

Alan Pollack, M.D., Ph.D.
Fox Chase Cancer Center

IMRT For Prostate Cancer

The Road To IMRT

From Conventional
To Conformal To
IMRT



3/3/03

Considerations In The Implementation Of IMRT

- Rationale for IMRT
- Dose Specification
- Target Motion
- Gains from IMRT
- Planning and Treatment at FCCC

Rationale For IMRT

- Dose escalation
- Normal tissue conformal avoidance
- Improved target coverage

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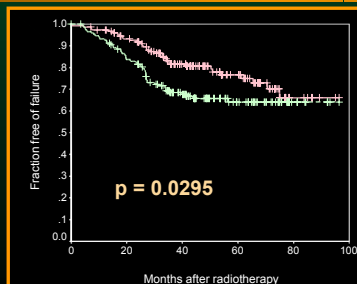
A Pollack, GK Zagars, JA Antolak, Eugene Huang, AC
von Eschenbach, DA Kuban, II Rosen
UT - MD Anderson Cancer Center

Prostate Cancer Dose Escalation Trial

70 Gy vs 78 Gy

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MDACC Randomized Trial 2001 All Patients

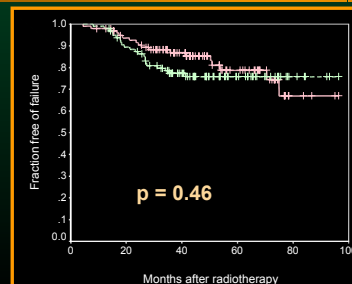


Median F/U
~60 mo

%6 yr FF
78 Gy: 70
70 Gy: 64

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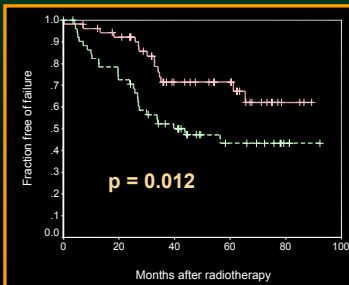
MDACC Randomized Trial 2001 PSA ≤10 ng/ml



%6 yr FF(n)
78 Gy: 74(97)
70 Gy: 76(98)

3/3/03

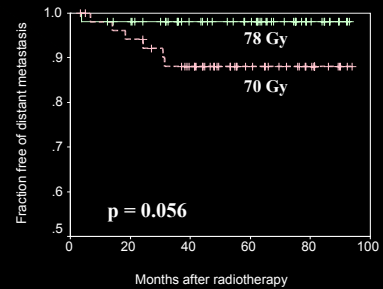
MDACC Randomized Trial 2001 PSA >10 ng/ml



%6 yr FF(n)
78 Gy: 62(53)
70 Gy: 43(53)

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MDACC Randomized Trial 2001: Freedom From DM For PSA >10 ng/ml



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MDACC 3D Protocol

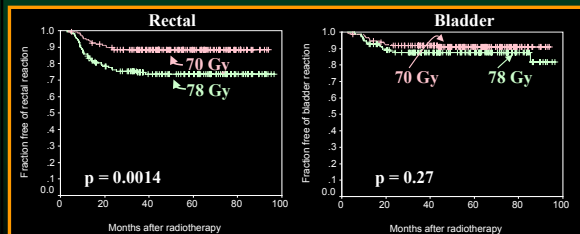
Complications

Prospective Evaluation For
Patients With ≥ 2 yr F/U

- Questionnaire
- Prospective Coding

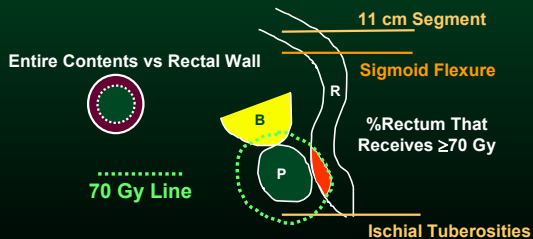
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MDACC Dose Escalation Trial 2001: Grade 2 or Higher Complications



