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# Comparing Long Term Treatment Results Of PROSTATE CANCER

## Prostate Cancer Results Study Group 2012



Peter Grimm, DO  
Prostate Cancer Center of Seattle

# Overview



- Long Term Comparative Results of All Treatments
- Why Different Treatments have Predictably Different Outcomes

# Prostate Cancer Results Study Group



- **Problem:** Patients and physicians need a simple means to compare prostate cancer control rates .
- **Since a randomized study is unlikely, we need a surrogate means to compare results**

# Prostate Cancer Results Study Group



- An assembled group of experts from key treating disciplines: Surgery, External Radiation, Internal (or Brachytherapy), High Frequency Ultrasound, and Proton Therapy
- The purpose of this work is to do a complete and ongoing review of the current literature on prostate cancer treatment

# Prostate Cancer Results Study Group

- Ignace Billiet, MD F.E.B.U., Urologist Kortrijk, Belgium
- David Bostwick, MD Bostwick Laboratories
- David Crawford, MD Univ Colorado, Denver
- Adam Dicker, MD Thomas Jefferson U Philadelphia, PA
- Steven Frank, MD MD Andersen, Houston Texas
- Peter Grimm, DO Prostate Cancer Center of Seattle
- Jos Immerzeel, MD De Prostaat Kliniek Netherlands
- Stephen Langley, MD St Luke's Cancer Centre, Guildford England
- Alvaro Martinez, MD William Beaumont , Royal Oak, MI
- Mira Keyes, MD BC Cancer Agency , Vancouver Canada
- Patrick Kupelian, MD UCLA Med Center Los Angeles
- Robert Lee , MD Duke University Medical Center
- Stefan Machtens, MD University Bergisch, Gladbach Germany
- Jyoti Mayadev, UC Davis Davis , California
- Brian Moran, MD Chicago Prostate Institute Chicago

# Prostate Cancer Results Study Group

- Gregory Merrick, MD Schiffler Cancer Center Wheeling West Virginia
- Jeremy Millar, MD Alfred Health and Monash University, Melbourne Australia
- Mack Roach, MD UCSF San Francisco California
- Richard Stock, MD Mt. Sinai New York
- Katsuto Shinohara, MD UCSF San Francisco California
- Mark Scholz, MD Prostate Cancer Research Institute Marina del Ray California
- Edward Weber, MD Prostate Cancer Center of Seattle
- Anthony Zietman, MD Harvard Joint Center Boston Ma
- Michael Zelefsky, MD Memorial Sloan Kettering New York
- Jason Wong, MD UC Irvine Irvine California
- Stacy Wentworth, MD Piedmont Radiation Oncology Greensboro , NC
- Robyn Vera, DO Medical College of Virginia Richmond Virginia

# ABOUT THIS REVIEW STUDY



- **18,000+ prostate studies were published between 2000 and 2010**
- **848 of those studies featured treatment results**
- **140 of those met the criteria to be included in this review study.**

# Criteria for Inclusion of Article\*



- 1. Patients should be separated into Low, Intermediate, and High Risk**
- 2. Success must be determined by PSA analysis**
- 3. All Treatment types considered: Seeds (Brachy), Surgery (Standard or Robotic), IMRT (Intensity Modulated Radiation), HIFU (High Frequency Ultrasound), CRYO (Cryo Therapy), Protons, HDR (High dose Rate Brachytherapy)**
- 4. Article must be in a Peer Reviewed Journal**

\* Expert panel consensus



# Criteria for Inclusion of Article (cont.)

- 5. Low Risk articles must have a minimum of 100 patients**
- 6. Intermediate Risk articles must have a minimum of 100 patients**
- 7. High Risk articles, because of fewer patients, need only 50 patients to meet criteria**
- 8. Patients must have been followed for a median of 5 years**

For additional criteria information contact: [lisa@prostatecancertc.com](mailto:lisa@prostatecancertc.com)

# % Articles Meeting Criteria



RP	EBRT/ IMRT	Cryo	Brachy	Robot RP	Proton	HIFU
9%	18 %	16%	31%	5%	15%	3%
24/260	39/222	5/31	66/213	3/59	2/13	1/30

Total of 848 Treatment Articles. Some articles addressed several treatments and were counted as separate articles for each treatment.

# LOW Risk Group Definition



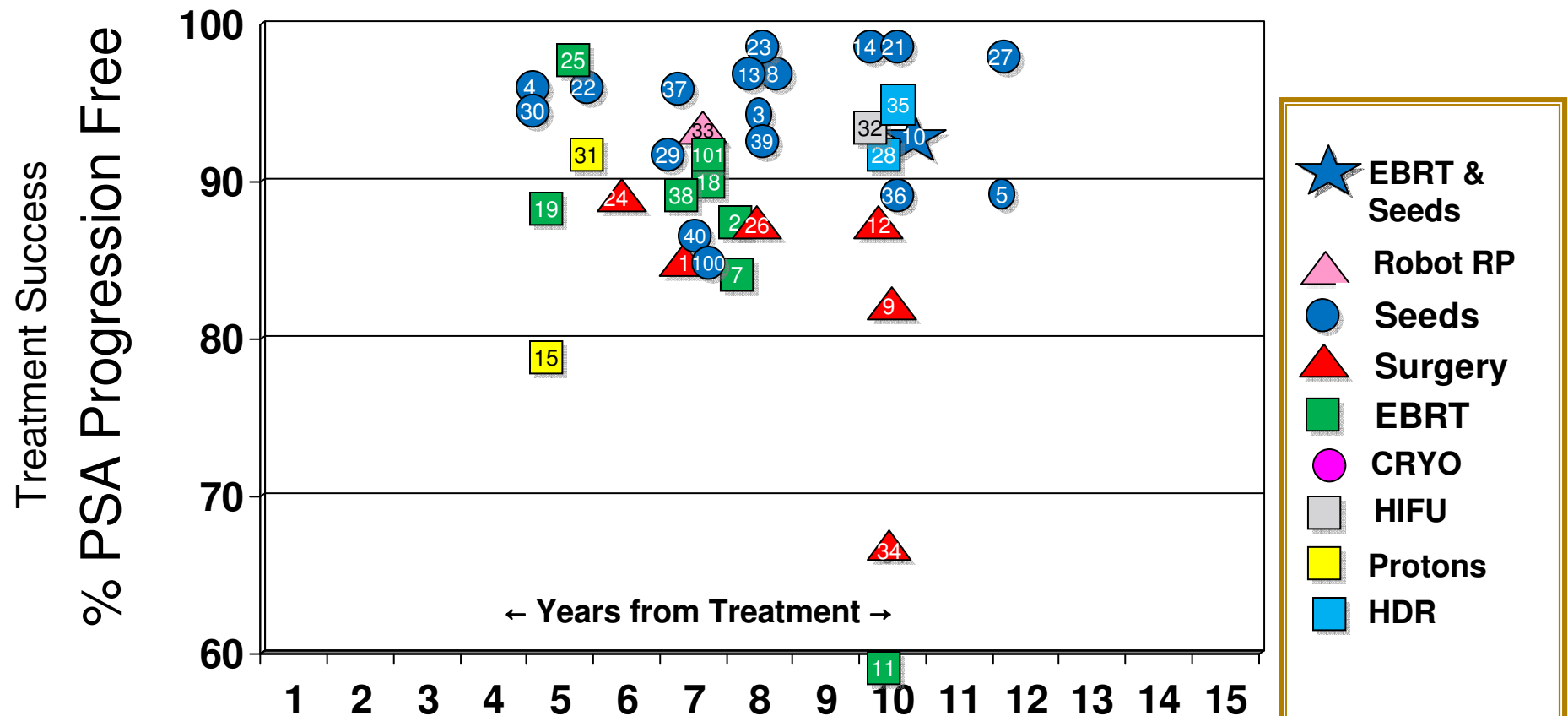
## Low Risk

Stage: T1 or T2a,b

Gleason Sum  $\leq 6$

PSA  $\leq 10$  ng/ml

# LOW RISK RESULTS



- Prostate Cancer Results Study Group
- Numbers within symbols refer to references

4/11/2012

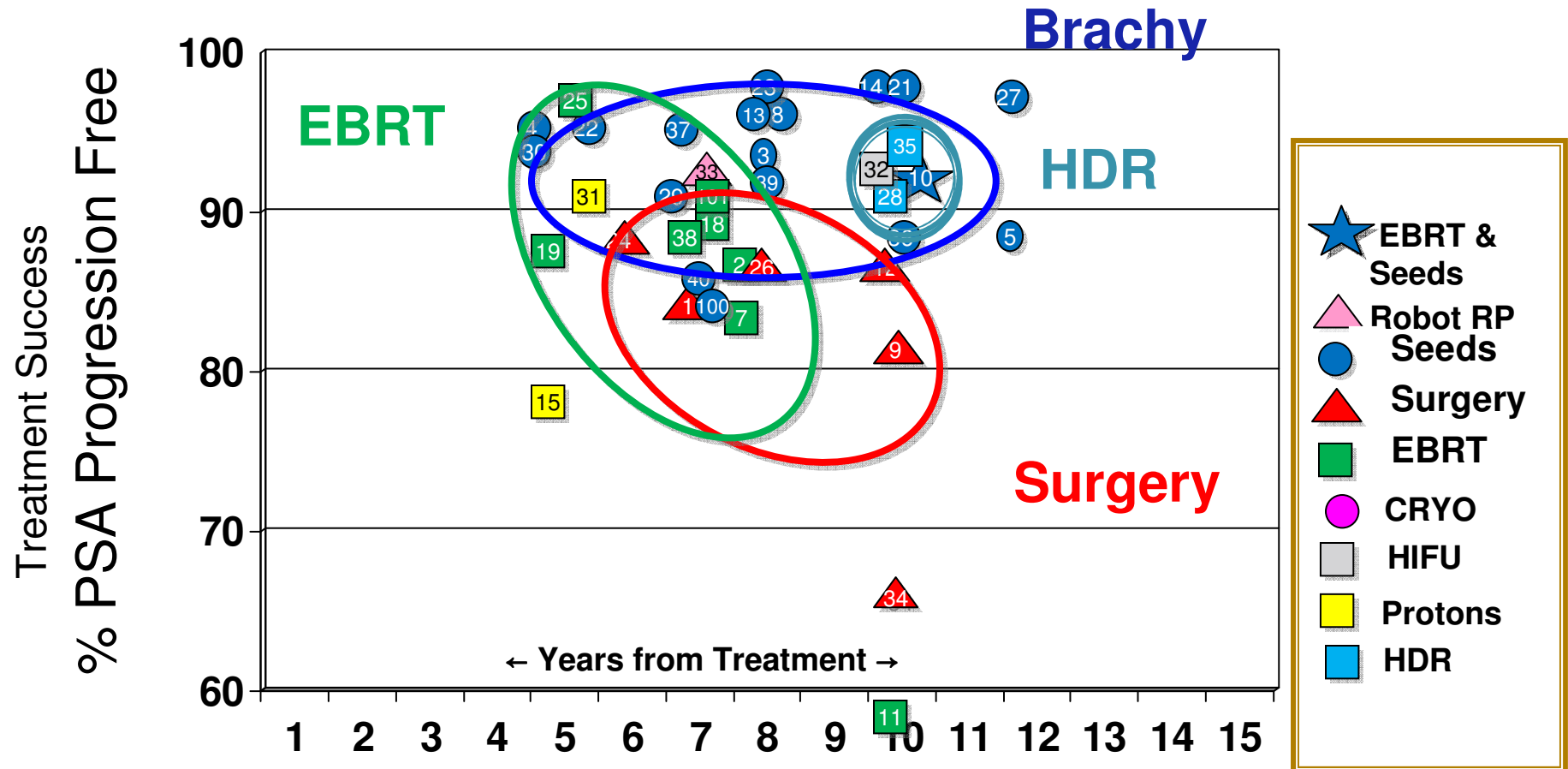
BJU Int, 2012, Vol. 109(Supp. 1)  
 22-29

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# LOW RISK RESULTS

Weighted



- Prostate Cancer Results Study Group
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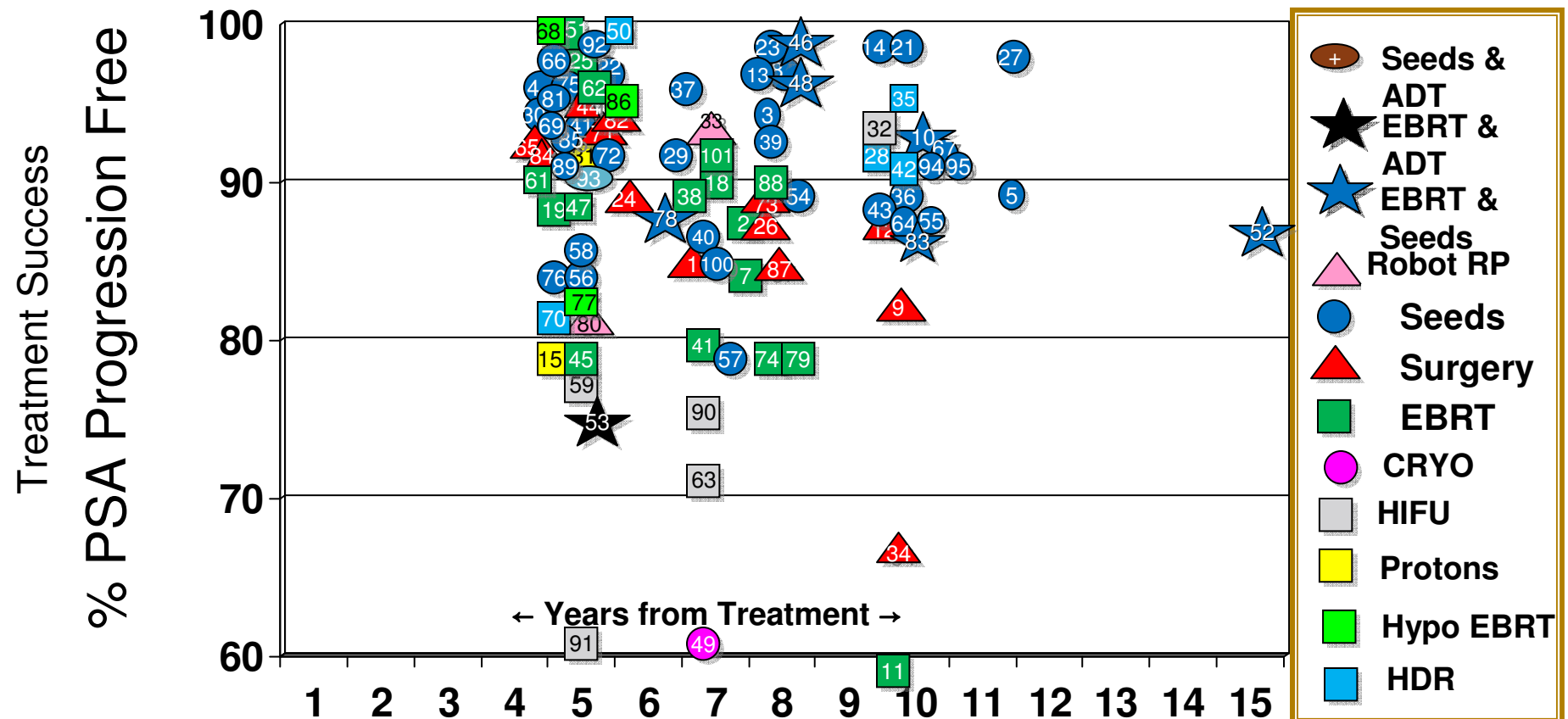
# Question about the Criteria



- “The PCRSF criteria is pretty strict and not a lot of studies fit. What happens if you include articles with only 40 months of follow up or have a long follow up but less than 100 patients?”

