

**Advances in Primary and
Adjuvant RT for Prostate Cancer:
Clinical Trials, Image-Guided
Radiotherapy and Brachytherapy**

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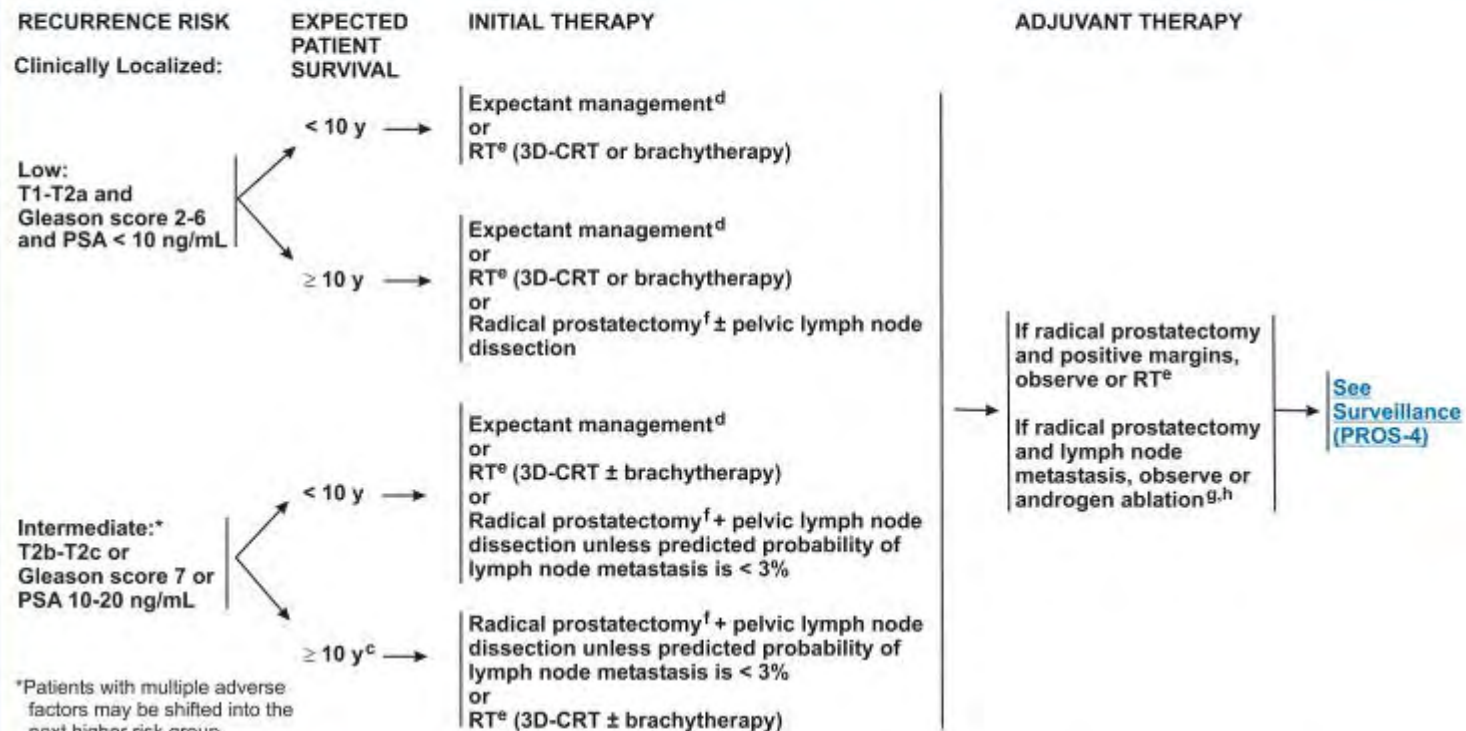
Topics and Trends

- **Risk groups and therapy selection**
- **Adjuvant RT: Clinical trials**
- **Trends in image-guided RT/Proton RT**
- **Brachytherapy results: Seeds and HDR**

NCCN Risk Groupings

- Low risk:
 - T1–T2a, Gleason ≤ 6 , *and*
PSA < 10 ng/ml
- Intermediate:
 - T2b–T2c, Gleason = 7, *or*
PSA 10 – 20 ng/ml
- High:
 - T3–4, Gleason 8 – 10, *or* PSA > 20

Risk Grouping and Treatment Options



^dExpectant management of intermediate and high risk clinically localized cancers is not recommended in patients with a life expectancy > 10 years (category 1).

^eExpectant management involves actively monitoring the course of disease with the expectation to intervene if the cancer progresses or if symptoms become imminent. See Principles of Expectant Management (PROS-B).

^fSee Principles of Radiation Therapy (PROS-C).

^gSee Principles of Surgery (PROS-D).

^hSee Principles of Hormonal Therapy (PROS-E).

ⁱSee Systemic Therapy (PROS-7).