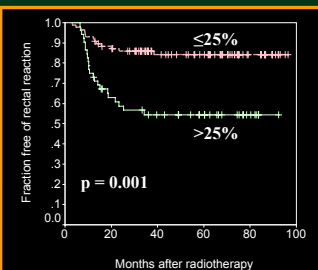
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Defining DVH Parameters: Rectum



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78 Gy Arm Grade 2 or Higher Late Rectal Complications: Divided by Percent Rectum Treated To ≥ 70 Gy



3/3/03

Huang EH, Pollack A, Levy L, Starkschall G, Dong L, Rosen I, Kuban DA

IJROBP 54:1314, 2002

**Late Rectal Toxicity:
Dose Volume Effects Of Conformal
Radiotherapy For Prostate Cancer**
M.D. Anderson Cancer Center

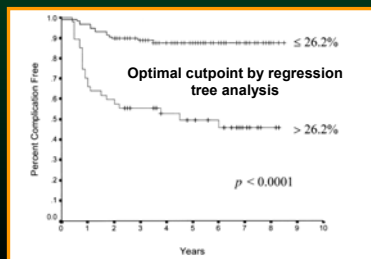
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**Determinants of Rectal Toxicity
Rectal DVH Parameter**

- Huang et al: 74 – 78 Gy
 - » Percent of rectum > absolute volume
 - ❖ >26.2% over 70 Gy
 - » History of Hemorrhoids
- Skwarchuk et al : ≥70.2 Gy
 - » 50% isodose line beyond rectal wall
 - » Smaller rectal wall volume
 - » Higher rectal Dmax
 - » Diabetes

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Huang et al, 2002



3/3/03

**Prostate Cancer Radiotherapy:
Dose & ≥Grade 2 Rectal Reactions**

Author	Year	Dose	GI Toxicity
Smit	1990	≤70 Gy	22%(2 yr Act)
		>70-75 Gy	20%
		>75 Gy	60%
Shipley	1995	67.2 Gy	12%(10 yr Act)
		75.6 CGE	32%
Lee	1996	<72 Gy	7%(18 mo Act)
		72-76 Gy	16%
		>76 Gy	23%
Zelevsky	1998	≤70.2	6%(5 yr Act)
		>75.6	17%
Pollack	2002	70 Gy	12%(5 yr Act)
		78 Gy	26%

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**Prostate Cancer Radiotherapy: Rectal
Volume Irradiated & ≥Grade 2 Reactions**

Author	Year	Dose	Rectal Vol	GI Toxicity
Benk	1993	75 CGE	<40%ARW	19%(40 mo Act)†
		75 CGE	≥40%ARW	71%
Lee	1996	74-76 Gy	Rect Block	10%(18 mo Act)
		74-76 Gy	No Block	19%
Dearnaley	1999	64 Gy	3DCRT	8%(5 yr Act)
		64 Gy	Conven-RT	18%
Boersma	1998	70 Gy	≤30%	0%(Crude)*
		70 Gy	>30%	9%
Pollack	2002	70 Gy	≤25%	16%(6 yr Act)
		70 Gy	>25%	46%

† Any rectal bleeding; *Severe rectal bleeding; ARW = anterior rectal wall.

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Impetus For Change To IMRT

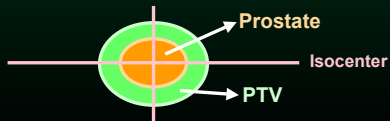
Rectal Toxicity

- 35% of protocol pts had unacceptable plans
- Limit rectum receiving ≥70 Gy to <25%
 - » 3DCRT and/or IMRT from day 1
 - » Reduced coverage of distal seminal vesicles

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Protocol Techniques

- Conformal used as a boost
 - » Antiquated approach
- Dose specification to the isocenter
 - » Now prescribe to the PTV



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Immobilization: MDACC



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Immobilization: FCCC



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Prostate Movement

Antolak et al, IJROBP, 42:661, 1998

- 17 Pts w serial prostate CTs during RT
 - » Pretreatment CT & 3 subsequent CTs
 - ❖ CTs at 2-3 wk intervals
- Bladder, Rectum, Prostate outlined
- Alignment w 1st CT: rigid body transformation based on bony anatomy.
 - » Compare bounding box limits & center of mass

