

Salvage radiotherapy for recurrent prostate cancer

Troy Scroggins Jr. MD
System Chair, Radiation Oncology
Ochsner Health

Disclosures

- NONE

Agenda

1. Post prostatectomy salvage irradiation
2. Post radiotherapy salvage
 - Brachytherapy
 - SBRT
3. Patient examples.

Personal Technological “Game Changers”

- IMRT – Inverse planning, VMAT
- IGRT – KVs, Cone beam CT, MRI guidance
- Drug eluting cardiac stents
- Prostate MRI 3T magnet, DWI sequences
- Pet Scans – F¹⁸- fluciclovine, Pifulfolastat F¹⁸ PSMA, GA⁶⁸- PSMA- 11,

Post prostatectomy salvage treatment

The addition of androgen deprivation therapy and pelvic lymph node treatment to prostate bed salvage radiotherapy. (NRG/RTOG 0534 SPPORT)

- 1792 patients / 283 cancer centers (USA, Canada, Israel)
- Detectable or rising PSA (0.1 – 2.0 ng/ml)
- Gleason score ≤ 9 , Performance status 0 – 1
- 592 pts., Prostate Bed Alone
- 602 pts., Prostate Bed with short term ADT
- 598 pts., Prostate Bed and Pelvic nodes with short term ADT
- Median Follow up 8.2 yrs.

NRG/RTOG - 0534

A

5-year rate

Group 1: 70.9% (95% CI 67.0-74.9)

Group 2: 81.3% (95% CI 78.0-84.6)

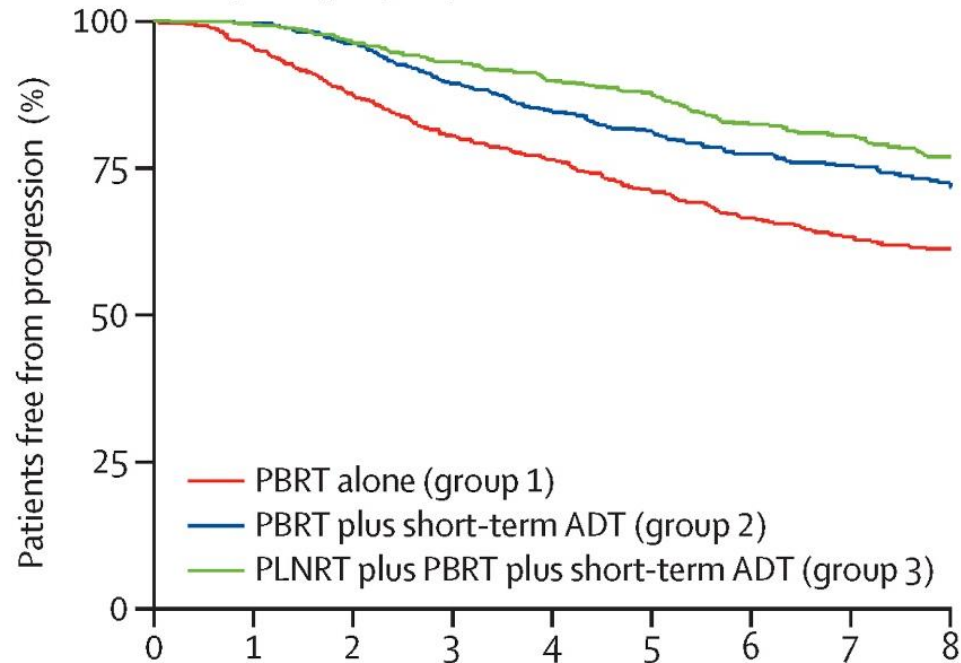
Group 3: 87.4% (95% CI 84.7-90.2)

5-year rate comparisons:

