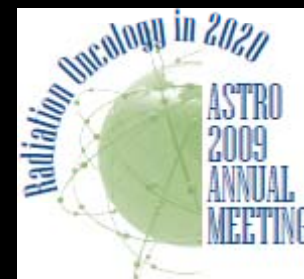


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# Comparative Effectiveness

## Prostate Cancer Results Study Group 2009



**Peter Grimm A-078**

Low and Intermediate Risk Prostate Cancer -  
Comparative Effectiveness of Brachytherapy,  
Cryotherapy, External Beam Radio Therapy,  
HIFU, Proton Therapy, Radical Prostatectomy

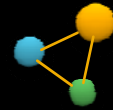
Peter Grimm, DO, John Sylvester, MD  
Seattle Prostate Cancer Center

# Prostate Cancer Results Study Group



- **Problem:** In the absence of randomized studies, patients, physicians, carriers, Medicare, etc: need a means to compare the **effectiveness of modern treatments**
- **Purpose:** The PCRSRG will compare and share results for prostate cancer that are utilizable for all those who are interested

# Expert Panel



- Ignace Billiet, MD Europe
- David Bostwick, MD Bostwick Laboratories
- David Crawford, MD Univ Colorado
- Peter Grimm, DO Seattle Prostate Cancer Center
- Jos Immerzeel, Netherlands
- Mira Keyes, MD BC Cancer Agency
- Kupelian, Patrick, MD MD Anderson Orlando
- Robert Lee Duke University Medical Center
- Stefan Machtens, MD Europe
- Brian Moran, MD Chicago Prostate Institute
- Greg Merrick, MD Schiffler Cancer Center
- Jeremy Millar, MD Australia

# Expert Panel



- Mack Roach, MD UCSF
- Richard Stock, MD Mt. Sinai New York
- Katsuto Shinohara, MD UCSF
- John Sylvester, MD Seattle Prostate Cancer Center
- Mark Scholz, MD Prostate Cancer Research Institute
- Ed Weber, MD Seattle Prostate Cancer Center
- Anthony Zietman, MD Harvard Joint Center
- Michael Zelefsky, MD Memorial Sloan Kettering
- Fellows Jason Wong, MD
- Residents: Jyoti Mayadev, MD U of Washington,  
Stacy Wentworth, MD Wake Forest,
- Robyn Vera, DO Medical College of Virginia

# Study



- **>15,000 articles** reviewed from 2000-2009
- Pub Med, Medline, Google Scholar, Elsevier
- **603 Treatment Results Articles Identified**
- Expert Panel Established **Criteria** for Inclusion
- Treatment **Articles screened** for study group criteria

# Criteria for Inclusion



1. Patients must be stratified into recognizable Pre-Treatment Risk groups: **Low, Intermediate, and High Risk** by either D'Amico, Zelefsky or NCCN stratification
2. **bRFS** standard endpoint ASTRO, Phoenix, and PSA < 0.2 (surgery)
3. **Clinical Staging No exclusions:** i.e. No Pathologic staging
4. **EBRT** must be minimum **72 Gy** IMRT / conformal

# Criteria for Inclusion



5. **All Treatment modalities** considered: Seeds, Surgery, IMRT, HIFU, CRYO Protons, HDR
6. Accepted results: Peer Reviewed Journals Only
7. Low Risk Accepted minimum number **100 pts**
8. Int Risk Accepted minimum number **100 pts**
9. High Risk Accepted minimum number **50 pts**
10. Minimum median **F/U** : 5 yr

# % Articles Meeting Criteria



RP	EBRT	Cryo	Brachy	Robot RP	Proton	HIFU
<b>15/206</b>	<b>7/165</b>	<b>2/26</b>	<b>20/157</b>	<b>0/53</b>	<b>1/9</b>	<b>0/27</b>
<b>7%</b>	<b>4%</b>	<b>8%</b>	<b>13%</b>	<b>0%</b>	<b>11%</b>	<b>0%</b>

Total 603 Treatment Articles. Some articles addressed several treatments

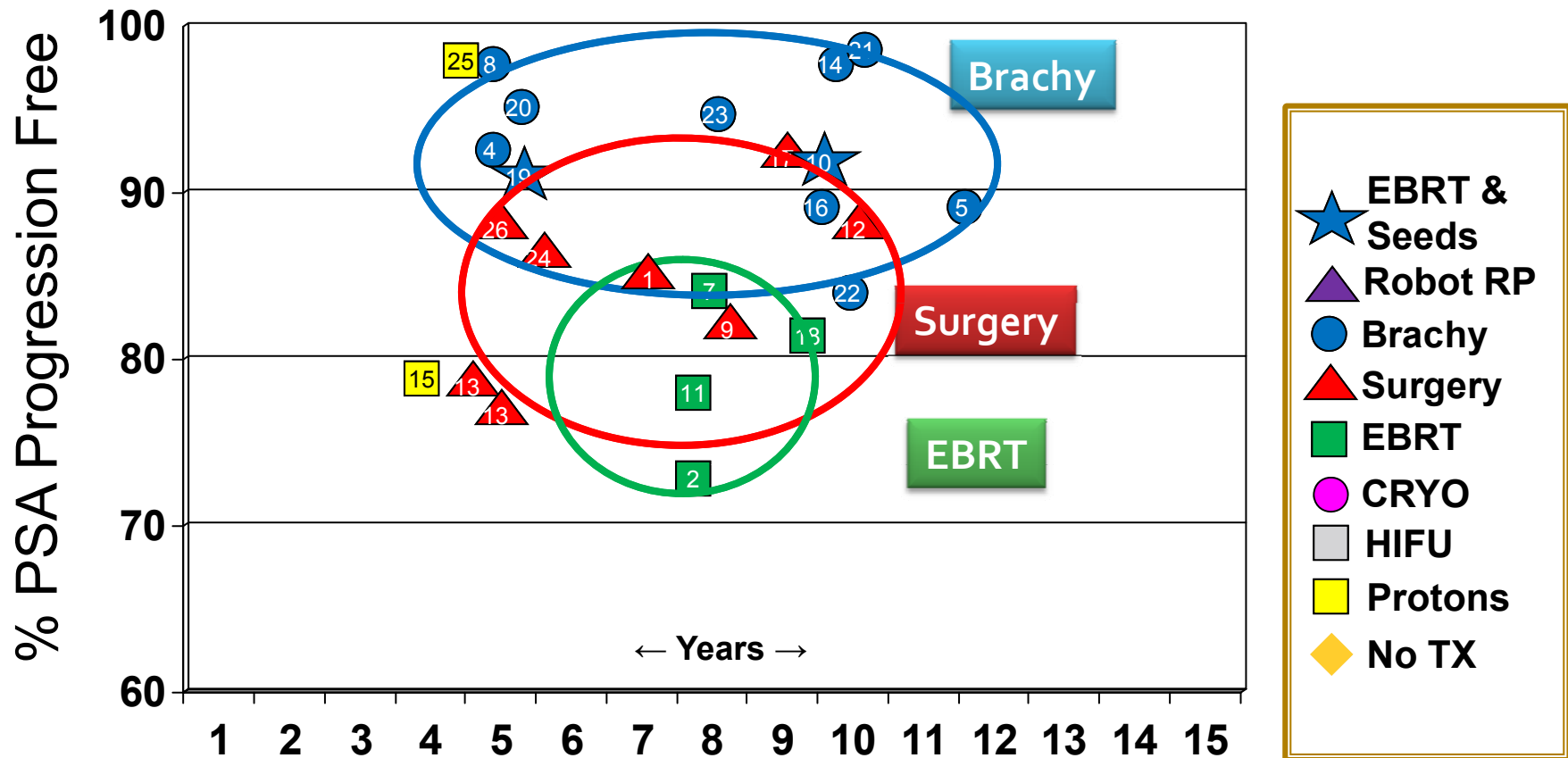


# Reason for Article rejection

	Strat	BR FS	Exc	<72Gy	<100pt	<5yr f/u	other
RP	68%	4	9	-	3	13	3
EBRT	31%	3	3	31	12	23	4
Brachy	29%	2	7	-	15	40	5
Cryo	10%	0	0	-	32	57	14
RobRP	64%	2	2	-	8	20	6
Proton	45%	0	0	-	18	36	0



# Low Risk PCSG Criteria



- Prostate Cancer Results Study Group 3/31/09
- Numbers within symbols refer to references

# Question

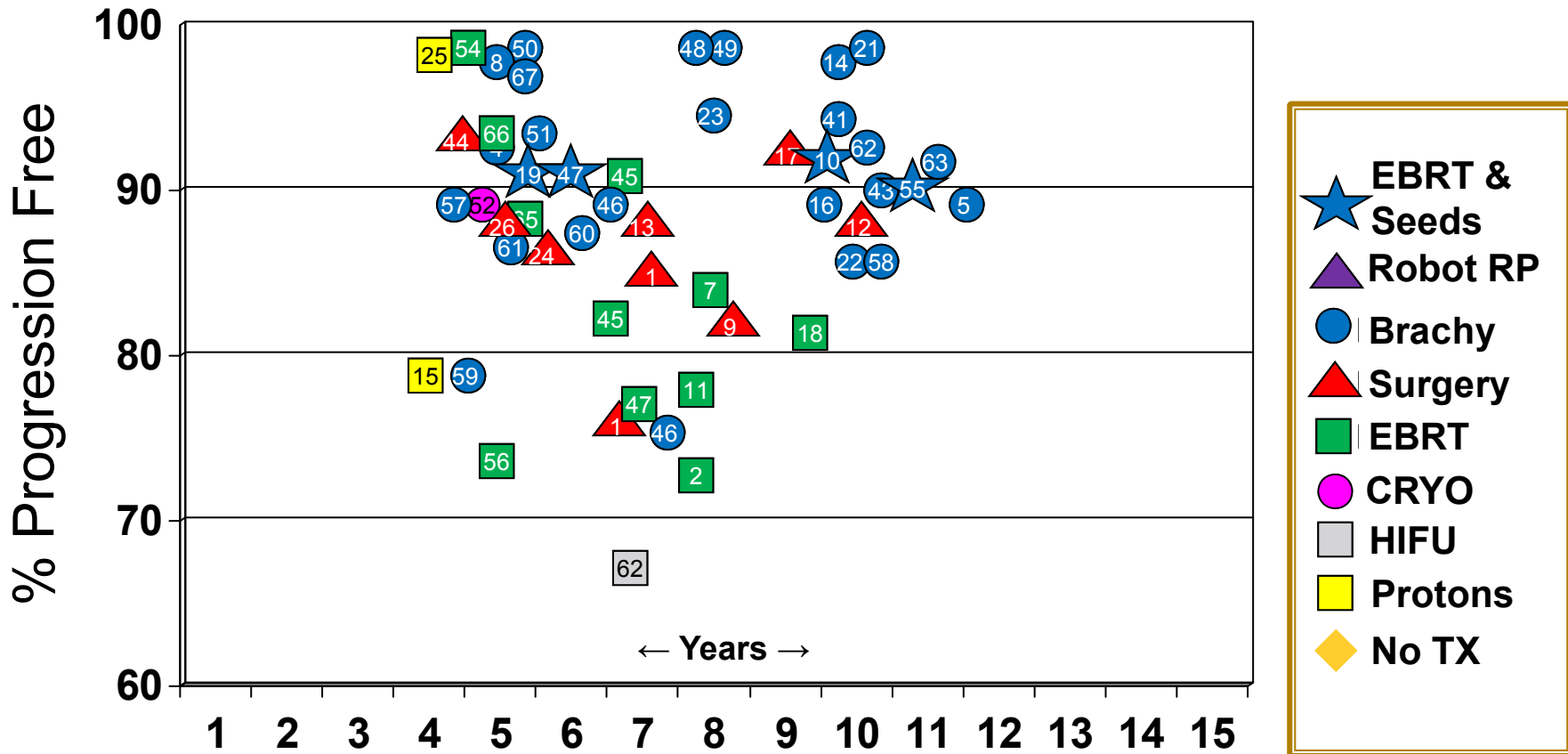


**Would changing the median f/u to 40 months, or relax # pts change the overall outcome ?**

# Low Risk



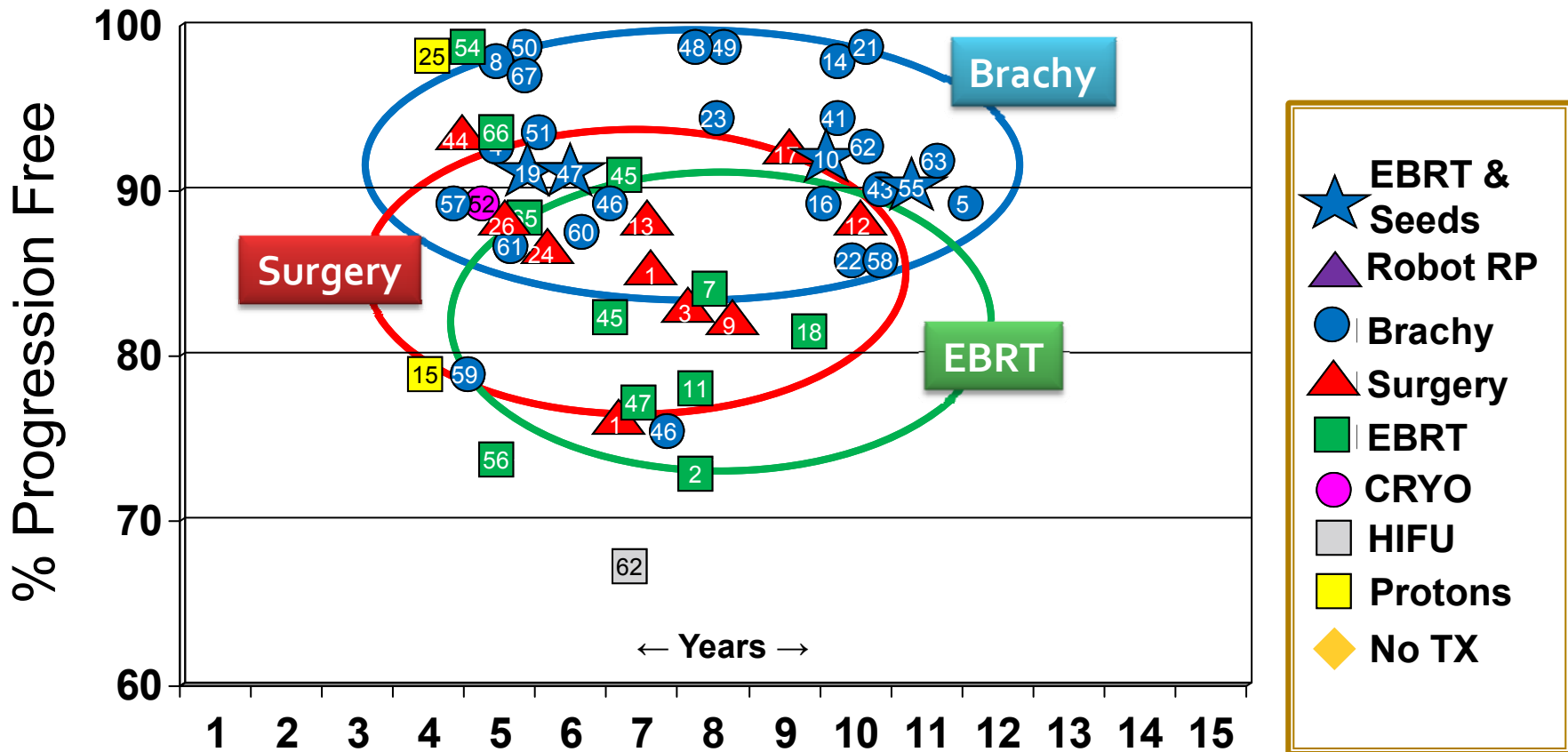
> 40 mo Med F/U or < 100 pts



- Prostate Cancer Results Study Group 3/31/09
- Numbers within symbols refer to references

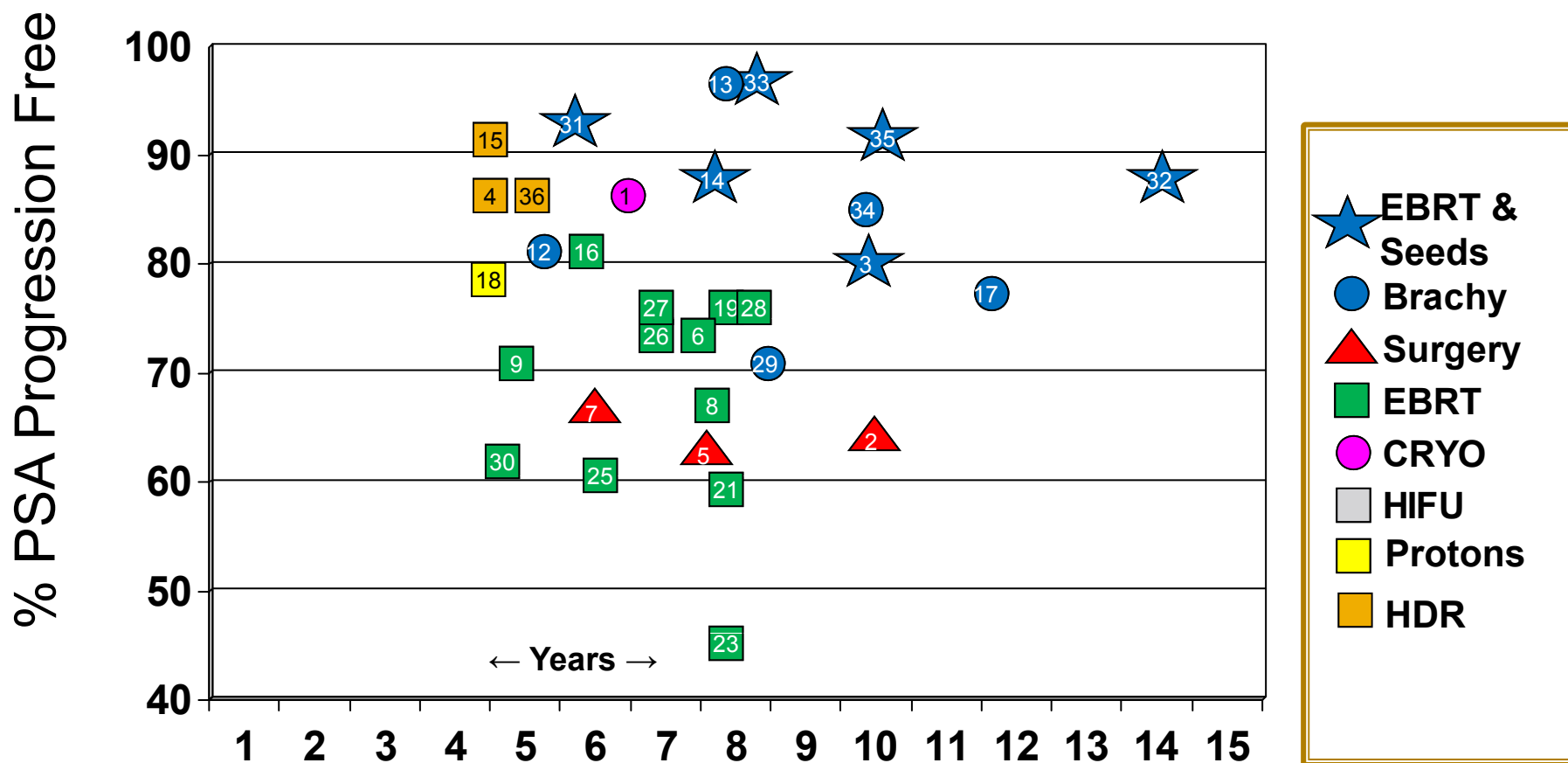
# Low Risk

> 40 mo Med F/U or < 100 pts



- Prostate Cancer Results Study Group 3/31/09
- Numbers within symbols refer to references

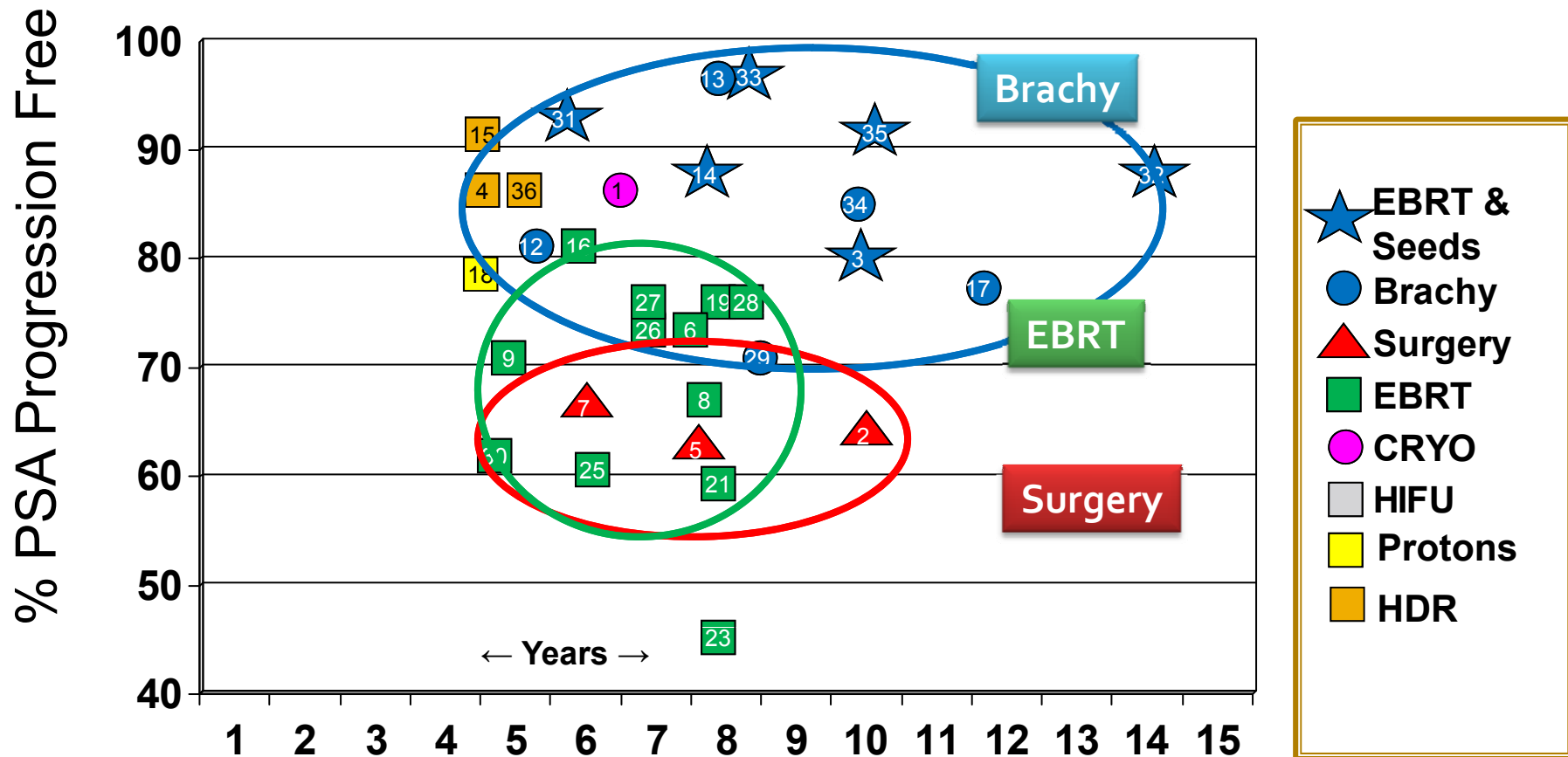
# Intermediate Risk PCRSWG Criteria



- Prostate Cancer Results Study Group 3/31/09
- Numbers within symbols refer to references