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Types of Radiation Treatment for Prostate Cancer

- **External beam radiotherapy (EBRT)**
 - Early adjuvant post-prostatectomy EBRT
 - Intensity-modulated radiotherapy (IMRT)
 - Daily prostate localization/cross-sectional imaging
- **Brachytherapy**
 - Permanent seed implants (I-125/Pd-103)
 - As monotherapy or with EBRT
 - New seed technology/intraoperative planning
 - Temporary high-dose-rate (HDR) after loading implants
 - With EBRT

Adjuvant and Salvage Radiotherapy Following RRP

- **Adjuvant—given after the primary therapy (RT after RRP)**
- **Salvage—given after the primary therapy has failed**

Post-op RT: Summary of The Randomized Trials

Group	n	Dose(Gy)	FFBF	P value
SWOG 8794/	211	None	44%(5yr)	<0.001
RTOG 9019	208	60-64	71%(5yr)	
EORTC	503	None	53%(5yr)	<0.0001
2291	502	60	74%(5yr)	
ARO 96-02	153	None	60%(4yr)	<0.0001
	108	60	81%(4yr)	

Salvage and Adjuvant RT After RRP: Indications and Evidence

1. Biopsy proven local recurrence	+++
2. Positive margins	+++
3. Rising PSA	++
4. Positive seminal vesicles	++
5. Extraprostatic extension (EPE)	+
6. High-grade cancer	-



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Prostate Nomogram - Post-Radical Prostatectomy

[Change Treatment Stage](#)

Pre-treatment PSA
 Prostate Capsule Inv ▾
 Pathology Gleason Sum
 Surgical Margins Pos
 Seminal Vesicle Inv
 Lymph Node Involvement
 Neo-Adjuvant Hormones
 Neo-Adjuvant XRT

Clear **Calculate**

Results

2 yr Progression-Free Probability	86%
5 yr Progression-Free Probability	70%
7 yr Progression-Free Probability	65%

To learn more about Progression-Free Probability, [click here](#). Results are accurate to +/- 8%. Print your results and discuss them with your doctor.

Print

ADDITIONAL TOOLS

- [Volume](#)
- [Life Expectancy](#)
- [PSA Doubling Time](#)

HELP

- [Glossary](#)
- [FAQ](#)

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Cancer Center

Prostate Nomogram - Post-Radical Prostatectomy

[Change Treatment Stage](#)

<input type="checkbox"/> Pre-treatment PSA	<input type="text" value="10"/>
<input type="checkbox"/> Prostate Capsule Inv	Est. <input type="button" value="v"/>
<input type="checkbox"/> Pathology Gleason Sum	<input type="text" value="7"/>
<input checked="" type="checkbox"/> Surgical Margins Pos	<input type="checkbox"/>
<input type="checkbox"/> Seminal Vesicle Inv	<input type="checkbox"/>
<input type="checkbox"/> Lymph Node Involvement	<input type="checkbox"/>
<input type="checkbox"/> Neo-Adjuvant Hormones	<input type="checkbox"/>
<input type="checkbox"/> Neo-Adjuvant XRT	<input type="checkbox"/>

Results

2 yr Progression-Free Probability	61%
5 yr Progression-Free Probability	33%
7 yr Progression-Free Probability	25%

To learn more about Progression-Free Probability, [click here](#). Results are accurate to +/- 8%. Print your results and discuss them with your doctor.

