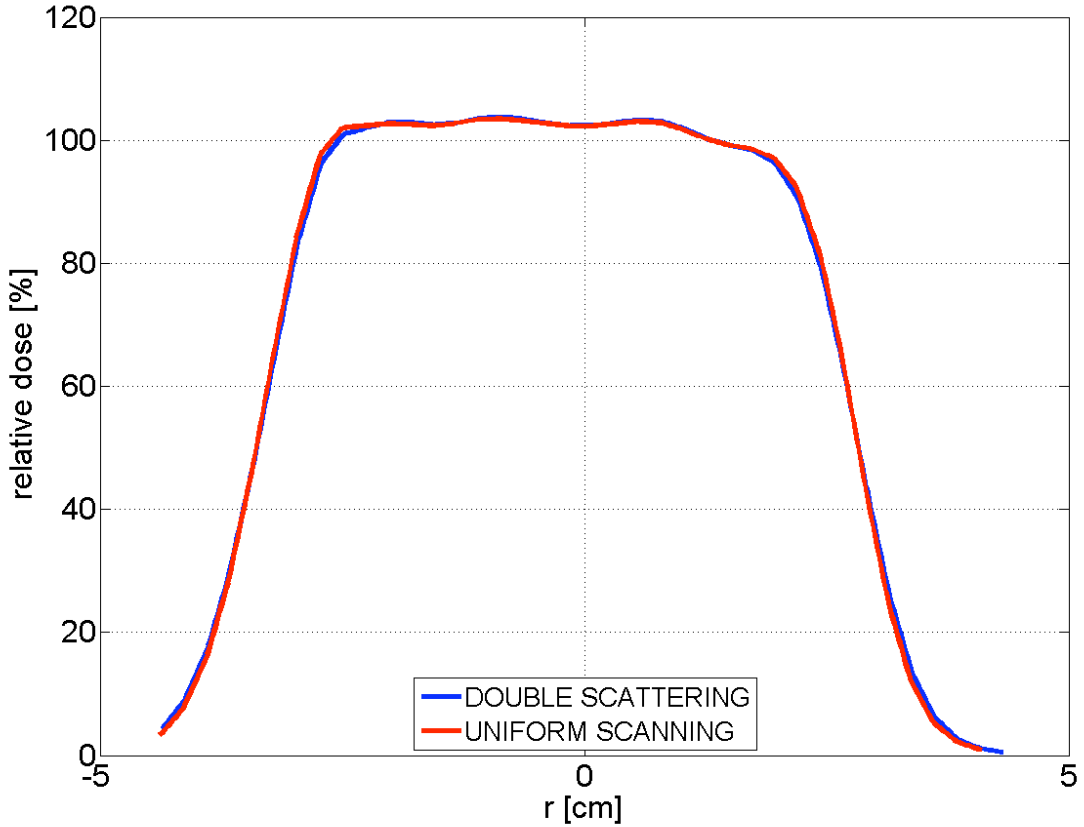

100
90
80
70
60
50
40
30
20
10
0
Volume
IMRT - MSK
3D CRT - MSK
IMRT - MGH
IMRT - UFPTI
Proton - MGH
Proton - UFPTI
The limit of the photon modality
10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85
Dose

Uniform vs. DS DVH



Provided by Roelf Slopsema, MS

Uniform vs. DS lateral penumbra



Provided by Roelf Slopsema, MS

Rectal dose comparison

	IMRT plans
	Rectum V70
MSKCC	14%
MGH	14.5%
MADCC	15.5%
UF	14%
Protons UF	**8%**

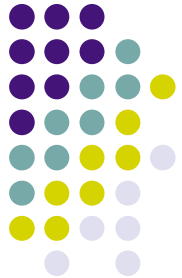
Zelefsky et al Radiotherapy and oncology 2000; 55:241-249

Trofimov et al IJROBP 2007; 69:pp. 444–453,

Zhang et al IJROBP 2007; 67: 620–629

Vargas et al IJROBP 2008; 70: pp. 744–751

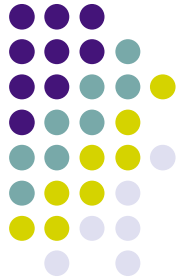
Uncertainties



- Two different sources of uncertainties: planning and delivery.
- For proton therapy dose depth deposition uncertainty is predictable and appropriate angle selection will determine the direction of the uncertainty.
- IMRT has also uncertainty. However, no DVH plan reflects this uncertainty.

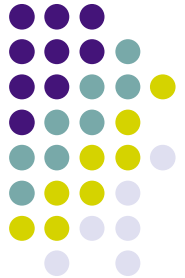
Jin et al Med Phys. 2005; 6:1747-56

IV. Uncertainties



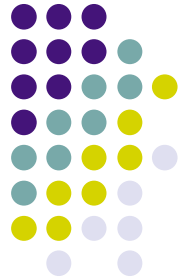
- Planning: for proton therapy we should account for the depth dose uncertainty and biologic effectiveness for IMRT the spatial and non-spatial disagreement between plan and delivery.

Proton Uncertainties



- Uncertainty for prostate proton therapy treatments has been quantified at UFPTI
- Our prostate uncertainty is 5-8mm in the direction of the beam and is corrected at planning.

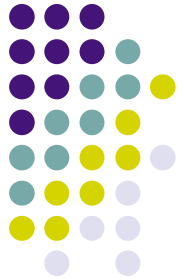
Uncertainties



- IMRT uncertainties in the low and high dose area should be corrected. However, this is not currently done.

"minimization of overall uncertainty during the treatment planning process will improve the quality of IMRT" Jin et al Med Phys 2008; 35: 983

Uncertainties



- The remainder uncertainties are related mostly to patient positioning, inter-fraction and intra-fraction error.