# Intermediate Risk PCRSWG Criteria



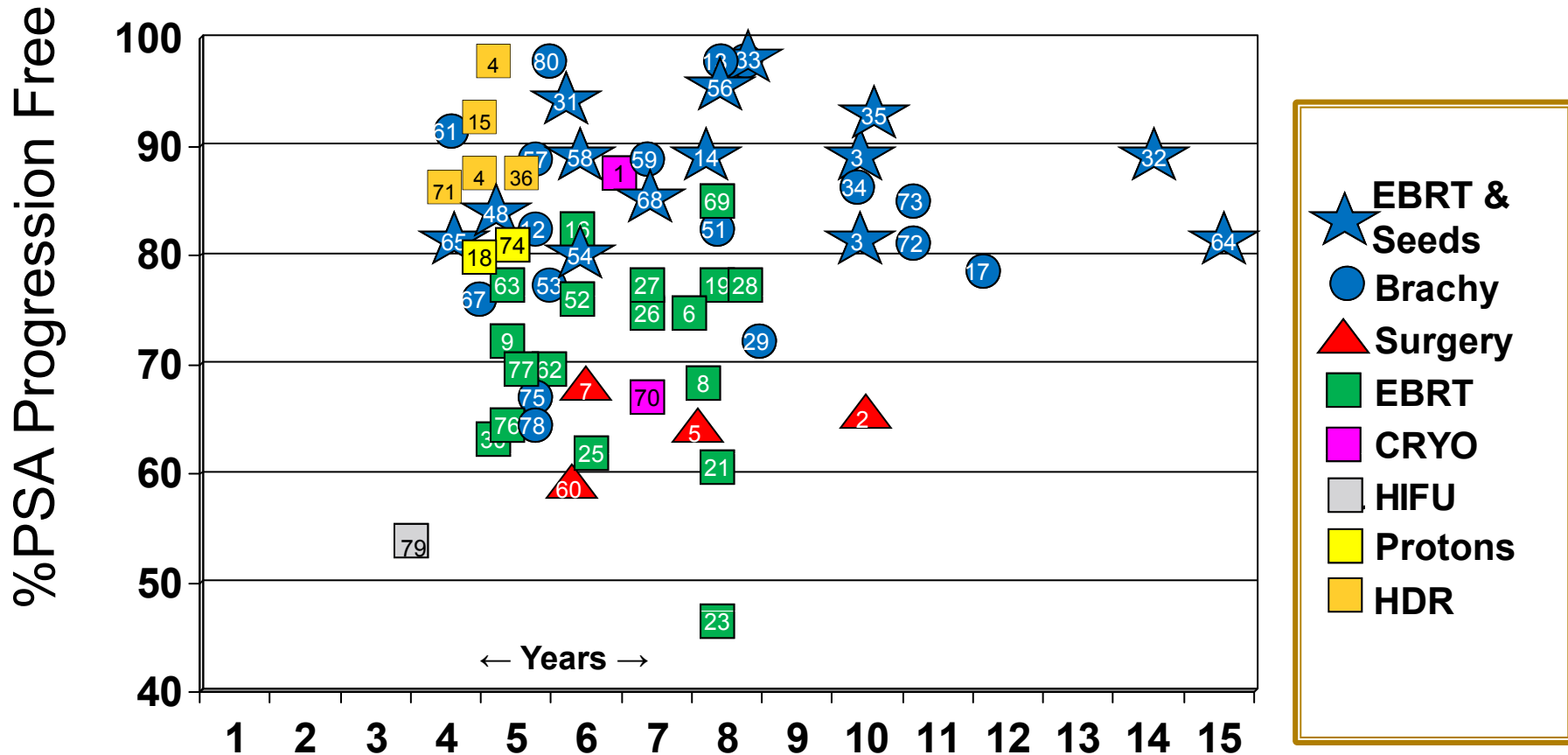
- Prostate Cancer Results Study Group 3/31/09
- Numbers within symbols refer to references



# Intermediate Comparison

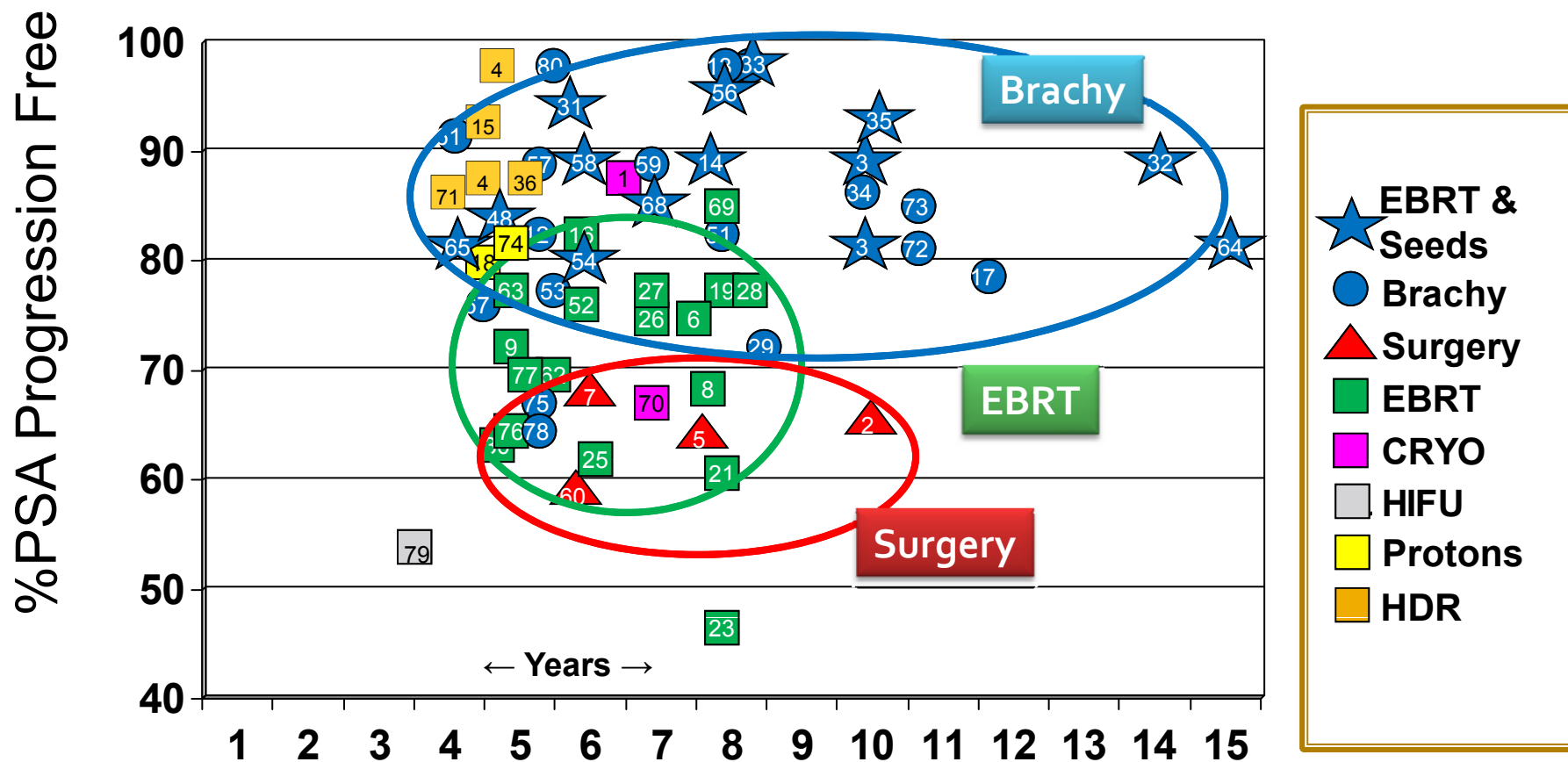


## >40 mo Med F/U or < 100 pts



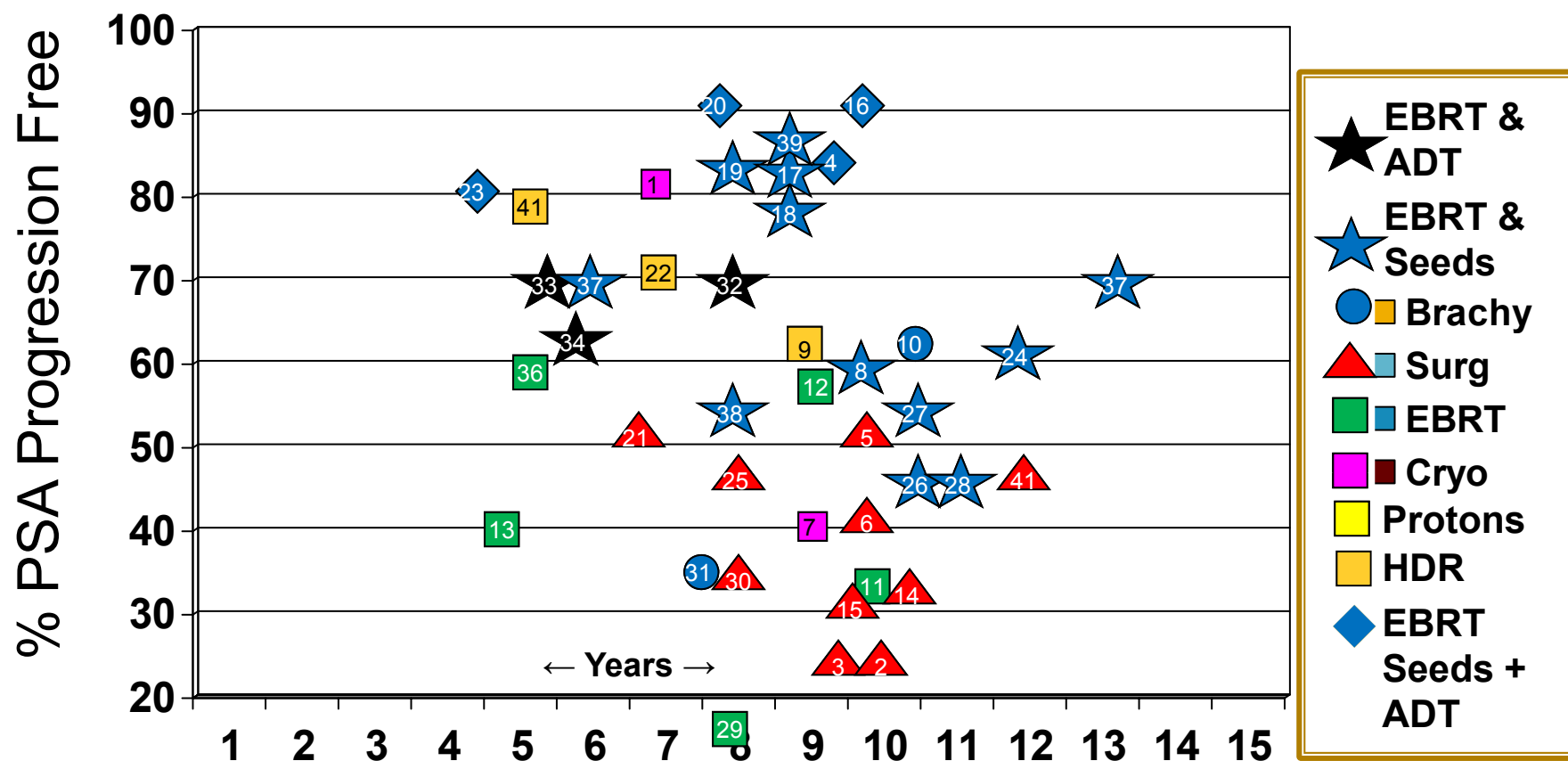
# Intermediate Comparison

>40 mo Med F/U or < 100 pts



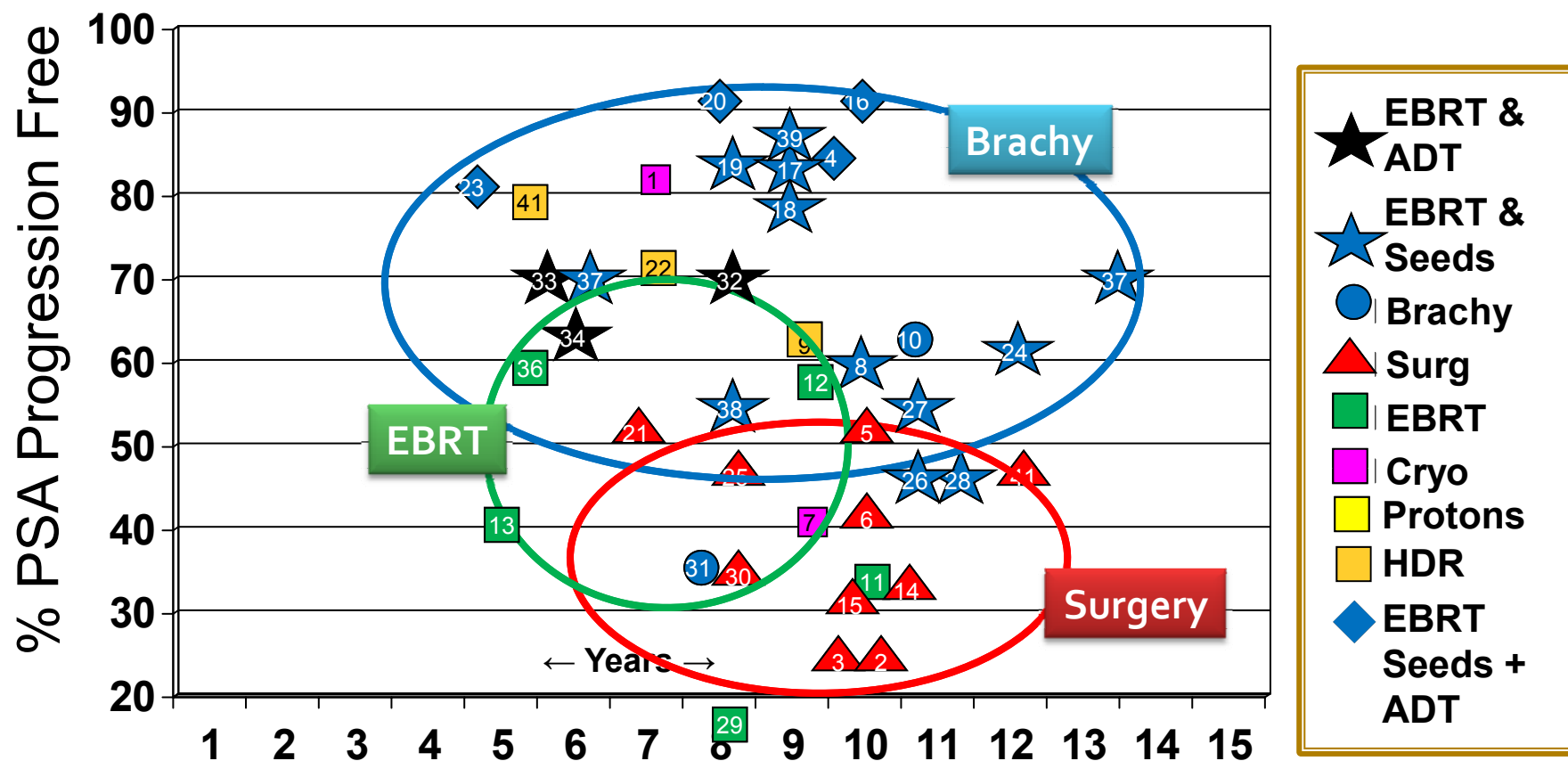
- Prostate Cancer Results Study Group 3/31/09
- Numbers within symbols refer to references

# High Risk PCRSWG Criteria



- Prostate Cancer Results Study Group 3/31/09
- Numbers within symbols refer to references

# High Risk PCRSNG Criteria

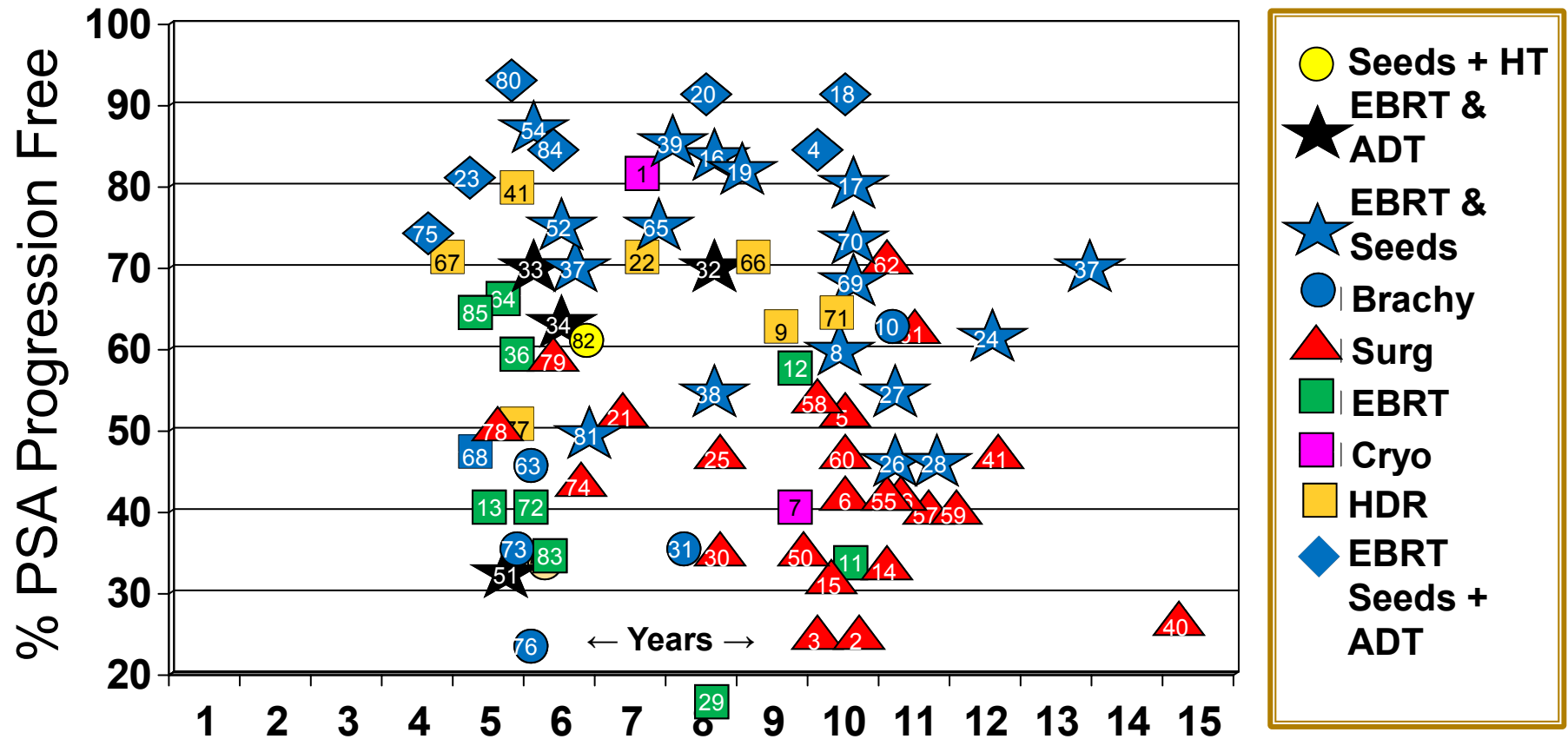


- Prostate Cancer Results Study Group 3/31/09
- Numbers within symbols refer to references