ADDITIONAL TOOLS

HELP

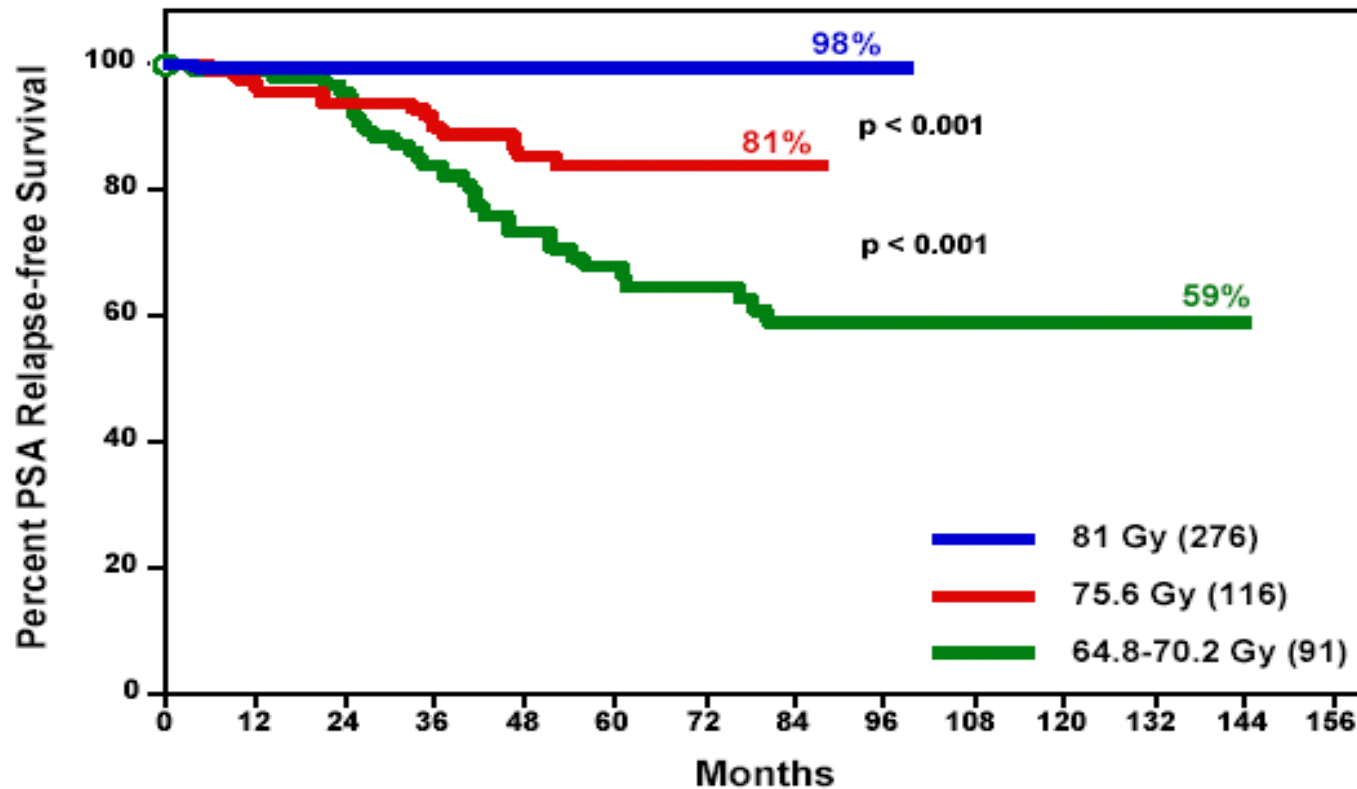
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Image Guided Radiation Therapy

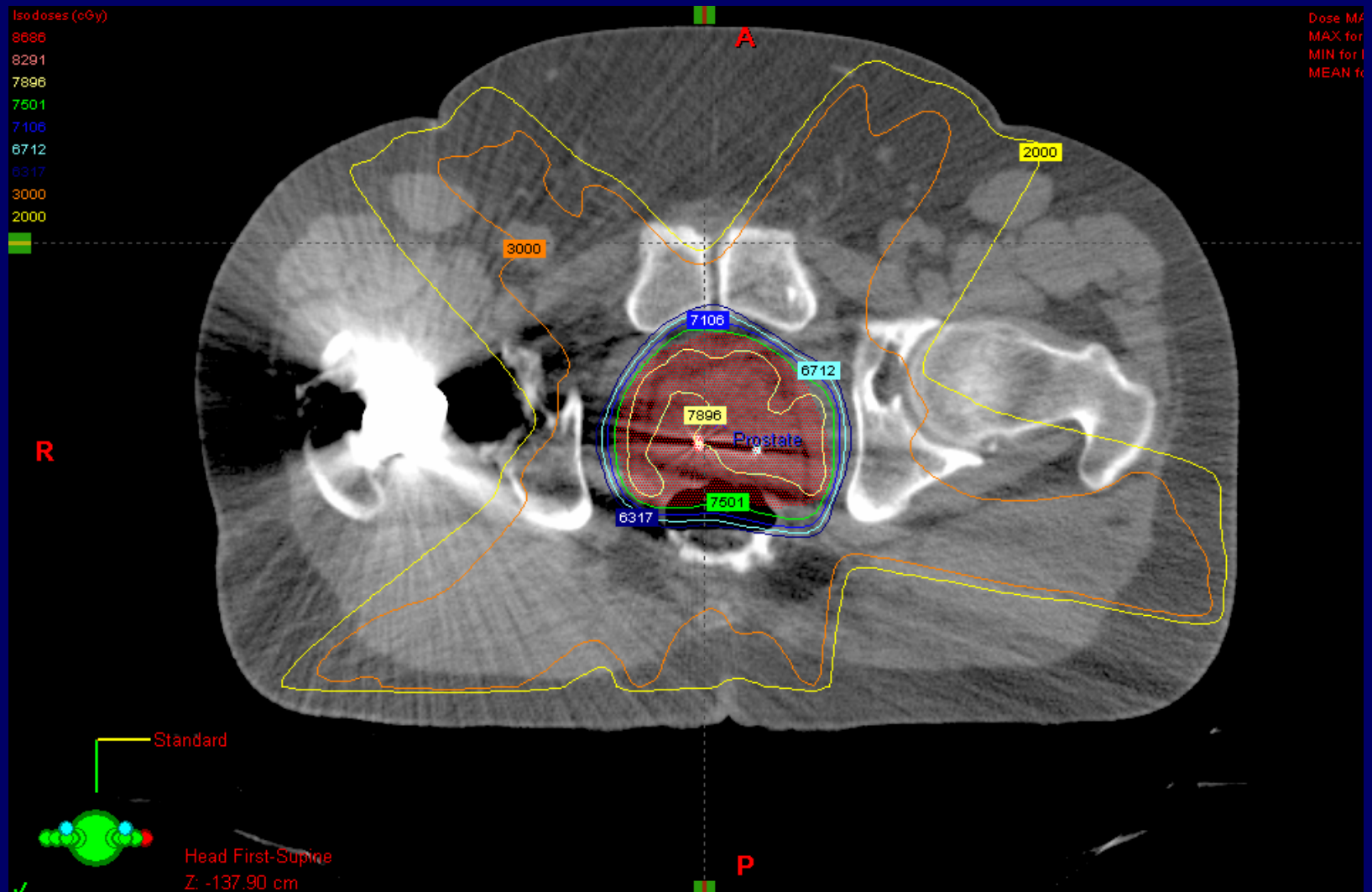
- External Radiotherapy
 - Intensity Modulated Radiation Therapy (IMRT)
 - Proton Radiotherapy/Heavy Ions
- Imaging Methods during Radiotherapy
 - Electronic Portal Imaging
 - kV Imaging
 - KV and MVCT
 - Ultrasound