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Recommendations For PTV Margins

- ICRU #50: Define PTV based on probable position of the CTV
- 95% prob that a point on the CTV in PTV
 - » 0.7 cm L-R
 - » 0.7 cm S-I
 - » 1.1 cm A-P
 - ❖ Add >0.5 cm to block for penumbra

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Bladder & Rectal Volume Changes

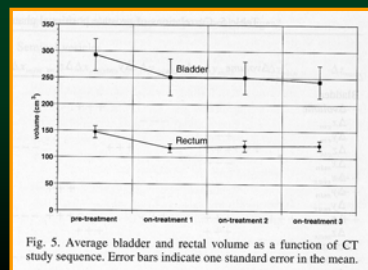
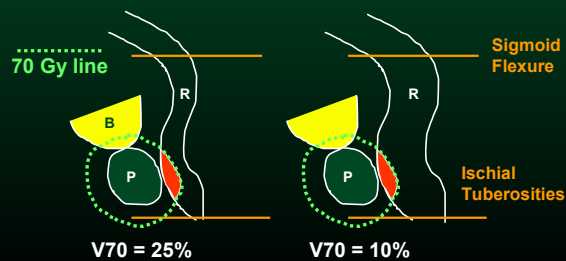


Fig. 5. Average bladder and rectal volume as a function of CT study sequence. Error bars indicate one standard error in the mean.

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Filling Effects on Rectal DVH Parameters



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Controlling For Prostate Movement

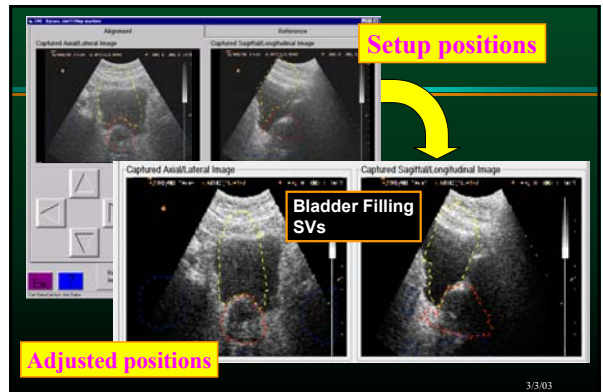
- New CT at 2-3 weeks
- Rectal Balloon
- Fiducial Markers & EPID
- BAT Ultrasound localization
- CT – LINAC
 - » CT-on-rails
 - » Cone beam CT

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B-mode Acquisition and Targeting System



3/3/03



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BAT Ultrasound vs. CT

- Lattanzi et al, Fox Chase Cancer Center
- 69 Daily CT and BAT images compared
- High correlation of paired CT-BAT shifts
 - » Ant/Post, $r = 0.88$
 - » Lateral, $r = 0.91$
 - » Sup/Inf, $r = 0.87$

3/3/03

A Chandra, L Dong, E Huang, DA Kuban, L O'Neil, II Rosen, A Pollack

M.D. Anderson Cancer Center
IJROBP, 2003

Quality and Consistency Of
Ultrasound-Based Daily Prostate
Localization During IMRT

3/3/03

Daily BAT Ultrasound For IMRT

- 147 consecutive patients
 - » 3509 procedures
 - » Image quality and alignment rated
- Quality: acceptable in 95%
- Alignment: acceptable in 97%
 - » For those with acceptable quality
 - » No alignment attempted in 22 pts

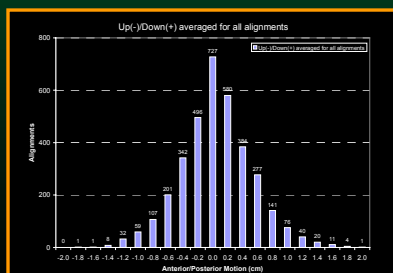
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BAT Alignment

Type	RL	AP	SI
Mean±SD(mm)	-0.55±2.77	0.50±4.86	0.71±4.40
Range(mm)	-14.1–14.5	-17.2–21.1	32.2–20.2
%>5 mm	9	28	23
%Misalign	0.1	1.7	1.5