# High Risk



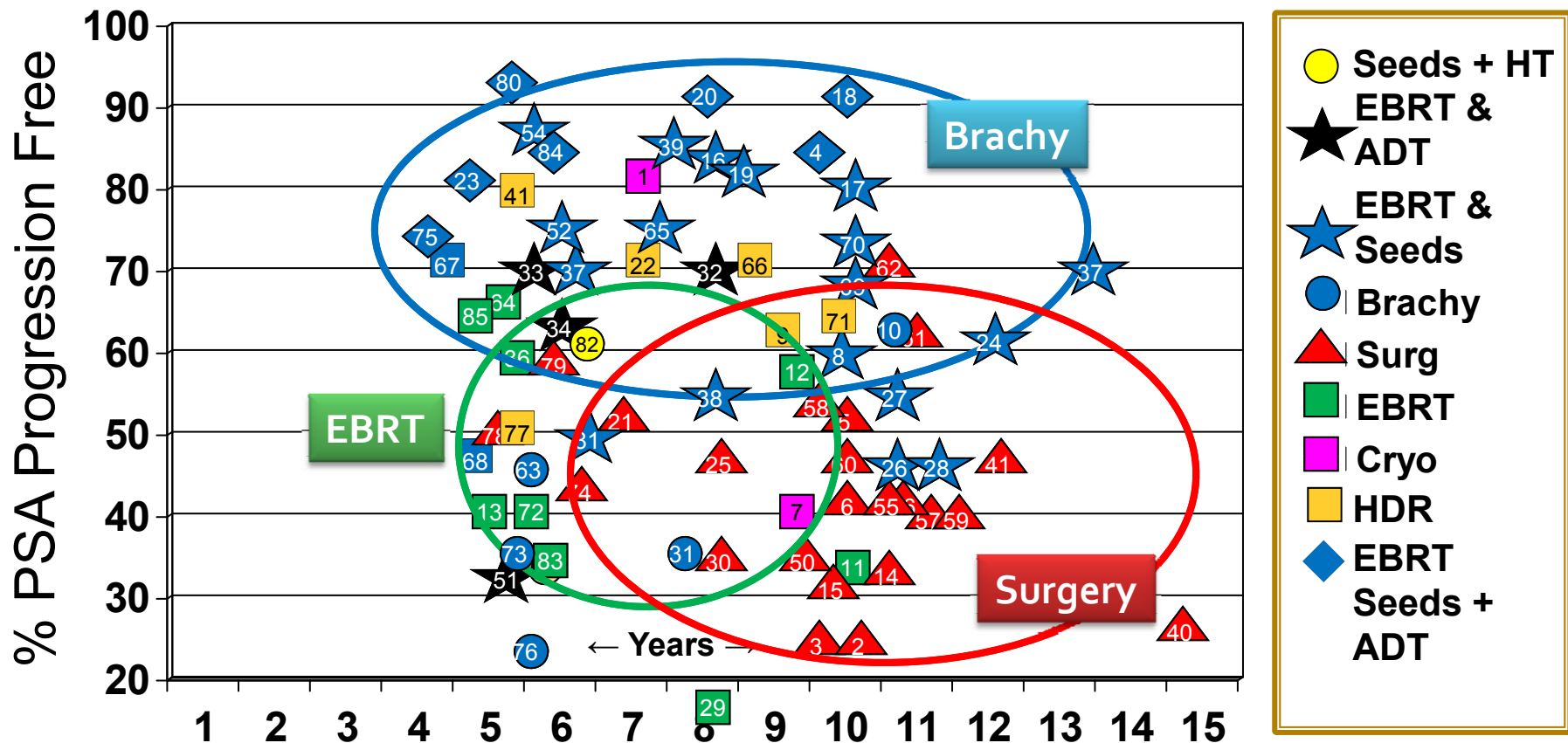
> 40 mo Med F/U or < 50 pts



- Prostate Cancer Results Study Group 3/31/09
- Numbers within symbols refer to references

# High Risk

> 40 mo Med F/U or < 50 pts



- Prostate Cancer Results Study Group 3/31/09
- Numbers within symbols refer to references

# Conclusions



- No Randomized studies to date
- **By BRFS control criteria Brachytherapy alone or Comb appears superior in all risk groups**
- Prostate studies to date rarely include Pre-treatment Risk Group stratification, confounding comparisons
- **Only a small % of studies to date conform to basic reporting criteria**

**David White**

Interstitial High Dose Rate (HDR) Brachytherapy + IMRT Versus  
HDR Monotherapy for Early-stage Prostate Cancer : Median 8 Year  
Follow-up in 387 Cases



# Interstitial High Dose Rate (HDR) Brachytherapy + IMRT Vs. HDR Monotherapy For Early Stage Prostate Cancer

**David White, CMD, Rufus J. Mark, MD, Paul J. Anderson, MD,  
Robin S. Akins, MD, Murali Nair, PhD**

**Joe Arrington Cancer Center and Texas Tech University, Lubbock Texas, USA**



# Introduction:

- The role of supplemental External Beam Radiation Therapy (EBRT) in brachytherapy is controversial.
- We compare our results of High Dose Rate HDR (HDR) + Intensity Modulated Radiation Therapy (IMRT)

vs.

HDR monotherapy.

# Materials & Methods

- 1997 - 2009, **387 patients** with T1 and T2.
- There were no Gleason Score or PSA exclusions.
  - **109 patients** elected **HDR + IMRT**
  - **278 patients** underwent **HDR monotherapy**.
- No patient received Hormonal Blockade.
- Median **Gleason Score was 7** (range : 4 to 10).
- Median **PSA was 9.8** (0.60 to 39.8).
- **Implant volumes** ranged from 36 cm<sup>3</sup> to 196 cm<sup>3</sup>.

## IMRT + HDR

45 Gy in 25 fractions (**IMRT**) and 16,5 Gy to 20 Gy in 3 fractions (**HDR**).

## HDR alone

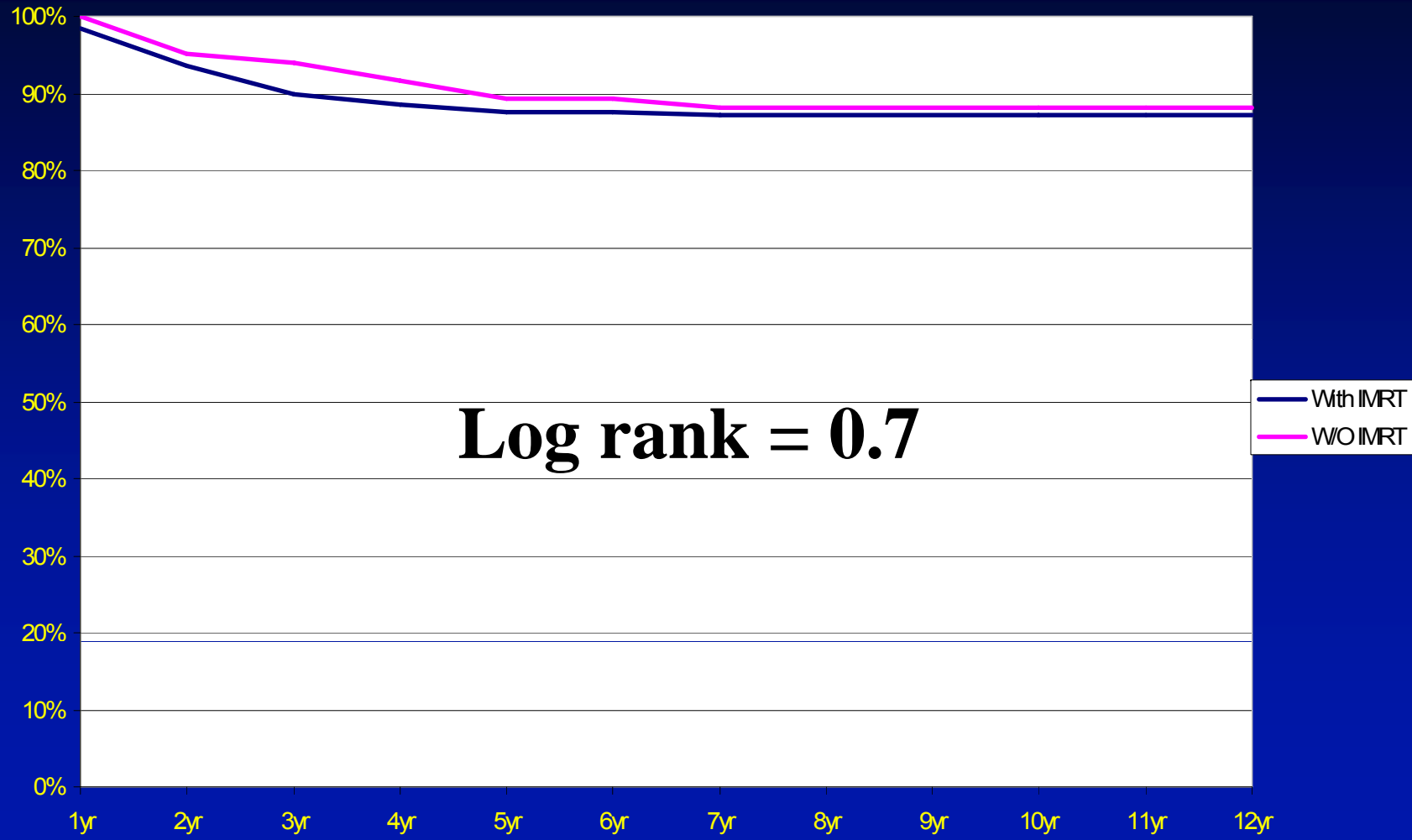
- Two HDR implants spaced 4 weeks apart,
- Each implant – 22,5 Gy in 3 fractions over 24 hours,
- Final dose to **45 Gy** in 6 fractions.

# Results:

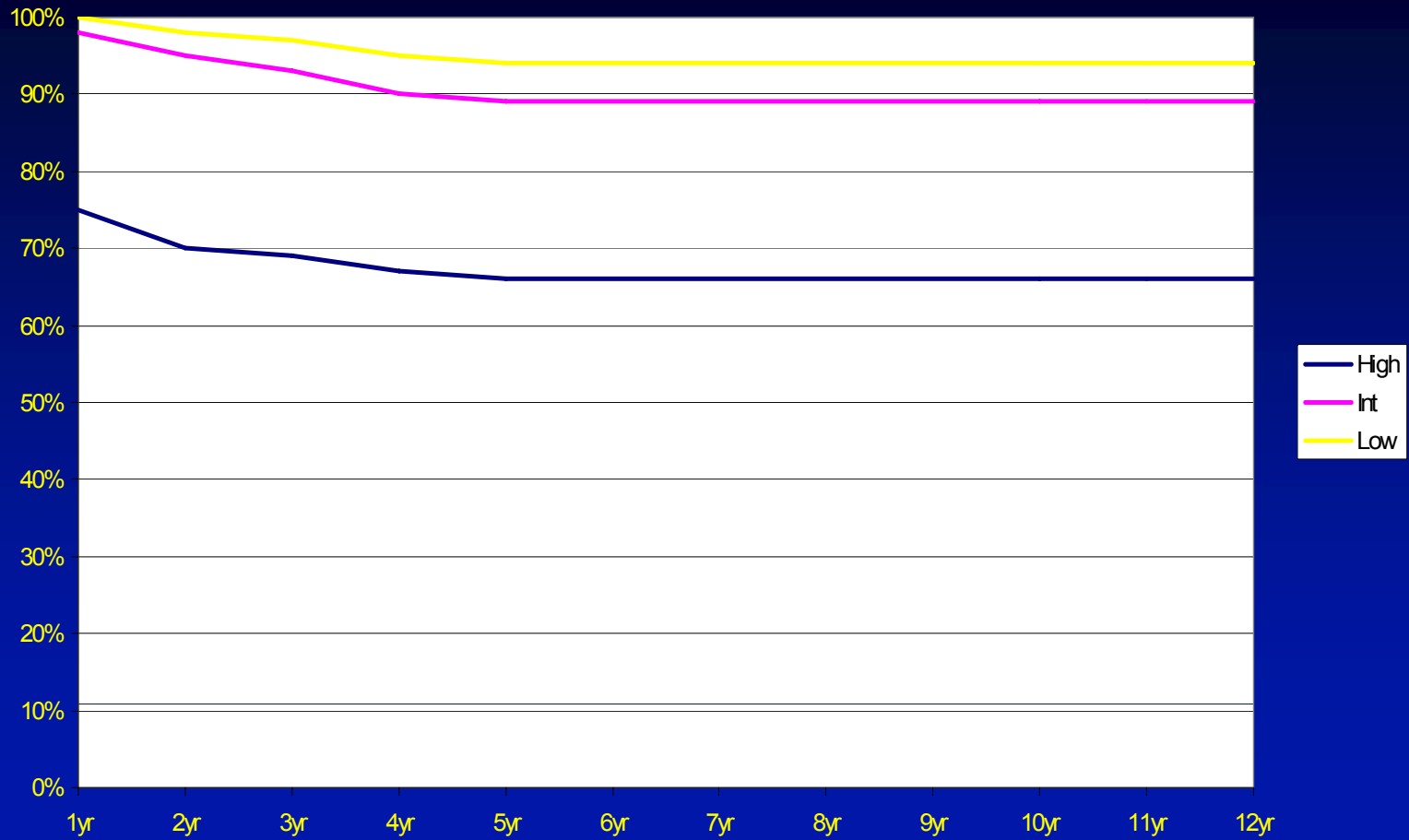
- There was **no significant difference between the treatment groups** with respect to T-Stage, Gleason Score, and PSA.
- With a median **follow-up of 96 months** (range : 6 months to 157 months), the overall **PSA disease free survival was 88.1%** (341/387).
- In patients undergoing **IMRT + HDR Implant**, PSA disease free survival was 87.1% (95/109) vs. 88.5% (246/278) for patients undergoing **HDR alone** (p=0.73).
- The **8 year actuarial survival** was 82% for the group receiving **IMRT + HDR** vs. 84% with **HDR monotherapy** (log rank = 0.7).
- **Urethral stricture** requiring dilatation has developed in 4.7% (18/387) of patients.

- **Urinary stress incontinence** has occurred in 3.1% (12/387).
- **RTOG late bladder toxicities** were : 0% Grade 4, 0% Grade 3, and 3.1% (12/387) Grade 2.
- **RTOG late rectal toxicities** were : 0.3% (1/387) Grade 4, 0% Grade 3, 2.8% (11/387) Grade 2, and 3.4% (13/387) Grade 1.
- **RTOG late rectal toxicity was higher in patients undergoing HDR + IMRT** with 15.6% (17/109) of patients experiencing Grade 2 and 1 symptoms, vs. 2.5% (7/278) receiving **HDR alone** (p=0.0001).

# PSA DFS : HDR + IMRT vs. HDR



# PSA DFS BY RISK GROUP



# Conclusions:

- With median 8 year follow-up, we have observed no significant difference in PSA disease free survival in patients undergoing HDR monotherapy vs. HDR + IMRT.
- Complications were similar, though RTOG Grade 1 and 2 late toxicity was higher in patients receiving HDR + IMRT.
- HDR monotherapy compares favorably to EBRT, LDR +/- EBRT, and HDR + IMRT, both with regard to PSA disease free survival, and complications.





# Dosimetric Comparison of HDR Monotherapy with IMRT for Treatment of Early Stage Prostate Cancer

Murali T. Nair<sup>1,2</sup> Ph.D, Rufus Mark<sup>1</sup> M.D, Paul J. Anderson<sup>1</sup> M.D,  
Thomas Neumann<sup>1</sup> M.D, Yunsil Ho<sup>1</sup> Ph.D, Marty White<sup>1</sup> CMD,  
Michel Banwo<sup>1</sup> CMD and Sndya Nair<sup>2</sup> B.S.

<sup>1</sup>Joe Arrington Cancer Center ,4101 22nd Place & <sup>2</sup>Texas Tech University , Lubbock,  
TX:79410.

# Purpose/Objective:

The purpose of this work is to compare dosimetry plans from **HDR brachytherapy** with **IMRT** for prostate cancer using Dose Volume Histogram

# Materials/Methods:

- **HDR monotherapy** has been used at our institution for treatment of stage **I and B prostate cancers**, **PSA  $\leq$  20** for the last 7 years.
- Dosimetry plans of **400 patients** have been compared.
- The implant procedure consists of using a commercial template with **stainless steel needles** under ultrasound guidance.
- The treatment plan was generated using axial **CT images** taken at 5mm thickness .
- **Graphical optimization** technique was used for uniform coverage and control of dose to urethra and rectum .
- The **dose fractionation** used for HDR and IMRT are presented in Table 1.

## Table 1:

Radiation therapy Fractionation Used for HDR monotherapy and IMRT

### 1. HDR Monotherapy

PTV dose:

- Prostate + SV **21Gy in 3 fx**+ 30d rest + **21Gy in 3 fx.**, CTV +5mm

#### Criteria used for DVH Analysis:

- **Ref. Dose (RD)** to 95 to 100% of PTV volume, 1.5RD to  $\leq$  30% of PTV volume and 2xRD to  $\leq$  10% of PTV volume,
- **Urethra:** Maximum dose  $\leq$  105% of PTV dose
- **Ant Rectal Wall:** 5% of volume  $\leq$  87% of PTV dose

## 2. IMRT Fractionated

### 2.1 Initial:

- Prostate +SV 50.4Gy in 28 fx,
- Margin CTV+15mm L/R,Ant, SI,
- CTV+10 mm Post

### 2.2 IMRT Boost Prostate

- 30.6 Gy in 17fx ,
- CTV +10mm L/R, Ant, S/I,CTV+ 5mm post
- Rectum: V10% < 71Gy and V30% < 50Gy
- Bladder: V60% < 60Gy

# Biological Dose:

- Using the published value for  $\alpha/\beta=1.5-2.0$  we have calculated biological dose for HDR monotherapy of 92 Gy.
- The biological dose for IMRT fractionation was 81 Gy at 1.8 Gy/fraction.
- Considering the **PTV volume ratio** for both HDR and IMRT we have applied an empirical **correction factor  $\lambda$**  to the BED calculation of HDR monotherapy

$$\frac{E}{\alpha} = nd \left\{ 1 + \frac{d}{(\alpha / \beta)} \right\}$$

n : # of fractions, d: dose per fraction  $\alpha/\beta$ : 2.0

### BRD Calculation

	Dose Fraction	BED total
HDR	7.0Gy x 3 fx. T=34d	94.5-(0.4x34) +94.5
	7.0Gy x 3 fx	Effective BED =175.4

Equivalent Fractionated dose = BED x  $\lambda$  / {1+d/  $\alpha/\beta$ }

The  $\lambda$ : dose volume reduction factor = 0.85 . Eq

.fractionated dose is 78Gy for 1.8 Gy/fraction

Fig 1a and b : IMRT treatment plan axial and sagittal plane with margin given for movement uncertainty

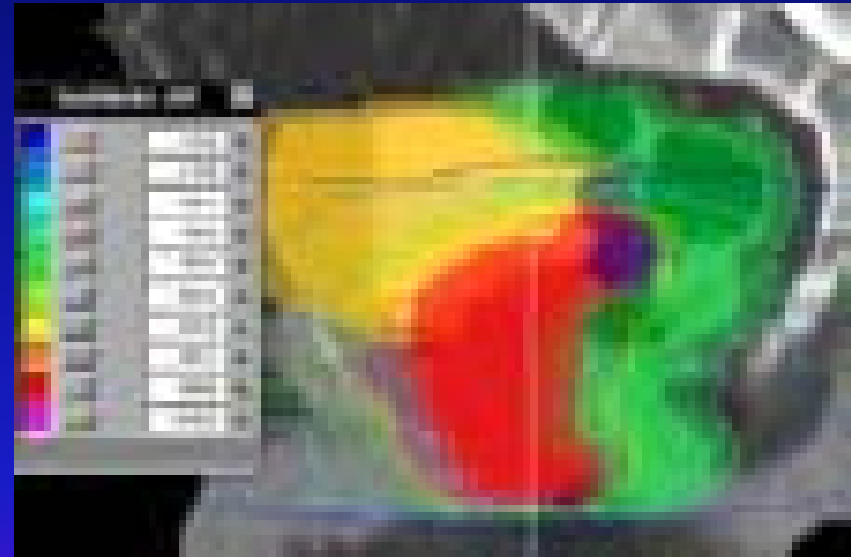
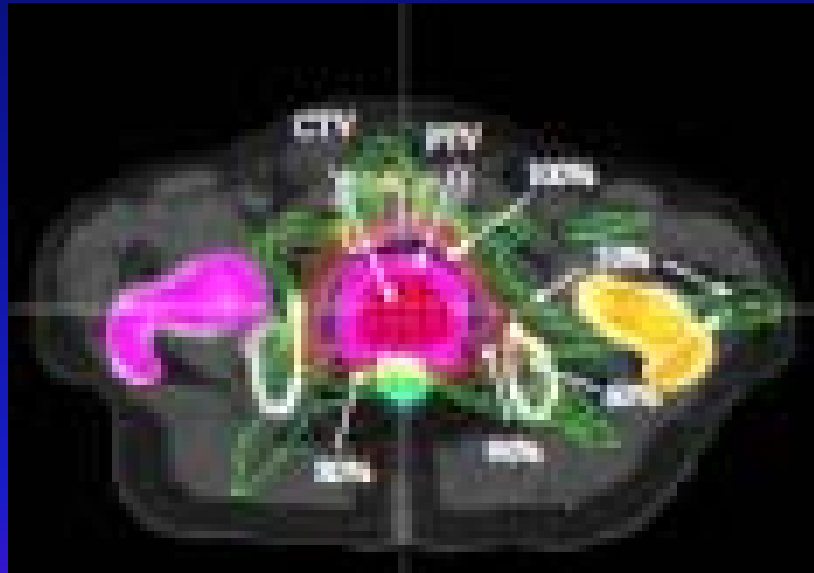
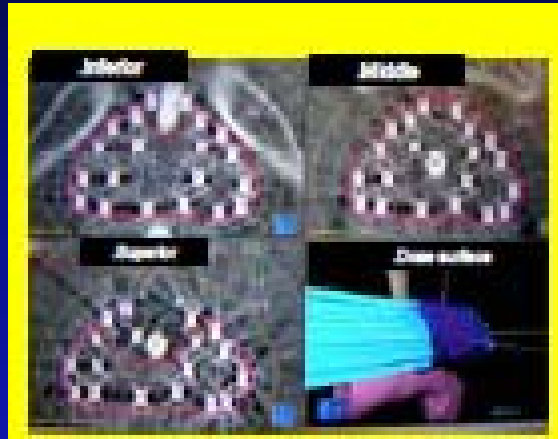




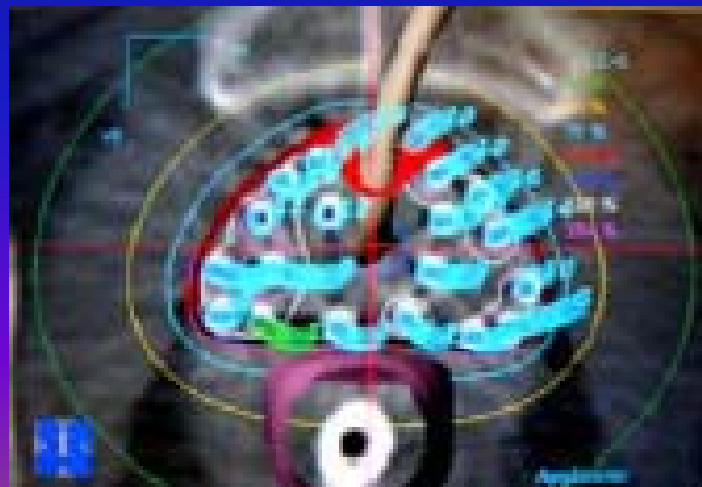
Fig 2. Dose Volume Histogram for IMRT prostate plan showing PTV,CTV,Seminal Vesicle (SV) Rectum and Bladder.