PSA Relapse-free Survival According to Dose for Favorable Risk Prostate Cancer Patients

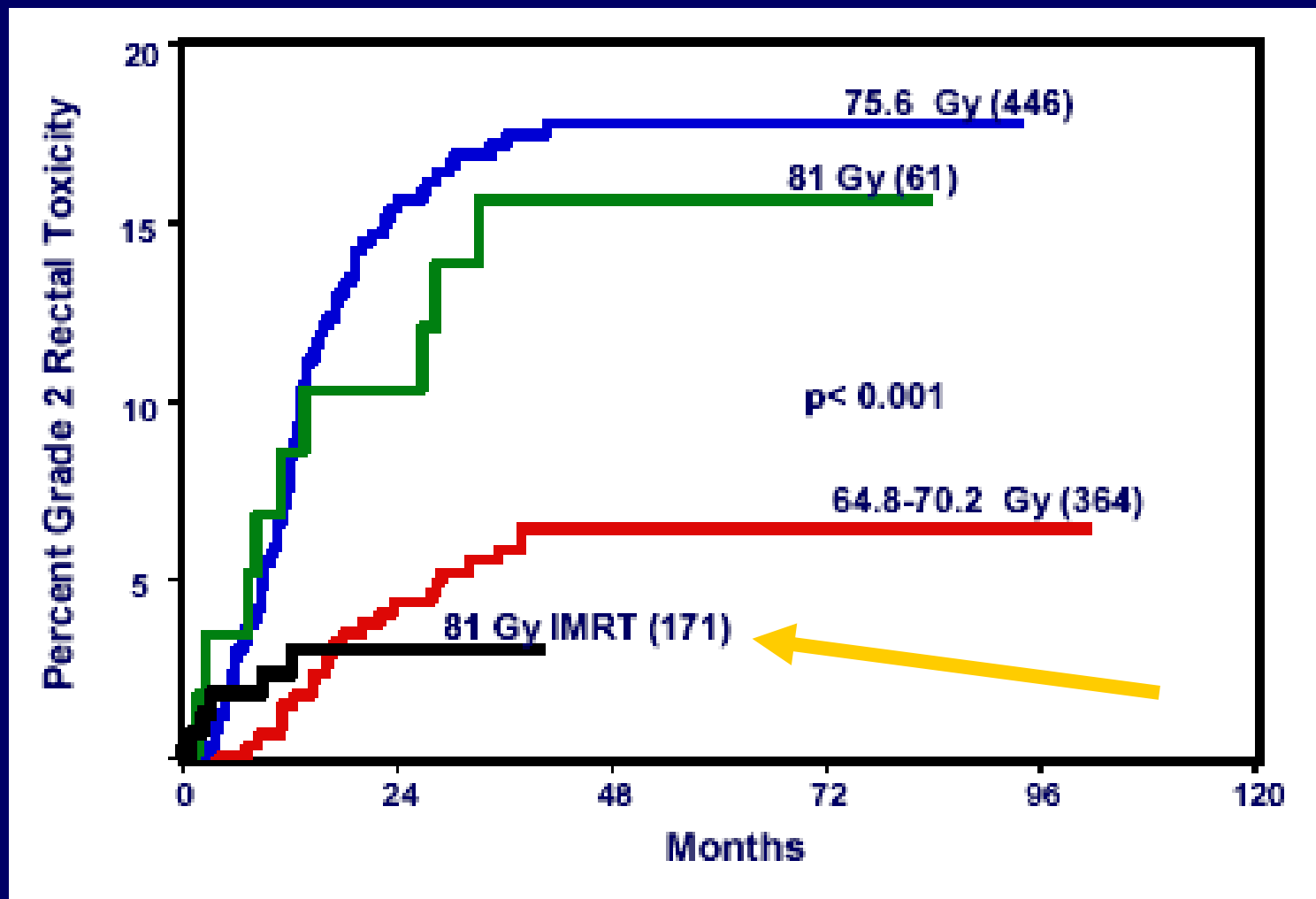


Favorable risk: T1-2, Gleason score \leq 6, PSA \leq 10

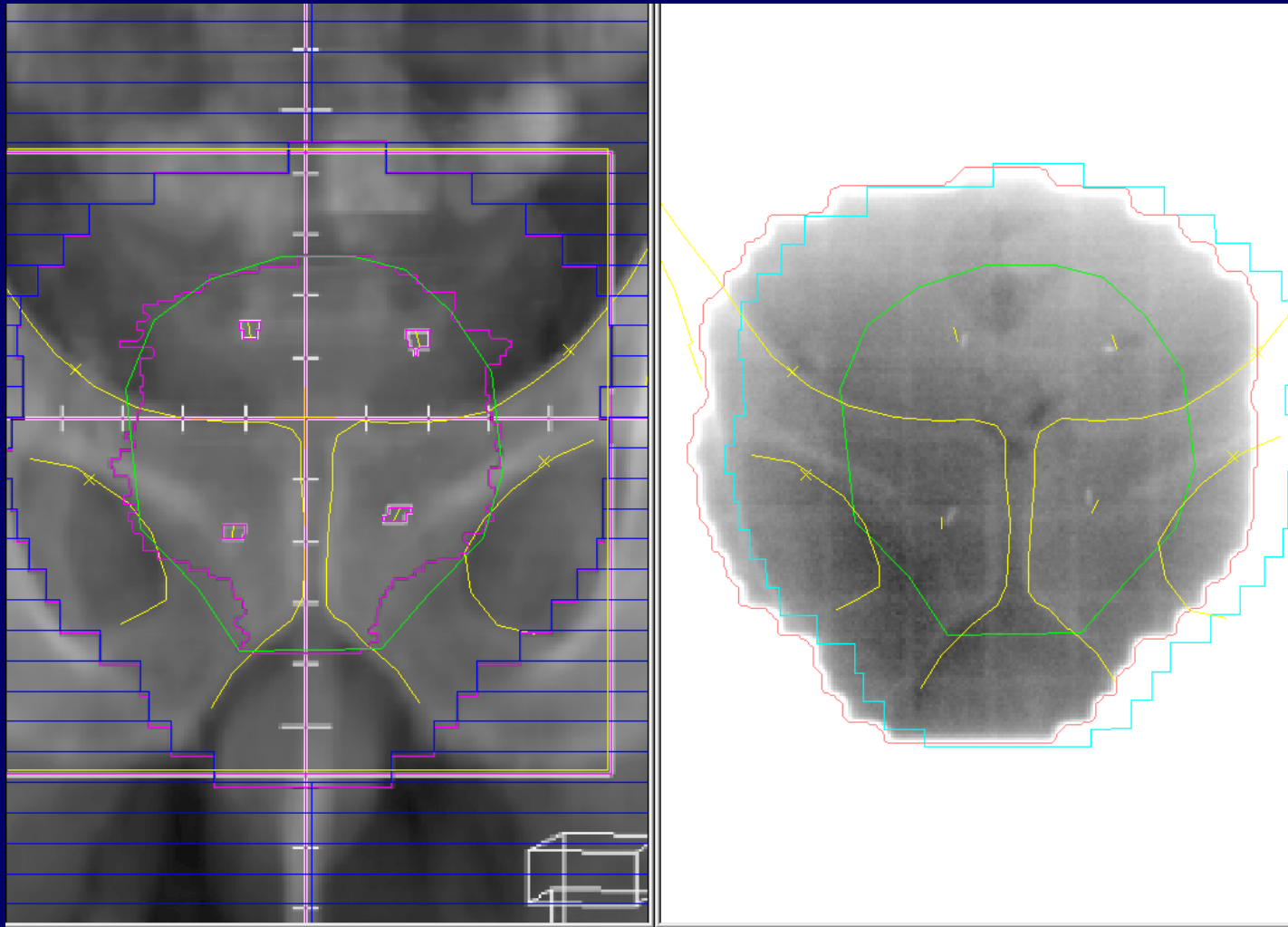
High-dose Intensity Modulated Radiation Therapy with Daily EPID Localization



Decreased Side Effects at Higher Radiation Dose with IMRT



Prostate Localization: Hitting a Moving Target



On Board Imaging (OBI) with kV X-rays: 'Cone Beam CT'



kV digital imaging mounted
at 90 degrees to the beam.

*kV CT scan on the table
Dose: 1.4 cGy



*Groh BA. et al., Med Phys 29(6): 967: 2002
Images: Varian Corp. and Henry Ford Hosp.