Inter-fraction error

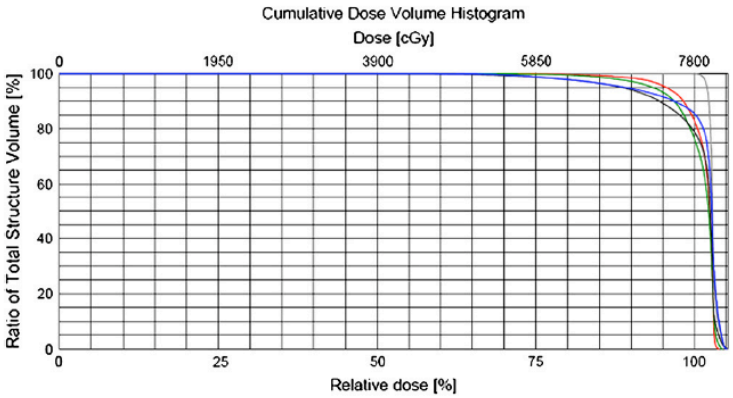


Fig. 3. Dose–volume curves for initial prostate position and prostate positions A–D for 1 case.

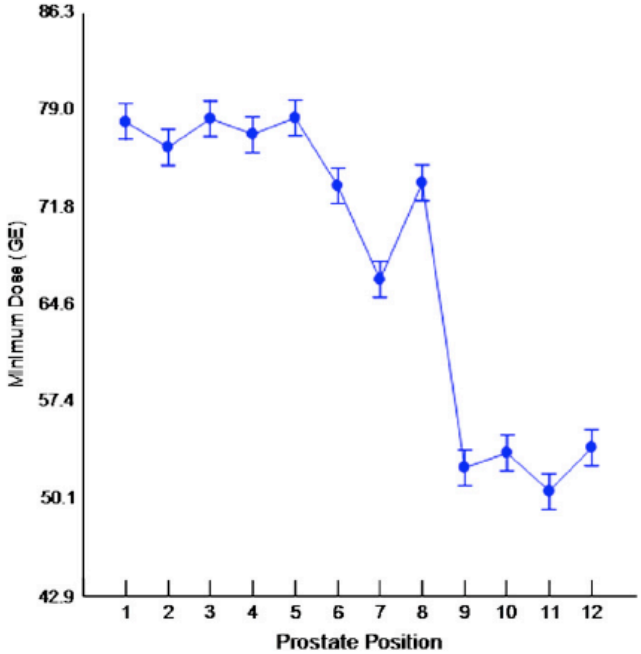


Fig. 5. Minimal prostate dose in several positions: 1, initial; 2, 5-mm anterior; 3, 5-mm inferior; 4, 5-mm posterior; 5, 5-mm superior; 6, 10-mm inferior; 7, 10-mm posterior; 8, 10-mm superior; 9, Point A; 10, Point B; 11, Point C; and 12, Point D.

Vargas et al IJROBP 2008: 70; 1492–1501

	No Image guidance (SD)	Image Guidance (SD)	p-value
5 mm Anterior			
Prostate V78 (%)	99.6(0.5)%	100% (0.03)%	**0.04**
Prostate Mean Dose	79.55(0.29) GE	79.47(0.32) GE	0.6
Prostate Minimum Dose	76.52(1.17) GE	78.15(0.27) GE	**0.001**
Prostate Maximum Dose	81.19(0.94) GE	81.08(0.89) GE	0.8
5 mm Inferior			
Prostate V78 (%)	99.6 (0.5)%	100% (0.03)%	**0.04**
Prostate Mean Dose	79.56(0.31) GE	79.54(0.29) GE	0.9
Prostate Minimum Dose	78.03(0.34) GE	78.19(0.23) GE	0.3
Prostate Maximum Dose	81.28(97.1) GE	81.15(0.92) GE	0.8
5 mm Posterior			
Prostate V78 (%)	99.4(0.8)%	100% (0.007)%	**0.05**
Prostate Mean Dose	79.43(0.28) GE	79.55(0.29) GE	0.4
Prostate Minimum Dose	76.75(1.49) GE	78.29(0.30) GE	**0.008**
Prostate Maximum Dose	81.16(96.6) GE	81.29(1.02) GE	0.8