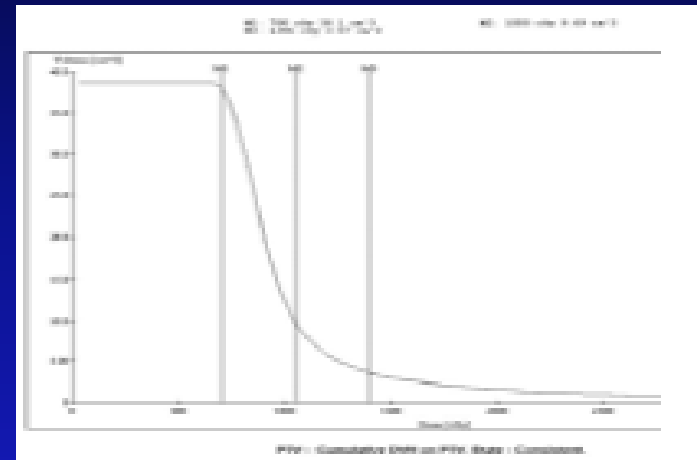
**Fig.3 HDR treatment plan showing the dose distribution on axial planes , inferior, middle and superior covering seminal vesicle. 3D dose cloud along with rectum and urethra are also presented**



**Fig.4. Planar section through mid axial indicating the dose fall off towards rectum**



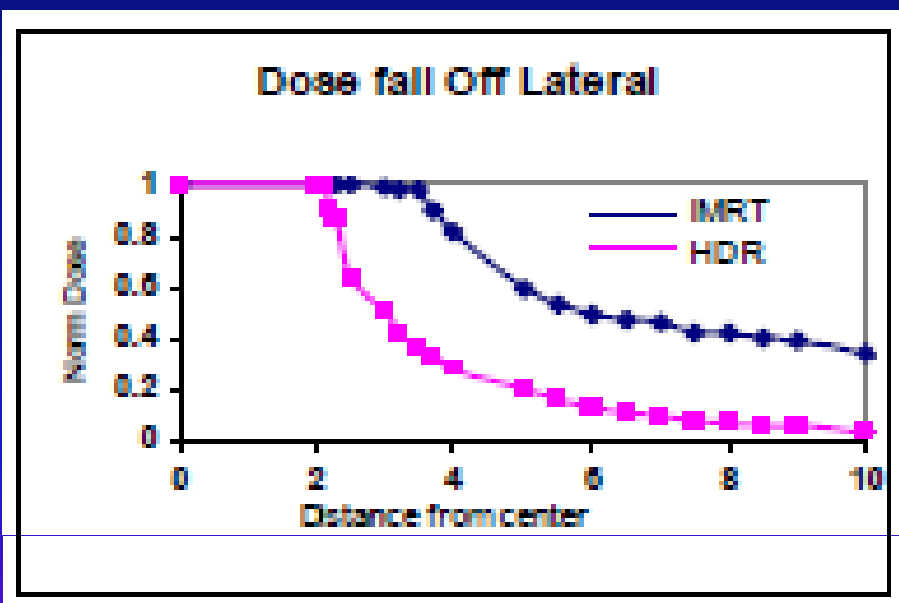
**Fig 5. Dose Volume Histogram for HDR Brachytherapy : M1 volume at Dref =7Gy, M2: Volume at 1.5 Dref, , Volume at Dref = 2.0 Dref**



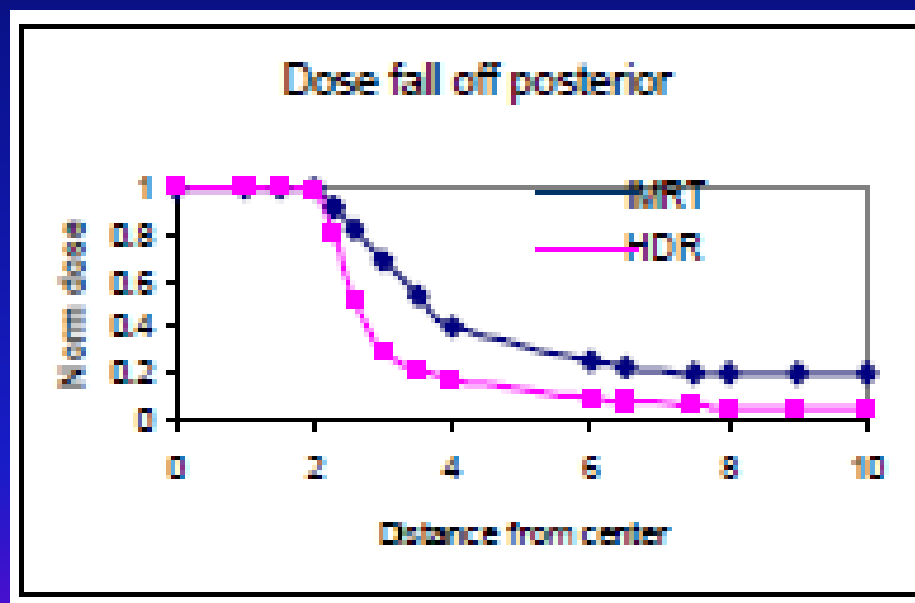
# Results

- The **dose fall off** from isocenter towards lateral along the X-axis for **IMRT and HDR** plans is presented in **Fig 6** and along posterior Y axis is presented in **Fig7** .
- From the plots the distances for 60%,50% ,30% and 10% drop are presented in **Table 2**.
- The **50% dose distance (d50)** laterally for HDR dosimetry is nearly half as compared to the same for IMRT dose distribution.
- Also the **d50 posteriorly** for HDR is 0.75 times that of IMRT dose.
- **This resulted in considerable reduction in integral dose for HDR monotherapy plans as compared to IMRT plans.**

**Fig 6. Dose plot from isocenter to pelvic wall for IMRT and HDR.**



**Fig 7. Dose plot from isocenter to posterior wall for IMRT and HDR.**



**Table 2 Comparison of the extent of % dose from isocenter for IMRT and HDR along lateral and posterior dimension.**

<i>IMRT dose</i>	60%	50%	30%	10%
Lateral dist.	5.2	5.8	10.5	17
Post. dist.	3.2	3.7	6	12
<i>HDR dose</i>				
Lateral dist.	2.7	3	3.8	6.7
Post. dist	2.5	2.6	3	6

# Conclusion

- Using the graphical optimization the **PTV for HDR** was extended to cover the extracapsular volume, while controlling the urethral and rectal dose to tolerance level .
- **Unlike IMRT , HDR monotherapy allows to confine**, the CTV precisely within the PTV reference dose volume, during the entire treatment, as the CTV moves along with the PTV dose .
- **Therefore the planned dose distribution can be maintained precisely without adding movement margins to the volume.**
- Therefore **the integral dose** was considerably less in HDR plan.
- Also in HDR, the **rectal and bladder volumes** are kept outside the reference dose volume, hence minimizing the rectal complication.

**Therefore HDR monotherapy is superior to  
IMRT for early stage prostate cancer.**



Prostate brachytherapy with iodine-125 implants in patients with intermediate risk prostate cancer: a highly efficient treatment when compared with high dose external beam radiotherapy.

**Naji Salem<sup>1,2</sup>, Thomas Duberge<sup>1</sup>, Jean Marie Boher<sup>1</sup>, Franck Bladou<sup>1</sup>, Michel Resbeut<sup>3,2</sup>, Gwenaelle Gravis<sup>1</sup>, Jorchen Walz<sup>1</sup>, Jean Michel Hannoun Levi<sup>4,2</sup>**

*<sup>1</sup>Institut Paoli Calmettes, Marseille, France, <sup>2</sup>Cercle des Oncologues Radiothérapeutes du Sud (CORS), Mougins, France, <sup>3</sup>Croix Rouge, Toulon, France, <sup>4</sup>Centre Antoine Lacassagne, Nice, France*



# Purpose:

- Data on prostate brachytherapy (BT) in patients with **intermediate risk** (IRP) features are scarce since these patients are usually treated with external beam radiotherapy (EBRT) **with or without short androgen deprivation** or by **radical prostatectomy**.
- We retrospectively analysed outcome of IRP treated in the department of radiotherapy at INSTITUT PAOLI CALMETTES either with **EBRT or BT as monotherapy.**

# Material/methods:

- 1995 - 2006,
- **751 patients** with low and intermediate risk characteristics without nodal involvement or metastasis received either  
EBRT (231 patients)  
or BT (520 patients);
- none received adjuvant hormonal therapy.
- According to D'Amico classification,
- **402 patients carried one or more intermediate risk factors** (two lobes extension, Gleason score 7, pre-treatment PSA 10-20);
- among these **229 received BT and 171 EBRT,**
- with 84% of these patients receiving neoadjuvant and concomitant **hormonal therapy.**
- Patients treated were not fully comparable based on pre-treatment characteristics (**Table 1**).

# Table 1: Pre-treatment characteristics of patients with IRP

	Brachytherapy (n=229 pts)	EBRT (n=171 pts)	p-value
<b>Age Median</b>	65 years	71 years	<0.01
<b>PSA Median</b>	9.97 ng/ml	11 ng/ml	<0.01
<b>1 lobe involvement</b>	51 %	41.5%	
<b>2 lobes involvement</b>	49%	58.5%	0.18
<b>Gleason ≤6</b>	84.7%	50.6%	
<b>Gleason 7</b>	15.3%	49.4%	<0.01
<b>Gleason 3+4</b>	10.1%	24.2%	
<b>Gleason 4+3</b>	5.2%	25.2%	
<b>Hormonal therapy</b>	33%	51%	<0.01
<b>Mean HT duration</b>	4.1 months	4 months	
<b>HT duration min-max</b>	1 -14 months	1 - 8 months	

- Median pre-treatment **PSA value**:  
    **EBRT** 11.0ng/ml,  
    **BT** 9.97ng/ml (p<0.01);
- **Gleason score =7**: EBRT 49.4%, BT 15.3% (p<0.01),
- **bilobar prostate involvement** on biopsy was detected in 49% in EBRT and in 58.5% in BT treated patients (p=0.18).
- BT using permanent stranded **iodine-125** (Rapid-strand, ONCURA<sup>®</sup>) with a preplanned intraoperative technique aimed to deliver **145 Gy** with a post-implant median D90 =148 Gy (extr.74-203 Gy).
- Median delivered dose to the prostate with **conformal EBRT** was **78 Gy** (extr.66-80 Gy) (**Table 2**).
- **Relapse** was defined according **ASTRO/Phoenix definition** PSA nadir+2ng/ml.

Statistical analyses were done with SAS program.

## Table 2: BT and EBRT characteristics

Brachytherapy (n=229 pts)		EBRT (n=171 pts)	
<b>Median D90</b>	148 Gy	<b>Prostate mean dose</b>	78 Gy
<b>Min D90</b>	74 Gy	<b>Prostate min dose</b>	66 Gy
<b>Max D90</b>	203 Gy	<b>Prostate max dose</b>	80 Gy
<b>Mean seed number</b>	79.9	<b>Seminal Vesicles mean dose</b>	44.3 Gy
<b>Min seed number</b>	36	<b>Pelvis 45-46 Gy</b>	74.8%
<b>Max seed number</b>	125	<b>Prostate boost with I-125</b>	2.9%
<b>Activity per seed</b>	0,36mci until 2002	<b>2 Gy/fraction</b>	97.7%
	0,505mci from 2003	<b>1.8 Gy/fraction</b>	2.3%

# Results:

- Five-year biochemical relapse free survival (BRFS) for all low and intermediate risk patients was 86%.
- In IRP, 67 patients experienced biochemical, local or metastatic relapse, 37 in BT and 30 in EBRT group.
- Five-year BRFS in IRP was 80% (CI=74-85) and was not significantly different ( $p=0.09$ ) whether patients were treated with BT (5-y BDFS=84% [76-89%]) or with EBRT (5-y BDFS=72% [60-82%]) (Fig. 1).

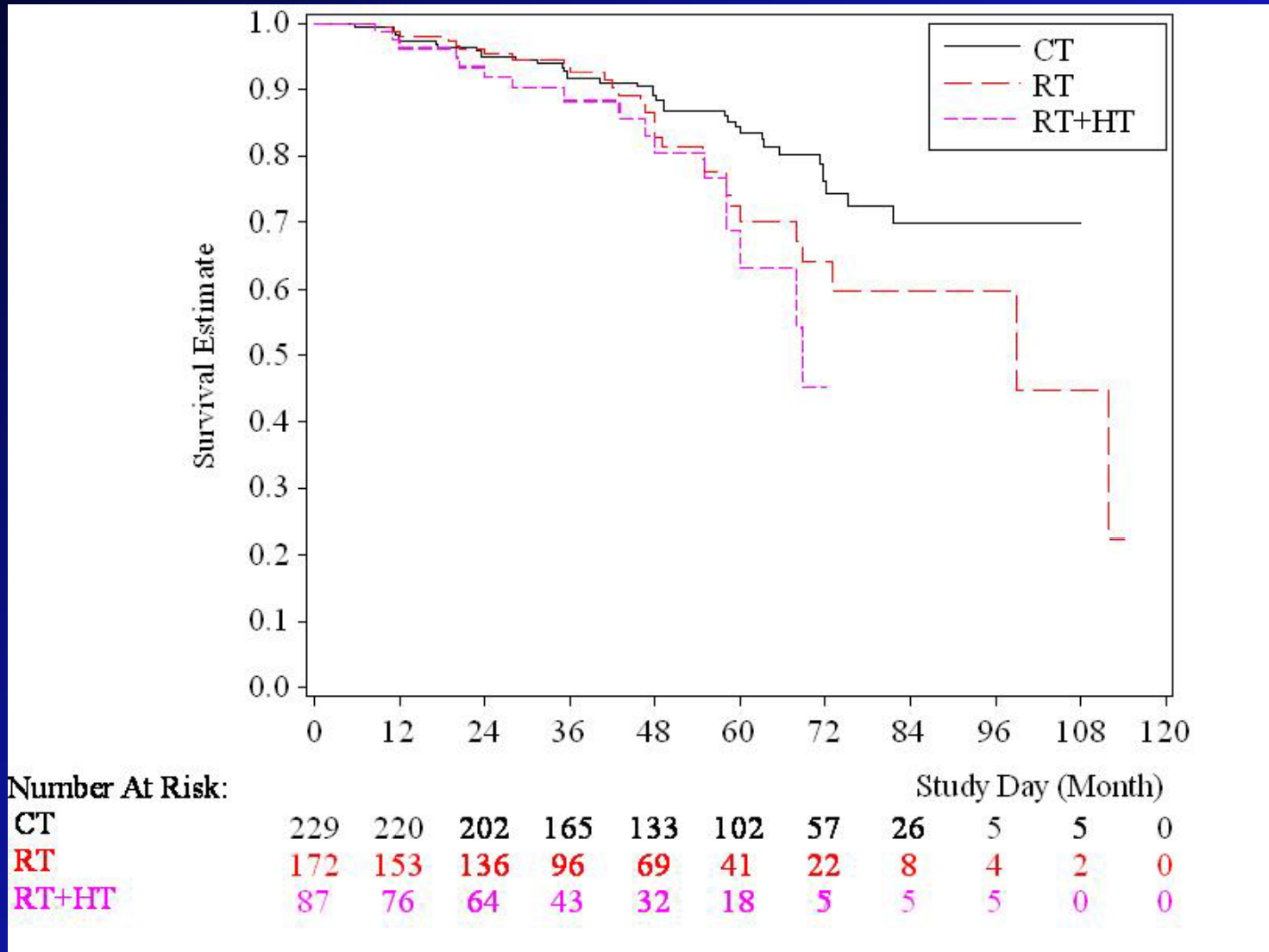
- In univariate analysis, none of the factors analysed Gleason score (<7 vs. 7), lobar involvement (1 vs.2), pre-treatment PSA value ( $\leq 10$  vs.  $>10$ ) were associated with better BRFS; only the number of the pre-cited clinical factors 1 vs. 2 or more showed high significance ( $p=0.008$ ) (Table 3).
- The number of pre-clinical factors 1 vs. 2 or more was an independent prognostic factor ( $p=0.021$ , HR=1.849 CI95=1.097-3.116) in multiple logistic regression.

# Table 3: Multivariate logistic regression

Factors	Hazard Ratio	95% CI	P-value
Gleason	1.609	[0.89,2.91]	0.12
Involved lobes	1.191	[0.70,2.02]	0.52
PSA	1.693	[0.96,2.98]	0.07
Treatment	0.970	[0.53,1.77]	0.92
Age	1.016	[0.97,1.06]	0.48
1 vs. 2 or 3 factors	1.935	[1.17,3.20]	0.01



Fig. 1: IRP relapse free survival curves according to delivered treatment (among the 172 EBRT patients, 87 received short androgen deprivation and are represented herein)



## Conclusion:

- In our series, **PB as monotherapy** yields excellent outcome when compared to EBRT with dose escalation.
- **The prognosis of IRP treated herein is different whether these patients carried one or more adverse prognosis factors.**

# Long-term Prostate Brachytherapy Outcomes With 10 Years Of *Minimum* Follow-up

**M Terk<sup>1</sup>, J Cesaretti<sup>1</sup>, R Nurani<sup>1</sup>, R. Hixson<sup>1</sup>, D Swartz<sup>2</sup>, M. Blasser<sup>3</sup>**

*<sup>1</sup>Florida Radiation Oncology Group, Jacksonville, FL, <sup>2</sup>Mclver  
Urological Clinic, Jacksonville, FL, <sup>3</sup>Urology Associates of N.E.  
Florida, Orange Park, FL*

**Mitchell Terk**

Long-term Prostate Brachytherapy Outcomes  
With 10 Years Of Minimum Follow-up



**Purpose:** Evaluate long-term, non-actuarial prostate **seed implant** outcomes with a *minimum* of 10 years of follow-up

**Methods:** A prostate seed implant program was initiated at our institution in July 1997. All patients were prospectively followed in a centralized database. This study evaluates the *initial 110 consecutive patients* treated from July 1997 to April 1999. All patients had a minimum follow-up of 10 years.



# Treatment:

Low Risk: 70% received 160 Gy I-125 monotherapy, 30% received combination 100 Gy Pd-103 + 45 Gy external radiation

Intermediate Risk: 68% combination therapy

High Risk: 90% combination therapy + median duration of 9 months of LHRH agonist treatment

Salvage Therapy: 100 Gy Pd-103 + 9 month LHRH agonist therapy



## March 2009 Results

- Low Risk: 93% biochemically NED
- Intermediate Risk: 95% bNED
- All High Risk: 66% bNED,  
    **High Risk (if pre-tx PSA < 70) = 77% bNED**
- Salvage therapy: 66% bNED
- **No failures after 5.5 years**
- Only 2% grade 3 toxicity, 0% grade 4

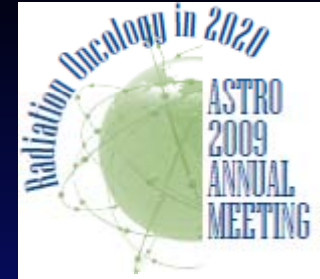
## November 2009 UPDATE: 158 consecutive pts

- Low Risk: 92%
- Intermediate Risk: 96%
- High Risk: 80%



# Conclusions:

- Prostate seed implant allows for excellent long-term outcomes across all risk-groups of prostate cancer
- No treatment failures occurred after 5.5 years, supporting the durability of outcomes
- Long-term GU and GI toxicities were minimal



# Targeted 3-D Stereotactic Brachytherapy as Monotherapy in Gleason's Score 8-10 Prostate Cancer

Daniel B. Fried<sup>1</sup>, Panos G. Koutrouvelis<sup>2</sup>, Niko Lailas<sup>2</sup>,  
Fred Hendricks<sup>3</sup>, James Sehn<sup>2</sup>, and Stuart Katz<sup>3</sup>

<sup>1</sup>Wake Forest University Health Sciences, Winston-Salem, North Carolina; <sup>2</sup>URO-Radiology Prostate Institute, Vienna, VA; <sup>3</sup>Urology, George Washington University Medical Center, Washington, DC;



# Purpose

To report the results for primary stereotactic  
brachytherapy alone in **GS 8-10**  
prostate cancer patients  
treated via  
posterior CT-guided stereotactic pararectal  
approach.