Improved Aiming for IMRT: Implantable Wireless Transponder for Prostate Tracking

Wireless Transponders

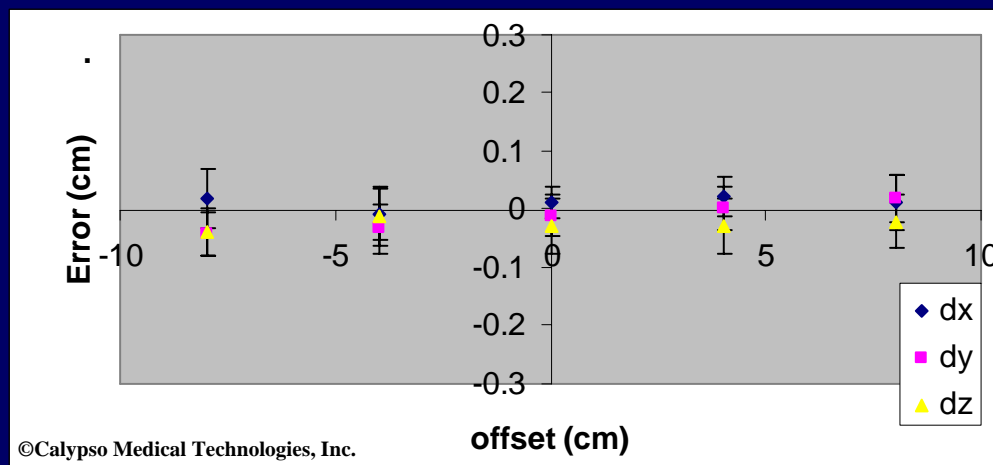
Calypso® 4D Localization System and
Beacon® Transponder

- Wireless 15 G, permanent implant
- Contains a AC magnetic resonant circuit
- Three, uniquely identifiable, time multiplexed, transponders define treatment isocenter
- No external lead wires or internal power supply
- Hermetically sealed, glass-encapsulated circuitry for permanent implantation
- Remains inactive until energized by system

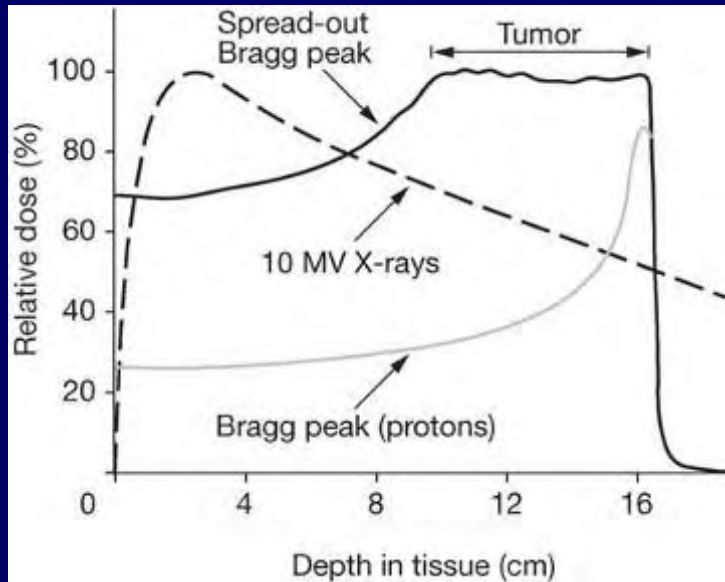


FDA limits use of this device to prostate treatments only.
©Calypso Medical Technologies Inc.

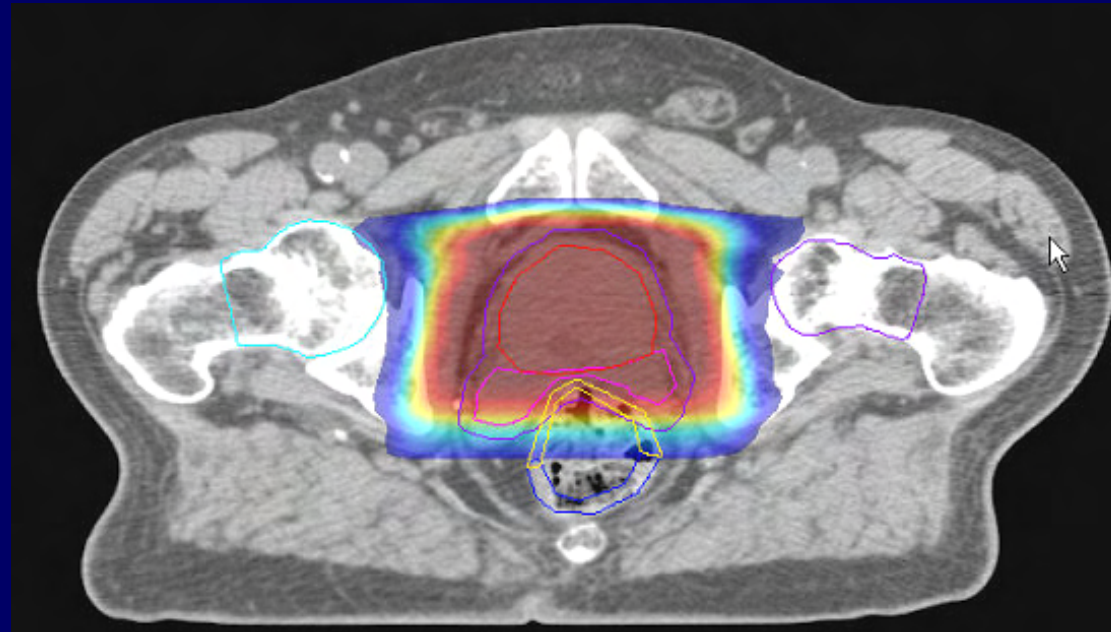
Accuracy at 27.4 cm from array



Why Protons?