Vargas et al IJROBP 2008: 70; 1492–1501

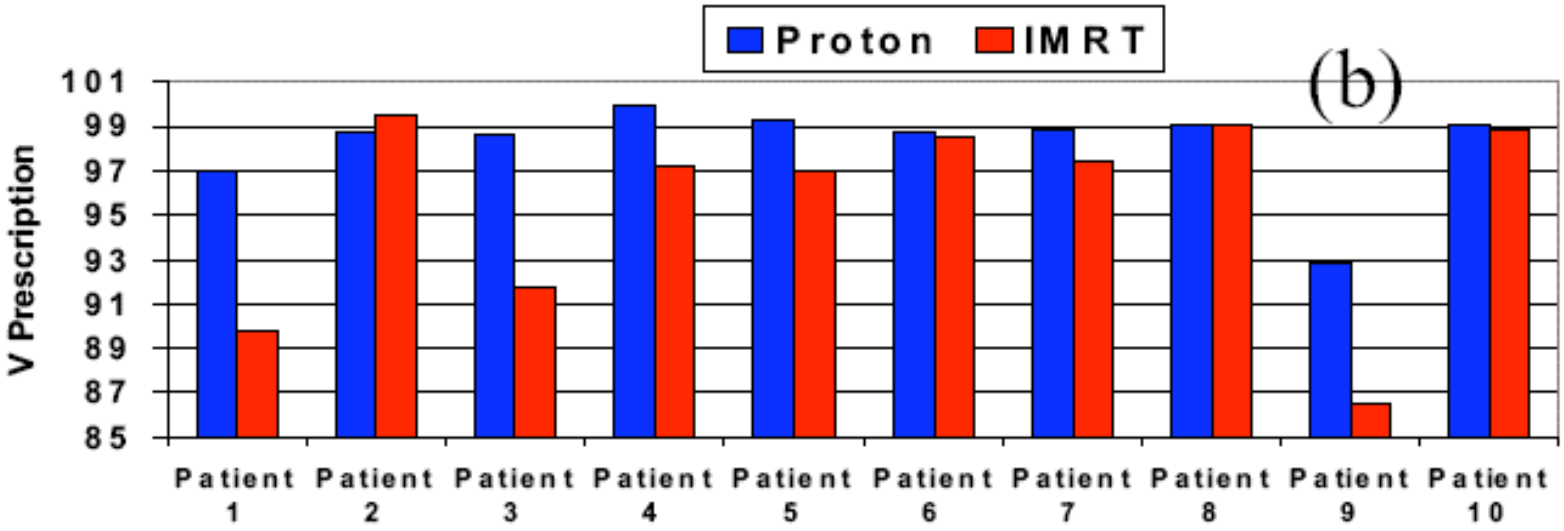
	No Image guidance	Image Guidance	p-value
10 mm Inferior			
Prostate V78 (%)	96.5% (1.2)%	100% (0.1)%	**<0.001**
Prostate Mean Dose	79.44 GE (0.30) GE	79.55 GE (0.27) GE	0.4
Prostate Minimum Dose	72.47 GE (0.90) GE	78.07 GE (0.27) GE	**<0.001**
Prostate Maximum Dose	81.30 GE (0.96) GE	81.17 GE (0.99) GE	0.8
10 mm Posterior			
Prostate V78 (%)	89.8% (3.9%)	100% (0.1)%	**<0.001**
Prostate Mean Dose	78.93 GE (0.31) GE	79.59 GE (0.29) GE	**<0.001**
Prostate Minimum Dose	64.75 GE (5.90) GE	78.31 GE (0.53) GE	**<0.001**
Prostate Maximum Dose	80.9 GE (0.83) GE	81.20 GE (0.83) GE	0.5
10 mm Superior			
Prostate V78 (%)	94.4%(2.0)%	100% (0.3)%	**<0.001**
Prostate Mean Dose	79.25 GE (0.26) GE	79.48 GE (0.31) GE	0.1
Prostate Minimum Dose	72.78 GE (0.70) GE	78.28 (0.41) GE	**<0.001**
Prostate Maximum Dose	81.00 GE (84.3) GE	81.23 GE (0.93) GE	0.6

Vargas et al IJROBP 2008: 70; 1492–1501

Point A			
Prostate V78 (%)	83.56% (4.7) %	98.49% (2.8) %	**<0.001**
Prostate Mean Dose	78.48 GE (0.39) GE	79.51 GE (0.34) GE	**<0.001**
Prostate Minimum Dose	52.92 GE (4.89) GE	77.59 GE (1.27) GE	**<0.001**
Prostate Maximum Dose	80.61 GE (0.6) GE	81.07 GE (0.73) GE	0.2
Point B			
Prostate V78 (%)	85.57% (3.3) %	90.16% (23.5) %	**<0.001**
Prostate Mean Dose	78.66 GE (0.31) GE	79.28 GE (0.38) GE	**0.002**
Prostate Minimum Dose	54.34 GE (4.57) GE	77.15 GE (0.77) GE	**<0.001**
Prostate Maximum Dose	81.02 GE (0.84) GE	81.04 GE (0.94) GE	0.9
Point C			
Prostate V78 (%)	82.6% (4.2) %	99.2% (1.9) %	**<0.001**
Prostate Mean Dose	78.39 GE (0.41) GE	79.57 GE (0.29) GE	**<0.001**
Prostate Minimum Dose	52.19 GE (5.58) GE	77.54 GE (1.09) GE	**<0.001**
Prostate Maximum Dose	81.10 GE (0.87) GE	81.19 GE (0.80) GE	0.8
Point D			
Prostate V78 (%)	86.53% (3.9) %	97.39% (3.4)%	**<0.001**
Prostate Mean Dose	78.73 GE (0.42) GE	79.31 GE (O.36) GE	**0.006**
Prostate Minimum Dose	54.93 GE (4.47) GE	76.60 GE (0.83) GE	**<0.001**
Prostate Maximum Dose	81.25 GE (0.95) GE	81.02 GE (0.99) GE	0.6

