



## Salvage Prostate Brachytherapy

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1996-2013

1515 combined HDR + EBRT

574 HDR monotherapy

36 Salvage

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2125 Total Patients

No Disclosure



## Recurrent Prostate Ca: The Situation

S/P Primary Radiation Therapy  
Brachytherapy (mostly seeds)  
EBRT (variable methods, doses, fields)

S/P Radical Prostatectomy +/- EBRT

S/P Primary Cryotherapy (little data)



## Estimated Incidence Isolated LR of PCA after RT

Prostate Ca in USA 200K year (x 50% RT) = 100K

LR after RT – (low estimate?) 10-20% = 10-20K

Assume 50% are isolated = 5-10K cases/yr

Demanes et al – Journal of Anecdotal Estimates 2014

## Recurrence Diagnostics

**Local recurrence serious but not hopeless situation**

Marcus et al Can J Urol 2012 19(6): 6534

**Rising PSA (first sign)** is nonspecific (Dx or Site)

**Prostate Bx needed** but can be misleading if too early

Get a bad bounce...  
you might make an error!





### Why or Why not Local Salvage?



#### Benefits

- Local Control
- Prevent DM
- Avoid systemic Rx
- Psychological benefit
- Cost effective (if it works)
- Good QoL (if no compl.)

#### Benefits

- Local Failure
- DM occur anyway
- GI or GU side effects
  - Fistula
  - ED
  - Poor QoL if compl.

### Metastatic w/u is insensitive & nonspecific

**Tc-99 Bone Scan** – not very helpful for early detection  
(F18 PET better?)

**Prostascint** – obsolete?

**MRI** – useful for local extent and targeting

**C11 PET** – useful, but hard to obtain



## Risk of Distant Metastasis

Original Low risk vs. Int/High (PSA >10 or GS >7)

PSA velocity < 2ng/ml per year

Time to PSA failure > 1-3 years

PSA doubling time > 8-12 months

Nguyen et al. Cancer 2007;110(7):1417

## Case Selection



Favorable risk group - preferred not essential

Favorable PSA profile

Long Disease Free Interval

Few, if any, GI or GU side effects or major symptoms

Motivated, well-informed, otherwise healthy patient



## Radiation Risks Analysis Prior Dose and Methods



EBRT 65-85 Gy  
Ant. Rectum = Urethra = Pros

Brachytherapy  
Urethra > Pros > Ant. Rectum

## Other Considerations

Effective alternatives to local Rx i.e systemic therapy  
BCC less important than CSS and QoL

Mistakes can really hurt...  
Patients live a long time with side effects

Some Pts Rx for local palliation – that's different  
Same admonitions about side effects



## Salvage Disease Control

SALVAGE	n	Yrs FU	BCC
Prostatectomy	500	5-10	47-87%
Cryotherapy	1000	1-7	34-77%
HIFU	250	1-2	46-61%
Seeds	250	2-5	51-87%
Seeds RTOG 2010	37	7	54%