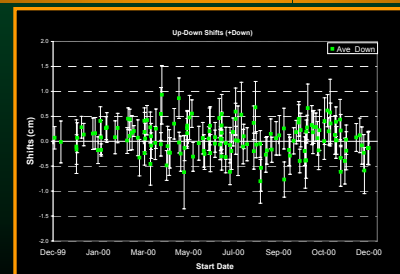
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BAT Alignments: Ant-Post



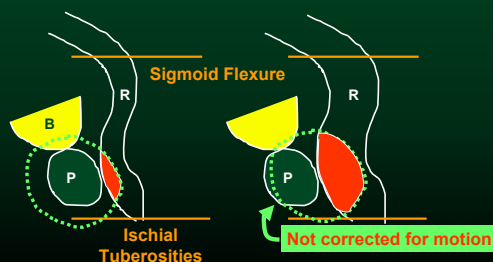
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Individual Patient BAT Alignment Averages



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Rectal Filling Effects: No Target Imaging During RT



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Huang E, Dong L, Chandra A, Kuban DA,
Rosen II, Evans A, Pollack A

Intrafraction Motion During IMRT For Prostate Cancer

3/3/03

Intrafraction Prostate Motion During IMRT: Patients and Methods

- 20 Patients studied over 10 Tx days
 - » IMRT: 75.6 Gy / 42 fx
- Pre- and Post-tx alignment images
 - » 400 BAT Procedures
- Performed by radiation therapists

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Intrafraction Motion For 200 Post-treatment Ultrasound Procedures

Direction	Mean $\pm$ SD mm (Range)	No Shift	Shift $\leq$ 2.5 mm	Shift $>$ 2.5 to 5 mm	Shift $\geq$ 5 mm
RL	(-) 0.01 $\pm$ 0.4 (2.5 to -2.4)	80.5%	19.5%	0%	0%
AP	0.2 $\pm$ 1.3 (6.8 to -4.6)	72.0%	21.5%	5.5%	1.0%
SI	0.1 $\pm$ 1.0 (3.5 to -6.8)	72.5%	23.5%	3.5%	0.5%

(-) denotes motion to the left, posteriorly, or inferiorly

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CT-LINAC Measurements Of Interfraction Motion

Int J Radiation Oncology Biol Phys, Vol. 55, No. 1, pp. 411-418, 2001
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0360-3016/01/\$ - see front matter

doi:10.1016/S0360-3016(01)00267-4

PHYSICS CONTRIBUTION

DEVELOPMENT OF A SEMI-AUTOMATIC ALIGNMENT TOOL FOR ACCELERATED LOCALIZATION OF THE PROSTATE

CHUNHO HUA, Ph.D.,* D. MICHAEL LOWELOCK, Ph.D.,* GRAS S. MAGRAN, Ph.D.,* MATTHEW S. KATZ, M.D.,† JAMES MICHALAKOS, Ph.D.,* EUGENE P. LEE, Ph.D.,* TIMOTHY HOLLISTER, M.D.,† WENDIE R. LUTZ, Ph.D.,* MICHAEL J. ZELINSKY, M.D.,† AND CLIFTON C. LING, Ph.D.*

Departments of *Medical Physics and †Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY

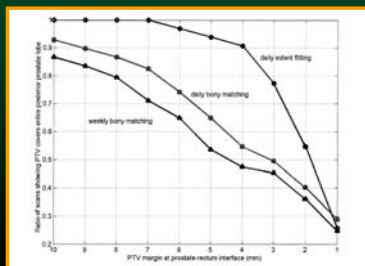
3/3/03

Hua et al, MSK

- “With daily CT extent-fitting correction, 97% of the scans showed that the entire posterior prostate gland was covered by PTV given a margin of 6 mm at the rectum-prostate interface and 10 mm elsewhere.
- In comparison, only 74% and 65% could be achieved by the corrections based on daily and weekly bony matching on portal images, respectively.”