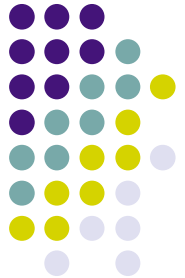
Vargas et al IJROBP 2008: In Press

Correcting Inter-fraction error



Zhang et al IJROBP 2007; 67: 620–629

Image Guidance Accuracy



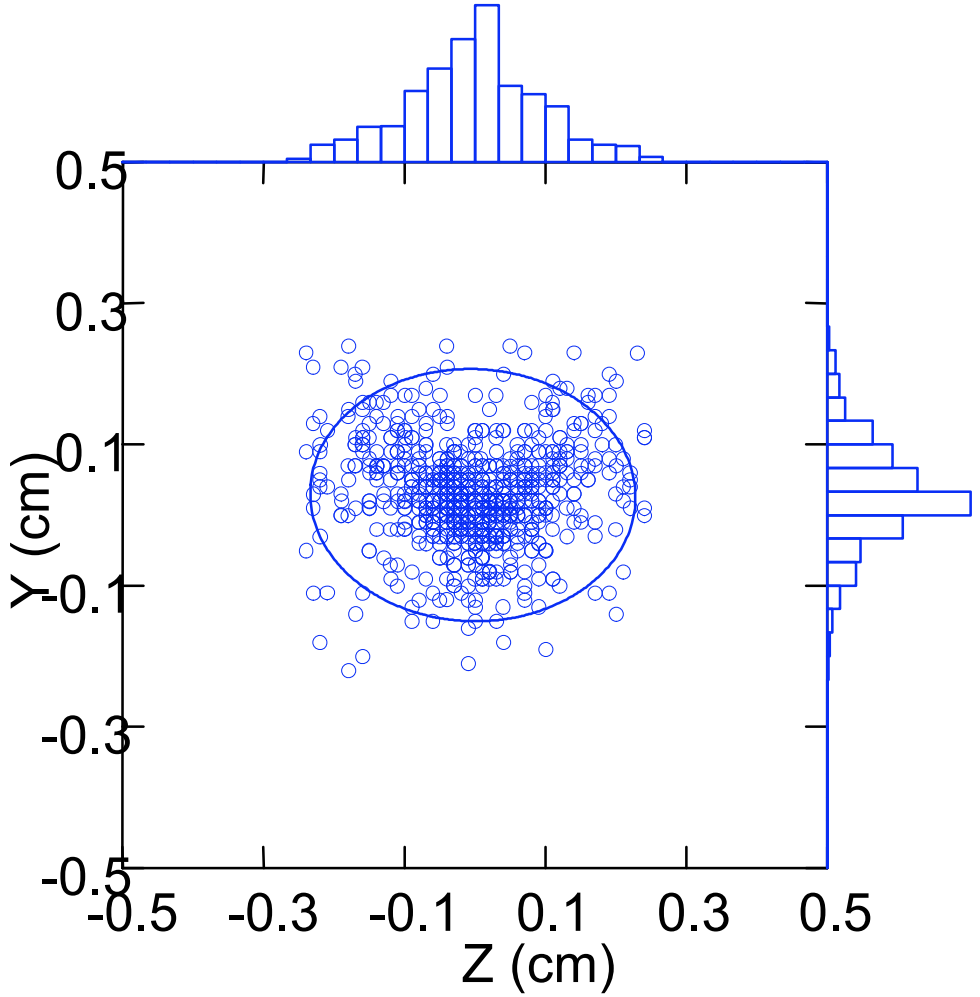
- The image guidance system and use will define the residual error for your IGRT system.

Corrections for an Action Level

	2.5mm action level			
Patient	0 Corrections	1 correction	2 corrections	3 corrections
Total	8.7 (67/772)	82.1 (634/772)	8.3 (64/772)	0.9 (7/772)
Cumulative	8.7%	90.8%	99.1%	100%