Group 3 vs group 1: $p < 0.0001$

Group 2 vs group 1: $p < 0.0001$

Group 3 vs group 2: $p = 0.0027$



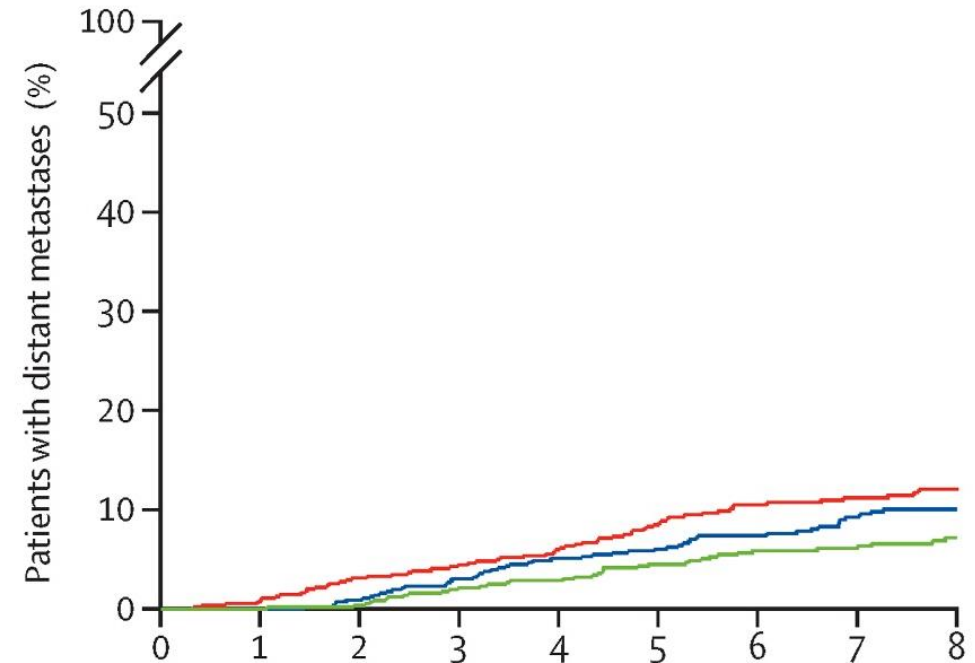
B

Log-rank tests:

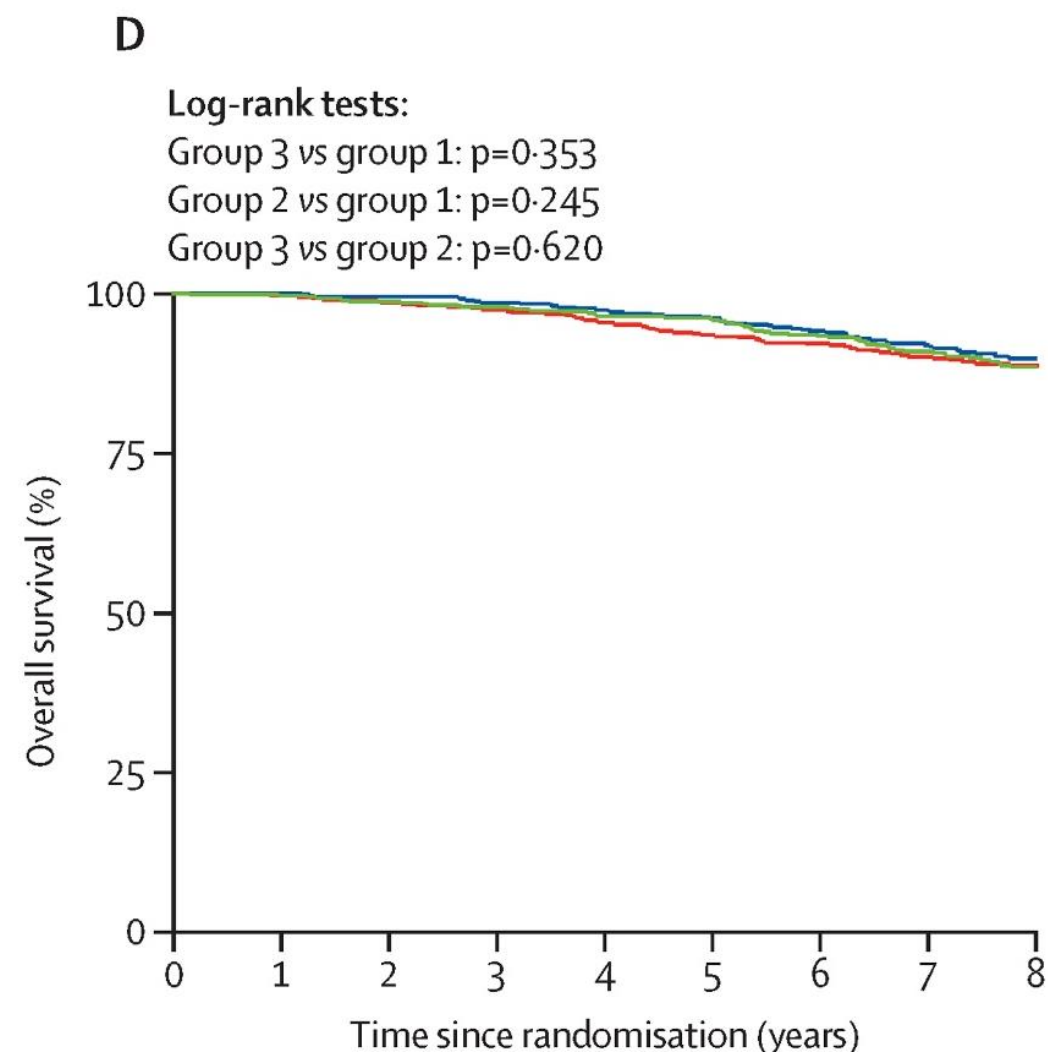
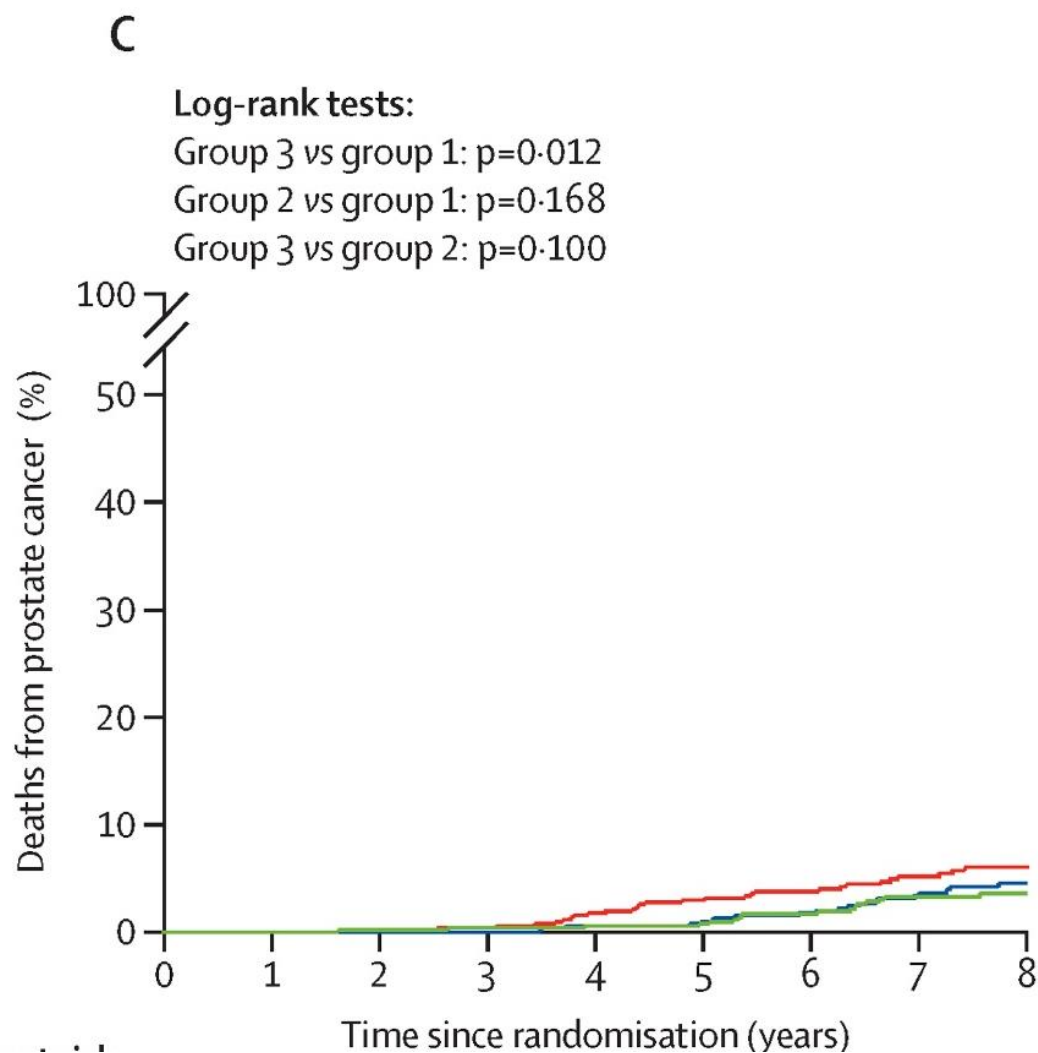
Group 3 vs group 1: $p = 0.0098$