...Bragg Peak leads to less exit dose



Cost: \$50 – 200 Million

US: 3 Centers open

more on the way

Worldwide: 22+

Protons: Phase III Trial CaP

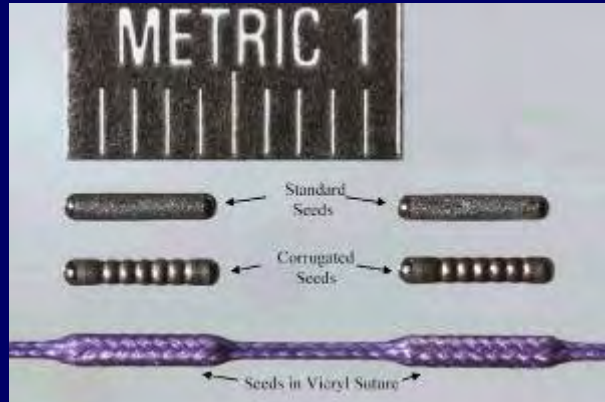
- MGH/Loma Linda – 393 pts (1996-99)
- 70.2 Gy vs 79.2 Gy = photons (50.4 Gy) + protons (19.8 vs 28.8 Gy)
- T1a – T2b with PSA < 15 and No mets
- No androgen deprivation allowed
- Low risk (58%), Intermediate (33.5%), and High risk (8.5%)
- Median follow-up 5.5 years
- **RESULTS**: 80.4% bNED vs 61.4%

Permanent Seed Implants

- **Advantages**
 - High intraprostatic dose
 - Convenient outpatient treatment as monotherapy
 - Excellent long-term results (10+ years)
 - Long-term morbidity low in appropriately selected patients
- **Disadvantages**
 - Difficult technique to master
 - Fewer patients eligible compared to EBRT
 - Acute urinary side effects greater than EBRT

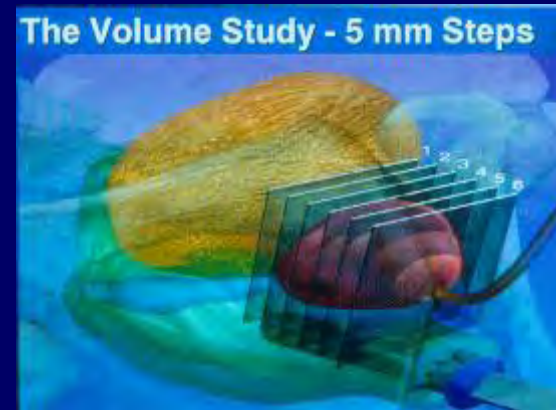
Permanent Seed Implants I-125/Pd-103 Brachytherapy

1. I-125/Pd-103 seeds



Adapted from Davis BJ, et al. Int J Radiat Oncol Biol Phys. 2003 Nov 15;57(4):1174-82.