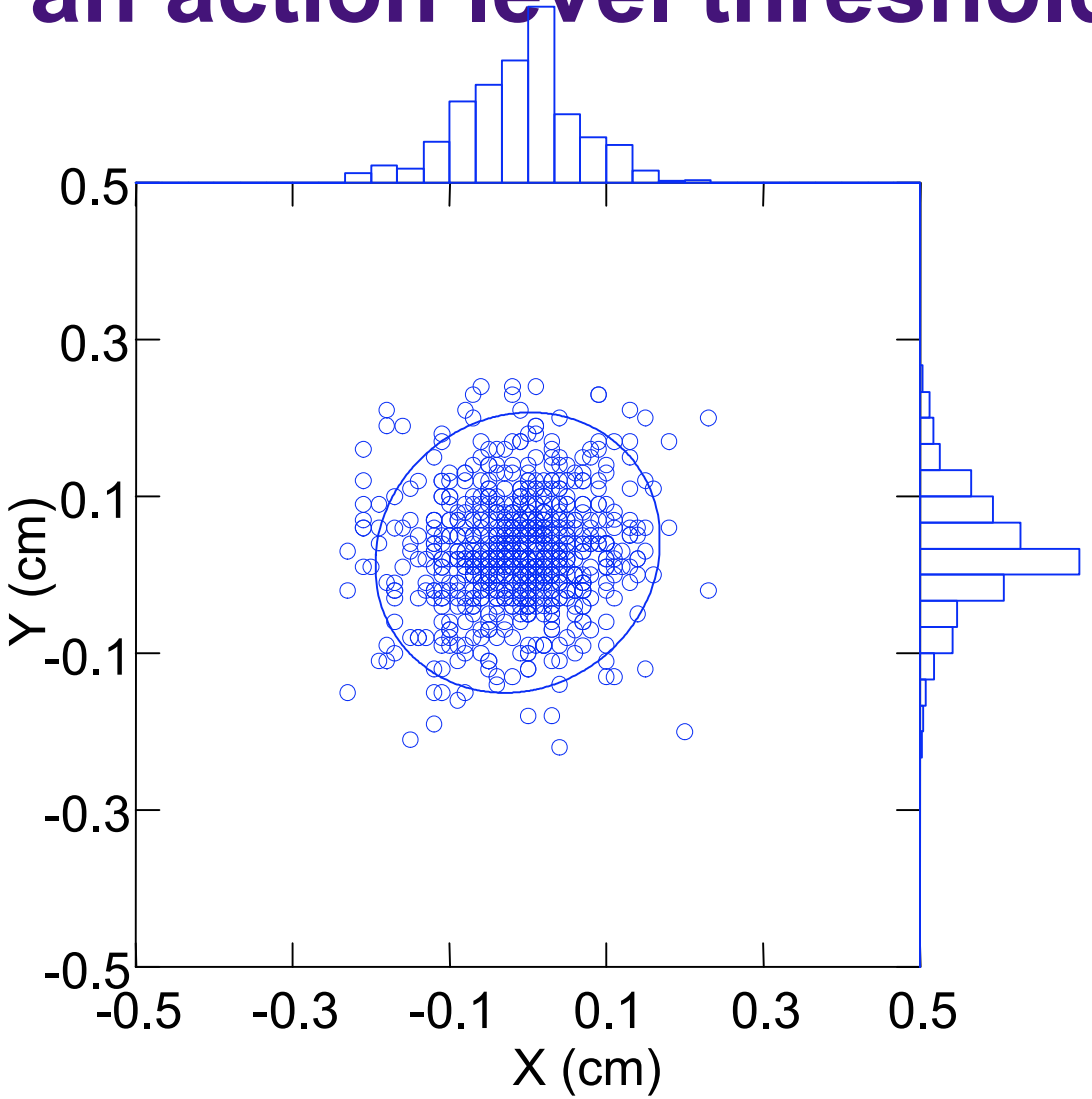
Vargas et al In press AJCO 2008

Residual prostate position with IGPT and an action level threshold



Vargas et al In press AJCO 2008

Residual prostate position with IGPT and an action level threshold



Vargas et al In press AJCO 2008

Intra-fraction error

AP	Supine WRB	Supine WORB	Prone WRB	Prone WORB
Average per patient	-0.13	0.37	0.27	-0.25
Average Range (mm)	-0.37 to 0.1	-0.1 to 1.0	-1.02 to 2.09	-0.55 to 0.31
SD per period	0.55	1.0	1.47	1.98
SD range (mm)	0.25 to 0.9	0.15 to 1.65	0.62 to 1.36	0.67 to 2.57
SI				
Average per patient	-0.18	-0.14	-0.03	0.20
Average Range (mm)	-0.48 to 0.01	-0.34 to 0.04	-0.18 to 0.09	-1.04 to 1.81
SD per period	0.85	0.66	1.06	0.41
SD range (mm)	0.01 to 1.40	0.09 to 0.99	0.2 to 1.68	0.13 to 0.87

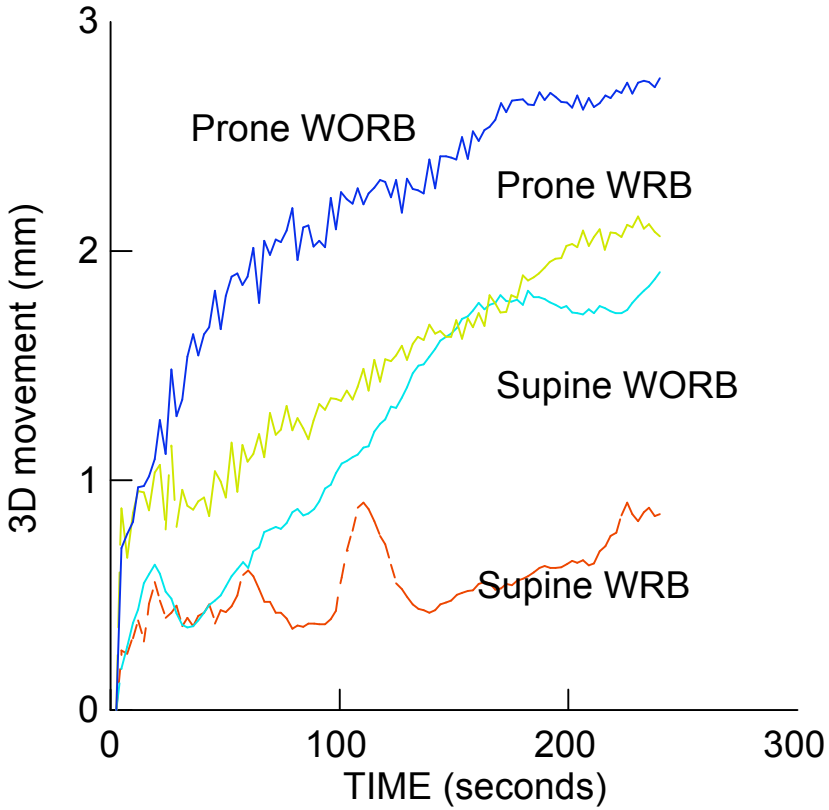
Provided by Vargas et al

Time and intra-fraction error

AP	Supine WRB	Supine WORB	Prone WRB	Prone WORB
0-2 minutes				
average	-0.14	0.17	0.15	-0.12
SD	0.48	0.57	0.85	1.58
2-4 minutes				
average	-0.11	0.56	0.38	-0.38
SD	0.62	1.44	1.19	2.39
SI				
0-2 minutes				
average	-0.10	-0.05	-0.02	0.12
SD	0.49	0.41	0.70	0.72
2-4 minutes				
average	-0.25	-0.23	-0.05	0.28
SD	1.22	0.91	1.42	0.92

Provided by Vargas et al

Time and Intra-fraction error



Movement over time

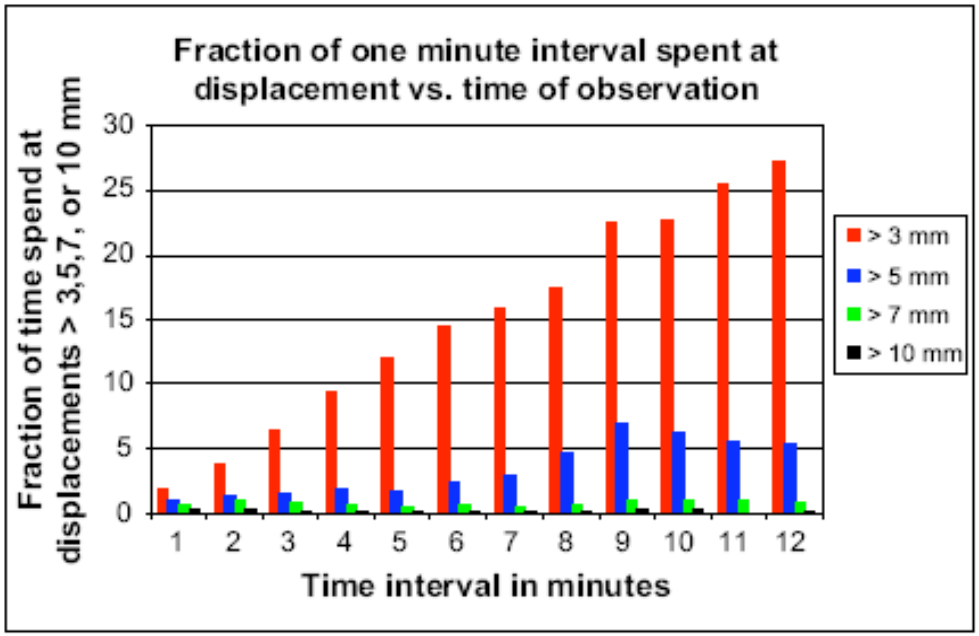
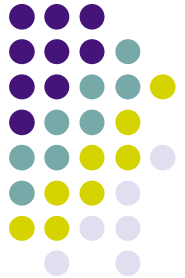