Group 2 vs group 1: $p = 0.083$

Group 3 vs group 2: $p = 0.043$



NRG/RTOG - 0534



ACUTE

Lower GI / Pelvis	Increased frequency or change in quality of bowel habits not requiring medication / rectal discomfort not requiring analgesics	Diarrhea requiring parasympatholytic drugs (e.g. Lomotil) / mucous discharge not necessitating sanitary pads / rectal or abdominal pain requiring analgesics	Diarrhea requiring parenteral support / severe mucous or blood discharge necessitating sanitary pads / abdominal distention (flat plate radiograph demonstrates distended bowel loops)	Acute or subacute obstruction, fistula or perforation; GI bleeding requiring transfusion; abdominal pain or tenesmus requiring tube decompression or bowel diversion
Genitourinary	Frequency of urination or nocturia twice pretreatment habit / dysuria, urgency not requiring medication	Frequency of urination or nocturia that is less frequent than every hour. Dysuria, urgency, bladder spasm requiring local anesthetic (e.g. Pyridium)	Frequency with urgency and nocturia hourly or more frequently / dysuria, pelvis pain or bladder spasm requiring regular, frequent narcotic / gross hematuria with/without clot passage	Hematuria requiring transfusion / acute bladder obstruction not secondary to clot passage, ulceration, or necrosis

LATE

Small/Large intestine	Mild diarrhea; mild cramping; bowel movement 5 times daily; slight rectal discharge or bleeding	Moderate diarrhea and colic; bowel movement > 5 times daily; excessive rectal mucus or intermittent bleeding	Obstruction or bleeding, requiring surgery	Necrosis / perforation fistula
Bladder	Slight epithelial atrophy; minor telangiectasia (microscopic hematuria)	Moderate frequency; generalized telangiectasia; intermittent macroscopic hematuria	Severe frequency & dysuria; severe telangiectasia (often with petechiae); frequent hematuria; reduction in bladder capacity (<150 cc)	Necrosis/contracted bladder (capacity < 100 cc); severe hemorrhagic cystitis
Bone	Asymptomatic; no growth retardation; reduced bone density	Moderate pain or tenderness; growth retardation; irregular bone sclerosis	Severe pain or tenderness; complete arrest of bone growth; dense bone sclerosis	Necrosis / spontaneous fracture