# LOW RISK RESULTS

>40 months follow-up or less than 100 patients

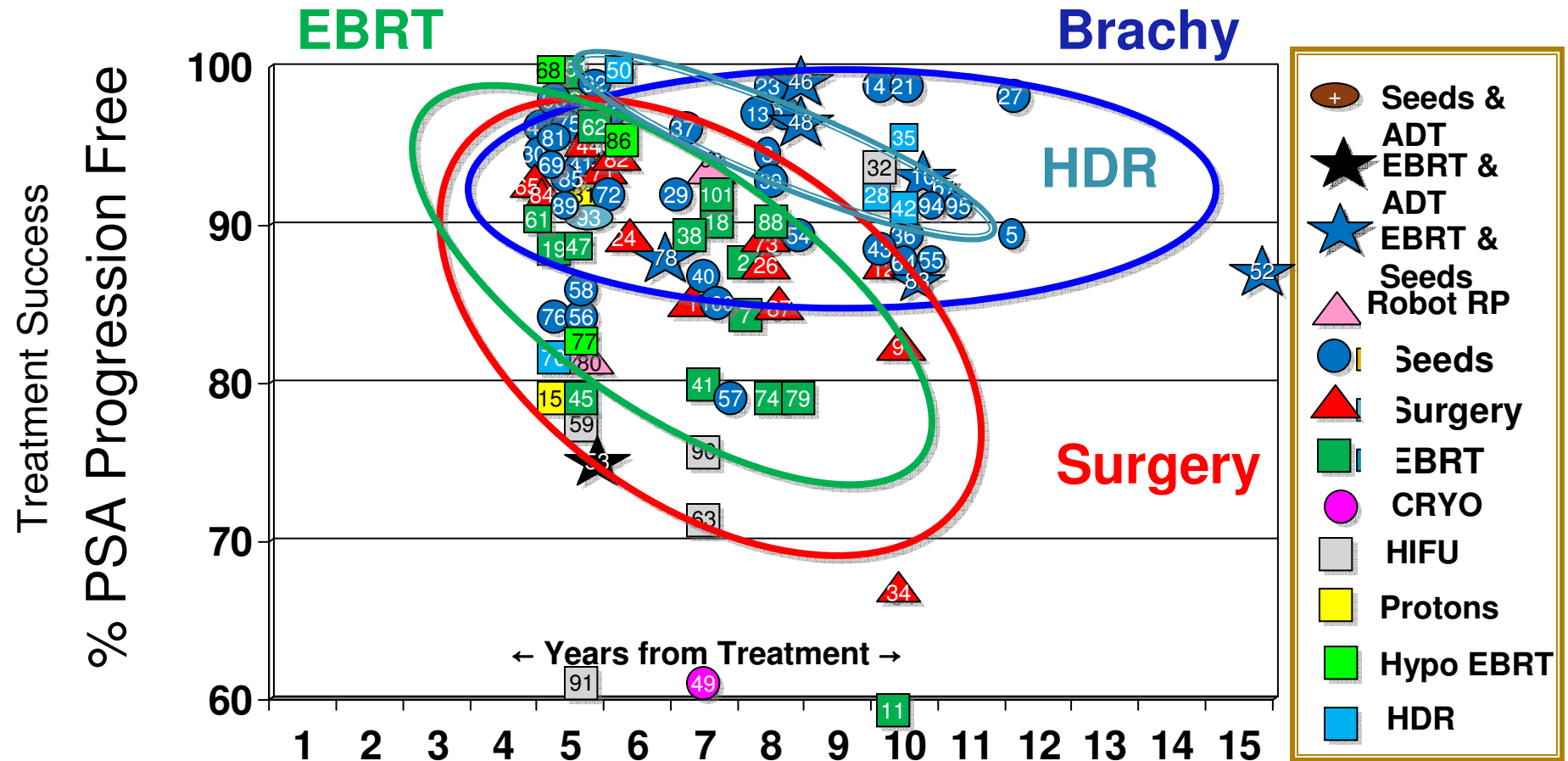


- Prostate Cancer Results Study Group
- Numbers within symbols refer to references

# LOW RISK RESULTS

>40 months follow-up or less than 100 patients

Weighted



- Prostate Cancer Results Study Group
- Numbers within symbols refer to references

4/11/2012

BJU Int, 2012, Vol. 109(Supp 1)22-29

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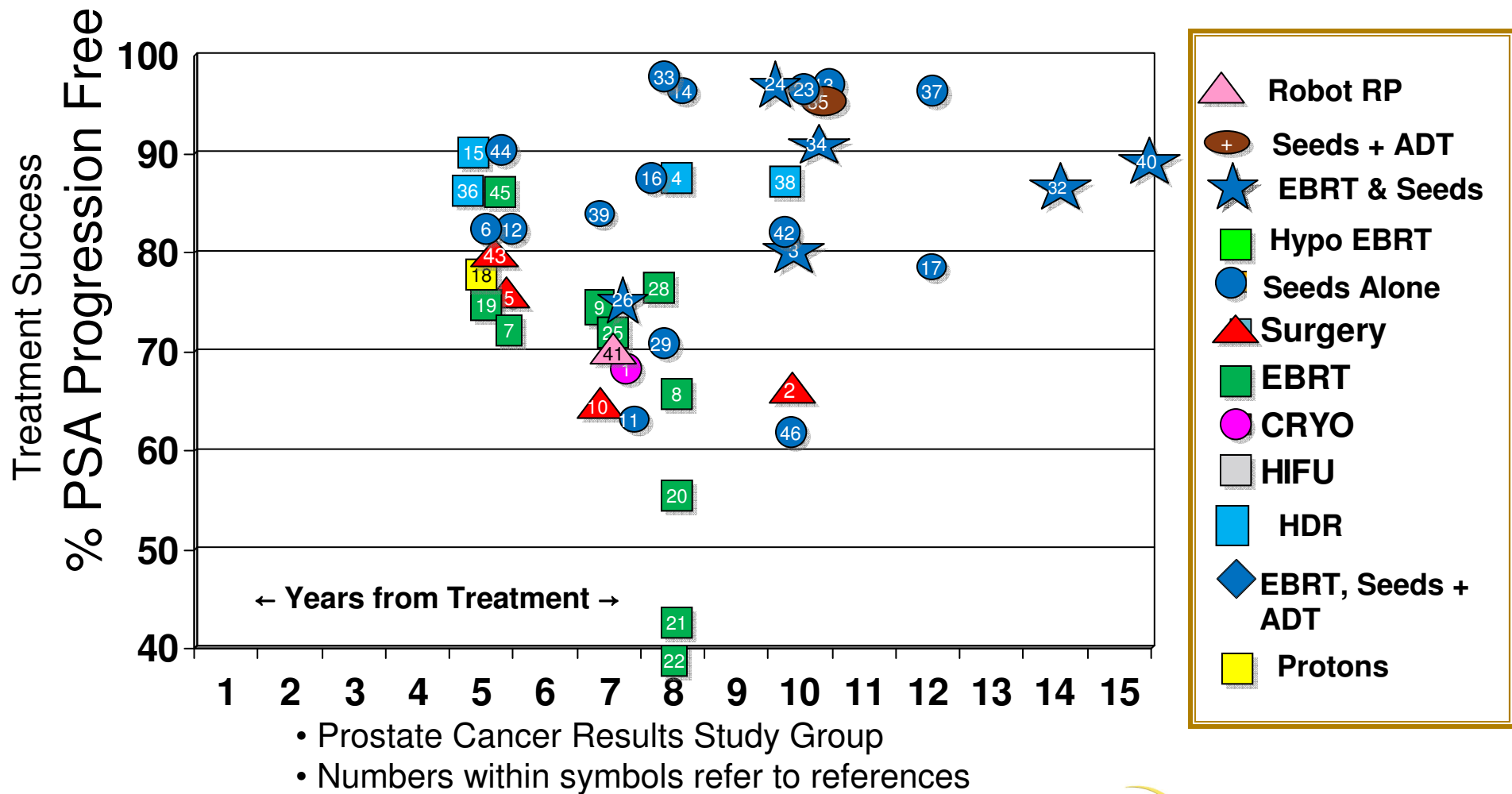
studymanager™ 16



# Intermediate Risk Patient Definition

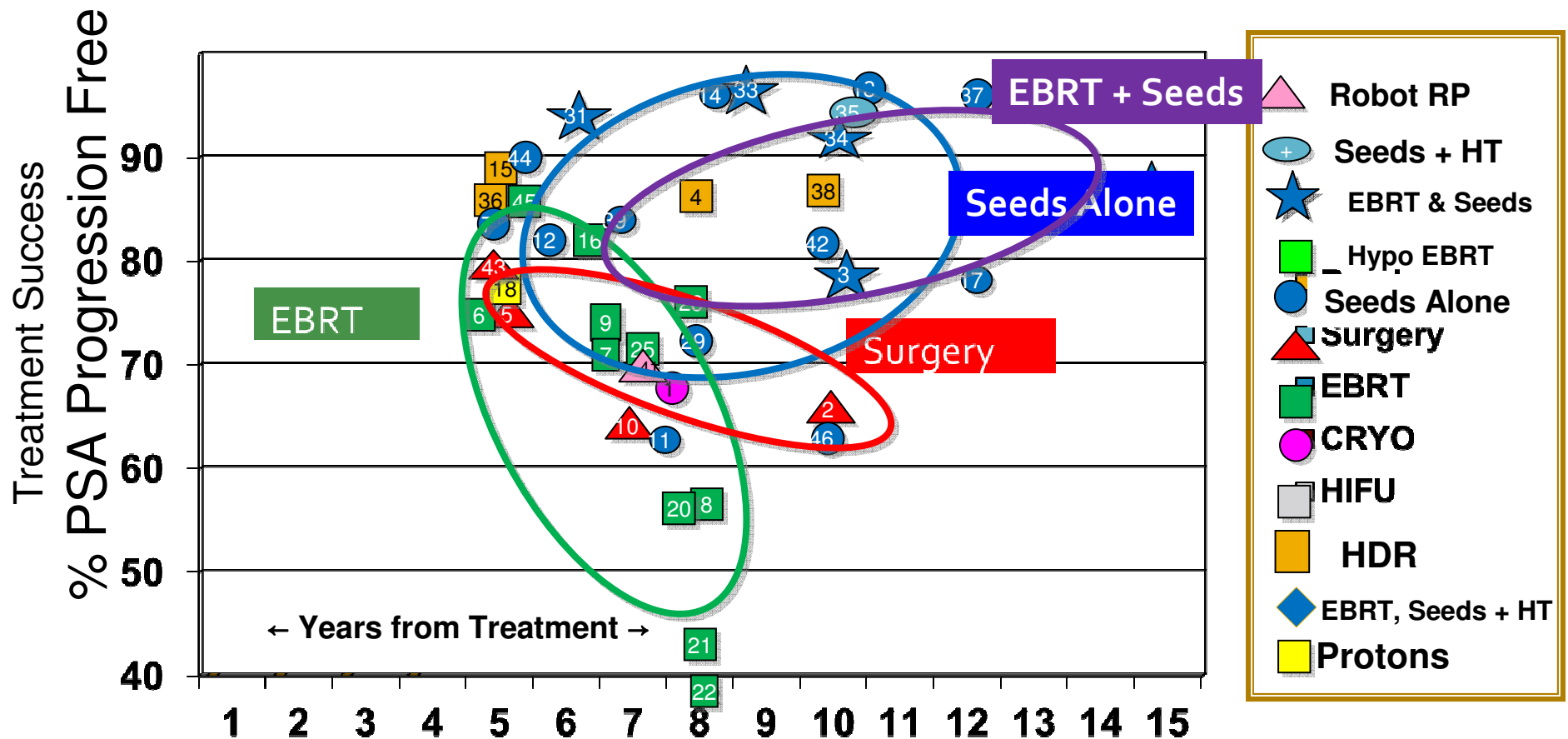
- Zelefsky definition
  - Only 1 factor
    - Clinical Stage T2c
    - Gleason score  $\geq 7$
    - PSA  $> 10$  ng/ml
- D'Amico definition
  - PSA 10-20 Gleason Score 7 or Stage T2b

# INTERMEDIATE RISK RESULTS



# INTERMEDIATE RISK Grouping

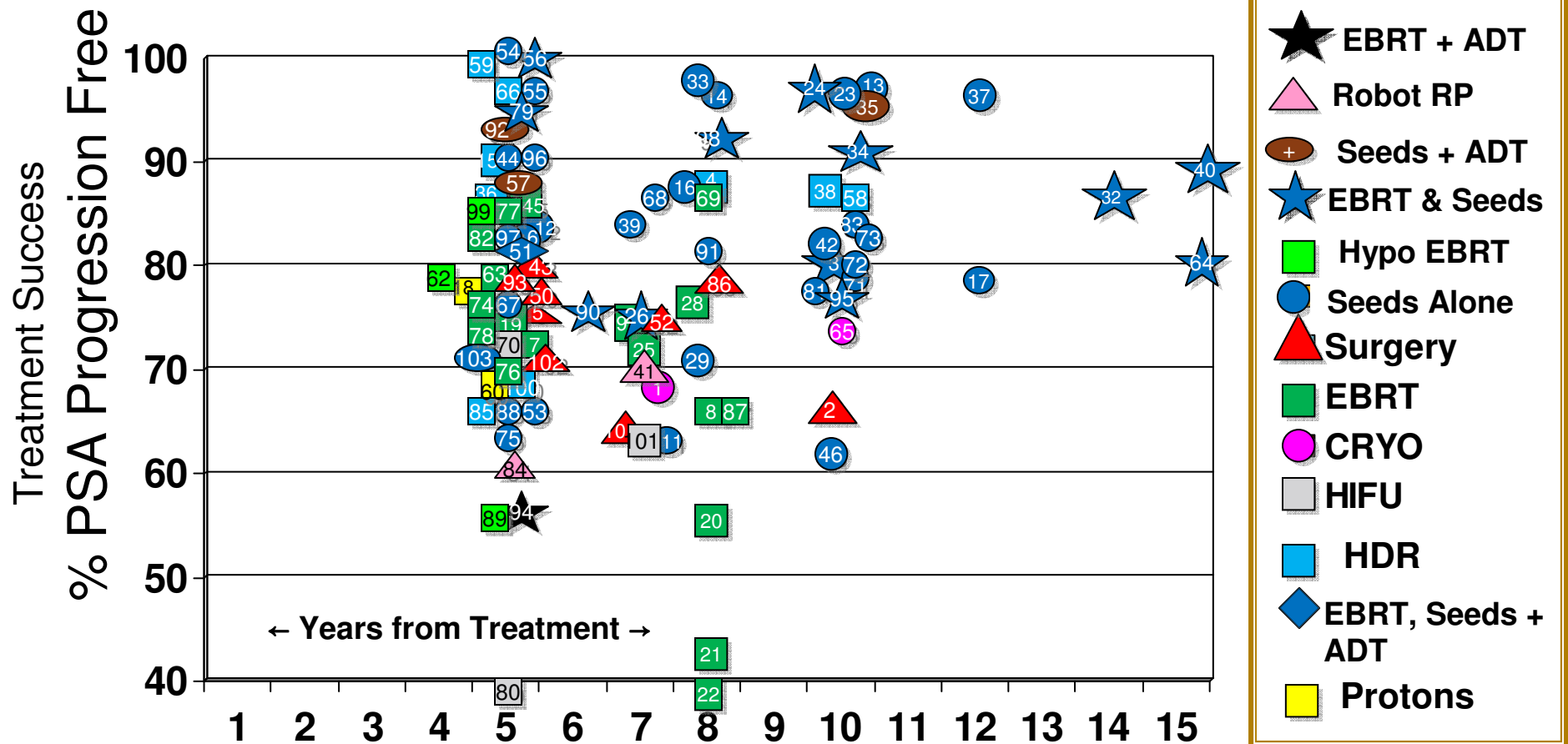
weighted



- Prostate Cancer Results Study Group
- Numbers within symbols refer to references