Fig. 4. Fraction of time that certain displacements were observed plotted vs. time of observations. For this plot, all first, second, and so forth, minutes from all tracking sessions were analyzed separately for prostate displacement. Likelihood of prostate displacement clearly increased with time elapsed after patient positioning.

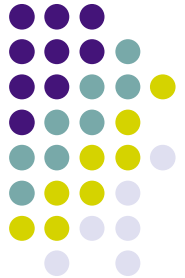
Langen et al 2008; 70: 1492-1501

Randomized Trials



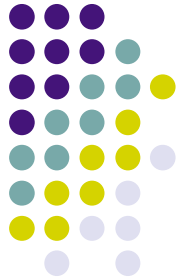
- Randomized trials provide non-biased answers to the a defined question. If proton therapy is compared to IMRT we will know if the proton therapy technique employed is superior or less toxic to IMRT.
  - However, which type of proton therapy will be used IG with an active level threshold with MRI simulation and patient specific optimization.
  - What will happen with uniform scanning, IMPT, integration with chemotherapy, hypofractionated regimes, dose escalation.
  - Furthermore, it will take several years to propose write and accrue patients. Followed by several years before and answer for a given proton technique the answer may be irrelevant at the time the results are available

Randomized Trials



- No comparison was done for 2D to 3D or from 3D to IMRT.
- Dosimetric analysis suggested a benefit for 3D and IMRT and clinical results followed.
- The benefit for Proton therapy compared to IMRT is larger than for 3D vs. IMRT for prostate cancer.
- Surrogates, as the studies quoted before, are available that show a clinical benefit for proton therapy the question that will remain will be magnitude of the benefit.

Randomized Trials



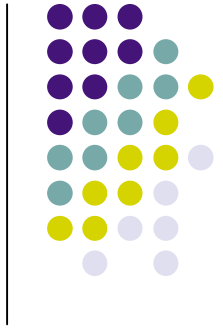
- Will resources be better spend in questions that can only be answered with this type of design?
  - Hypofractionation for proton therapy
  - Dose escalation
  - Integration of chemotherapeutic/other agents

Radiation Oncology Pool

Radiation Oncology Pool *Physician Part B		
		%Change from Prior
2001	$ 810,000,000	
2002	$ 1,002,000,000	24%
2003	$ 1,163,000,000	16%
2004	$ 1,330,000,000	14%
2005	$ 1,460,000,000	10%
2006	$ 1,599,000,000	10%
Overall Change 2001-2006		**97%**

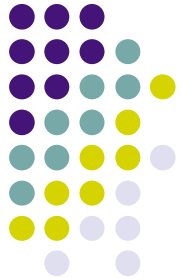
Provided by Tim Williams, MD

IMRT



2003 Ranked By Charges	HCPCS	2003 Allowed Charges	2003 Allowed Services	2006 Ranked By Charges	2006 Total Allowed Charges	2006 Total Allowed Services	Change in Allowed Charges	% Change in Total Allowed Charges	Change in Rank
2	99214	$3,819,014,159	50,029,969	2	$4,986,587,681	61,709,522	$1,167,573,522	30.6%	0
64	77418	$185,933,213	295,962	20	$581,612,048	870,083	$395,678,835	212.8%	44
8	78465	$855,761,471	2,751,144	5	$1,159,131,442	3,274,533	$303,369,971	35.5%	3