## Salvage Surgery

### Preop PSA Predicts bNED Outcome

<4ng/ml = 86%

4-10ng/ml = 55%

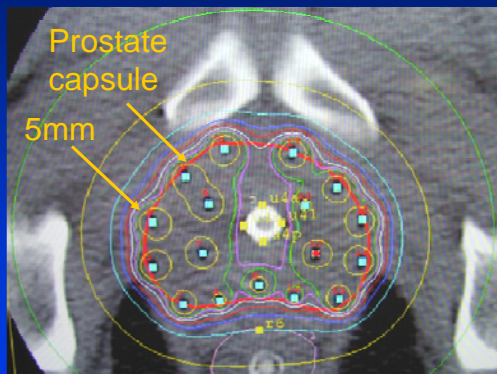
>10ng/ml = 25%



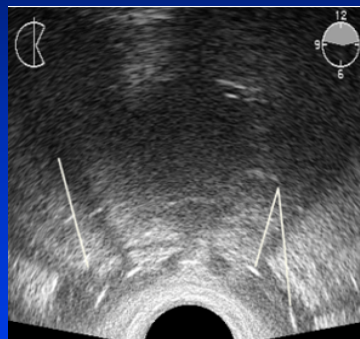
## Salvage Complications

	n	FU	Incont.	Strict or Retention GU G3/4	Rectal or Fistula GI G3/4
Prostatectomy	500	5-10	15-68%	9-32%	0-15%
Cryotherapy	1000	1-7	4-73%	2-67%	0-3%
HIFU	250	1-2	7-50%	10-50%	3-7%
Seeds	500	2-5	0-31%	0-47%	2-20%
Seeds RTOG 2010	37	7	8%	10%	2.5%

## HDR – Reliable treatment within & beyond prostate



Gy	%
9.0	150
7.5	125
7.2	120
6.6	110
6.0	100
5.4	90
4.5	75

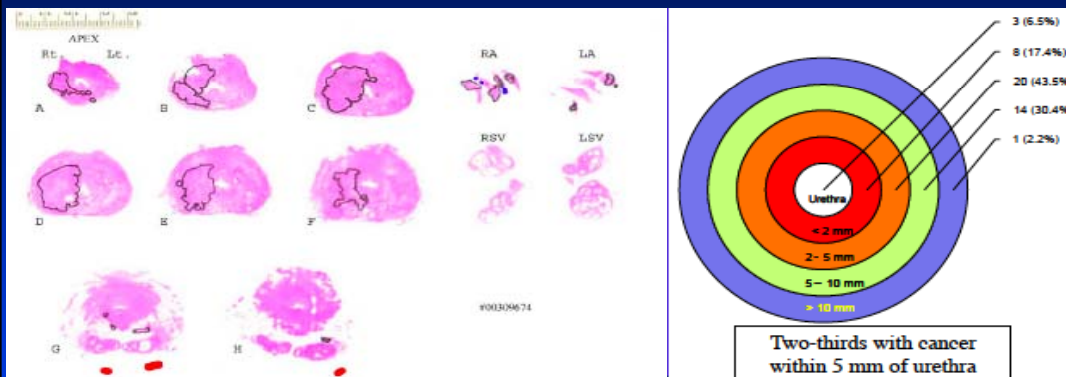


**HDR hypofractionation radiobiology different than EBRT or LDR**





## 2/3s have cancer within 5mm of the urethra



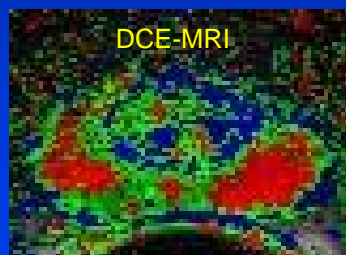
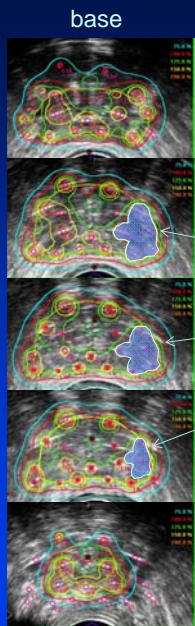
Huang et al. J Urol 2007 177(4): 1324-9

## HDR Dose sculpting

Dose de-escalation

Focal therapy

150%  
of prescribed dose



Courtesy Ghilezan et al





DISEASE CONTROL	n	Yrs FU	BCC
Prostatectomy	500	5-10	47-87%
Cryotherapy	1000	1-7	34-77%
HIFU	250	1-2	46-61%
Seeds	250	2-5	51-87%
Seeds ROTG 2010	37	7	54%
<b>HDR Indiana (Tharp) 7 Gy x 6</b>	<b>7</b>	<b>5</b>	<b>71%</b>
<b>HDR UCSF (Chen) 6 Gy x 6</b>	<b>52</b>	<b>5</b>	<b>51%</b>
<b>HDR MSKCC (Yamada) 8 Gy x 4</b>	<b>42</b>	<b>3</b>	<b>70%</b>
<b>HDR+HT (Kulkielka) 10 Gy x 3 (6 wk)</b>	<b>25</b>	<b>1</b>	<b>64%</b>
<b>HDR focal (Jo) 11 Gy x 2</b>	<b>11</b>	<b>2</b>	<b>74%</b>