		Group 1 (n=547, acute; n=545, late)	Group 2 (n=563, acute; n=559, late)	Group 3 (n=563, acute; n=562, late)	p value [*]	Group 2 vs group 1		Group 3 vs group 2	
						OR [‡] (95% CI)	p value [‡]	OR [‡] (95% CI)	p value [‡]
Acute adverse events [‡]									
All									
	Grade ≥2	98 (18%)	201 (36%)	246 (44%)	<0.0001	2.55 (1.93–3.37)	<0.0001	1.39 (1.10–1.77)	0.0034
	Grade ≥3	18 (3%)	41 (7%)	63 (11%)	<0.0001	2.31 (1.31–4.07)	0.0019	1.60 (1.06–2.42)	0.012
Blood or bone marrow									
	Grade ≥2	12 (2%)	10 (2%)	29 (5%)	0.0016	0.80 (0.34–1.88)	0.692	3.01 (1.45–6.26)	0.0016
	Grade ≥3	3 (1%)	1 (<1%)	15 (3%)	0.0012	0.32 (0.03–3.11)	0.836	15.38 (2.03–116.85)	0.0041
Gastrointestinal									
	Grade ≥2	11 (2%)	22 (4%)	38 (7%)	0.00041	2.01 (0.96–4.19)	0.032	1.76 (1.03–3.03)	0.020
	Grade ≥3	1 (<1%)	5 (1%)	4 (1%)	0.286	4.89 (0.57–42.01)	0.074	0.80 (0.21–2.99)	0.631
Renal or genitourinary									
	Grade ≥2	49 (9%)	68 (12%)	67 (12%)	0.177	1.40 (0.95–2.06)	0.046	0.98 (0.68–1.40)	0.544
	Grade ≥3	5 (1%)	5 (1%)	8 (1%)	0.622	0.97 (0.28–3.37)	0.518	1.61 (0.52–4.95)	0.203
Late adverse events [‡]									
All									
	Grade ≥2	308 (57%)	322 (58%)	350 (62%)	0.116	1.04 (0.82–1.32)	0.367	1.22 (0.96–1.55)	0.054
	Grade ≥3	65 (12%)	87 (16%)	96 (17%)	0.047	1.36 (0.96–1.92)	0.040	1.12 (0.81–1.53)	0.246
Blood or bone marrow									
	Grade ≥2	20 (4%)	10 (2%)	25 (4%)	0.038	0.47 (0.22–1.01)	0.973	2.60 (1.23–5.47)	0.0060
	Grade ≥3	3 (1%)	2 (<1%)	7 (1%)	0.181	0.65 (0.11–3.90)	0.682	3.51 (0.73–17.0)	0.059
Gastrointestinal									
	Grade ≥2	56 (10%)	57 (10%)	51 (9%)	0.753	0.99 (0.67–1.46)	0.518	0.88 (0.59–1.31)	0.738
	Grade ≥3	4 (1%)	5 (1%)	8 (1%)	0.488	1.22 (0.33–4.57)	0.384	1.60 (0.52–4.92)	0.206
Renal or genitourinary									
	Grade ≥2	202 (37%)	194 (35%)	223 (40%)	0.226	0.90 (0.71–1.16)	0.793	1.24 (0.97–1.58)	0.043
	Grade ≥3	29 (5%)	37 (7%)	45 (8%)	0.201	1.26 (0.76–2.08)	0.182	1.23 (0.78–1.93)	0.1

Post prostatectomy salvage treatment

The addition of androgen deprivation therapy and pelvic lymph node treatment to prostate bed salvage radiotherapy. (NRG/RTOG 0534 SPPORT)

Significant Covariate Effects

- PSA 0.1 – 1.0 ng/ml vs. >1.0 - <2.0 ng/ml
- Seminal Vesicle involvement
- Gleason score 8 – 9 vs. ≤ 7
- Median PSA 0.35 ng/ml if < median, groups 2 -3 were sig better than 1, if > than median group 3 was better but not sig.