# Materials and Methods

- **691 prostate cancer patients** underwent 3-D stereotactic pararectal brachytherapy implant
- between **January 1999 and December 2007** for whom dosimetric data are available
- **81 patients (11.7%)** had **GS 8-10** disease
- **58** of these 81 patients were suitable for analysis
- Patients were **omitted** for the following reasons:
  - Brachytherapy given as boost (16)
  - Less than 1 year of follow-up (7)
- All implants were performed using a **posterior pararectal approach**
- **Seminal vesicle (SV) biopsies were performed on all patients**
  - 12 core biopsies (6 from each SV)
  - Cores taken from proximal, mid, and distal SV

- **17 patients (29%)** had pathologically confirmed SV invasion and received implant to the prostate and SVs
- Patients received **androgen ablation** for 3-12 months post-implant
- Median **follow-up** was **32 months**
- Biochemical failure was defined by the Phoenix definition of PSA nadir plus 2 ng/mL

# Biopsy Technique

- **Seminal Vesicle Biopsy:**
  - 3-D stereotactic system
  - CT-guided posterior pararectal approach
  - Positions needle in three dimensions
  - Template adjustment avoids:
    - Penetration of rectum
    - Obstruction of needle by coccyx
  - Correct 3-D position of biopsy needle verified via CT prior to biopsy

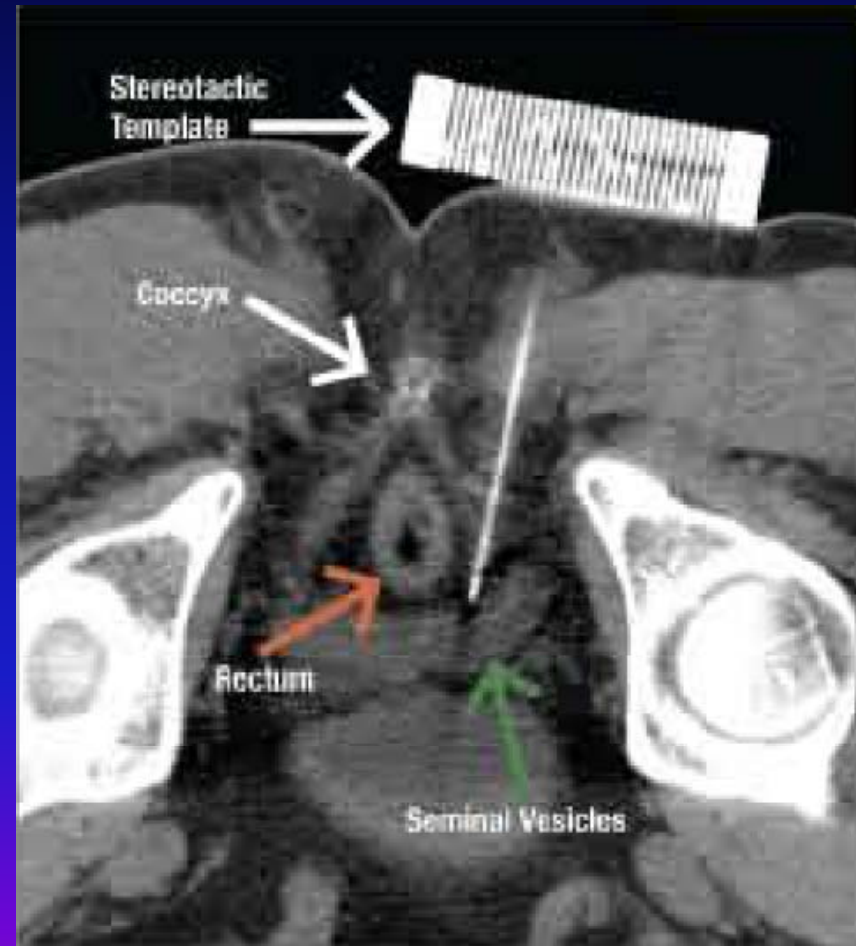


Figure A SV biopsy

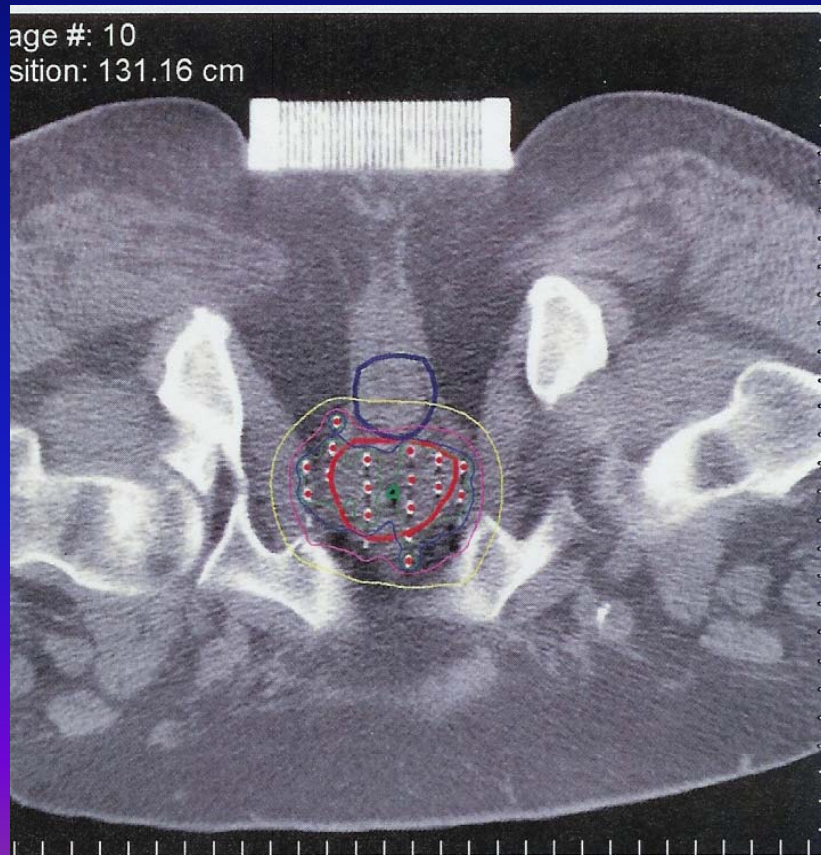
# Implant Technique

- 3-D Stereotactic I-125 implant:
- Posterior pararectal approach
- Real-time CT guidance
- 2.5 mm perforations in 3-D template correlate to CT x,y,z coordinates of needle path

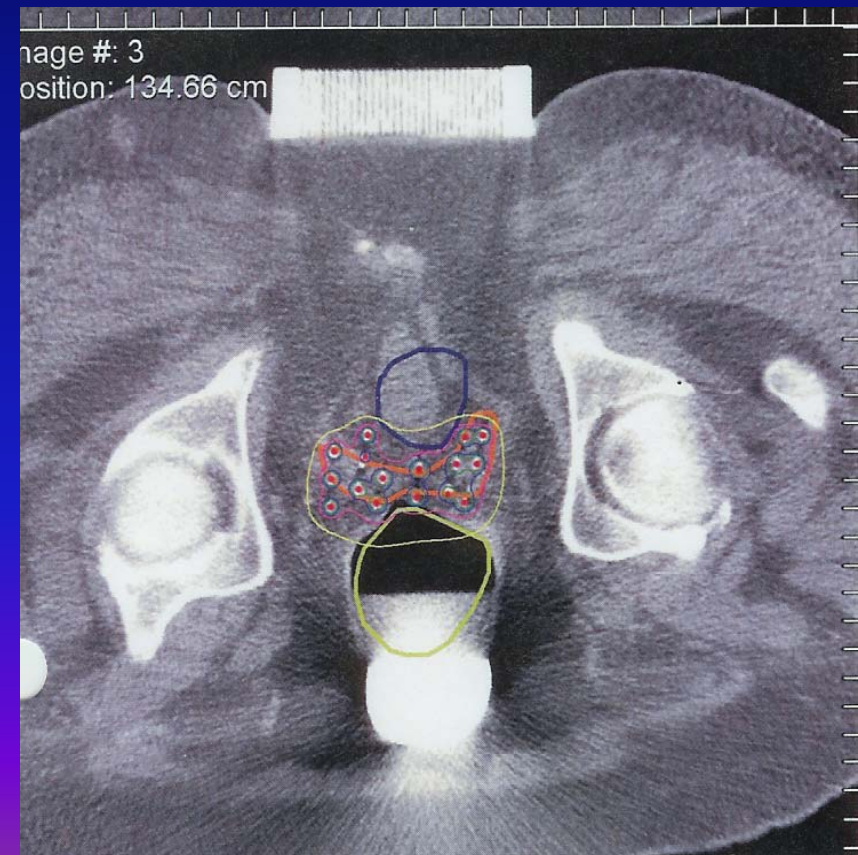


**Figure B Setup for 3-D stereotactic system**

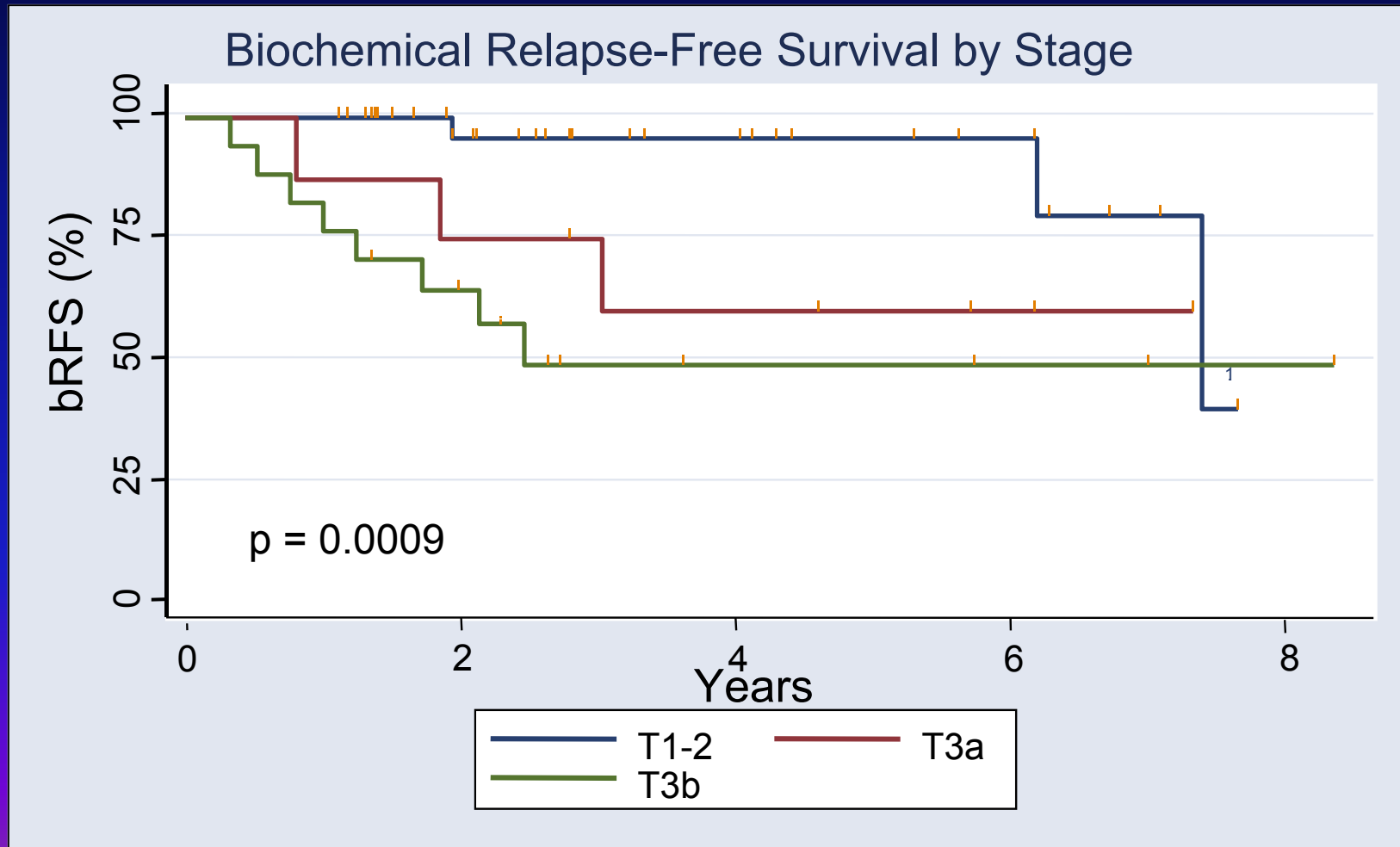
**Figure C Prostate outlined in red, rectum in blue, 100% isodose line in purple**



**Figure D SV outlined in red, rectum in blue, 100% isodose line in purple**

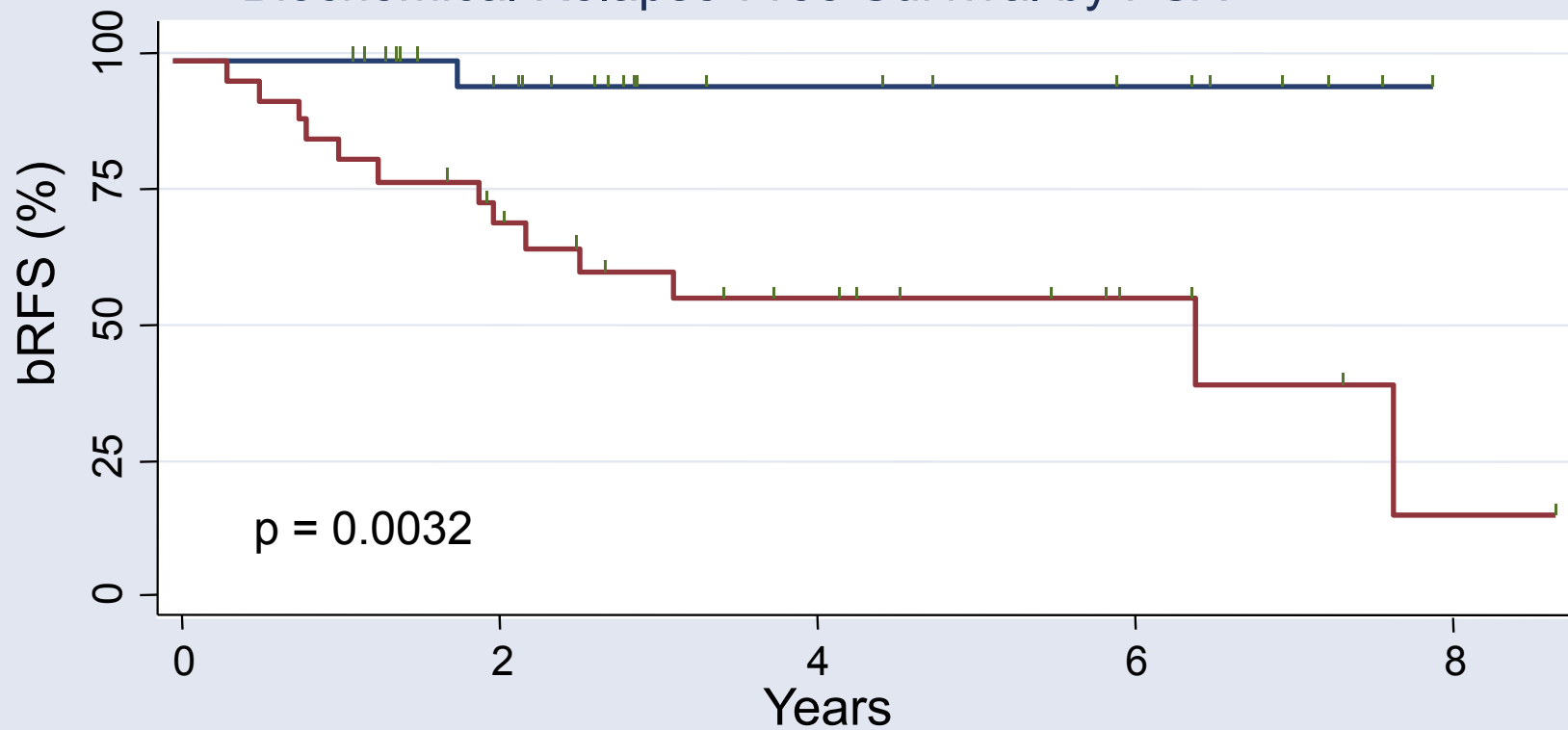


# Results





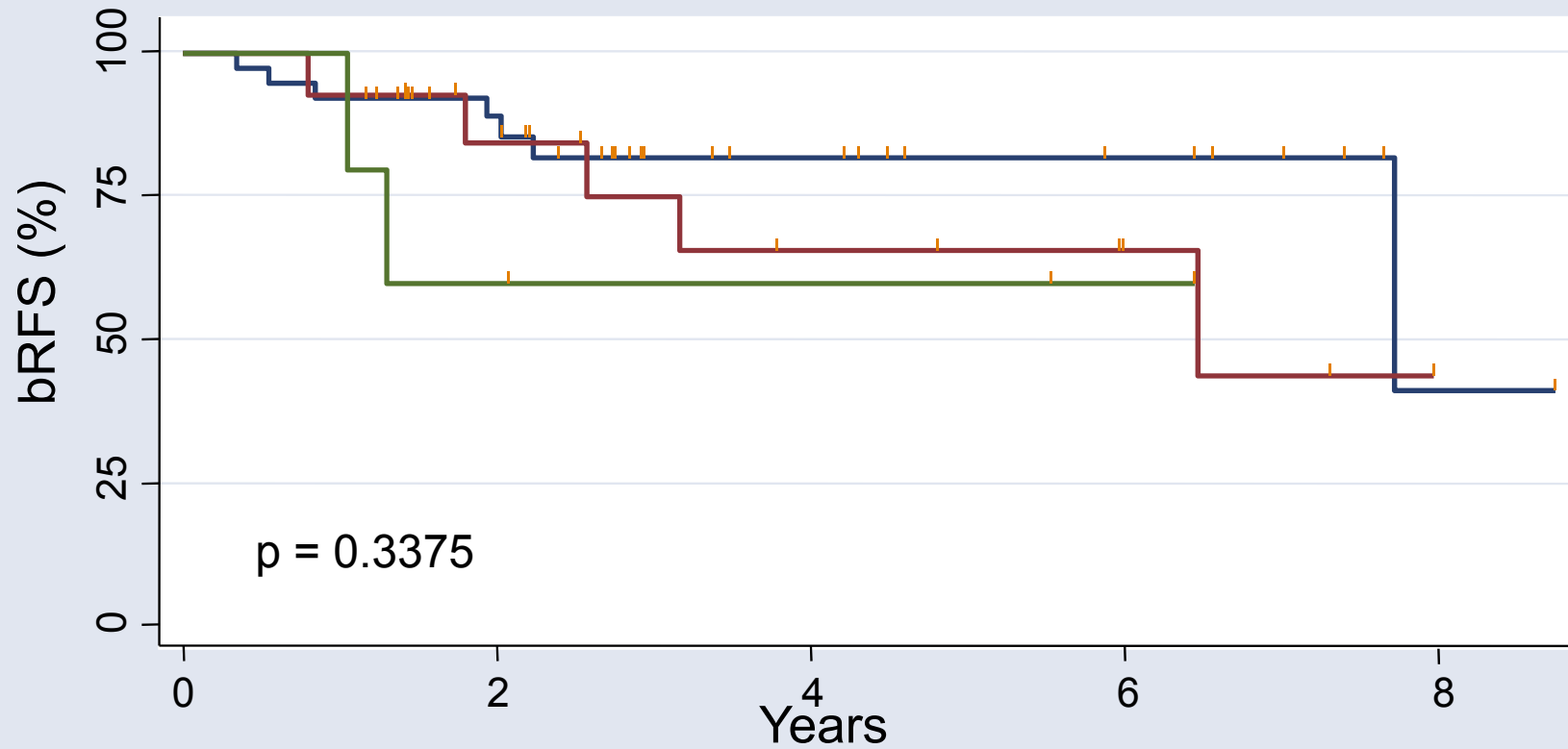
### Biochemical Relapse-Free Survival by PSA



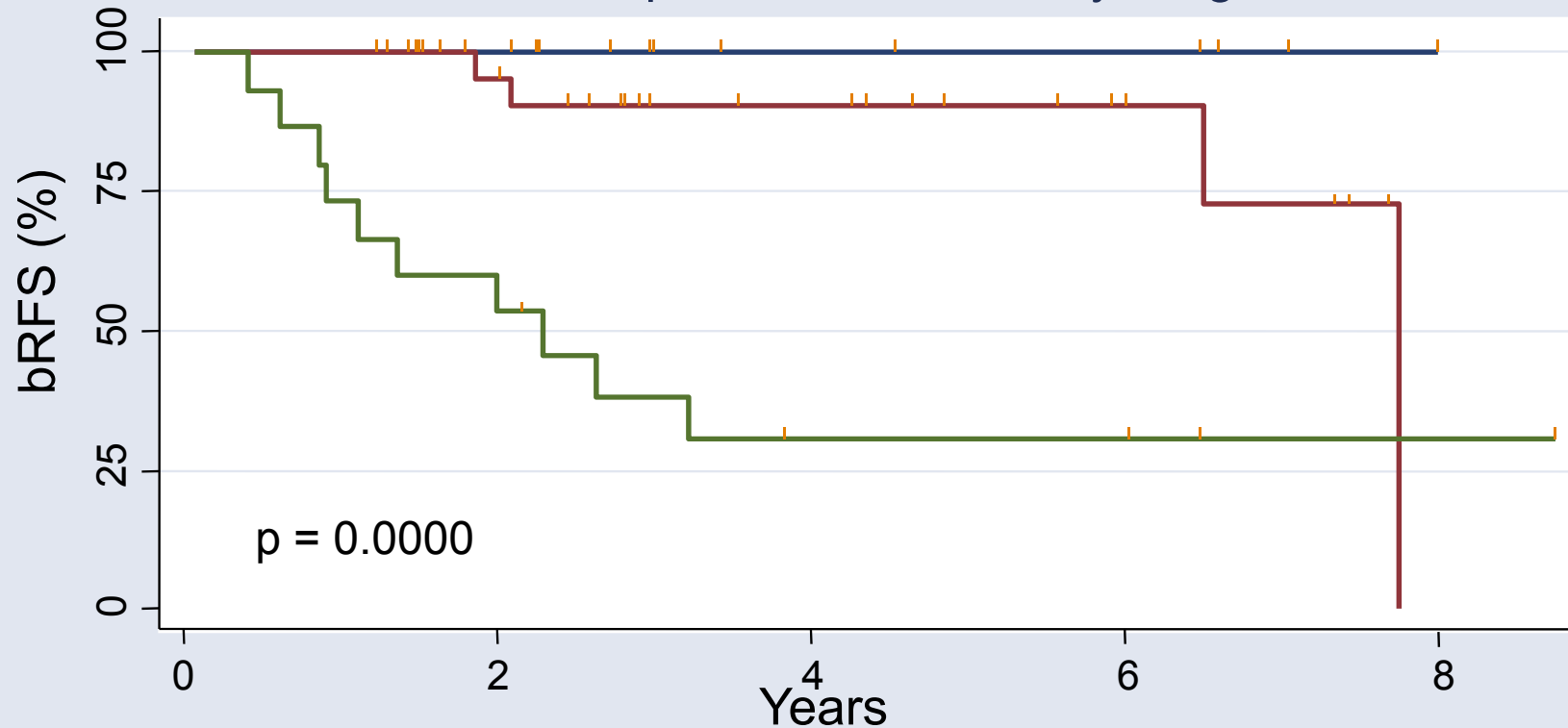
— PSA < 10      — PSA ≥ 10



## Biochemical Relapse-Free Survival by Gleason Score



### Biochemical Relapse-Free Survival by Stage and PSA



— T1-2 and PSA < 10 — T3 or PSA ≥ 10  
— T3 and PSA ≥ 10

# 58 GS 8-10 patients received primary brachytherapy

- 5-yr bRFS 82% for GS 8
  - 5-yr bRFS 66% for GS 9
  - 5-yr bRFS 60% for GS 10
- 
- 5-yr bRFS 95% for PSA < 10
  - 5-yr bRFS 59% for PSA ≥ 10
- 
- 5-yr bRFS 96% for T1 – T2
  - 5-yr bRFS 60% for T3a
  - 5-yr bRFS 49% for T3b
- 
- 5-yr bRFS 100% for PSA < 10 and T1-2
  - 5-yr bRFS 91% for PSA ≥ 10 or T3
  - 5-yr bRFS 30% for PSA ≥ 10 and T3

# Conclusions

- **3-D stereotactic targeted brachytherapy** alone for patients with **GS 8-10** disease provides adequate radiation coverage of the prostate and SVs
- **5-yr bRFS for patients with iPSA <10 and/or early T-stage** is excellent (95 - 100%)
- 5-yr bRFS of 75% for the entire cohort is **comparable to results for combined EBRT and brachytherapy** and is superior to rates for **prostatectomy or EBRT alone**
- **Cost and morbidity are reduced** relative to the combination of EBRT and brachytherapy



# **Interstitial High Dose Rate (HDR) Brachytherapy For Early Stage Prostate Cancer**

**Rufus J. Mark, M.D., Paul J. Anderson,  
M.D., Robin S. Akins, M.D., Murali Nair,  
PhD**

**Joe Arrington Cancer Center and Texas Tech  
University, Lubbock Texas, USA**

# Introduction:

- Transrectal Ultrasound (TRUS) guided interstitial implant for prostate cancer using **Low Dose Rate (LDR)** and **High Dose Rate (HDR)** technique has been reported with results

**comparing favorably**

to **surgery** and **External Beam Radiation Therapy.**

- Often, HDR and LDR interstitial implant is combined with EBRT.
- There is little published data on HDR alone.