Provided by Tim Williams, MD

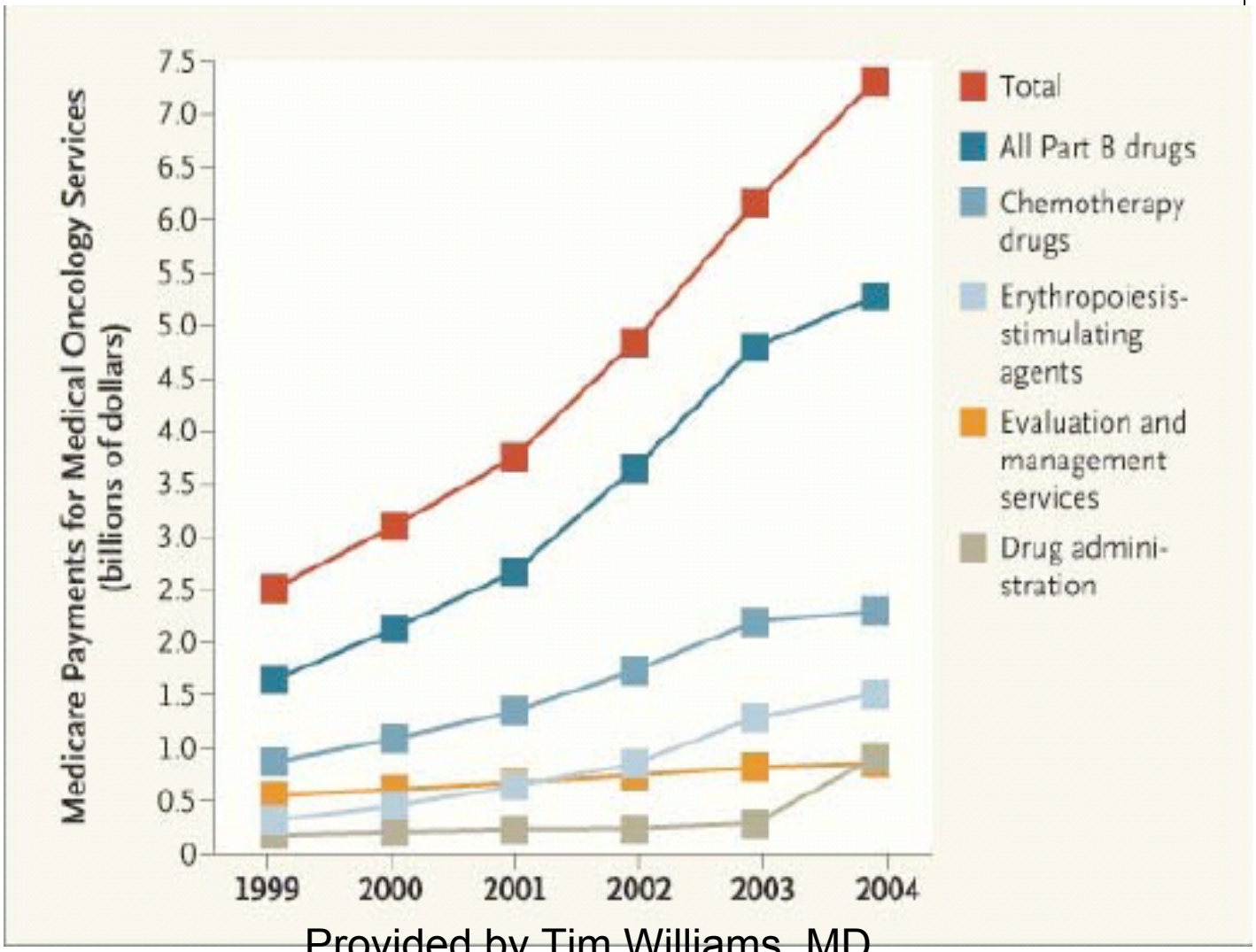


How Big is our Pool?

As a percent of 2006 total allowed charges under the physician fee schedule ($75.819 billion), radiation oncology allowed charges ($1.599 billion) = 2.1%.

Provided by Tim Williams, MD

Medicare Spending: Medical Oncology Services



Provided by Tim Williams, MD

Cost

	IMRT	Proton	Proton
Fractions	40	40	28
Global	$44 K	$54 K	$41 K
We can hypo-fractionate better with protons			
Using LCD rates, daily IGRT UFPTI PR04 is open!			

Provided by Sameer Keole, MD

Brachytherapy Monotherapy Toxicity

- RTOG 9805

Table 2. Acute toxicity (n = 94)

Toxicity	Grade (n)				
	1	2	3	4	5
Skin	4	0	0	0	0
Cardiovascular (general), edema not otherwise specified	2	0	0	0	0
Constitutional symptoms	8	0	0	0	0
Endocrine	1	0	0	0	0
Gastrointestinal	18	9	0	0	0
Hemorrhage	4	4	3	0	0
Infection, febrile neutropenia	0	0	1	0	0
Musculoskeletal	0	1	0	0	0
Neurology	1	0	0	0	0
Pain	7	3	0	0	0
Renal/genitourinary	35	43	4	0	0
Sexual/reproductive function	11	8	2	0	0
Other*	0	1	0	0	0
Worst overall	28	49	8	0	0

* Swollen prostate reported.

Lawton et al IJROBP 2007: 67; 39–47

Brachytherapy Toxicity

- RTOG 9805

Table 3. Toxicity during follow-up according to RTOG late scoring criteria (n = 93)

Toxicity	Present/not graded	Grade 1	2	3	4	5
Bladder	0	20	19	2	0	0
Bowel	0	11	5	0	0	0
Impotence	5	0	0	0	0	0
Liver	0	1	0	0	0	0
Other	1	0	0	0	0	0
Worst overall	2	19	22	2	0	0

	Mild	Moderate	Severe
Impotence	3	6	3
Other	3	1	0
Pain	2	0	0
Worst overall	8	7	3

Abbreviation: RTOG = Radiation Oncology Group.

Lawton et al IJROBP 2007: 67; 39–47, 2007

Brachytherapy Boost

- RTOG 0019

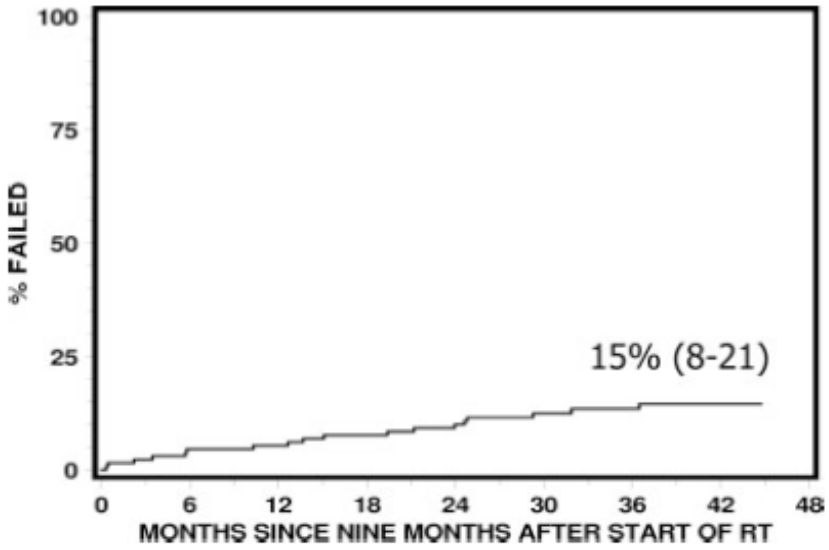


FIGURE 1. Time to late grade ≥3 genitourinary/gastrointestinal toxicity. RT indicates radiotherapy.