Post radiotherapy Salvage

- Salvage prostatectomy
- HIFU
- Cryotherapy
- Brachytherapy
 1. High Dose Rate
 2. Low Dose Rate
- SBRT (Stereotactic Body Radiotherapy)

Salvage LDR Brachytherapy

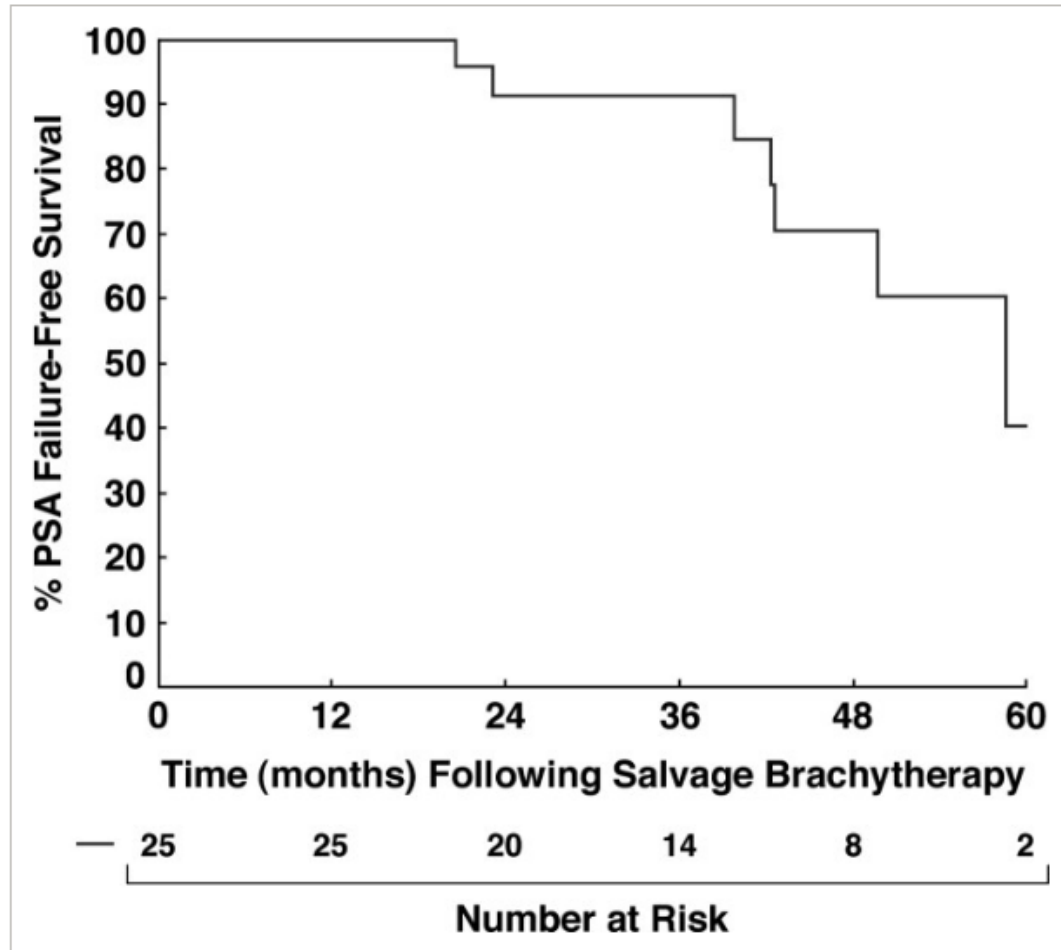


Figure 3 [Open in figure viewer](#) [Download PowerPoint](#)

Estimates of prostate-specific antigen (PSA) failure-free survival after salvage magnetic resonance image-guided prostate brachytherapy.