SALVAGE COMPLICATIONS	n	FU	Incont.	Strict or Retention GU G3/4	Rectal or Fistula GI G3/4
Prostatectomy	500	5-10	15-68%	9-32%	0-15%
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HIFU	250	1-2	7-50%	10-50%	3-7%
Seeds	500	2-5	0-31%	0-47%	2-20%
Seeds RTOG 2010	37	7	8%	10%	2.5%
<b>HDR Indiana (Tharp) 7 Gy x 6</b>	<b>7</b>	<b>5</b>	<b>28%</b>	<b>41%</b>	<b>0%</b>
<b>HDR UCSF (Chen) 6 Gy x 6</b>	<b>52</b>	<b>5</b>		<b>2%</b>	<b>0%</b>
<b>HDR MSKCC (Yamada) 8 Gy x 4</b>	<b>42</b>	<b>3</b>	<b>2%</b>	<b>7%</b>	<b>0%</b>
<b>HDR+HT (Kulkielka) 10 Gy x 3 (6 wk)</b>	<b>25</b>	<b>1</b>	<b>0%</b>	<b>0%</b>	<b>0%</b>
<b>HDR focal (Jo) 11 Gy x 2</b>	<b>11</b>	<b>2</b>	<b>0%</b>	<b>0%</b>	<b>0%</b>



SUMMARY	Year	Rx	N	FU Yr	bNED / FFP*	FU Yrs	G 3-4
Stephenson Bianco	2004	RP	100	5	55%*	5	13-33%
Heidenreich	2009	RP	55	2	87%*	2	15%
Izawa	2002	Cryo	131	5	40%	5	NR
Bahn	2003	Cryo	59	7	50-62%	7	NR
Ismail	2007	Cryo	100	3	59%	3	3%
Grado	1999	LDR	49	5	34%	5	16%
Beyer	1999	LDR	17	5	53%*	5	NR
Wong	2006	LDR	17	4	75%	4	47%
Allen	2007	LDR	12	4	63%	4	0%
Nguyen	2007	LDR	25	4	70%	4	30%
Lee	2008	LDR	21	3	38%	5	0%
Aaronson	2009	LDR	24	3	88%	3	4%
Burri	2010	LDR	37	7	54%	10	11%
Chen	2013	HDR	52	5	51%	5	10%
Yamada	2013	HDR	42	3	70%	3	8%

## Conclusions

Considerable need for effective salvage

HDR has good biologic and technical rationale

HDR BCC 50-70% (4-5 yrs) - hard to compare

Careful patient selection

Proper measures to avoid/manage toxicity



## References: Salvage Reviews

Touma et al. *J Urol* 2005;173:373  
Nguyen et al. *Cancer* 2007;110:1417  
Kimura et al. *BJUI* 2009;105:191  
Warde *Nature Reviews Urology* 2010;7:472  
Marcus et al *Can J Urol* 2012;19(6):6534

## References: HDR Salvage Articles

Tharp et al *Brachytherapy* 2008;7:231  
Lee et al (UCSF) *IJRBP* 2007;67(4);1106  
Chen et al (UCSF update) *IJRBP* 2013;86(2);324  
Yamada et al (MSKCC) *Brachytherapy* 2014;13:111  
Jo et al *BJUI* 2011;109;835  
Kukielka et al *Strahlenther Onkol* 2014;190:165