Lee et al Cancer 2007;109:1506–12.

Brachytherapy Boost

- RTOG 0019

TABLE 2
Reported Late Grade ≥3 Genitourinary/Gastrointestinal Toxicity in Recent Radiation Therapy Oncology Group Trials of Men With Clinically Localized Prostate Cancer

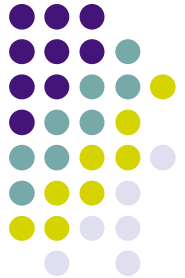
Study no.	Radiotherapy dose	No. of patients	Median FU, mo	% Late grade ≥3 GU/GI toxicity
0019	45 Gy in 1.8-Gy fractions and 108 Gy I–125	130	49	15 at 48 mo
9406 (Level III)	79.2 Gy in 1.8-Gy fractions	170	56–62	1–2 at 24 mo*
9406 (Level V)	78 Gy in 2-Gy fractions	218	29	5–7 at 24 mo*
9509	79.2 Gy in 1.8-Gy fractions	195	66	1–2*
9805	145 Gy I–125	94	64	<3 at 60 mo

FU indicates follow-up; GU/GI, genitourinary/gastrointestinal; Gy, grays; I–125, iodine-125.

* Represents a crude percentage: Actuarial figures are not provided.

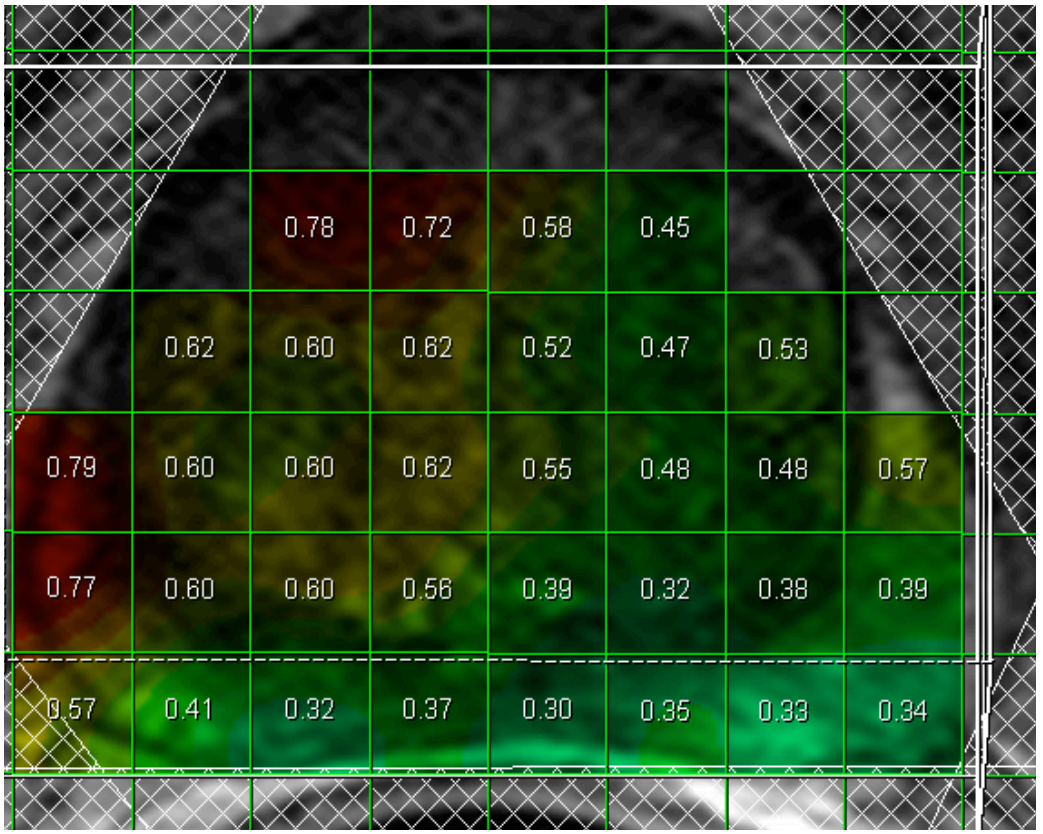
Lee et al Cancer 2007;109:1506–12.

Summary



- Acute toxicity is high.
- Late toxicity profile for IMRT and brachytherapy is similar for monotherapy and high for combined modality.
- Is an invasive procedure.
- Control rates are not better than conventional.

Future directions-Biologic guidance

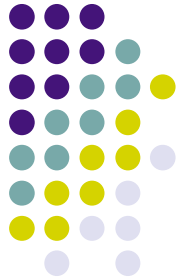


Provided by Carlos Vargas, MD

At the end

- Scanned proton therapy will decrease exposure outside the field potentially decreasing second malignancies.
- Optimally done proton plans will decrease doses to normal structures.
- Image guided proton therapy is superior to image guided IMRT
- Shorter treatment and beam on times will decrease intra-fraction error further reducing necessary margins and decreasing doses to normal structures
- Lower integral doses may allow the appropriate use with systemic agents
- Hypofractionated proton courses as proposed by us and implemented at UF are cheaper than IMRT (44-45fx)

In summary



Prostate is in an ideal location for optimal proton therapy.

Current DS proton therapy for prostate cancer is superior to IMRT.

However, we do not stop here US and IMPT will further improve our treatments and the clinical benefit.