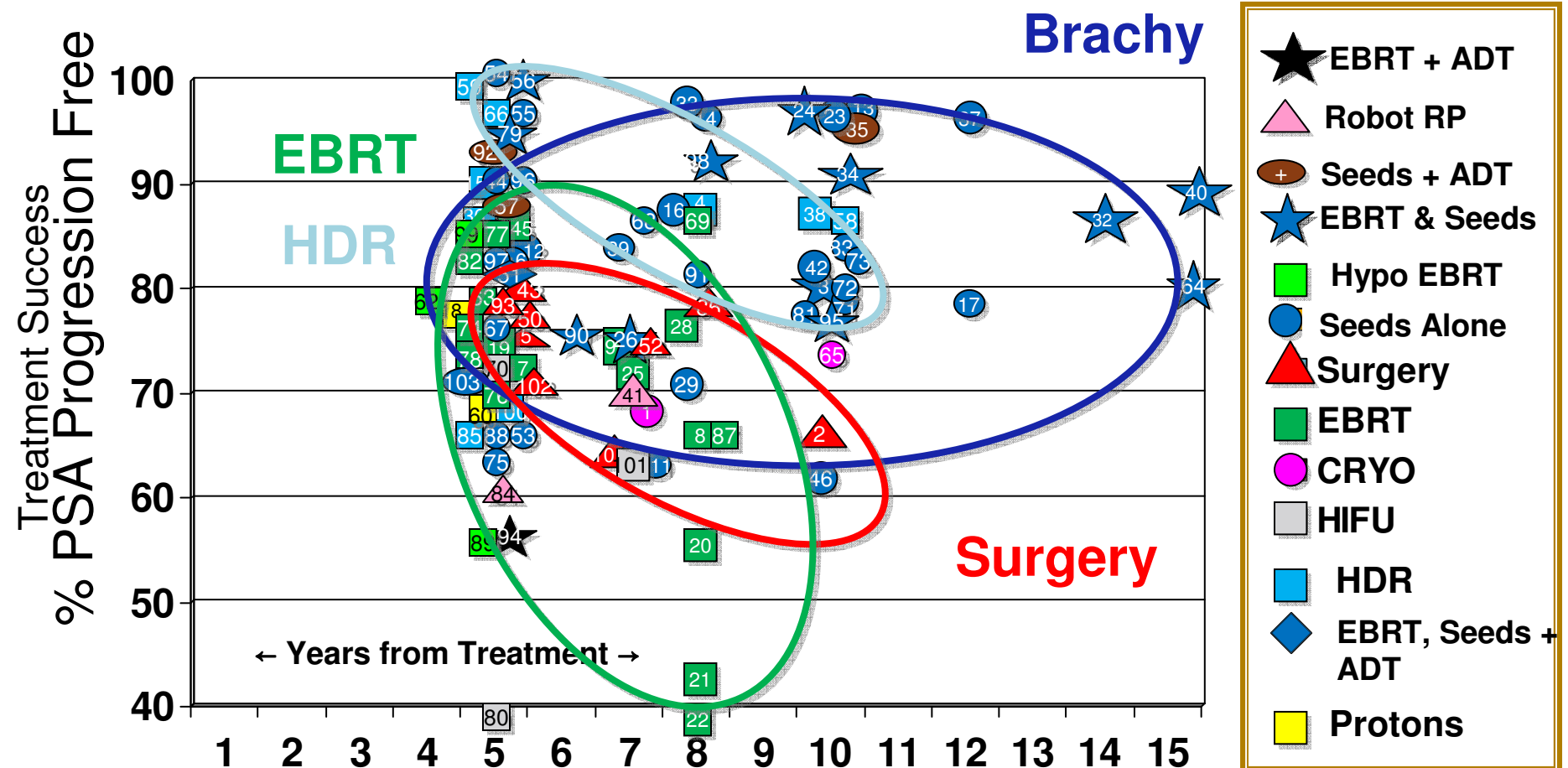
# INTERMEDIATE RISK RESULTS

>40 months follow-up or less than 100 patients



# INTERMEDIATE RISK RESULTS weighted

>40 months follow-up or less than 100 patients



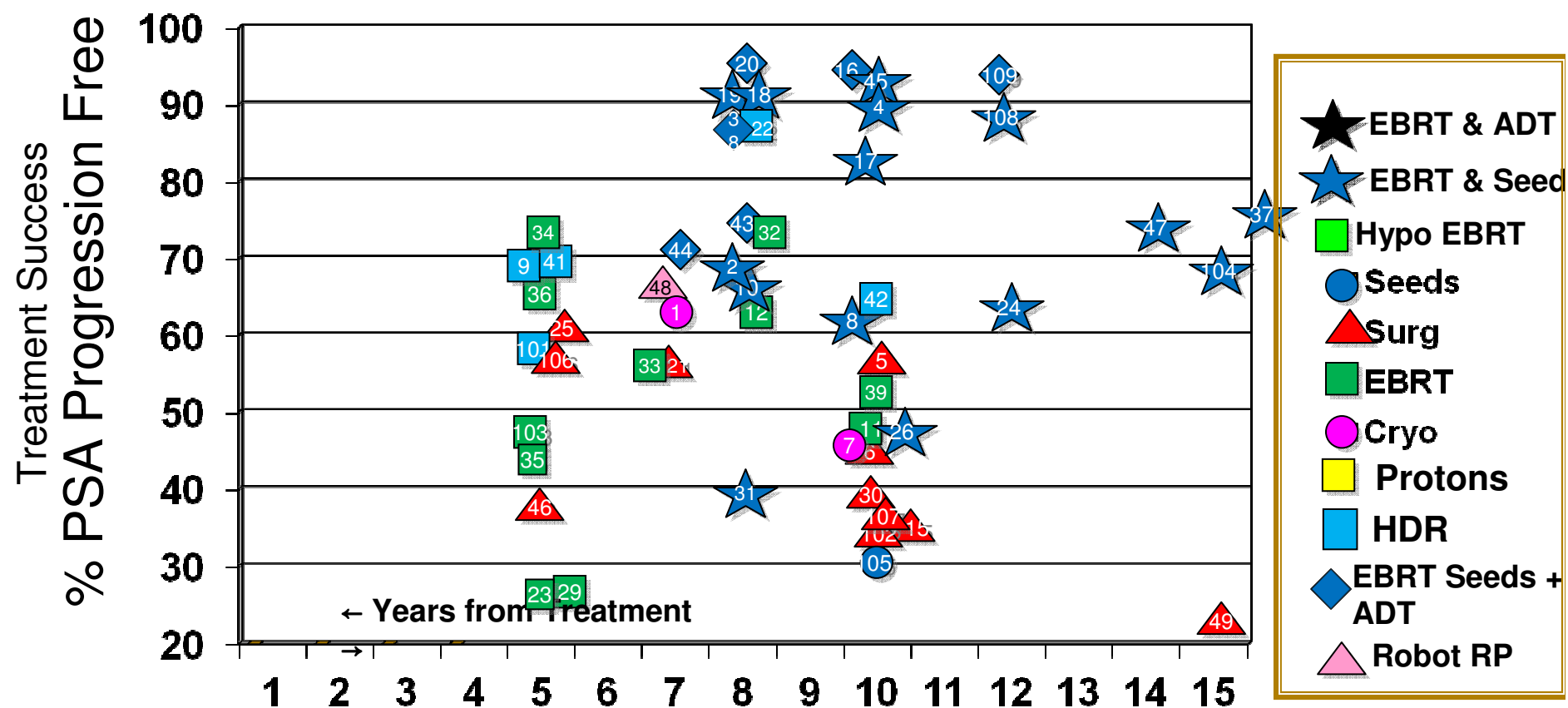
- Prostate Cancer Results Study Group
- Numbers within symbols refer to references

# High Risk Patient Definition



- Zelefsky definition
  - 2 or more factors
    - Gleason > 7
    - PSA 10-20 Clinical Stage T1c- T2b
- D'Amico
  - Gleason Score 8-10
  - PSA >20

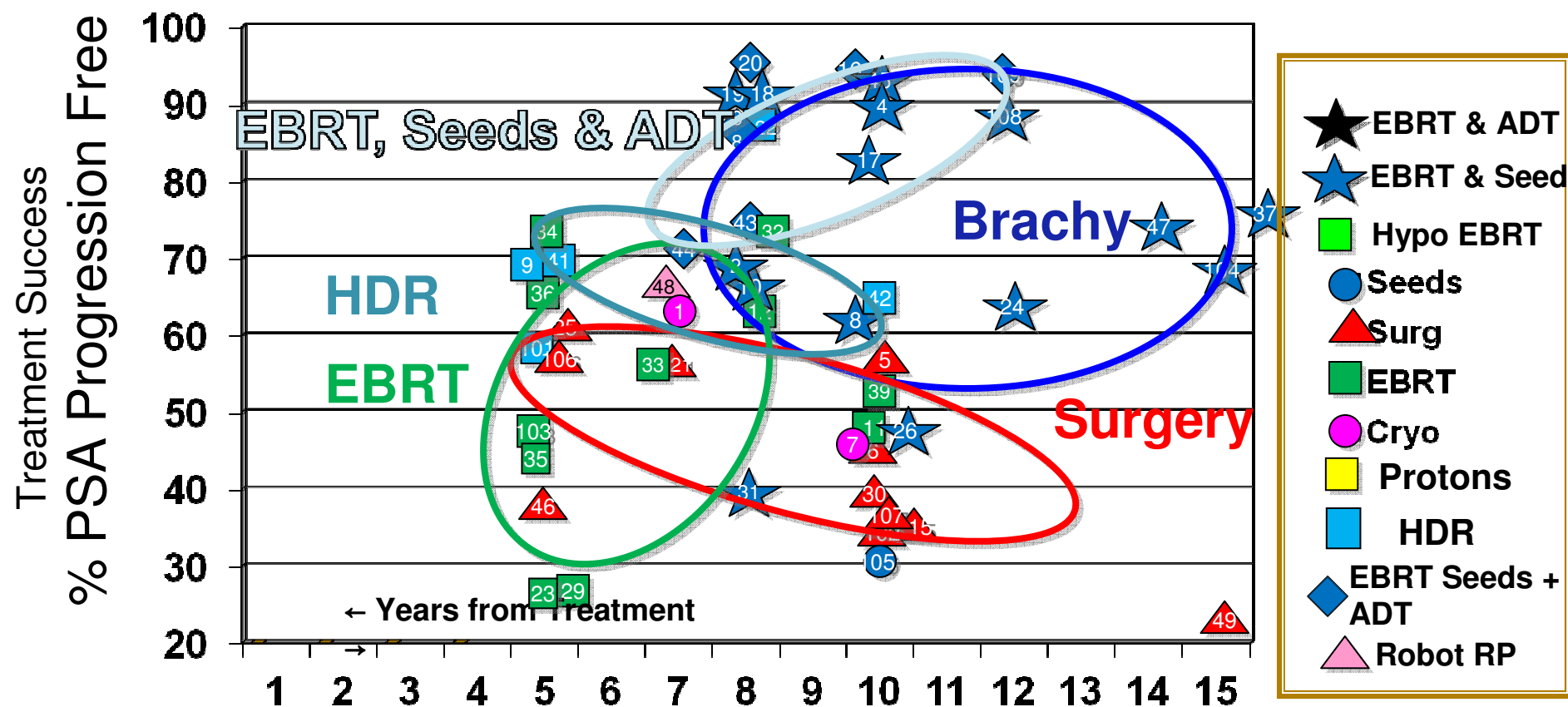
# HIGH RISK RESULTS



- Prostate Cancer Results Study Group
- Numbers within symbols refer to references

# HIGH RISK RESULTS

Weighted

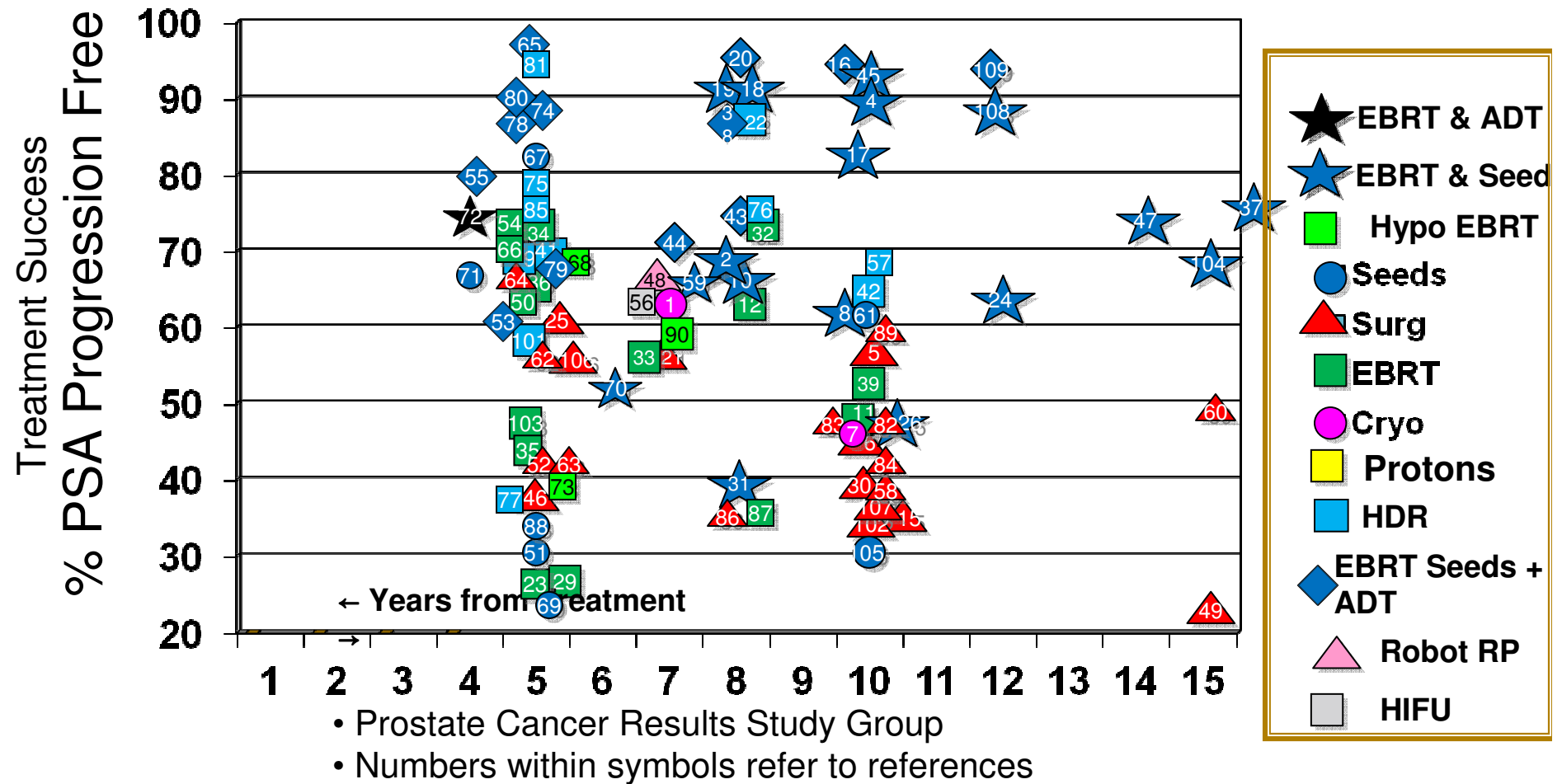


- Prostate Cancer Results Study Group
- Numbers within symbols refer to references