3/3/03

Hua et al, MSK



3/3/03

Real Time Prostate Motion Using Fiducials

CLINICAL INVESTIGATION

Prostate

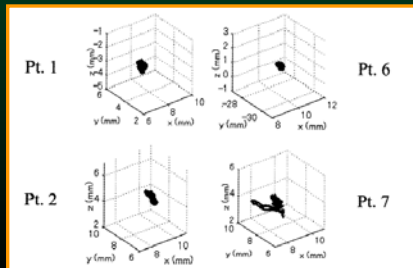
THREE-DIMENSIONAL INTRAFRACTIONAL MOVEMENT OF PROSTATE MEASURED DURING REAL-TIME TUMOR-TRACKING RADIOTHERAPY IN SUPINE AND PRONE TREATMENT POSITIONS

KEN KITAHARA, M.D.,* HIROKI SHIRATO, M.D.,* YUJIE SEPPENWOOLDE, Ph.D.,† RIKIYA ONIMARU, M.D.,* MASATO ODA, R.T.,* KATSURISA FUJITA, R.T.,* SHINICHI SHIMIZU, M.D.,* NORIO SHINDOHARA, M.D.,† TORU HARABAYASHI, M.D.,† AND KAZUO MIYASAKA, M.D.,*

Departments of *Radiology and †Urology, Hokkaido University School of Medicine, Sapporo, Japan; †Department of Radiotherapy, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Huis, Amsterdam, The Netherlands

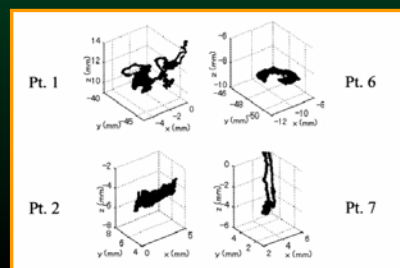
3/3/03

Kitamura, et al: Prostate Motion - Supine



3/3/03

Kitamura, et al: Prostate Motion - Prone



3/3/03

IJROBP 53:1111-1116, 2002

CLINICAL INVESTIGATION **Prostate**

HIGH-DOSE INTENSITY MODULATED RADIATION THERAPY FOR PROSTATE CANCER: EARLY TOXICITY AND BIOCHEMICAL OUTCOME IN 772 PATIENTS

MICHAEL J. ZELEFSKY, M.D.,* ZVI FUKS, M.D.,* MARGIE HUNT, B.A.,† YOSHITAYA YAMADA, M.D.,* CHRISTINE MARON, B.A.,* C. CLIFTON LING, Ph.D.,‡ HOWARD AMOS, Ph.D.,‡ E. S. VENKATRAMAN, Ph.D.,‡ AND STEVEN A. LEBEL, M.D.†

Departments of *Radiation Oncology, †Medical Physics, and ‡Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY

Median follow-up 24 mo

3/3/03

Zelevsky et al, 2002

- 772 Pts treated with IMRT
 - » 81 Gy 698 Pts
 - » 86.4 Gy 74 Pts
- Median follow-up 24 months
- Constraints
 - » Rectal wall: 40% of prescription dose
 - » PTV overlap 88% of prescription
 - » Bladder wall: 50% of prescription dose
 - » PTV overlap 98% of prescription

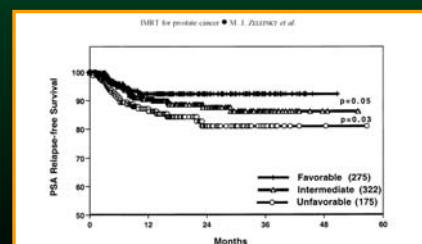
3/3/03

Zelevsky et al, 2003

- Prone position
- Thermoplastic shell immobilization
- No target localization daily
- Standardized beam arrangement
 - » 5 field