**We report our results with HDR alone.**

## Materials & Methods :

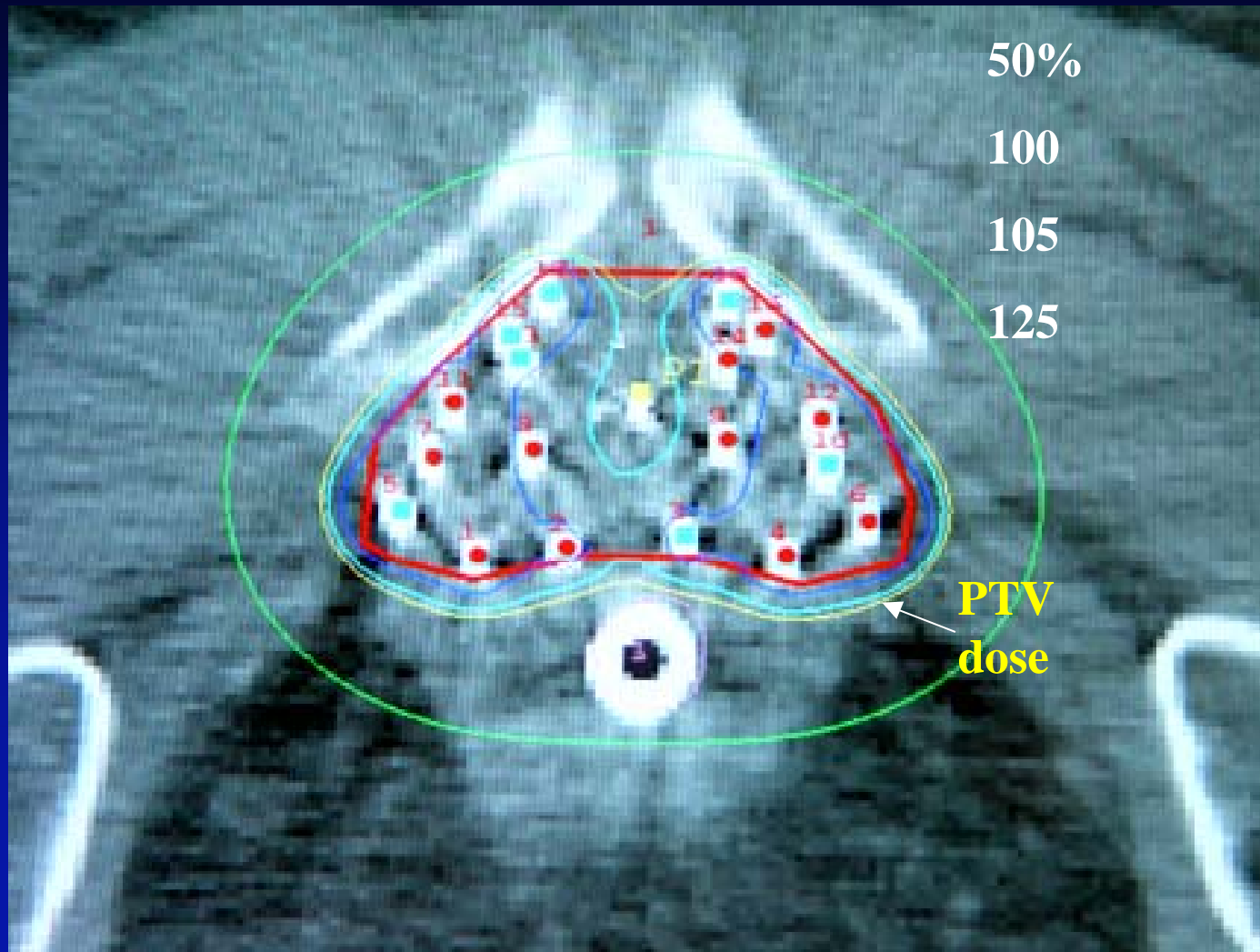
- 1997 - 2009,
- **278** patients, **T1 and T2**,
- TRUS guided interstitial implant,
- There were no Gleason Score or PSA exclusions.
- No patient received EBRT or Hormonal Blockade.
- Median **Gleason Score was 7** (range : 4 to 10).
- Median **PSA was 9.3** (2.7 to 39.8).
- **Treatment volumes ranged from 36 cm<sup>3</sup> to 196 cm<sup>3</sup>.**
- Treatment volume included the prostate and seminal vesicles in all cases.

# Materials & Methods:

- Our protocol for HDR alone, has called for **two HDR Implants**, spaced 4 weeks apart.
- The treatment volume received **22,5 Gy in 3 fractions** prescribed to the 100% Isodose line, given over **24 hours**.
- A **2nd implant** was performed 4 weeks later, delivering a further 22,5 Gy in 3 fractions, bringing the final dose to the prostate to **45 Gy in 6 fractions**.
- **Urethral dose points** (12-16) were followed, and limited to < 105% of the prescription dose.



# CT - HDR TREATMENT PLAN



# Results:

- Median **follow-up - 94 months** (range: 6 to 157),
- Overall PSA Disease Free Survival (**DFS**) was

**88.5% (246/278)**

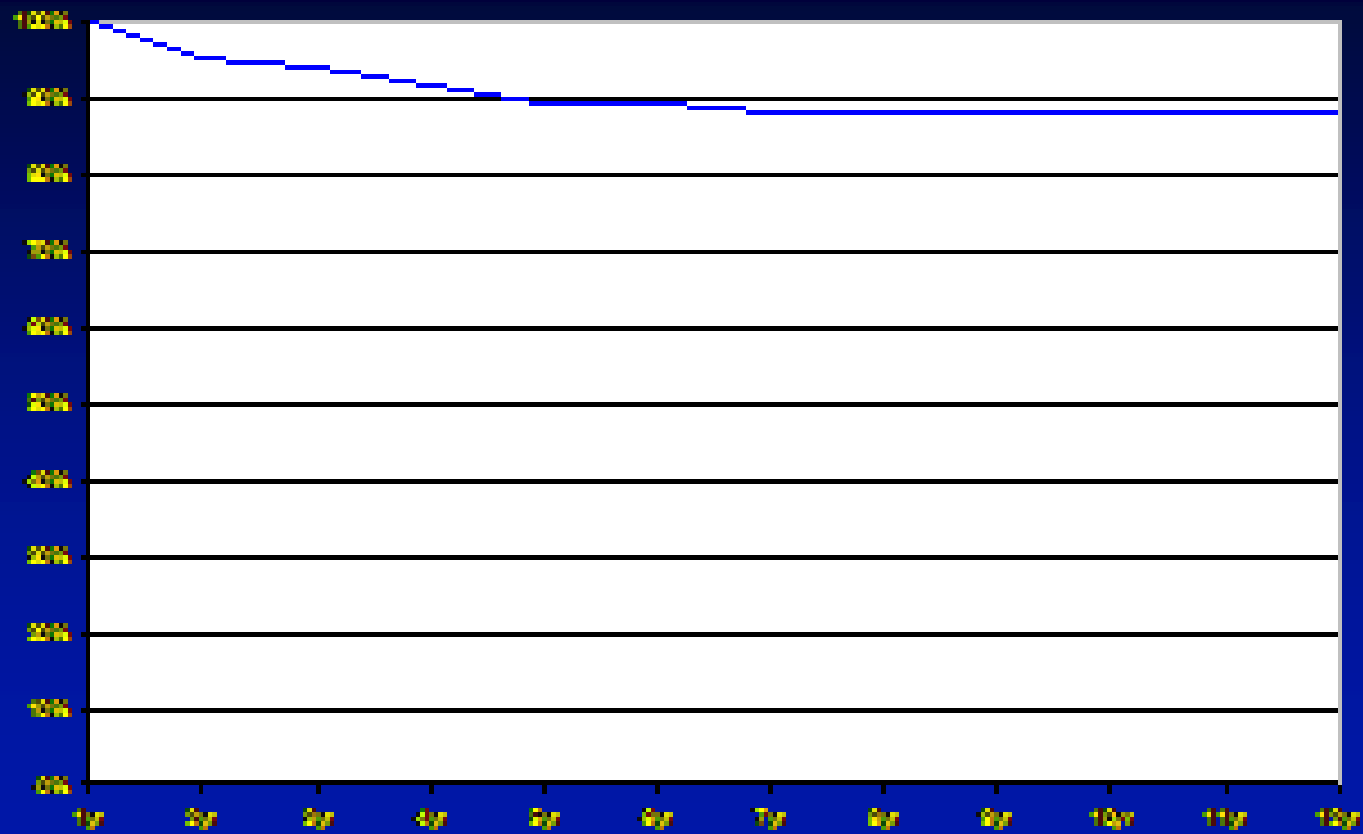
## By risk group PSA DFS:

- low risk - 94.3% (67/71),
  - intermediate risk - 89.4% (161/180),
  - high risk disease - 66.7% (18/27).
- Acute and chronic **complications** were uncommon.

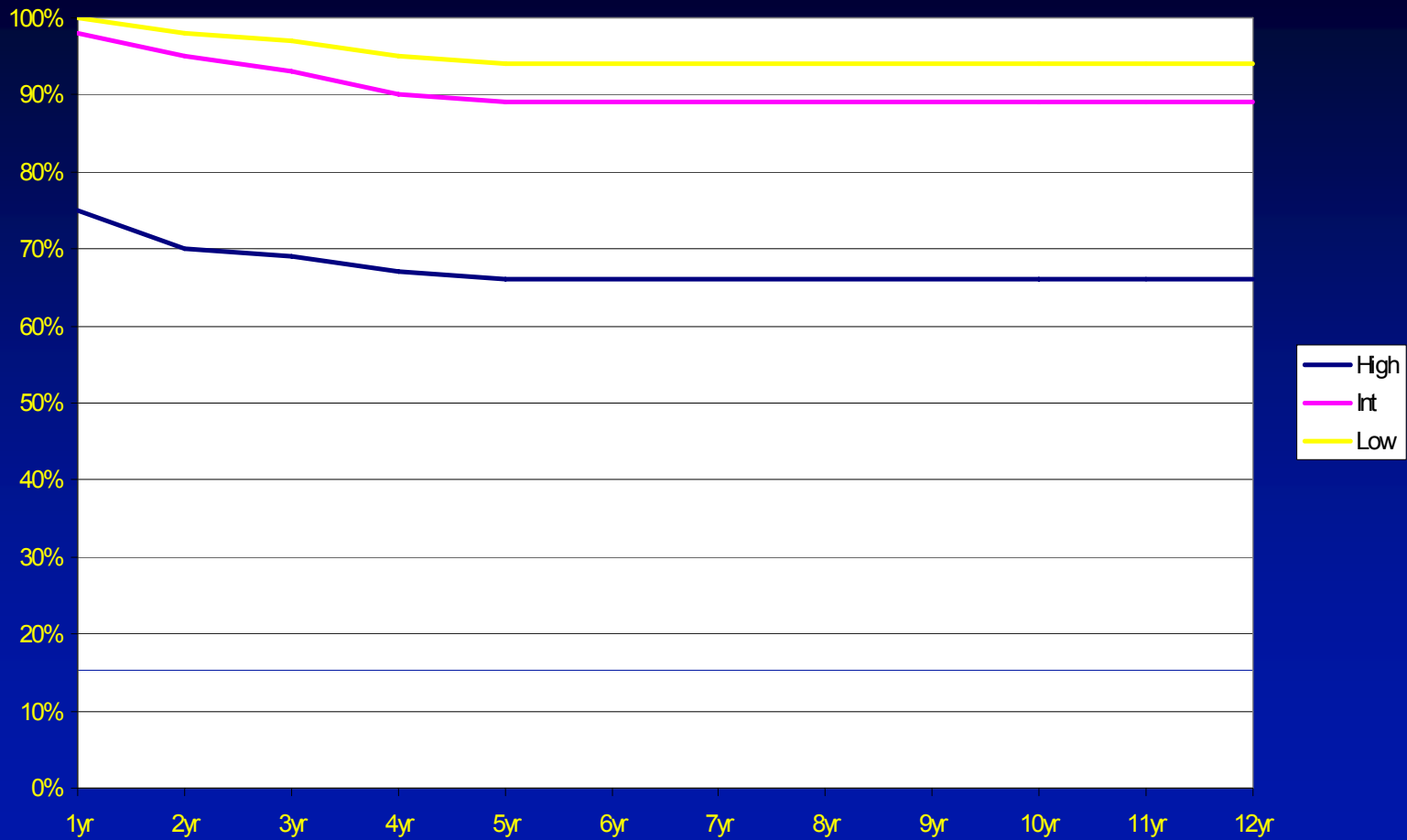
# Complications:

- **Acute urinary retention** occurred in 5.0% (14/278) of the patients, requiring temporary insertion of an indwelling foley catheter.
- **Deep venous thrombosis** occurred within one month of HDR in 1.4% (4/278) of the patients.
- **Urethral stricture** requiring dilatation has developed in 6.1% (16/278) of patients.
- **Urinary stress incontinence** has occurred in 3.2% (9/278).
- **RTOG late bladder toxicities** were : 0% Grade 4, 0% Grade 3, and 3.2% (9/278) Grade 2.
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# PSA DFS



# PSA DFS BY RISK GROUP



## **? HDR vs. LDR**

- **No worries re : Seed Supply.**
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- **No worries re : Radiation Exposure.**
- **No worries re : Seed Migration.**
- **No worries re : Seed Emboli.**
- **No worries re : pre-plan matching.**
- **No worries re : EPE.**
- **No worries re : SV.**
- **No worries re : Pubic Arch.**
- **No worries re : Volume.**

# Conclusions:

1 . Eight-year results with HDR implant alone compare favorably

to EBRT, LDR +/- EBRT, and HDR + EBRT, both with regard to PSA DFS, and complications.

2. HDR offers other advantages over LDR, such as:  
no radiation exposure to hospital personnel,  
no seed migration,  
greater dose flexibility  
precision of radiation dose delivery.

Larger volumes can be treated with HDR.