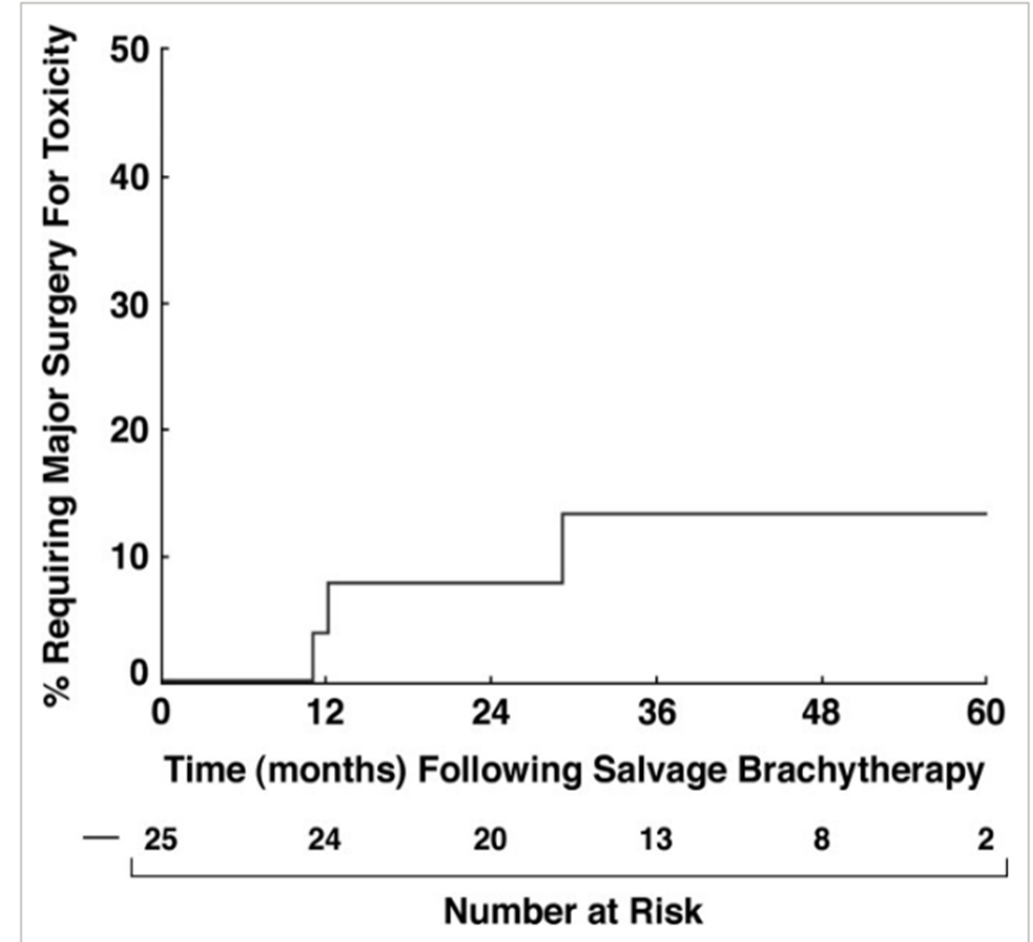


Figure 2 [Open in figure viewer](#) [Download PowerPoint](#)

Estimates of men who required surgery to repair late complications of radiation after they underwent salvage magnetic resonance imaging-guided prostate brachytherapy.

Salvage LDR Brachytherapy

- Low / intermediate grade
- Biopsy Proof of recurrent disease (timing of biopsy)
- Staging
- PSA and PSADT (< 10, > 12 months)
- Performance Status
- Prior radiotherapy dose

Salvage LDR Brachytherapy

LDR prostate brachytherapy following local recurrence after external beam radiotherapy - NRG / RTOG 0526

- 92 patients, low to intermediate risk
- 140 Gy I – 125 or 120 Gy Pd – 103
- Median EBRT dose 74 Gy
- 16% received androgen ablation.