3/3/03

Zelevsky et al, 2002



3/3/03

Dong L, O'Daniel J, Smith LG, Kuban D,
Bounds S, Rosen IL, and Pollack A

Dosimetric Gains From IMRT In Low Risk Prostate Cancer

3/3/03

Assessing Gains From IMRT Dong L, et al, MDACC

- 20 favorable patients planned
 - » All favorable with <50% of SVs outlined
 - » Structures outlined on AcQSim
- Multiple plans: 75.6 Gy in 42 fractions*
 - » 4 Field conformal throughout
 - » 10 Field: 4 field + 6 field conformal boost*
 - ❖ 78 Gy in 39 Fxs to isocenter
 - » 7 Field conformal with 40% from laterals
 - » 7 Field conformal with 50% from laterals
 - » IMRT using MIMiC, 6 MV
 - » IMRT using sMLC, 6 MV 10 field

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Definition of Normal Structures

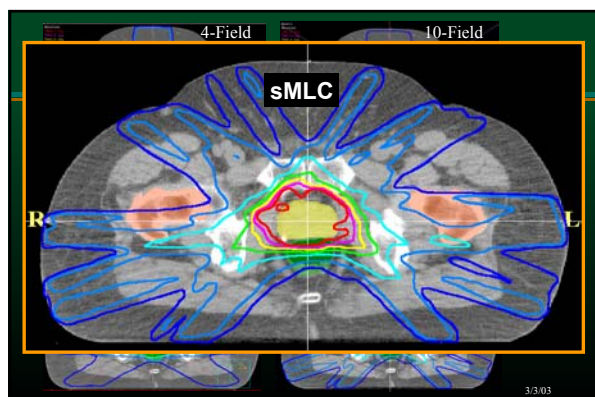
- Bladder:
 - » Entire structure
- Rectum:
 - » Ischial tuberosities to sigmoid flexure
 - » Entire contents (not just wall)
- Femurs:
 - » Down to between greater & lesser trochanters

3/3/03

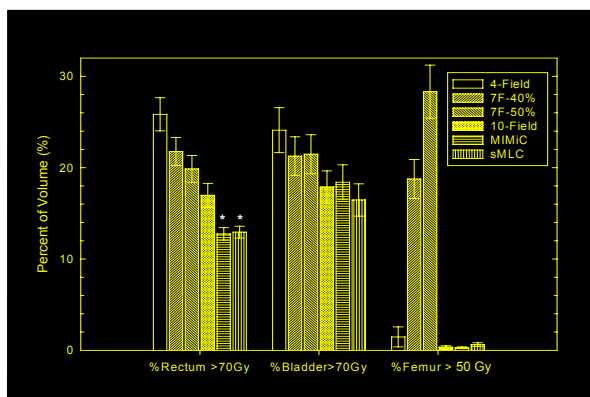
PTV Used

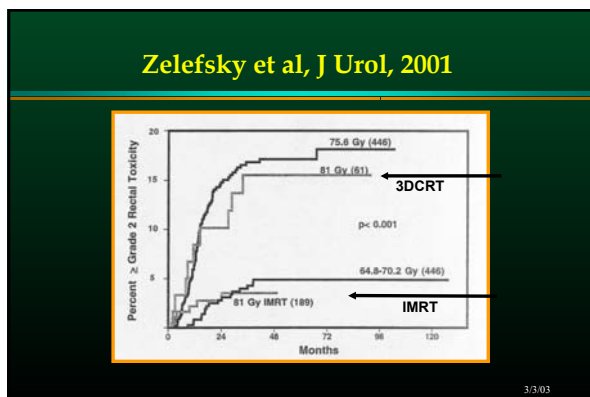
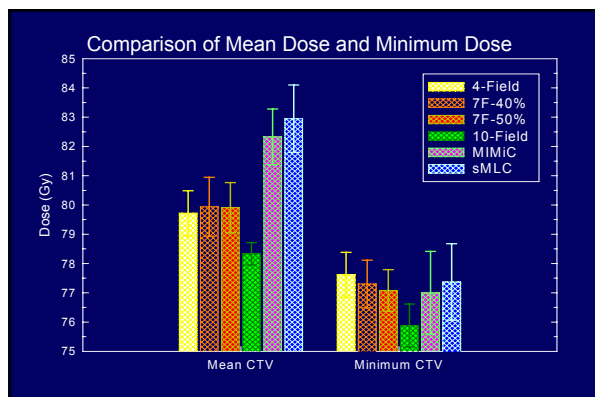
- 1.0 cm except posteriorly:
 - » Effective PTV: 1.0-1.5 cm for IMRT
- 0.5 cm posteriorly:
 - » Effective PTV: 0.4-0.8 cm for IMRT