2. Acquisition of prostate volume by TRUS for planning

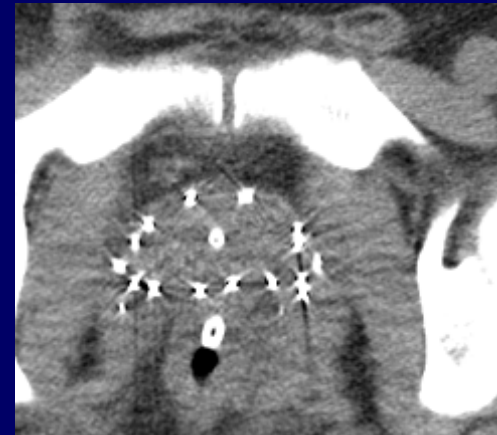


3. Outpatient implant procedure; TRUS guidance



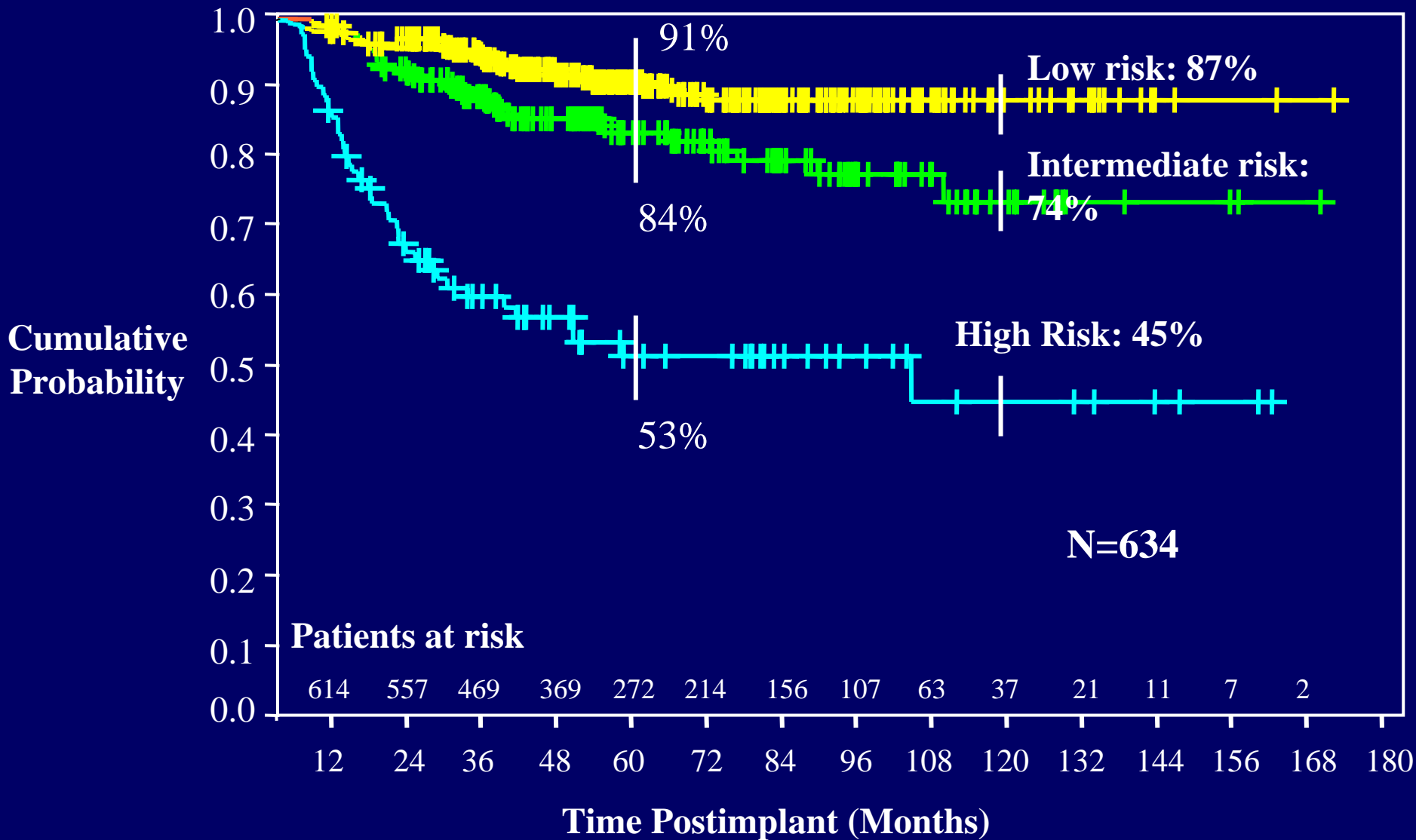
TRUS=transrectal ultrasound

4. Postimplant assessment of implant quality by CT



I-125/Pd-103 Implant \pm EBRT

bNED by MSKCC Risk Grouping



RTOG 98-05: Prospective HRQOL on Prostate Brachytherapy Patients

- **98 patients treated with I-125 monotherapy from 24 institutions**
- **Patients with T2a, PSA <10 ng/mL, Gleason ≤6**
 - **Prospectively evaluated at 3, 6, 9, and 12 months with patient-administered forms**
 - **FACT-P, Sexual Assessment Questionnaire (SAQ)**
 - **International Prostate Symptom Score (IPSS)**

RTOG 98-05: Prospective HRQOL on Prostate Brachytherapy Patients

- **Results**
 - **Urinary incontinence (any use of pads)**
 - **14% at 6 months**
 - **<1% at 12 months**
 - **ED: 73% potent before PB**
 - **57% at 1 year**
 - **65% unassisted before PB and 36% unassisted at 1 year**

Erectile Function 6 Years After Brachytherapy

Pre-Rx Status	#	Post-Rx Unchanged Potent	Sildenafil Response	Overall Potency (IIEF ≥ 11)
Normal	125	50%*	95%	92%
Suboptimal	56	13%	70%	30%

*57% for men <60 years

HDR + IMRT vs. HDR MONOTHERAPY FOR EARLY STAGE PROSTATE CANCER :

Mark et al., ABS 2007

6 YR PSA DFS

<u>Treatment</u>	<u>#PTS</u>	<u>PSA DFS</u>
HDR +/- IMRT	302	88.4% (267/302)
HDR + IMRT	109	88.1% (96/109)*
HDR	193	88.6% (171/193)*

*p = 0.6

Take-home Points

- **All modern radiotherapy approaches demonstrate better outcomes and less morbidity than in the past.**
 - **Dose escalation with image guidance and IMRT**
- **Technologies driving further improvements**
 - **Cone beam CT scanning/prostate tracking and positioning/proton radiotherapy**
- **Data supporting the use of adjuvant and salvage radiotherapy has increased.**
 - **EORTC, SWOG and ARO trials**

Thank You!