# HIGH RISK RESULTS

>40 months follow-up or less than 100 patients

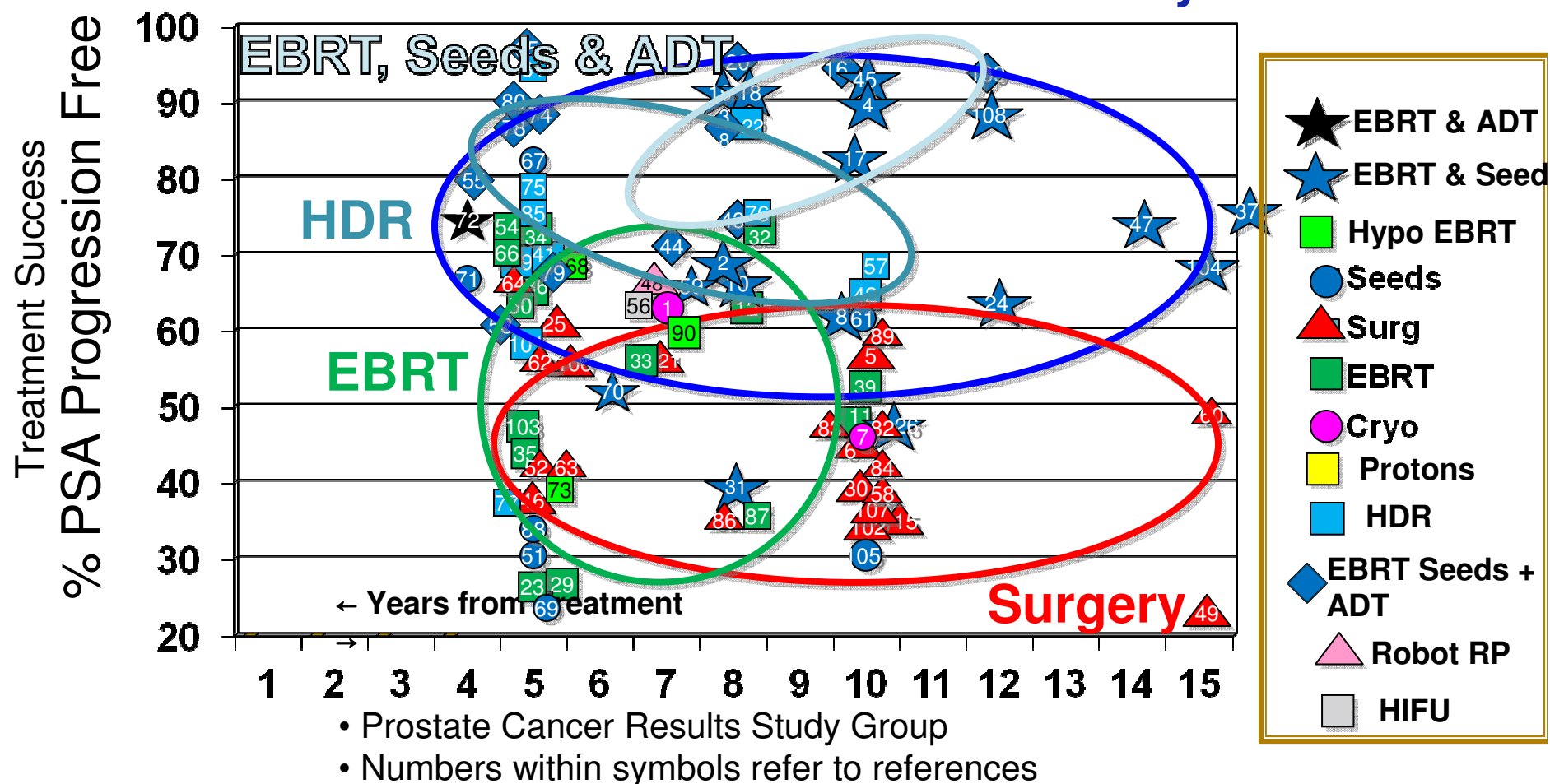


# HIGH RISK RESULTS

>40 months follow-up or less than 100 patients

Weighted

Brachy



# OBSERVATIONS



- For most low risk patients, most therapies will be successful.
- There appears to be a higher cancer control success rate for Brachy over EBRT and Surgery for all groups. Patients are encouraged to look at graphs and determine for themselves
- Serious side effect rates must be considered for any treatment
- Relaxing the report selection criteria doesn't seem to impact the results substantially

# **Why Different Treatments Have Predictably Different Outcomes**

# Cancer Control



- Three factors determine outcome in Prostate cancer
  - **1. Local Disease Control**
  - **2. Extracapsular disease (ECE)**
  - **3. Distant Disease**

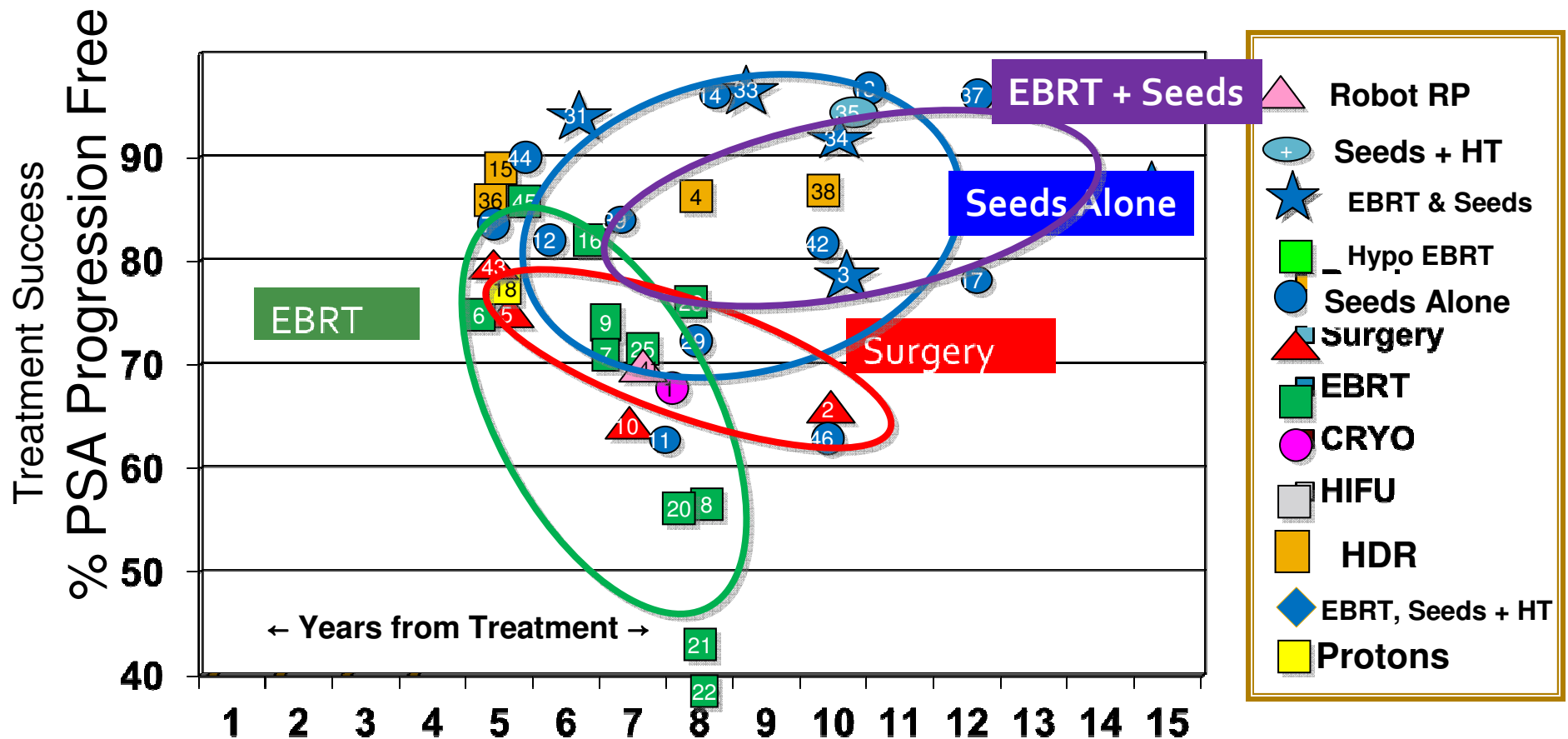
# Local Disease Control



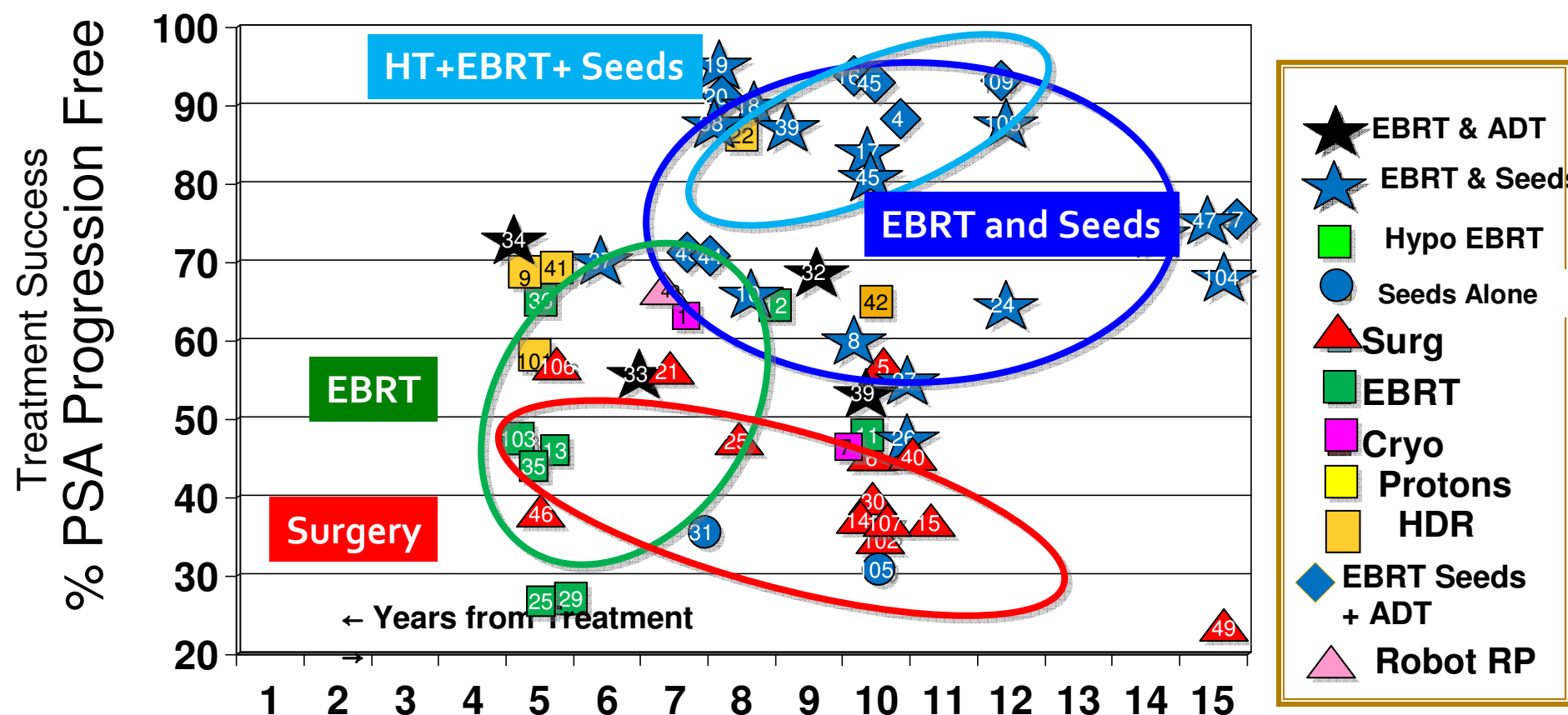
- **Radical Prostatectomy**
  - Removes prostate Excellent Local Control
- **EBRT- IMRT/Protons/ Cyberknife**
  - Enough dose to control disease?
- **Brachytherapy Seeds/ HDR**
  - Higher dose = Better Local Disease Control?