3. By omitting EBRT, bladder and rectal complications **costs** appear to be significantly reduced.

# PROSTATE CANCER RESULTS WITH HDR ALONE

<u>INST.</u>	<u>#PTS</u>	<u>GS</u>	<u>STAGE</u>	<u>PSA</u>	PSA <u>DFS</u>	<u>F/U</u>
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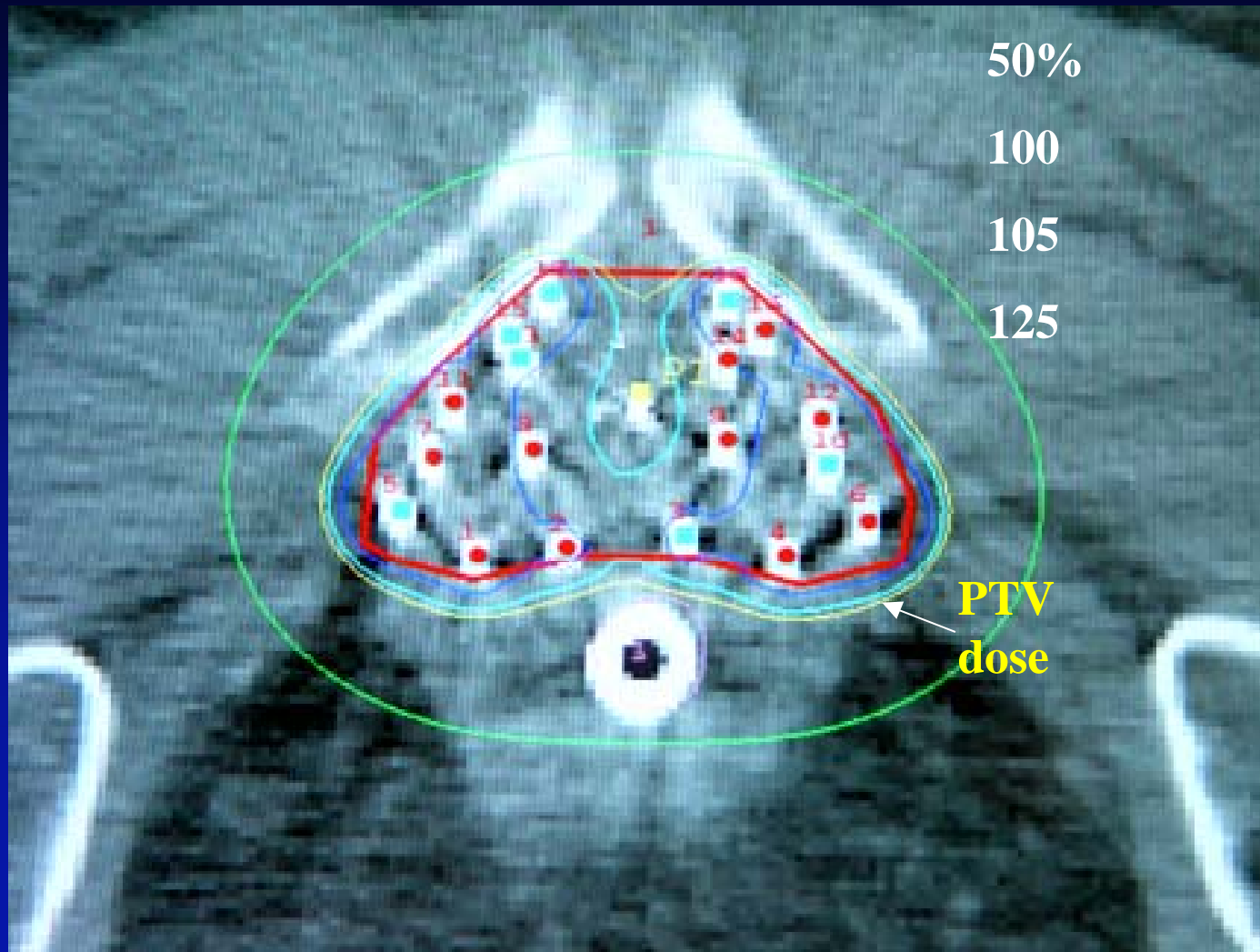
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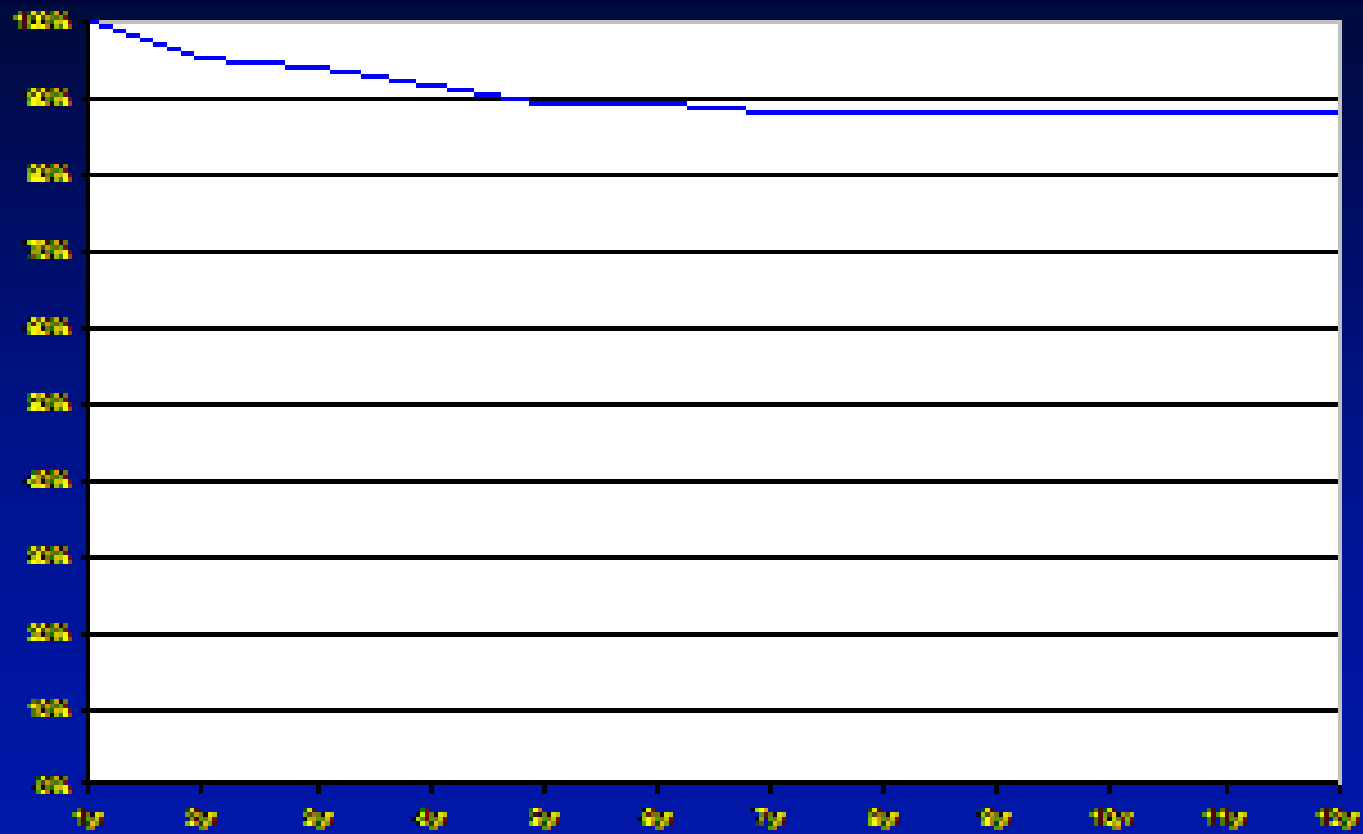
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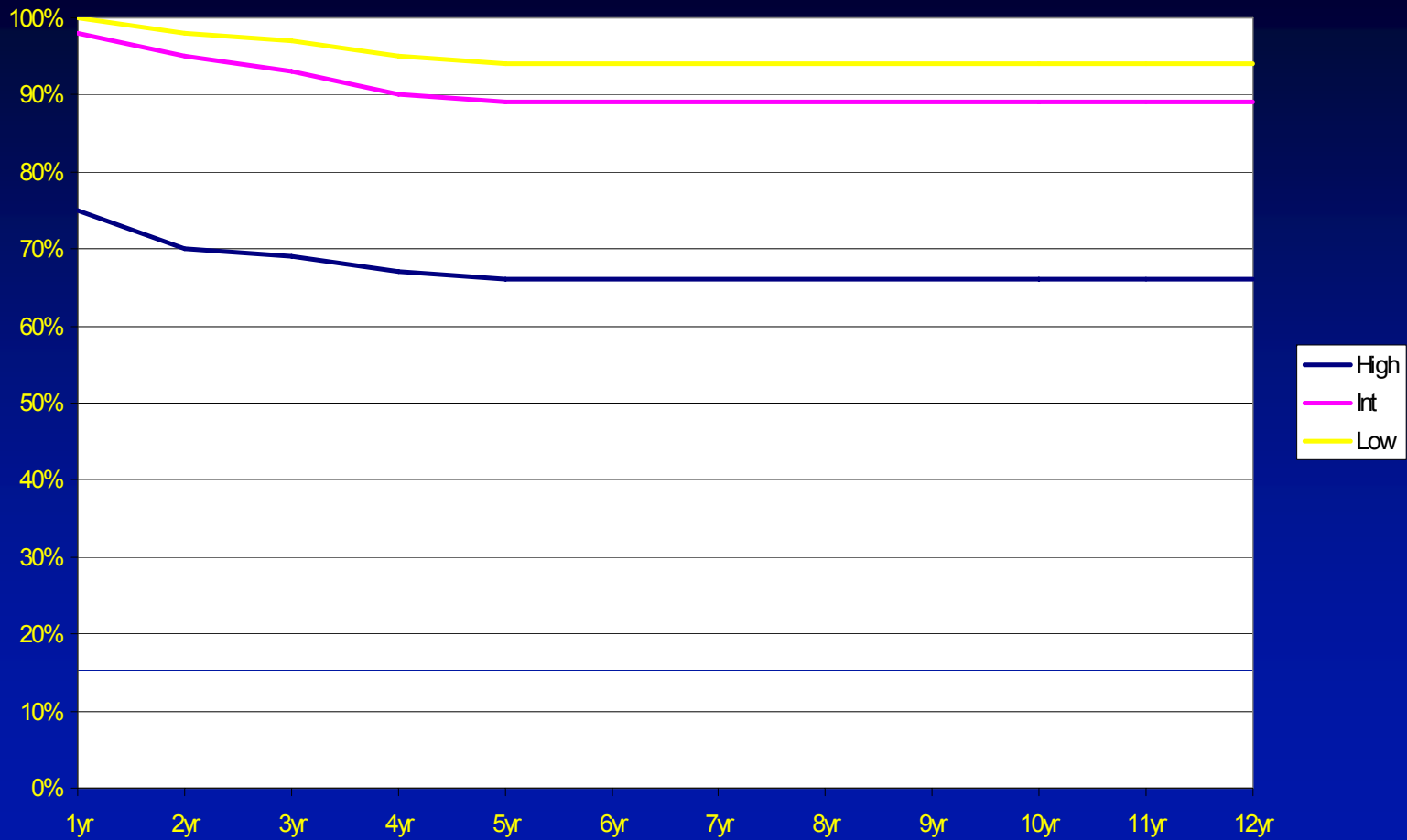
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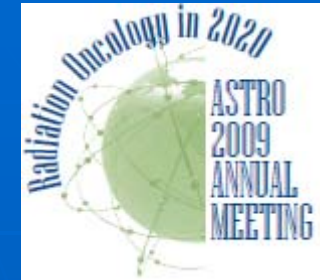
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**Thomas Shanahan A-099**  
AnchorSeed™ for the Reduction of Source  
Movement in Prostate Brachytherapy with the  
Mick Applicator Implant Technique



# AnchorSeed for the Reduction of Source Movement in Prostate Brachytherapy

**Thomas G. Shanahan, MD FACRO**  
**University Radiologists**

**Clinical Professor**  
**Urology and Radiation Oncology**  
**Southern Illinois University**  
**School of Medicine**  
**Springfield, Illinois**

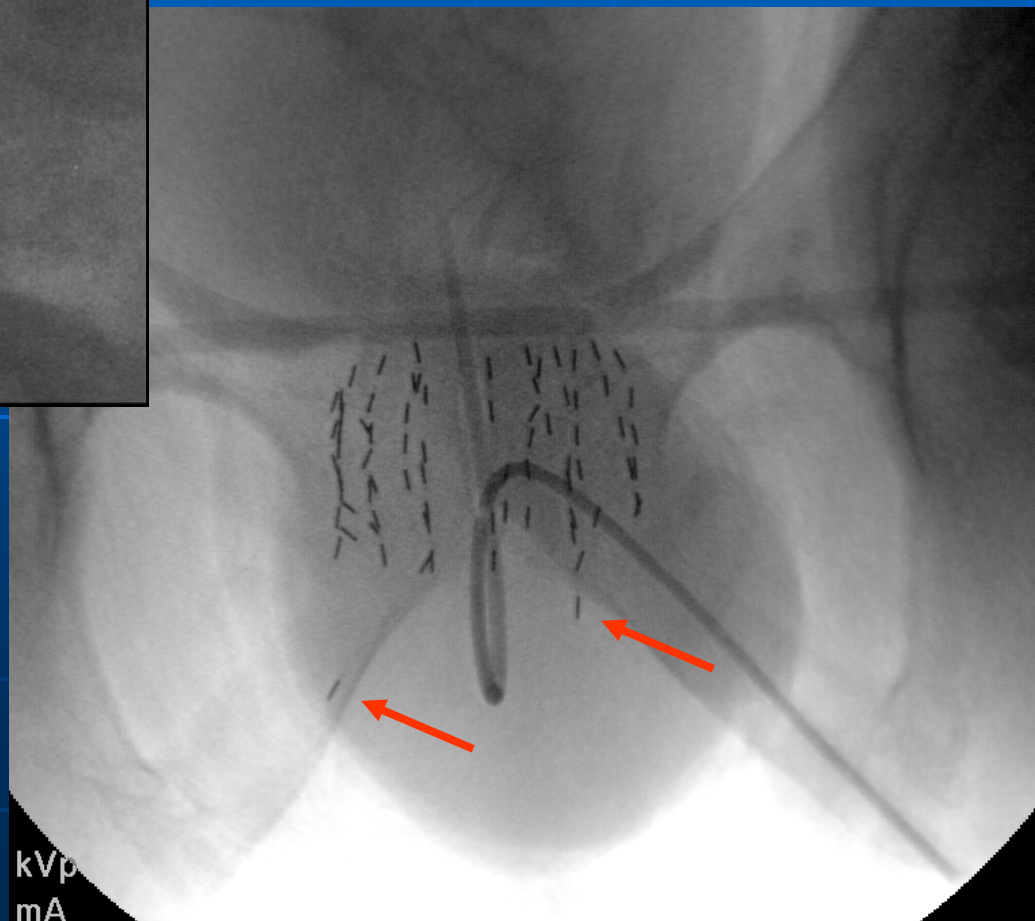
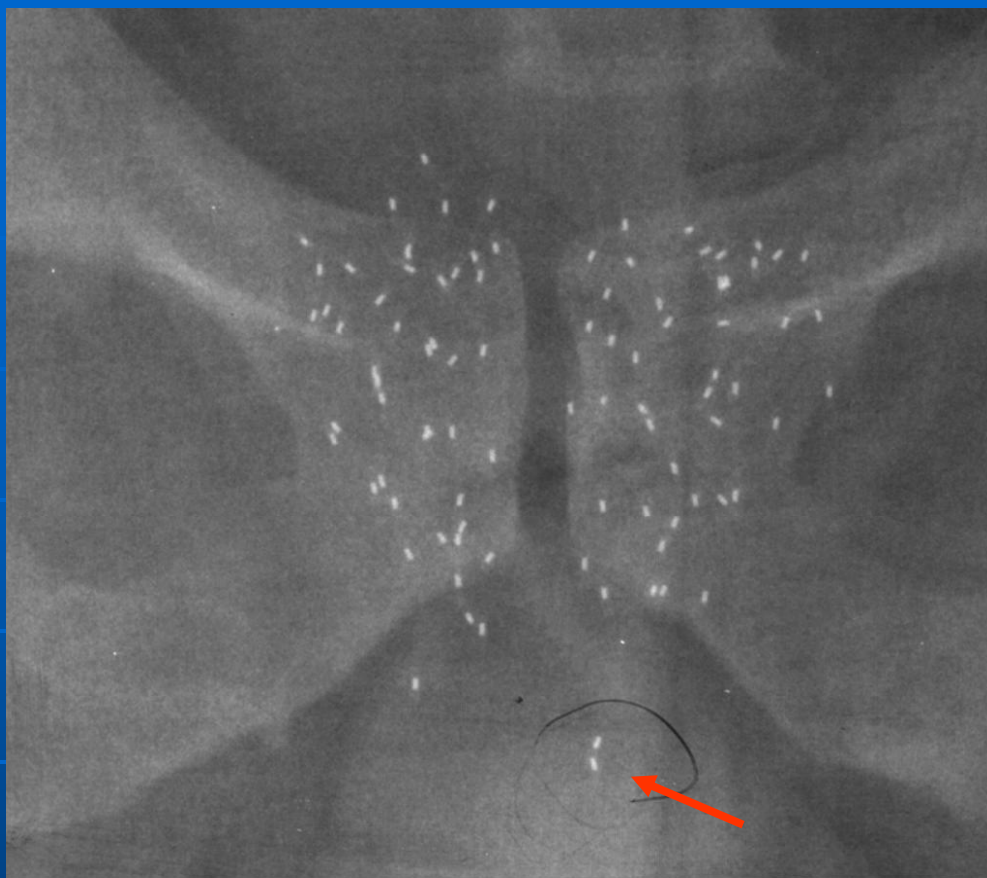


# SEED MIGRATION

- Blood
- Ejaculate
- Bladder
- Slippage or “waking”



Loose



kVp  
mA



Stranded

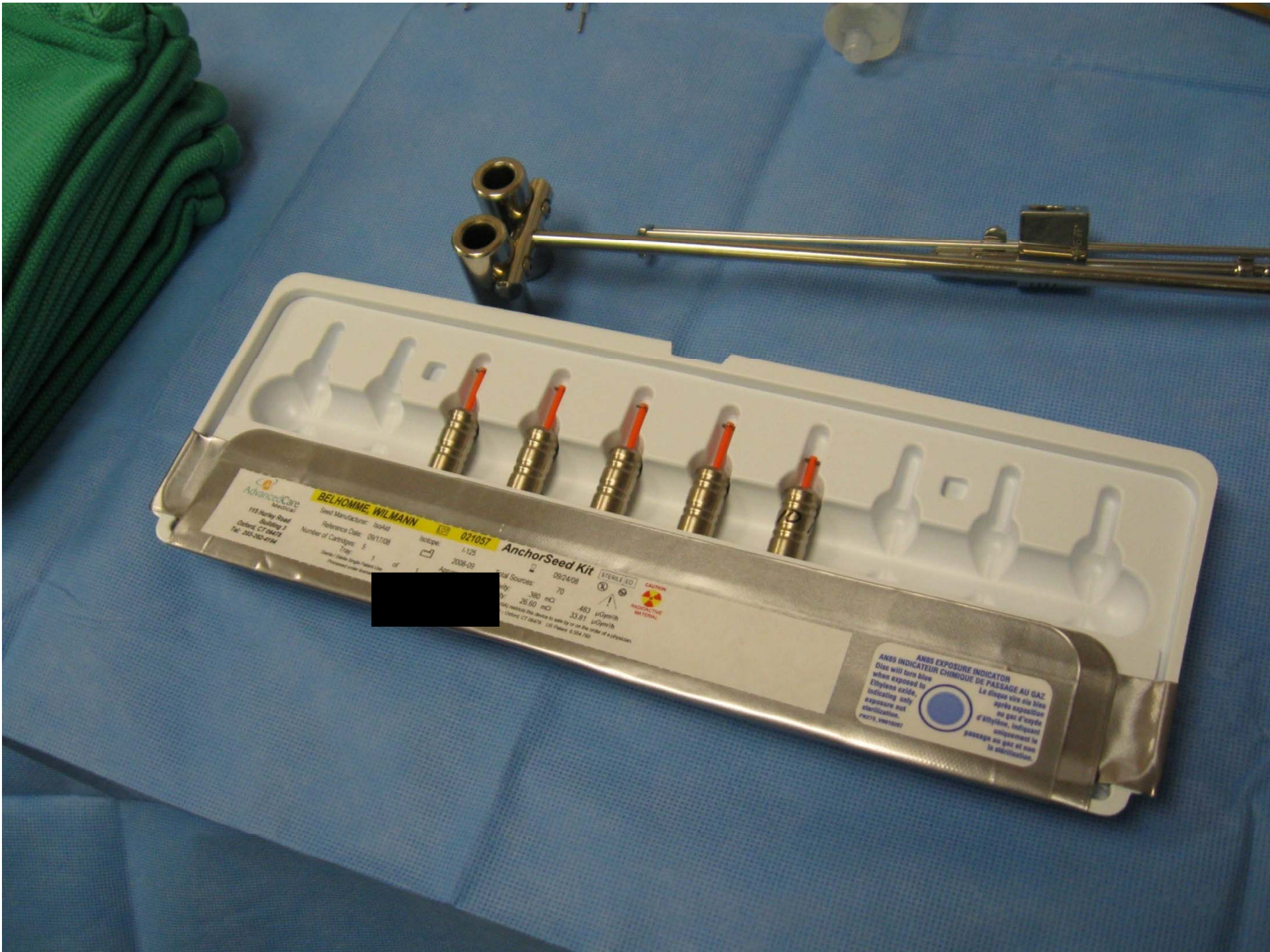


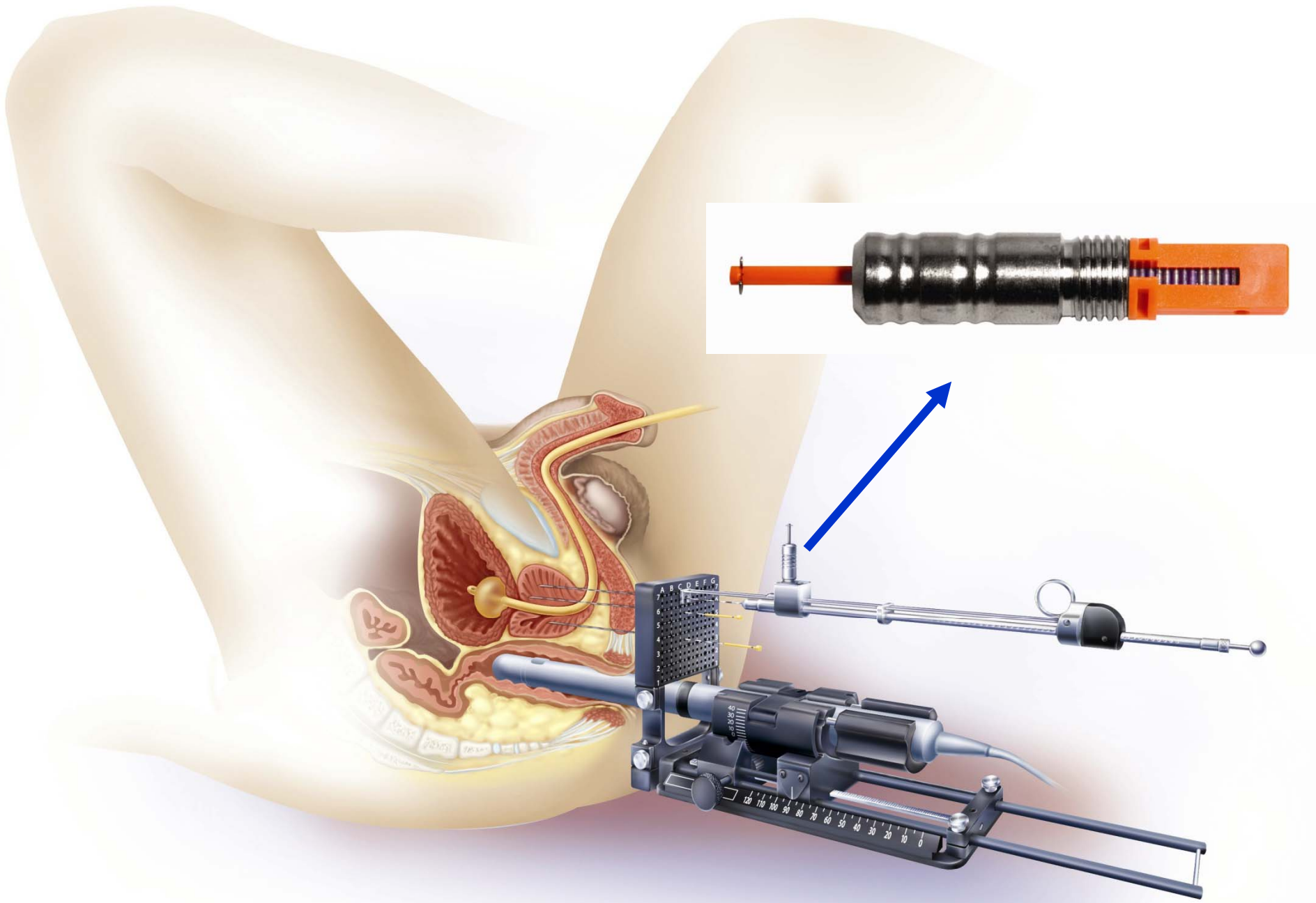
# SETUP

- Needles
- Cartridges w/ seeds
- Mick Applicator
- Seed passer
- Rectal suction tip
- Foley Catheter w/ contrast
- Sharpened needle for gold fiducial marker.
- Basin for sharps
- Bowl for perineal pressure











# IMAGE GUIDANCE AT IT'S BEST



AUG 15 2007

# ANCHORSEED STUDY

- 178 patients
- 89 Anchorseed      89 "bare seed"
- Same treatment technique
- Day 0 Fluoro films and CT
- 13,512 seeds were placed in 178 patients
- Ave: 76 seeds and 16 needles
- Measured inferior seed slippage