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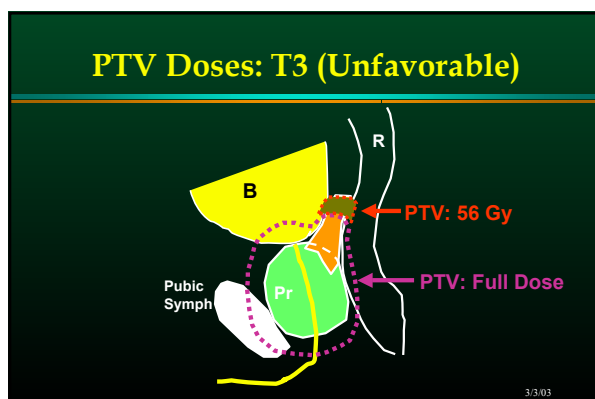
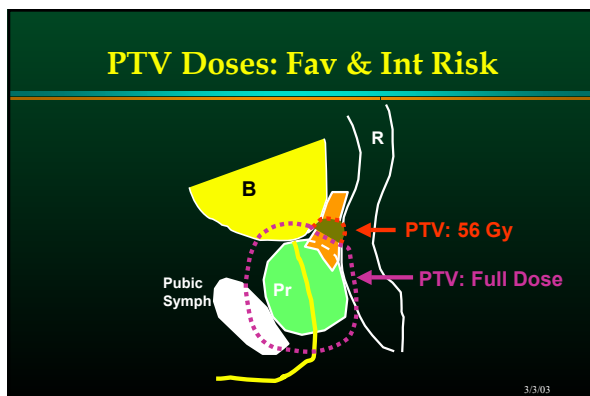
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IMRT For Prostate Cancer At Fox Chase

- **Favorable Risk**
 - » PTV: 74 Gy at 2 Gy/Fx
 - ❖ ±SVs, proximal: 56 Gy
- **Intermediate Risk**
 - » PTV: 76-78 Gy at 2 Gy/Fx
 - ❖ SVs ≤50%: 56 Gy
- **High Risk**
 - » PTV: 76-78 Gy at 2 Gy/Fx
 - ❖ SVs, proximal: 76-78 Gy
 - ❖ SVs, >50%: 56 Gy
 - ❖ Periprostatic LNs: 56 Gy
 - » Androgen Ablation x2 yr



Planning Constraints

- **PTV Constraints**
 - » Absolute: DVH, PTV Min PTV Max
 - » Effective: Prescription isodose coverage
- **Normal Tissue DVH Constraints**
- **Normal Tissue Dose Gradient Constraints**
 - » Examine transverse cuts
 - ❖ 100%, 90%, and 50% lines

Absolute and Effective PTV Constraints

- **Absolute (Hard) Constraints**
 - » $D_{95} \geq$ Prescription dose
 - » Min dose: <1% under 65 Gy
 - » Max dose 17% over prescription dose
- **Effective (Soft) Constraint**
 - » 100% line coverage varies
 - ❖ Examine slice by slice
 - ❖ If small margin check dose gradient

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PTV Used

- 8 mm except posteriorly:
 - » Effective PTV: 6-13 mm
- 5 mm posteriorly:
 - » Effective PTV: 4-8 mm

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DVH Planning

- **Prostate**
 - » Based on PTV
 - ❖ Considers uncertainties
- **Rectum and Bladder**
 - » Based on planning CT outline
 - ❖ Does not consider uncertainties

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Normal Tissue DVH Criteria

- **Rectum**
 - » $\leq 17\%$ to ≥ 65 Gy
 - » $\leq 35\%$ to ≥ 40 Gy
- **Bladder**
 - » $\leq 25\%$ to ≥ 65 Gy
 - » $\leq 50\%$ to ≥ 40 Gy