# INTERMEDIATE RISK Grouping

weighted



- Prostate Cancer Results Study Group
- Numbers within symbols refer to references



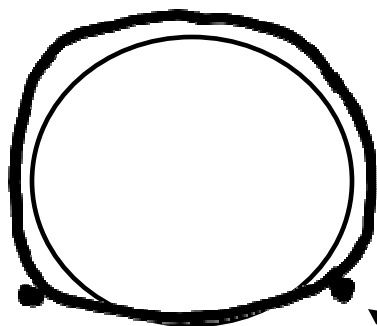
- Prostate Cancer Results Study Group
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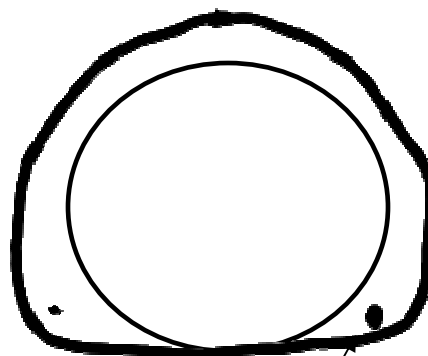
# Target Volumes



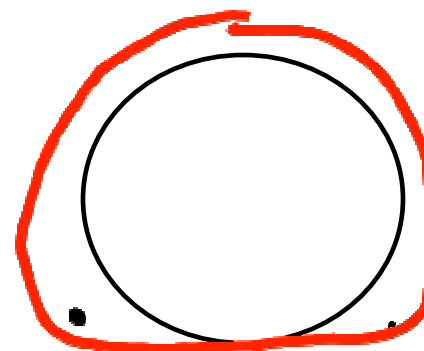
**Robot  
Surgery**



**IMRT**



**Seeds**



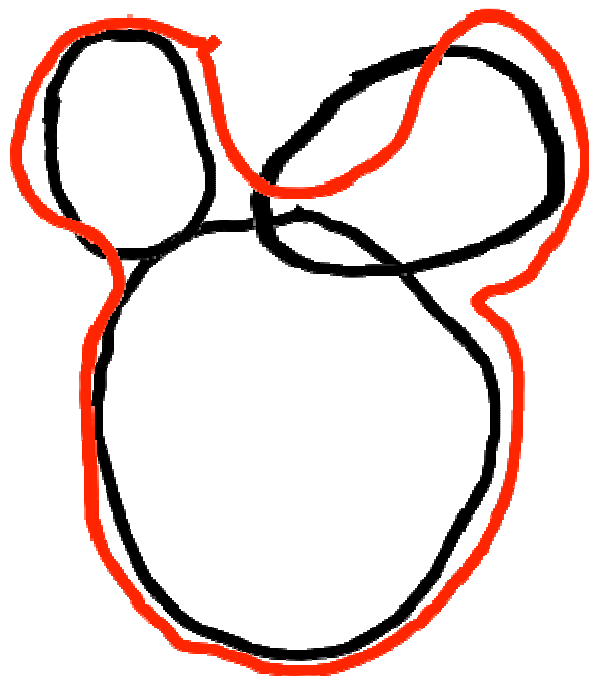
**Nerve**



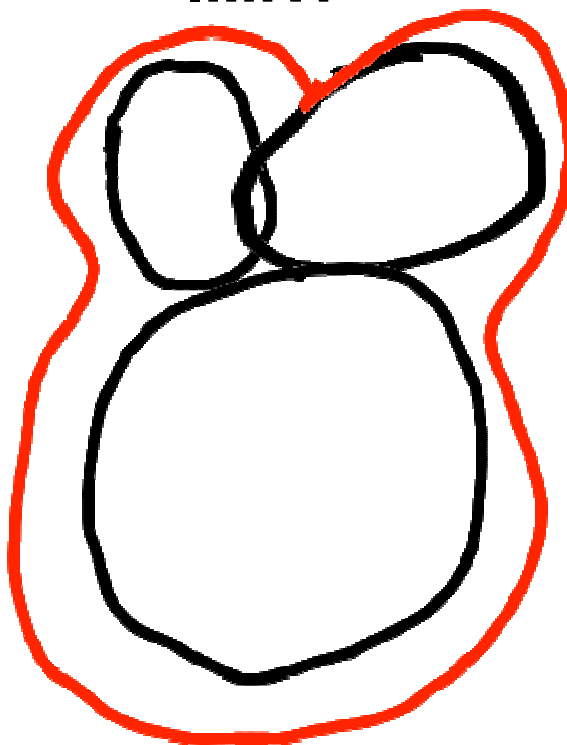
# Target Volumes



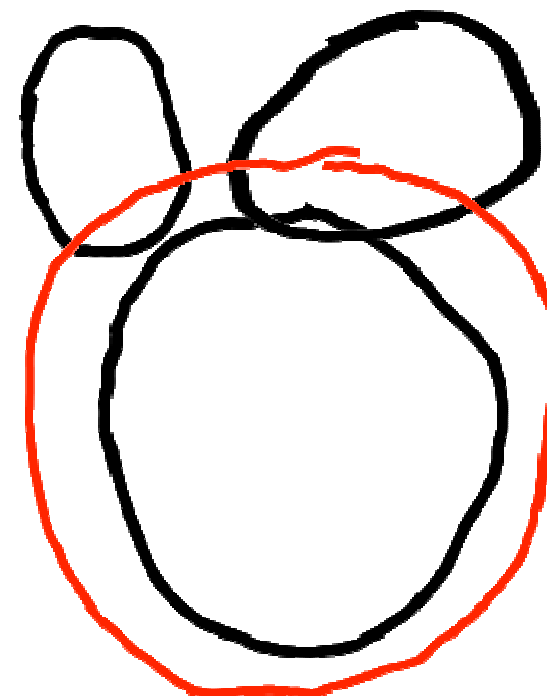
Surgery



IMRT



Seeds



# Local Disease Control Surgery



- Robotic surgery new standard of care
  - Effective in removing prostate
  - Reduces hospital stay
- **But**, No evidence to date that RRP has improved the cancer control rates over traditional RP
- 90% of robotic surgeries in US are nerve sparing
- Most failures are local <sup>1</sup>

1. Swanson, G, (SWOG 8794) Predominant Treatment failure after RP Patients is local J Clin Oncol 2007;25: 2225-2229

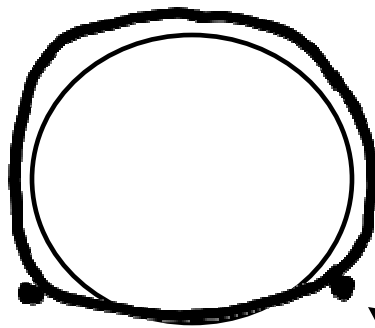


# Local Control IMRT

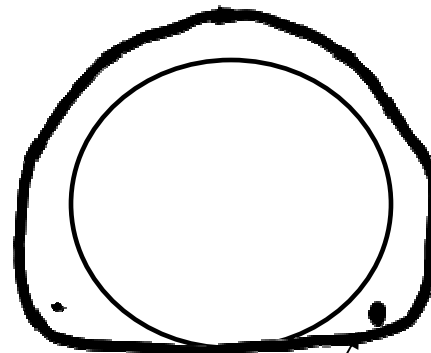
# Target Volumes



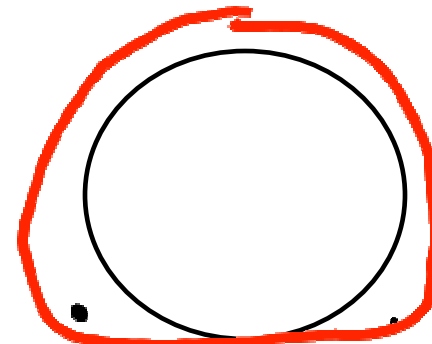
**Surgery**



**IMRT**



**Seeds**



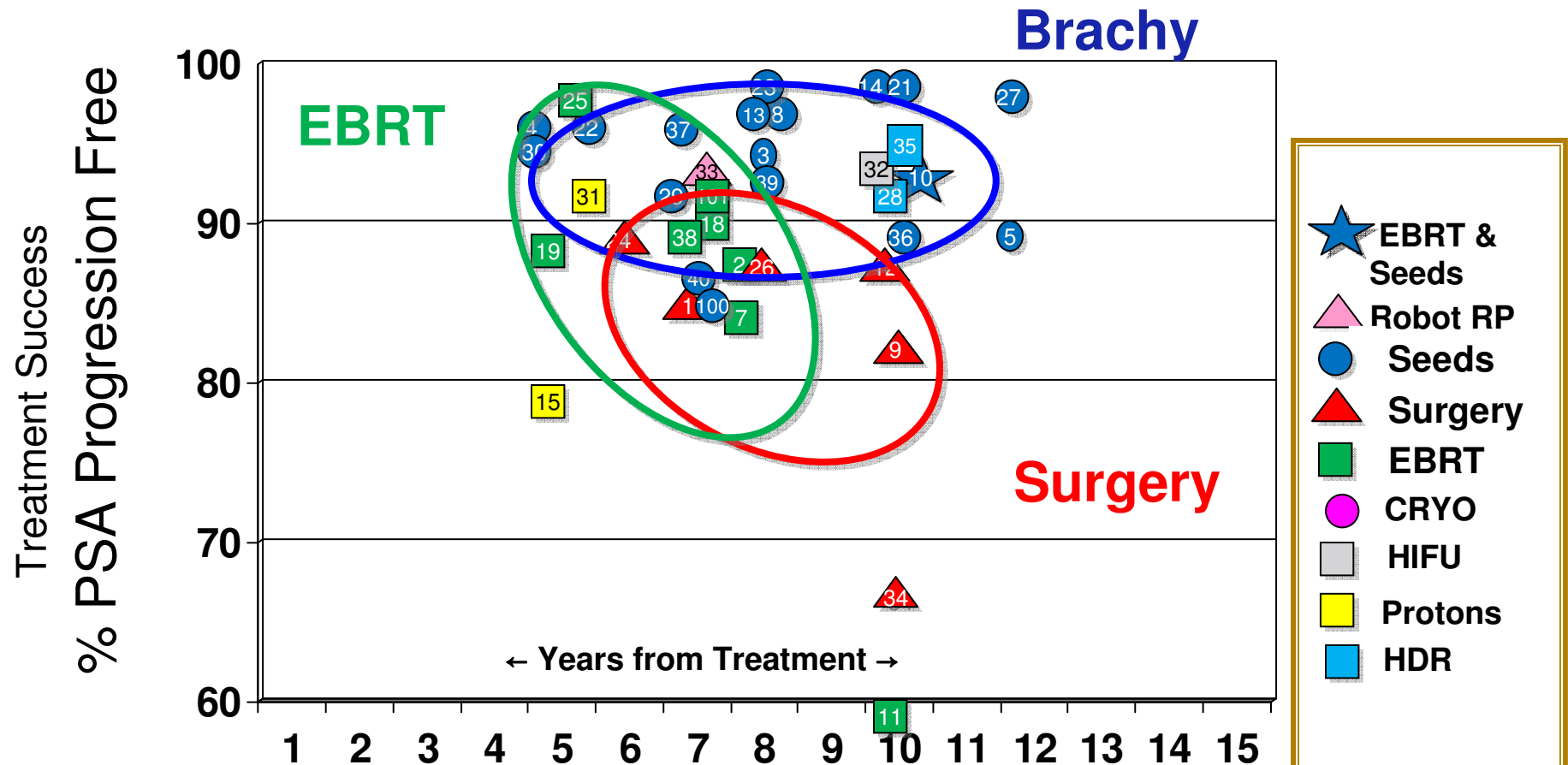
**Nerve**

**Why IMRT Fail? Dose @75Gy >2yr +Bx rate 51%**

\*Nichol et al (Prin Margaret) Radiotherapy and Oncology 76;11-17,2005

# LOW RISK RESULTS

Weighted



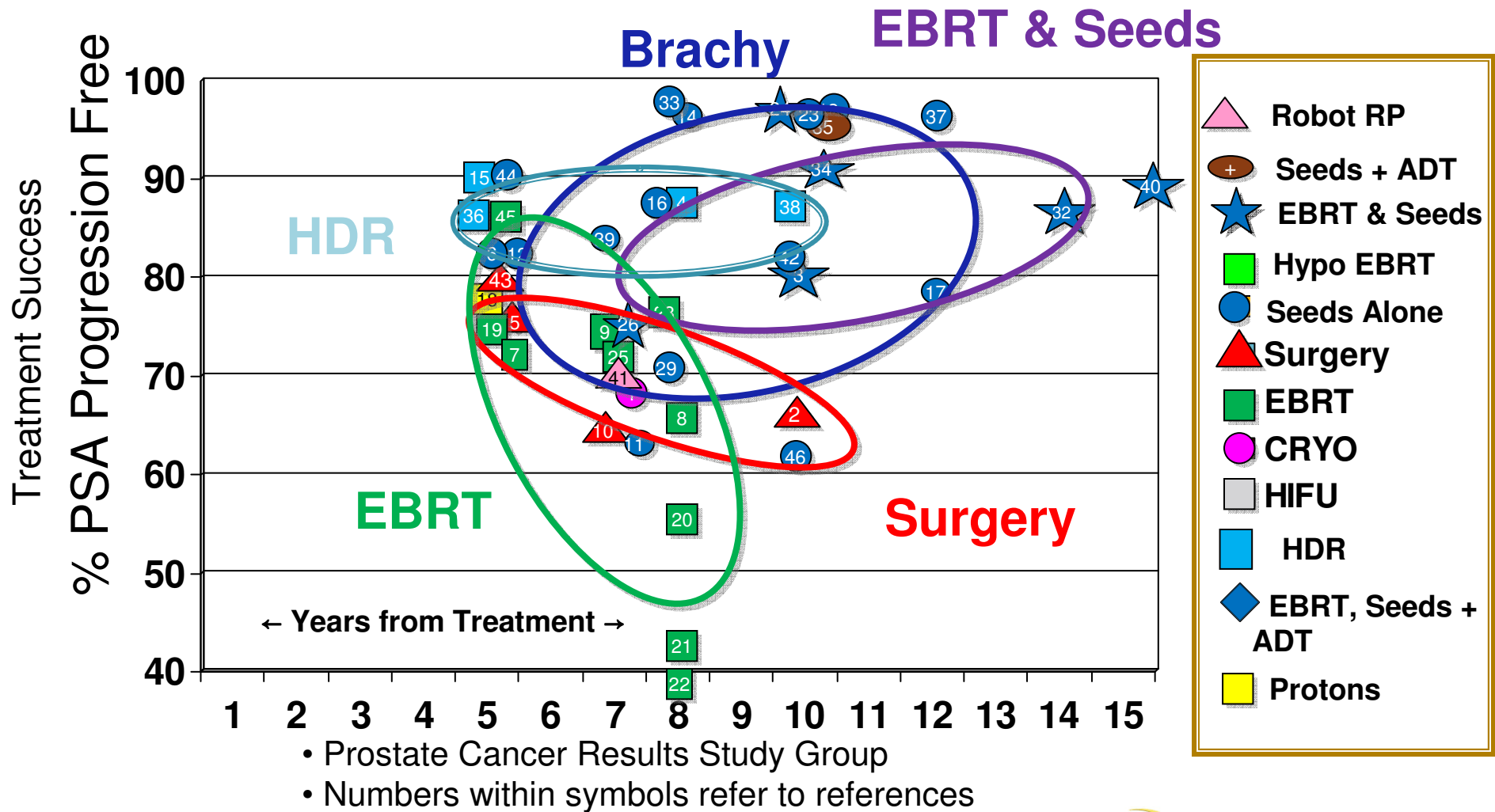
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# INTERMEDIATE RISK RESULTS

Weighted



# DOSE MATTERS

## 5-yr BRFS Low Risk

<b>UCSF</b>	<b>EBRT &gt;72 Gy 88%</b>		<b>Seeds 145Gy 93%</b>
<b>MSKCC*</b>	<b>IMRT 81Gy 88%</b>	<b>IMRT 86Gy 98%</b>	<b>Seeds 98%</b>

Cahlon et al (MSKCC) Ultrahigh dose IMRT for localized PCA Int J Rad Onc Biol. Phys. 2:4-8,2007

\*Zelevsky et al Long term outcome of IMRT for pts with clinically Localized PCa J Urol 176;1415-1419,2006