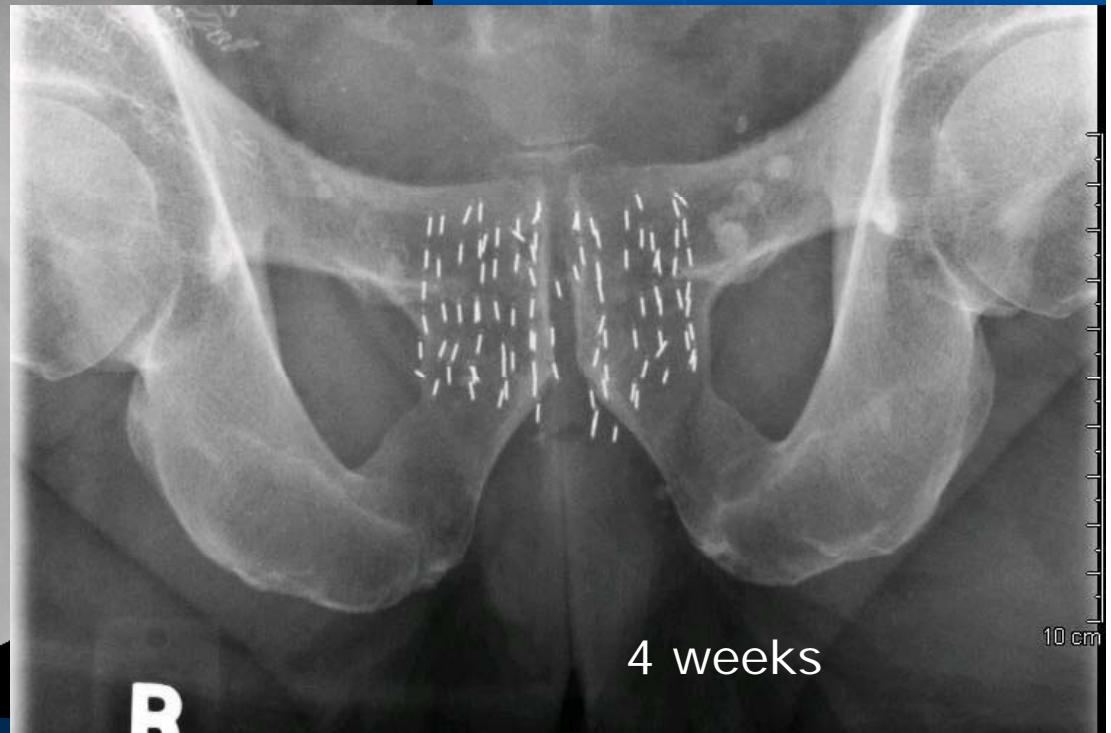
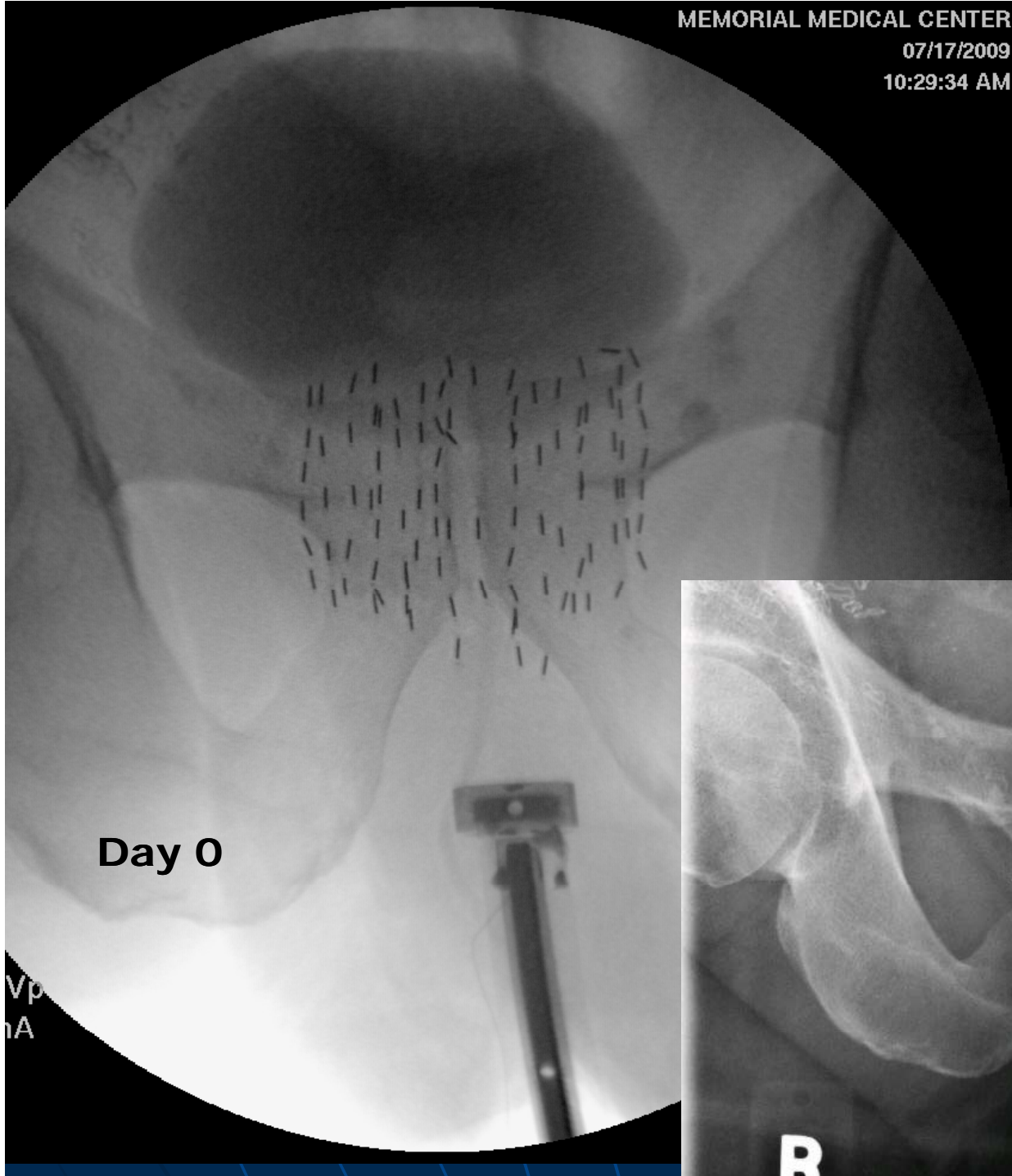
Table 1 Mean change in values according to seed type

Coated	Label	Mean	Std Dev	Median	25th	75th	p-value
No	Time of procedure(min)	38.60	6.40	37.50	35.00	40.00	0.0542
	Fluoro minutes	2.43	0.65	2.34	2.10	2.57	0.0001
	Seed Slippage(mm)	4.14	3.45	5.00	0.00	5.00	0.0016
	rV100 (cc)	0.08	0.10	0.05	0.00	0.12	0.0001
	uD30%	119.43	12.82	119.05	111.15	127.77	0.0185
	V100%	93.13	7.12	95.21	92.00	96.27	0.0015
	V150%	48.68	14.28	47.65	40.39	57.19	0.1148
	D90%	108.46	8.27	110.00	104.00	114.00	0.0052
Yes	Time of procedure(min)	36.93	3.82	35.00	35.00	40.00	
	Fluoro minutes	1.83	0.66	1.59	1.34	2.22	
	Seed Slippage(mm)	2.43	2.85	1.50	0.00	5.00	
	rV100 (cc)	0.04	0.13	0.00	0.00	0.03	
	uD30%	114.64	15.98	113.64	103.85	124.43	
	V100%	92.02	4.64	92.81	90.16	95.20	
	V150%	45.39	12.64	44.73	36.56	54.34	
	D90%	105.67	8.48	105.50	100.00	109.50	

MEMORIAL MEDICAL CENTER

07/17/2009

10:29:34 AM

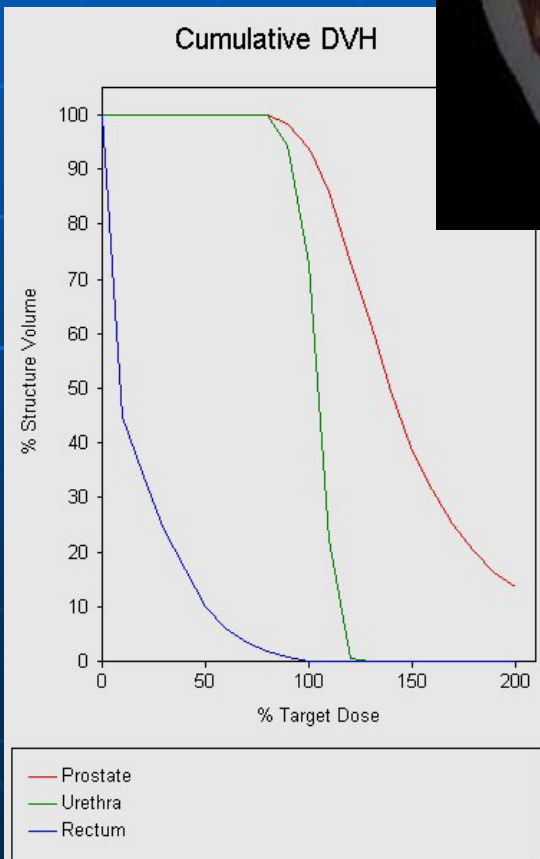
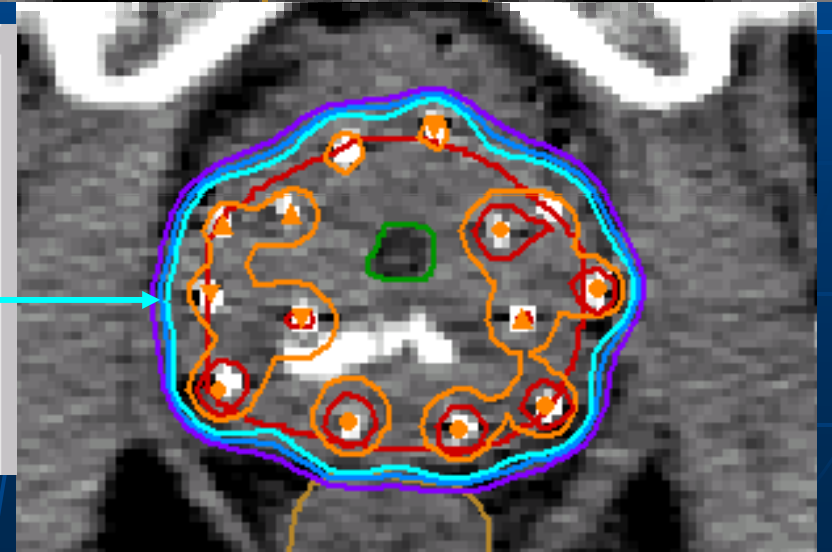
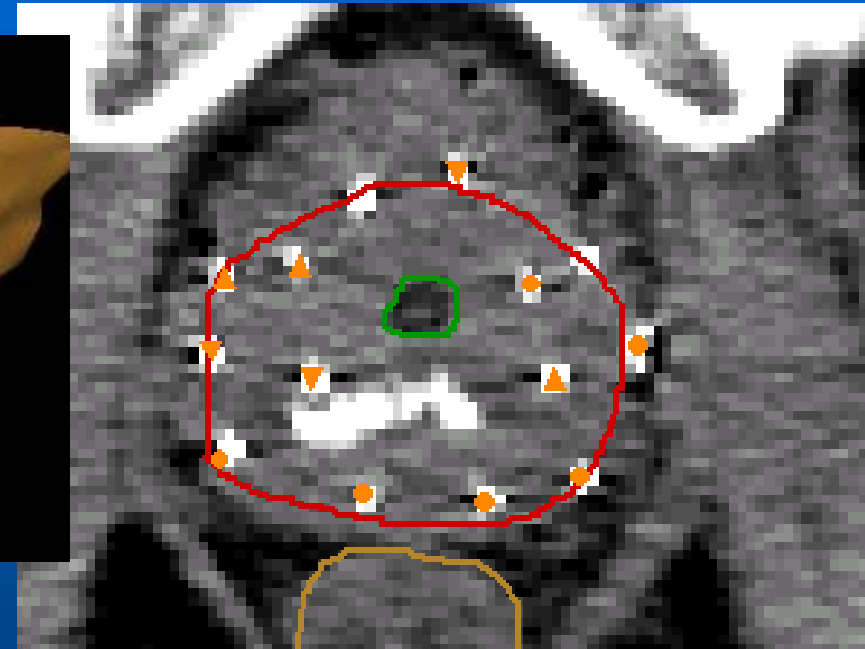


# RESULTS

- Less fluoro time
  - Better coverage of prostate
  - No seed slippage in Anchorseed
  - Lower Rectal dose
- 
- Same incidence of vascular migration

# DAY 0 POST IMPLANT CT

## VARISEED 8.0



Target Dose/Isodose Levels

145.0 Gy Modify...

Level (Gy)	Level (%)	Color
<input checked="" type="checkbox"/> 290.0	200 %	Red
<input checked="" type="checkbox"/> 217.5	150 %	Orange
<input checked="" type="checkbox"/> 145.0	100 %	Cyan
<input checked="" type="checkbox"/> 130.5	90 %	Blue
<input checked="" type="checkbox"/> 116.0	80 %	Purple

# VariSeed: Study Summary Report [Page 1]

Memorial Medical Center - 5/22/2009 11:58:37 AM

Name: [REDACTED] PID: [REDACTED] Dept. ID: [REDACTED]	Study: Post op Day 0 Variation: Default Images: 1d	Source: 1725 (UJ-235) Comment: Sources: TU Anisotropy: Memorial Point Model Source Activity: 0.381 U   0.381 mCi   Total Activity: 34370 U   34.622 mCi
Procedure Date: 5/21/2009	Prescription Dose: 184.0 Gy	Total Activity: 34370 U   34.622 mCi

Study Type: Post-Op

## Dose Information

### Prostate:

Total Volume:	35.57 cc	
V200 %:	8.05 cc	[22.62 %]
V150 %:	18.51 cc	[52.04 %]
V100 %:	33.85 cc	[95.16 %]
V80 %:	34.72 cc	[97.61 %]
D90 %:	181.69 Gy	[111.51 %]
D85 %:	170.78 Gy	[117.78 %]

### Urethra:

Total Volume:	0.80 cc	
V200 %:	0.00 cc	[0.00 %]
D30 %:	187.86 Gy	[115.77 %]
D5 %:	178.49 Gy	[123.10 %]

### Rectum:

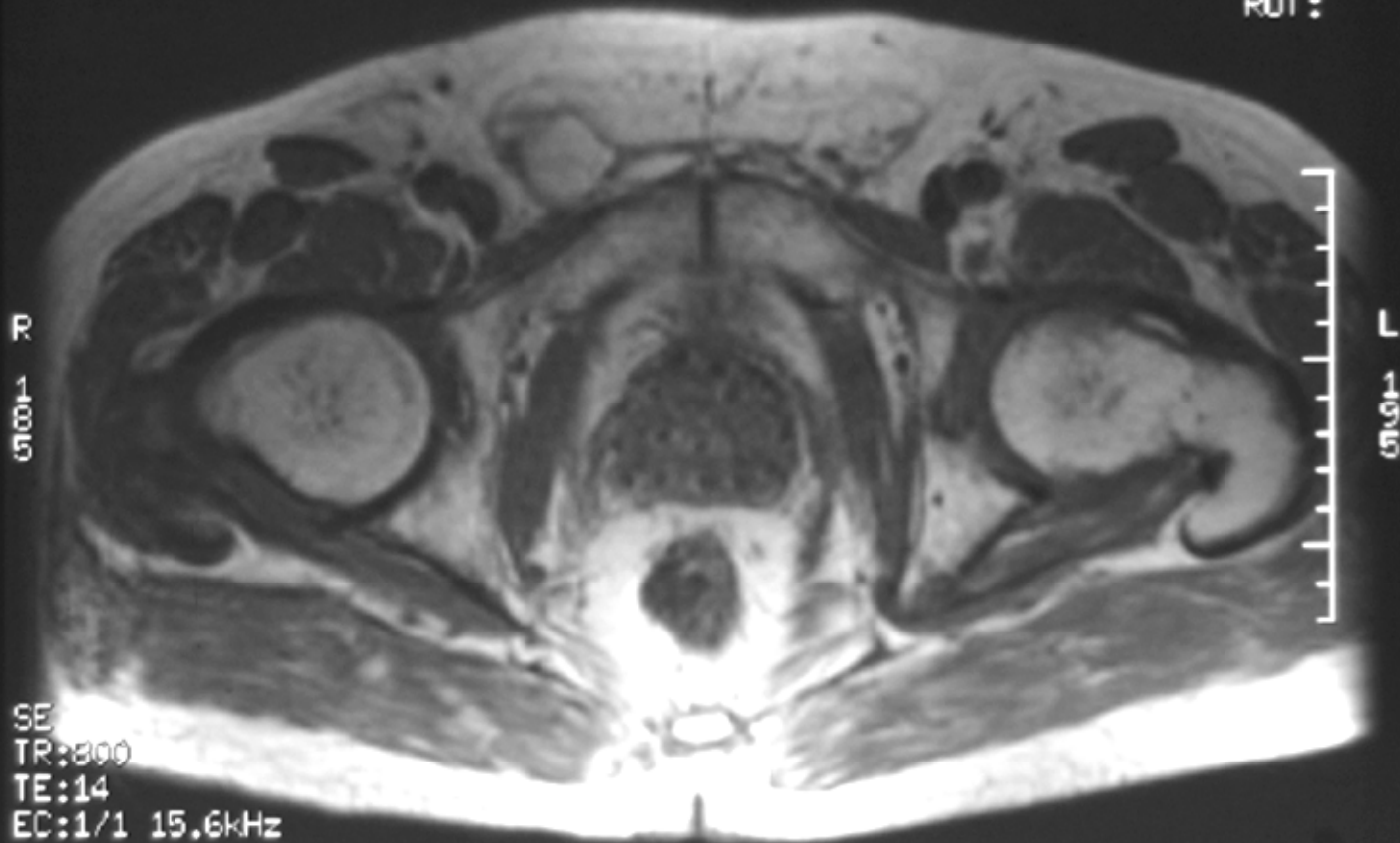
Total Volume:	39.11 cc	
V100 %:	0.00 cc	[0.00 %]
D30 %:	24.17 Gy	[16.67 %]
D5 %:	61.58 Gy	[42.47 %]



Signa 1.5T SYS#GEMS1234  
Ex: 17913  
Se: 8  
In: 11  
Ax: I29.4

A 194

01:27:35 PM  
Mag = 1.0  
FL:  
ROT:

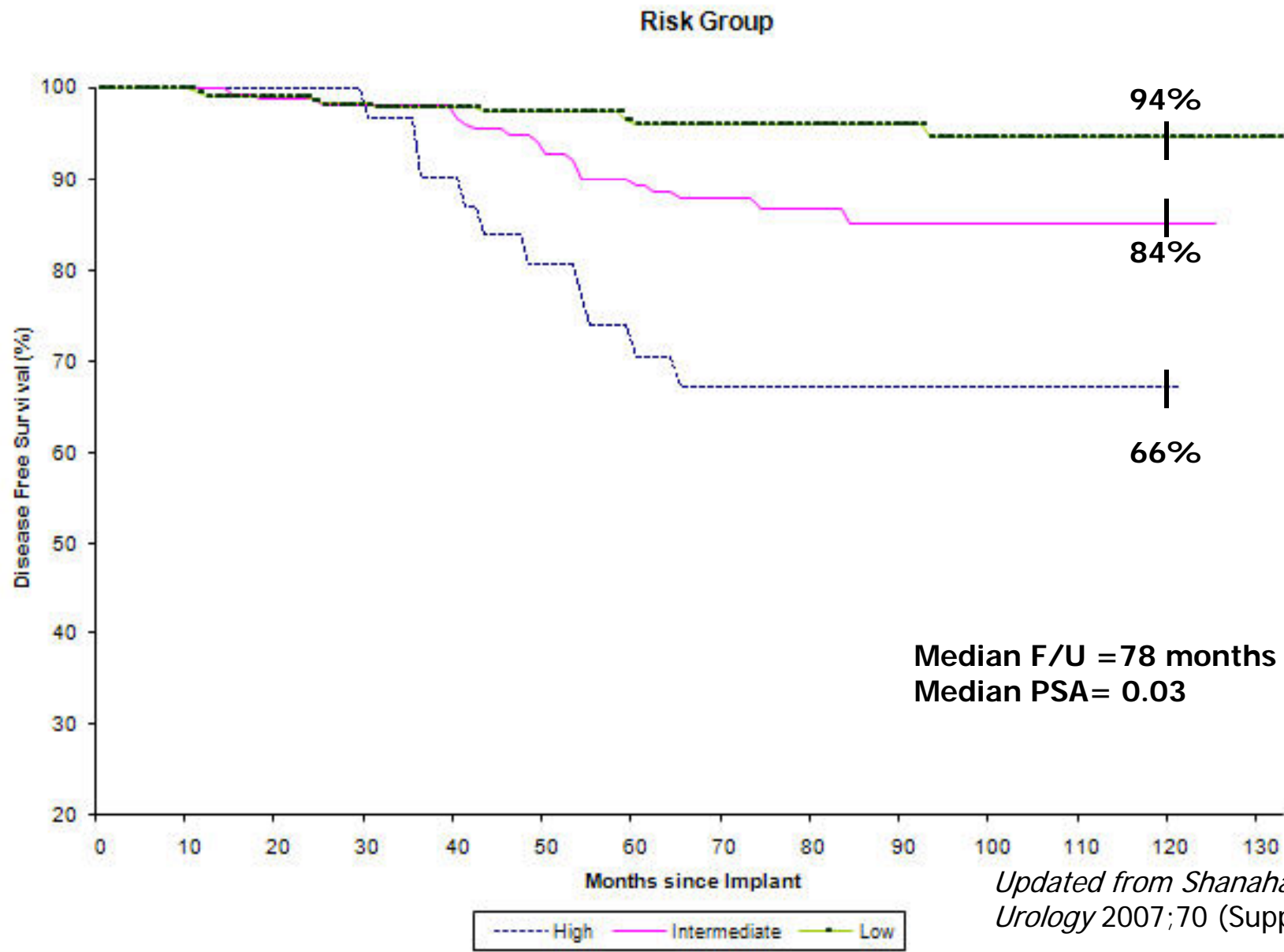


SE  
TR:800  
TE:14  
EC:1/1 15.6kHz

TORSO  
FOV:38x38  
5.0thk/1.0sp  
26/03:47  
256X256/1.00 NEX  
St:SI/NP/VB

P 186

W = 1230 L = 546



Median F/U = 78 months  
 Median PSA = 0.03

*Updated from Shanahan et al.  
 Urology 2007;70 (Suppl 3A):1*