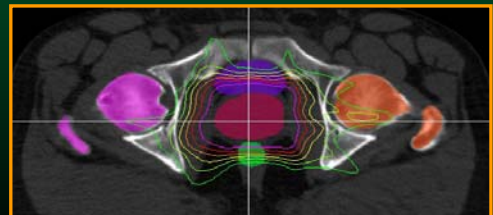
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Normal Tissue Dose Gradient Constraints

- **Sharp dose fall-off desired**
 - » Check slice by slice
- 90% line < half rectal width
- 50% line < full rectal width

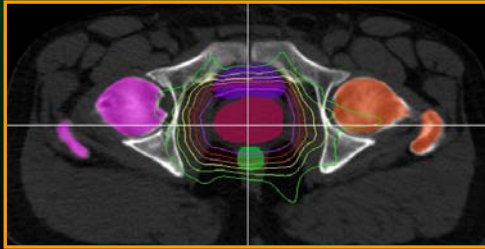
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Normal Tissue Dose Gradient: Acceptable



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Normal Tissue Dose Gradient: Unacceptable



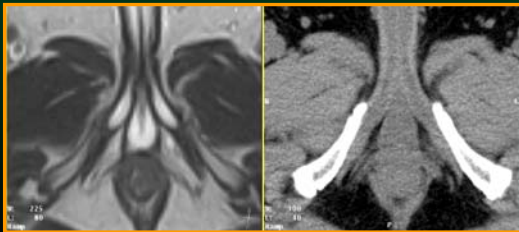
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MR-Sim For Prostate



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Penile Bulb/Cavernosal Bodies



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MRI vs CT: GTV Delineation



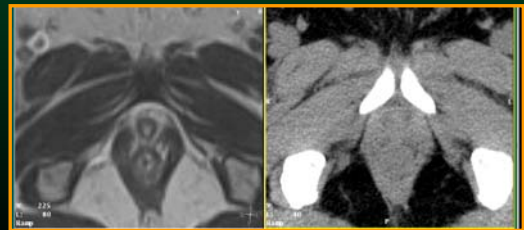
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MRI vs. CT: Prostate Apex



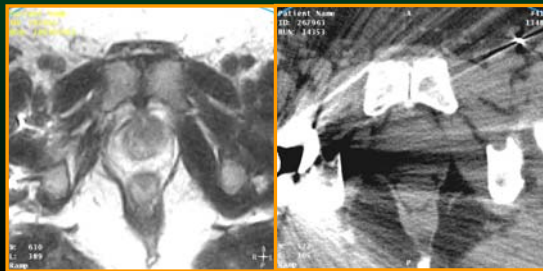
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Below Prostate Apex



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MRI vs. CT: Hip Replacement



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Gains From IMRT

- Dose escalation
- Normal tissue conformal avoidance
- Improved target coverage

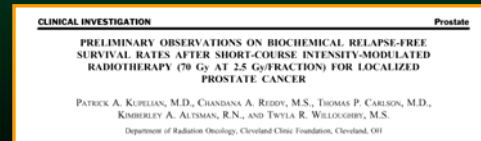
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FCCC Prostate Cancer Dose Escalation Trial

- Hypotheses:
 - » Further dose escalation beneficial
 - » Prostate cancer behaves like a late reacting tissue
- Dose escalation using hypofractionation
 - » Duchesne and Peters
 - » Brenner and Hall
 - » King et al
 - » Fowler et al
- Conventional Fx vs Hypofractionation

3/3/03

Hypofractionation For Prostate Cancer Cleveland Clinic Experience



IJROBP 2002

3/3/03

Prostate Hypofractionation Trial

Intermediate – High Risk Prostate Cancer

Standard Fractionation
76 Gy in 38 (2.0 Gy) fxs

Hypofractionation
70.2 Gy in 26 (2.7 Gy) fxs
Biologically equivalent to
84.3 Gy at 2.0 Gy

Stratified by Pretreatment PSA: ≤10 vs >10-20 vs >20 ng/ml;
GI ≤7 vs 8-10; Stage T1b-T2 vs T3; neoadj AA vs no AA;
long term AA vs no long term AA

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