Zelevsky (MSKCC) ASTRO 2007 #1074



# DOSE MATTERS

## BRFS Low Risk

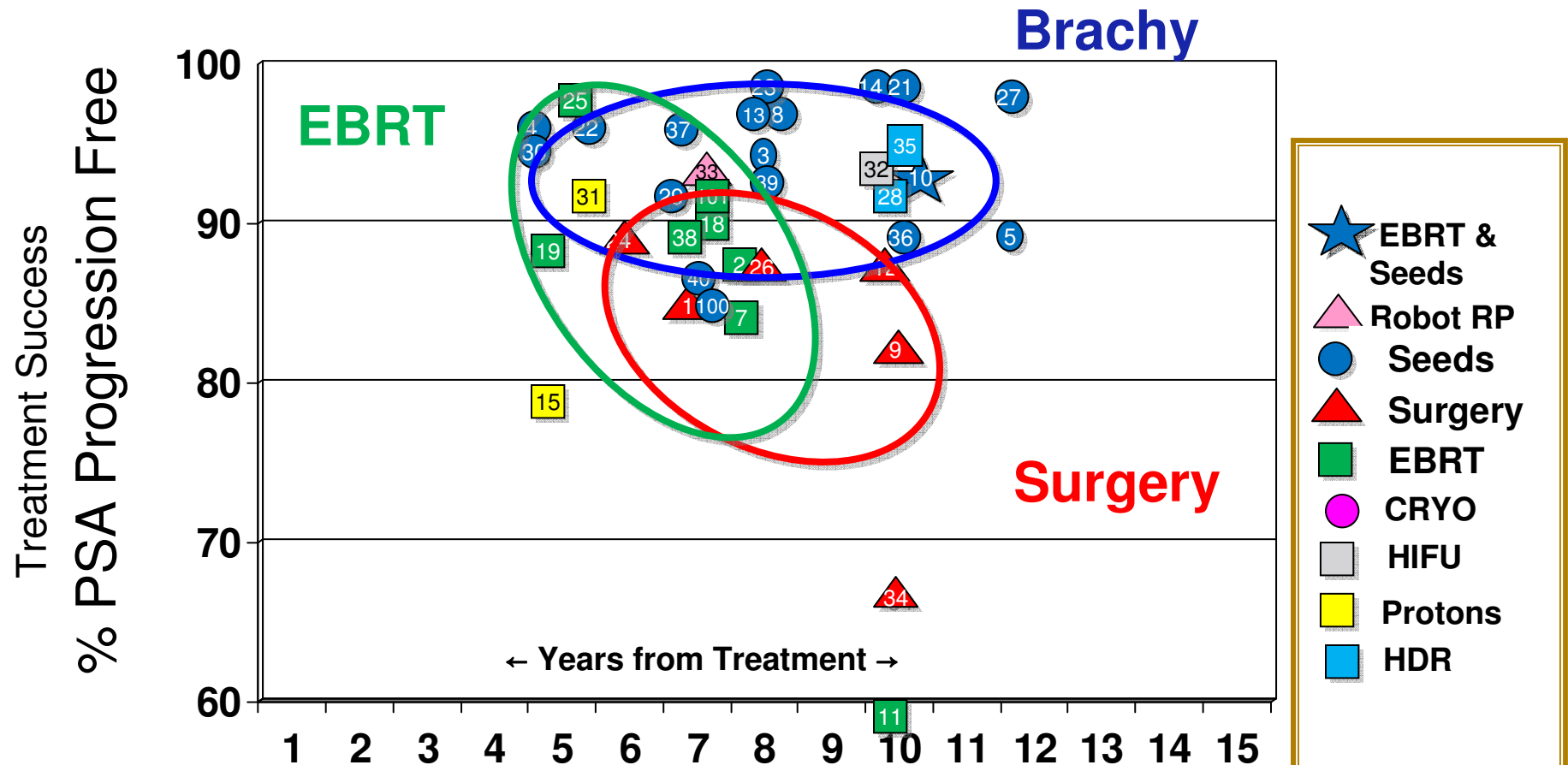


	7yr	10yr
<b>MSKCC Brachy 145 GY</b>	<b>95%</b>	<b>93%</b>
<b>MSKCC IMRT 81 Gy</b>	<b>89%</b>	<b>81%</b>

[Cancer.](#) 2011 Apr 1;117(7):1429-37. doi: 10.1002/cncr.25467. Epub 2010 Nov 8.

# LOW RISK RESULTS

Weighted



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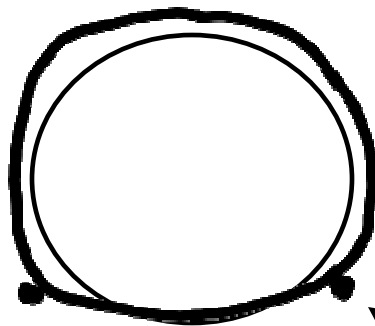


# Local Control Seeds

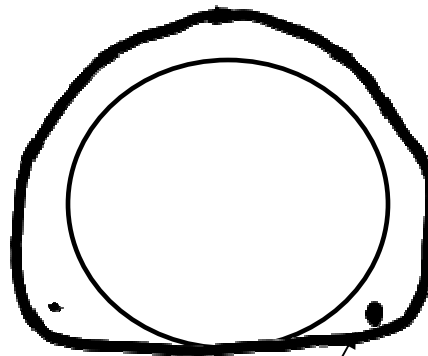
# Target Volumes



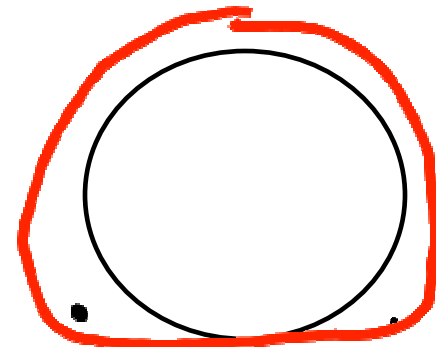
**Surgery**



**IMRT**



**Seeds**



**Nerve**

**Why Fail?**

**Rare LF**

**Distant**

**studymanager™**



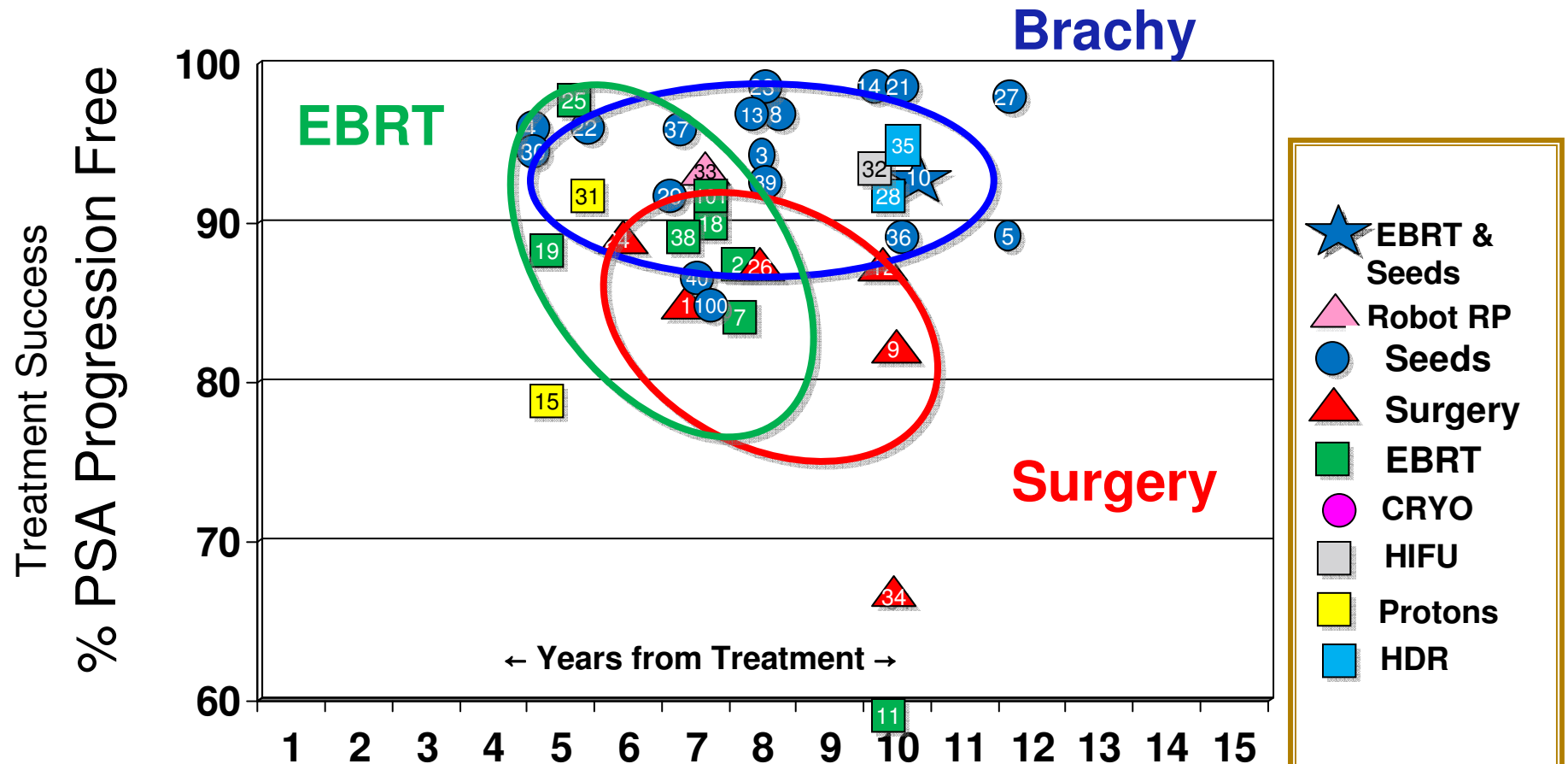
# **Is the Brachytherapy Dose High Enough?**

# Dose vs LR after Brachy

Low	4/28 <b>14.3%</b>	6/124 <b>4.8%</b>	3/104 <b>3%</b> <b>P=0.5</b>
Intermediate	5/34 <b>14.7%</b>	4/63 <b>6.3%</b>	2/38 <b>5.3%</b> <b>0.265</b>
High	13/59 <b>22%</b>	5/57 <b>8.8%</b>	1/51 <b>2%</b> <b>0.003</b>
Overall	<b>18%</b>	<b>6.3 %</b>	<b>3.1%</b> <b>&lt;0.001</b>

# LOW RISK RESULTS

Weighted



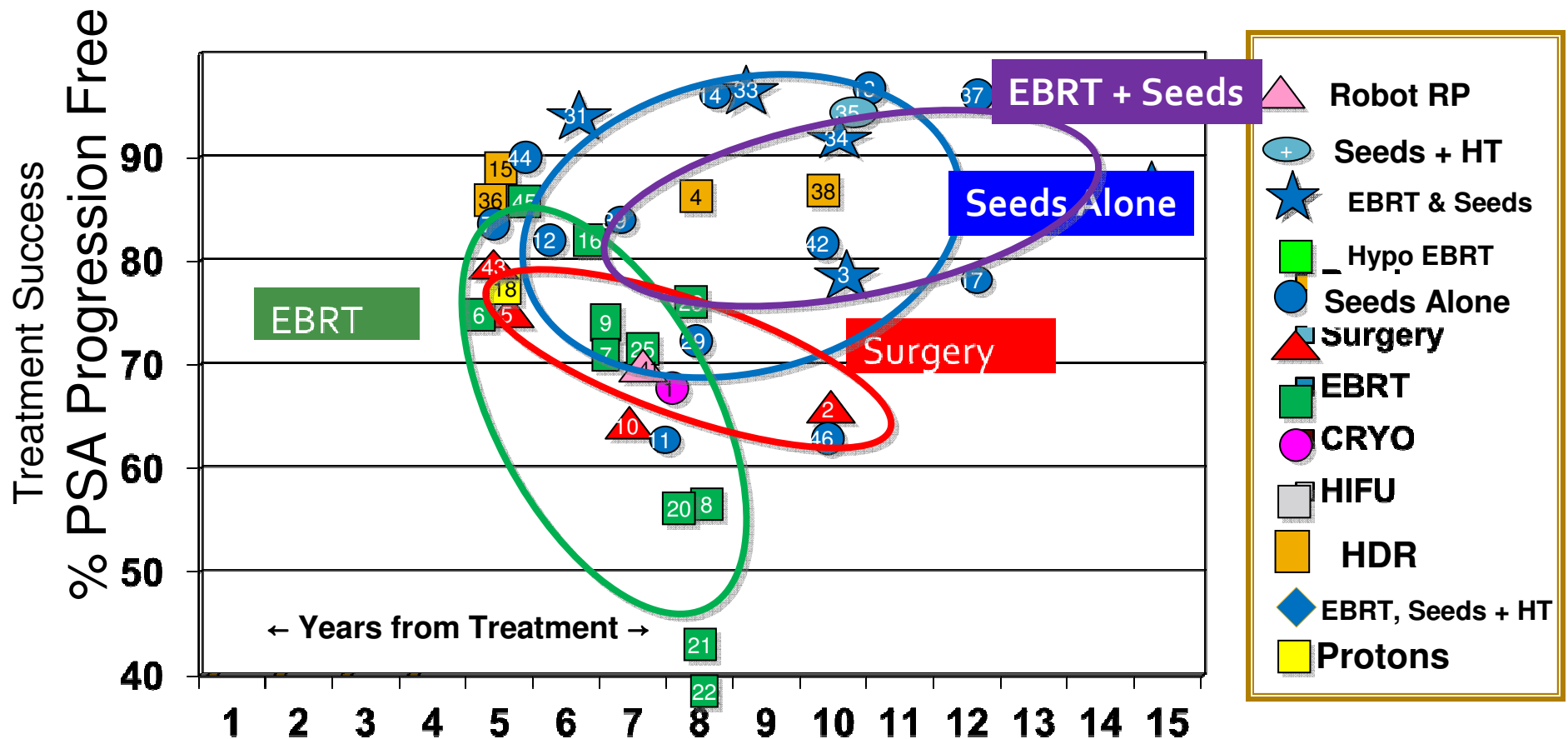
- Prostate Cancer Results Study Group
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4/11/2012

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# INTERMEDIATE RISK Grouping

weighted

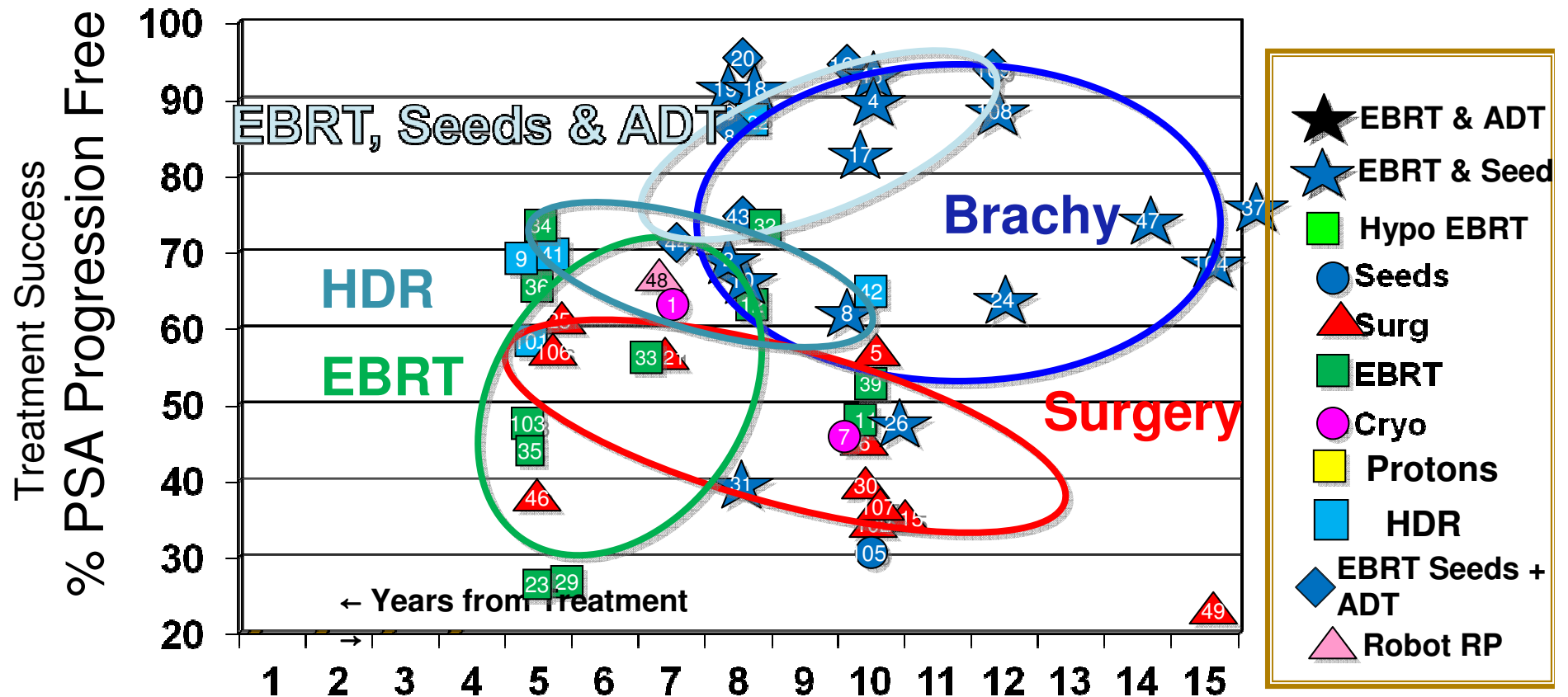


- Prostate Cancer Results Study Group
- Numbers within symbols refer to references



# HIGH RISK RESULTS

Weighted



- Prostate Cancer Results Study Group
- Numbers within symbols refer to references

# Local Control Bottom Line



- You have either to:
- Remove the prostate or,
- Deliver a high dose, even in Low risk disease

# Extra Capsular Disease Control

**ECE occurs in all risk groups**

**Low risk patients 20-50%**

**Intermediate Risk- 20-60%**

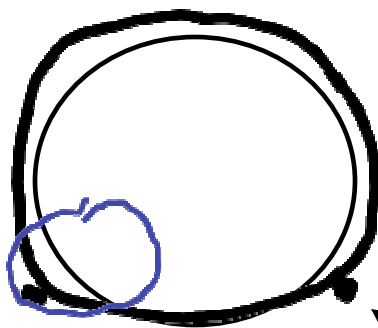
**High Risk – 16-57%**

**(Partin Tables)**

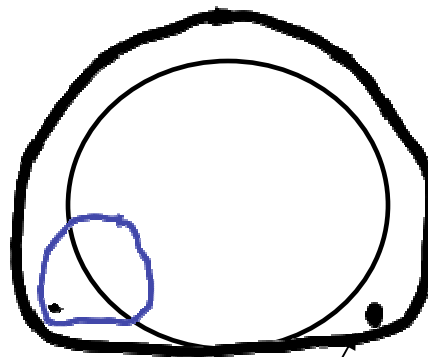
# Target Volumes



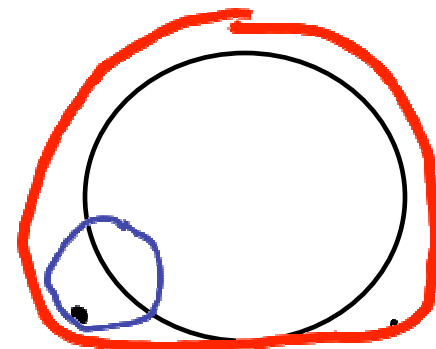
**Surgery**



**IMRT**



**Seeds**



**Nerve**

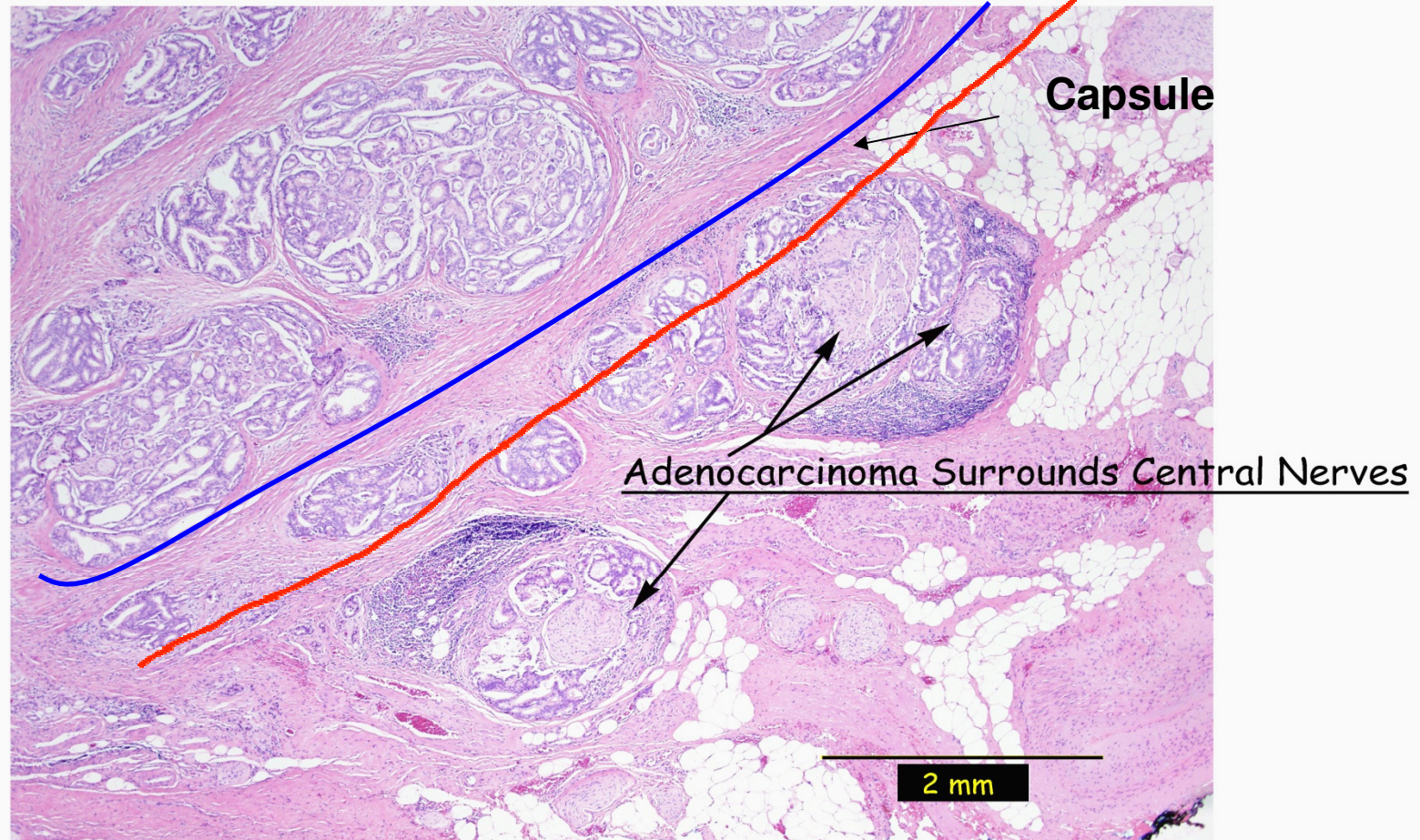
**Why Fail?**

# Extracapsular (ECE) Disease



- Surgery
  - Nerve sparing = ECE sparing ?
- IMRT
  - Treats Extracapsular disease routinely
- Seeds/HDR
  - Treats Extracapsular disease routinely

## Extracapsular Extension Via Growth Along Neurovascular Bundle



- Chao, et al. **Clinicopathologic Analysis of Extracapsular Extension (ECE) in**
- **Prostate Cancer: Should the CTV Be Expanded Posterolaterally to Account For Microscopic Extension?**
- IJROBP*; 65(4): 999-1007, 2006. (William Beaumont)

# Positive Margins vs Risk Group

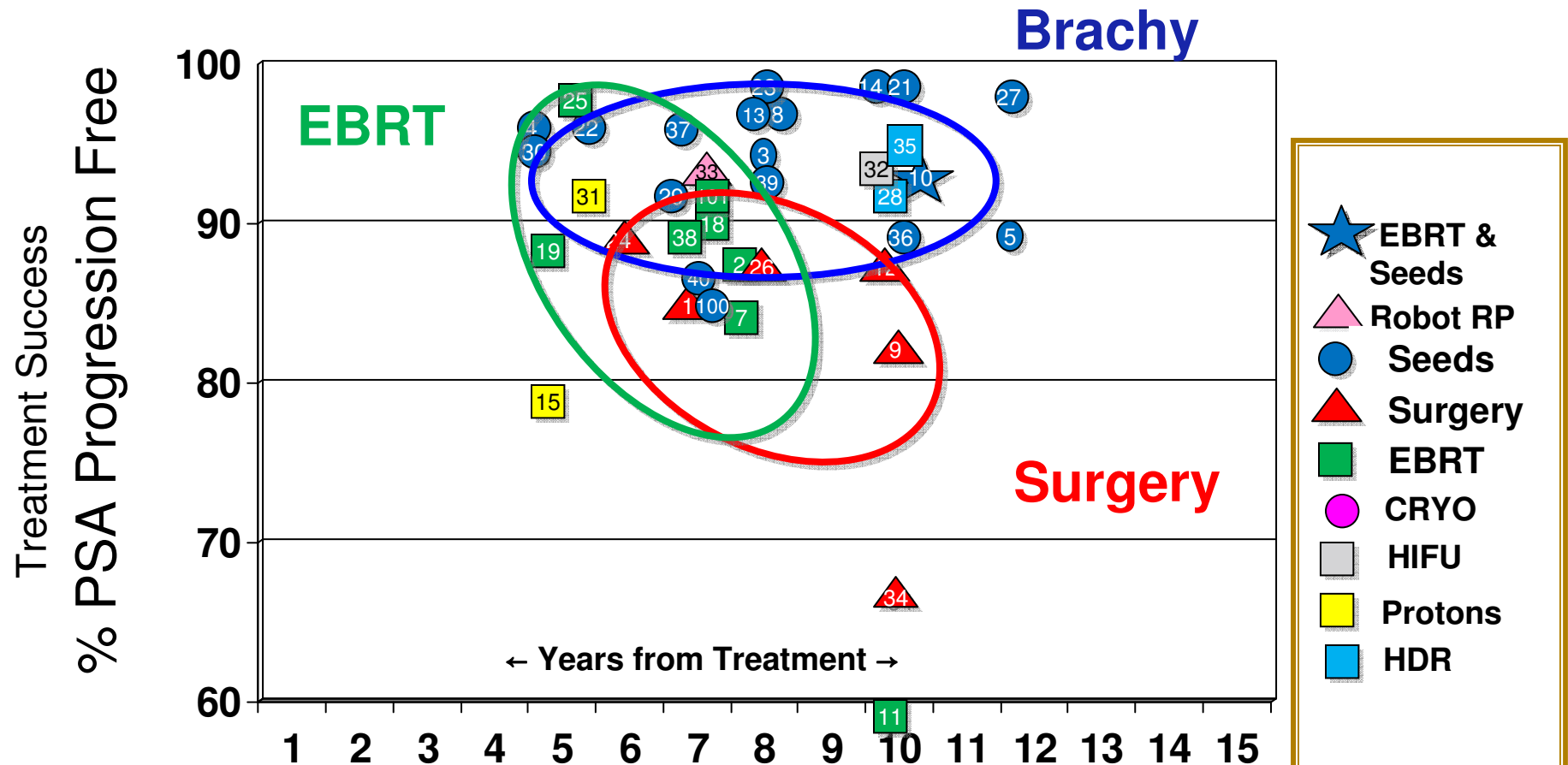
<b>Low</b>	<b>15%</b>
<b>Intermediate</b>	<b>22%</b>
<b>High</b>	<b>35%</b>

. Alkhateeb Impact of Surg Margins after RP by Risk Group J Urol Vol 183, 145-150, 2010



# LOW RISK RESULTS

Weighted



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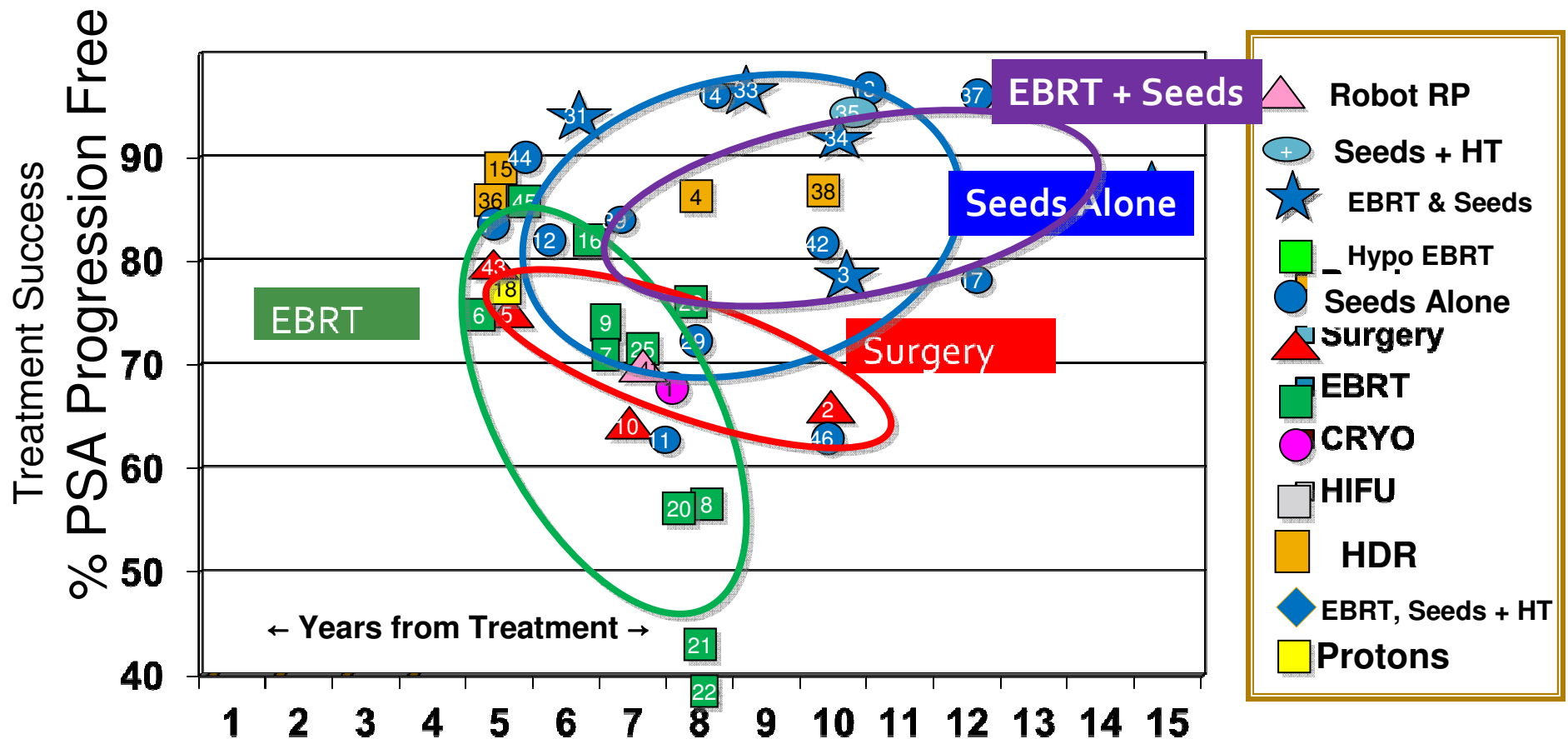
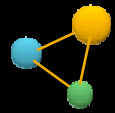
4/11/2012

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# INTERMEDIATE RISK Grouping

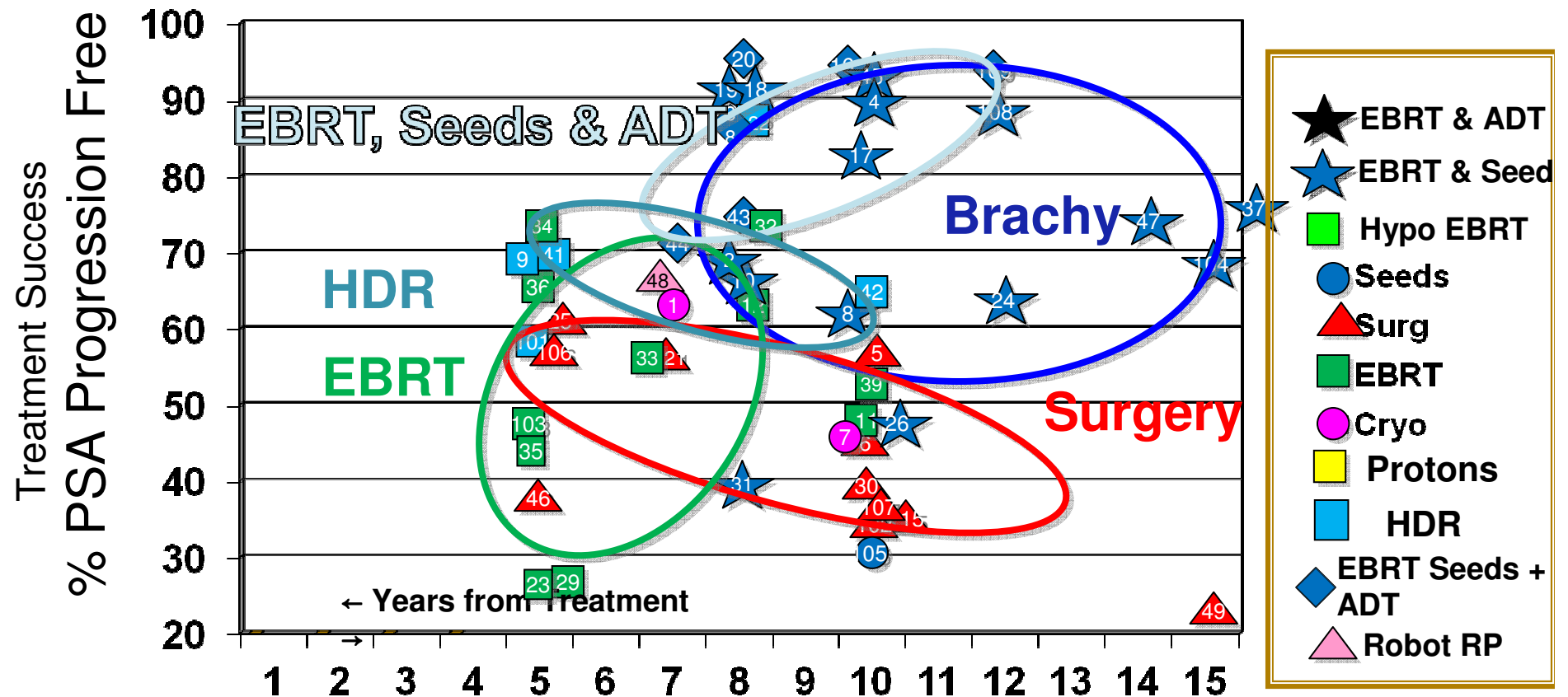
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- Prostate Cancer Results Study Group
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# HIGH RISK RESULTS

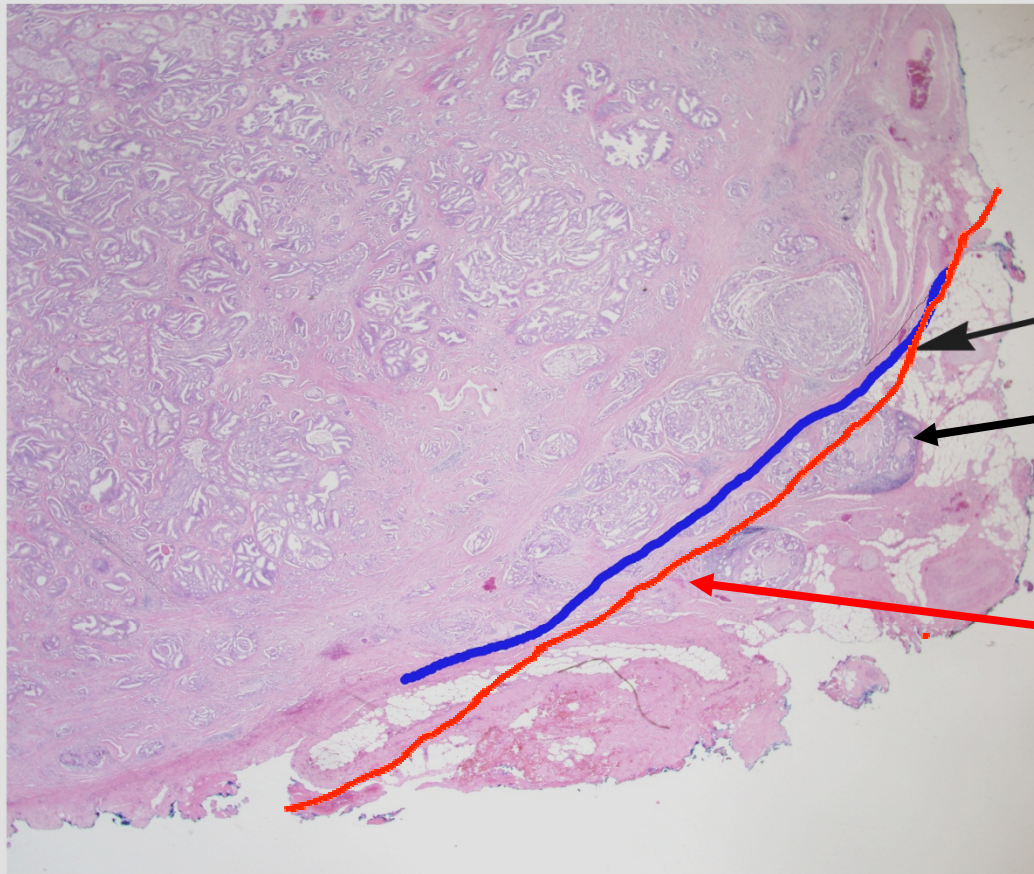
Weighted



- Prostate Cancer Results Study Group
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# Nerve Sparing Surgery

## Right: (+) Extracapsular Extension



Prostatic Capsule

Nerve

Nerve Sparing  
Margin

Chao, et al. **Clinicopathologic Analysis of Extracapsular Extension (ECE) in Prostate Cancer: Should the CTV Be Expanded Posterolaterally to Account For Microscopic Extension?**  
*IJROBP*; 65(4): 999-1007, 2006. (William Beaumont)

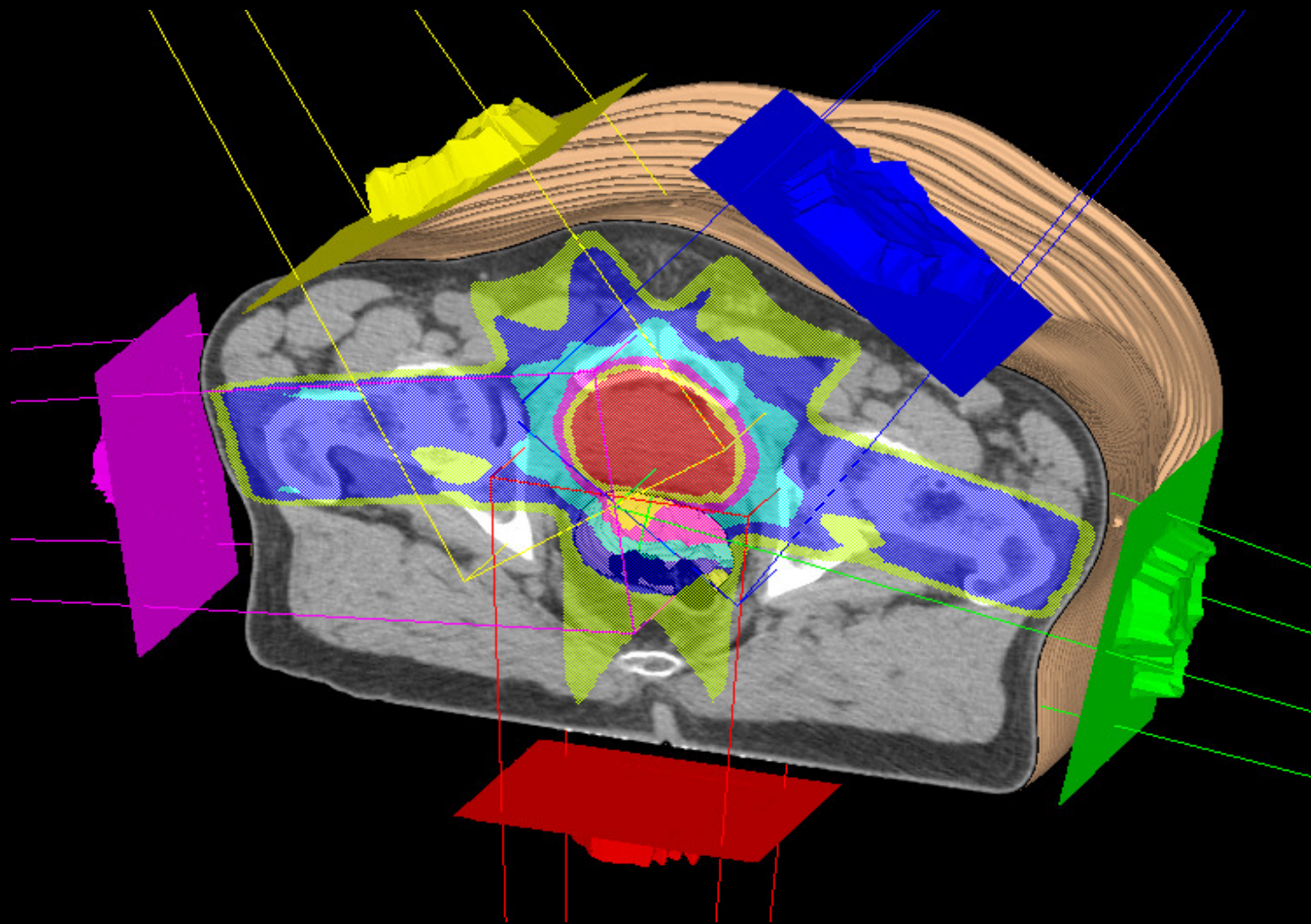
# ExtraCapsular Disease



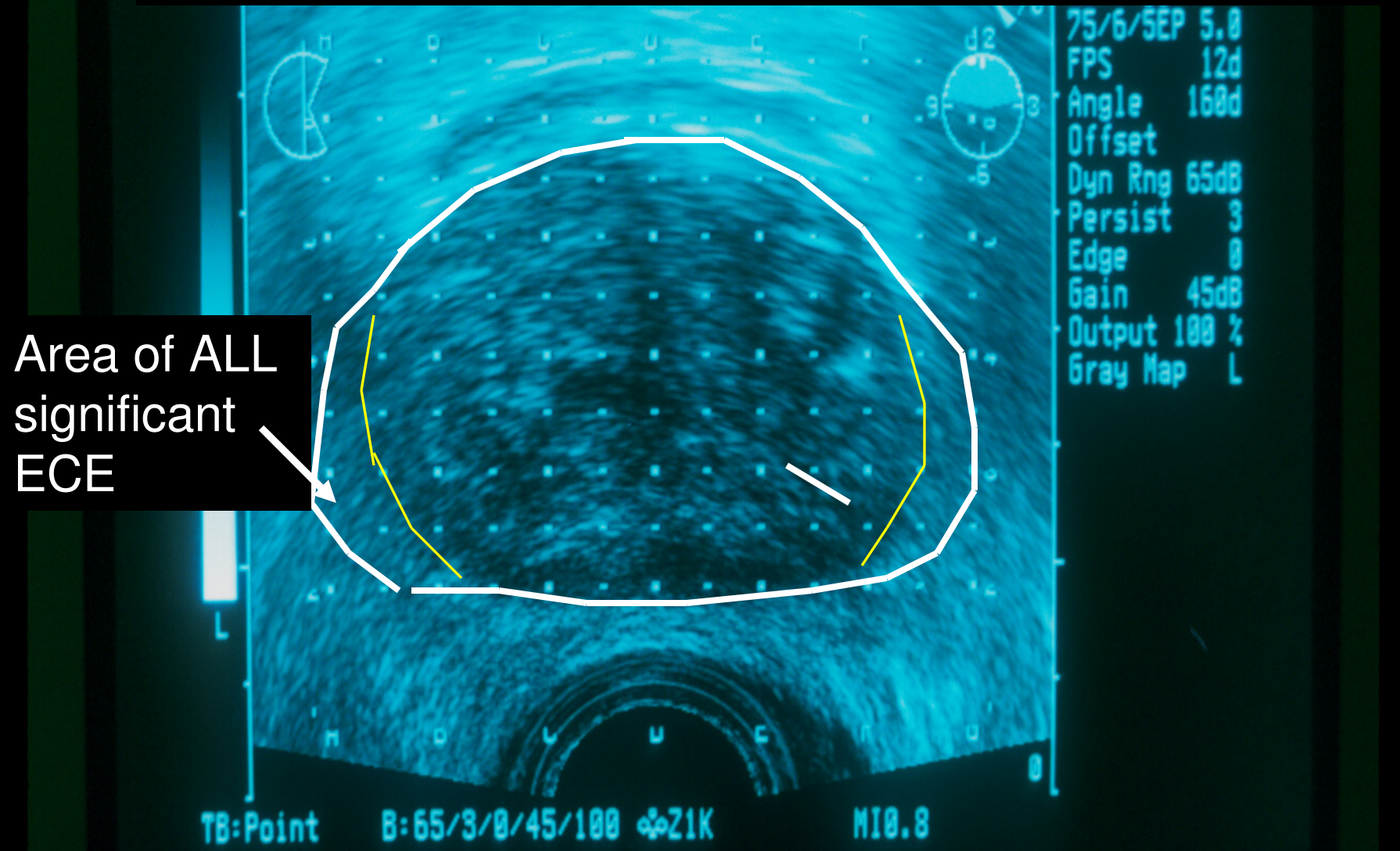
- From Current Data, it is possible for a standard or Robotic surgeon to predict from pre-op clinical factors, (Stage, Grade ,PSA) the likelihood of a positive margin (extra prostatic disease)



# IMRT And ECE



# Brachytherapy Target Volume



# Bottom Line

## Extra Capsular Disease



- 1. Surgery, especially nerve sparing, surgery fails to adequately address ECE
- 2. EBRT/IMRT effectively covers majority of ECE
- 3. Seed implantation effectively covers majority of ECE

# For Patient Version



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  - Or ProstateCancerTC.com
- Or contact PCRSBG member
- Prostate Cancer Treatment Center website
  - [www.Prostatecancertreatmentcenter.com](http://www.Prostatecancertreatmentcenter.com)