Salvage LDR Brachytherapy

LDR prostate brachytherapy following local recurrence after external beam radiotherapy - NRG / RTOG 0526

- Median follow up of 6.9 yrs.
- 5 yr. bRFS 68% 10 yr. bRFS 48%
- 10 yr. rate of distant failure was 19%
- 14% Grade 3 GI or GU late effects.

Salvage LDR Brachytherapy

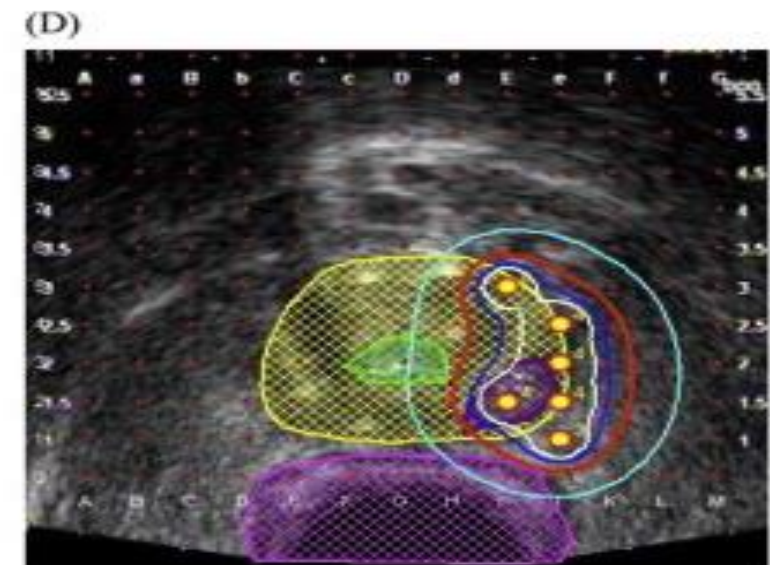
MRI Guided Boost or Partial Implantation

- UCSF – 24 patients, 3 with Gleason 8 disease
- 108 Gy to prostate, 144 Gy to the MRI lesion
- Median follow p 30 months, bRFS 88%
- 5 patients gross hematuria. , 1 stricture 1 rectal hemorrhage

Salvage LDR Brachytherapy

MRI Guided Boost or Partial Implantation

- Hsu, *et al*, 15 patients with I – 125 partial salvage
- 3 year bRFS 71%
- 5 pts. with Grade 2 GU no Grade 3
- No Grade 2/3 GI toxicity
- 87% maintained erections (87% PDE5 inhibitors)



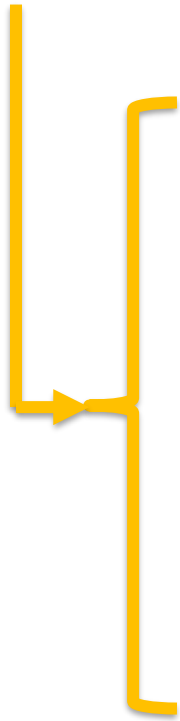
Hsc CC, et al, *IntJRad Onc Biol Phys*, 2013

Salvage LDR Brachytherapy

- Attractive option, low to intermediate risk, PSA < 10 with PSADT > 12 months
- 5 yr. bRFS 50 – 60% range, 10 yr. bRFS 30-40% range
- Late GU Grade 3/4 toxicity is 5 – 25%
- Late GI Grade 3/4 toxicity is 5 – 10%
- Expertise

Salvage SBRT

- **Conventional** fractionation: 1.8 to 2.0Gy / fraction
- **Hypofractionation**: smaller number of larger dose fractions

- 
- **Moderate** hypofractionation
 - 2.4 to 3.4Gy / fraction
 - **Extreme** (or Ultra) hypofractionation
 - ≥ 5.0 Gy / fraction
 - **SBRT** (stereotactic body radiotherapy)
 - ≤ 5 fractions

2 months



~ 1.5 months



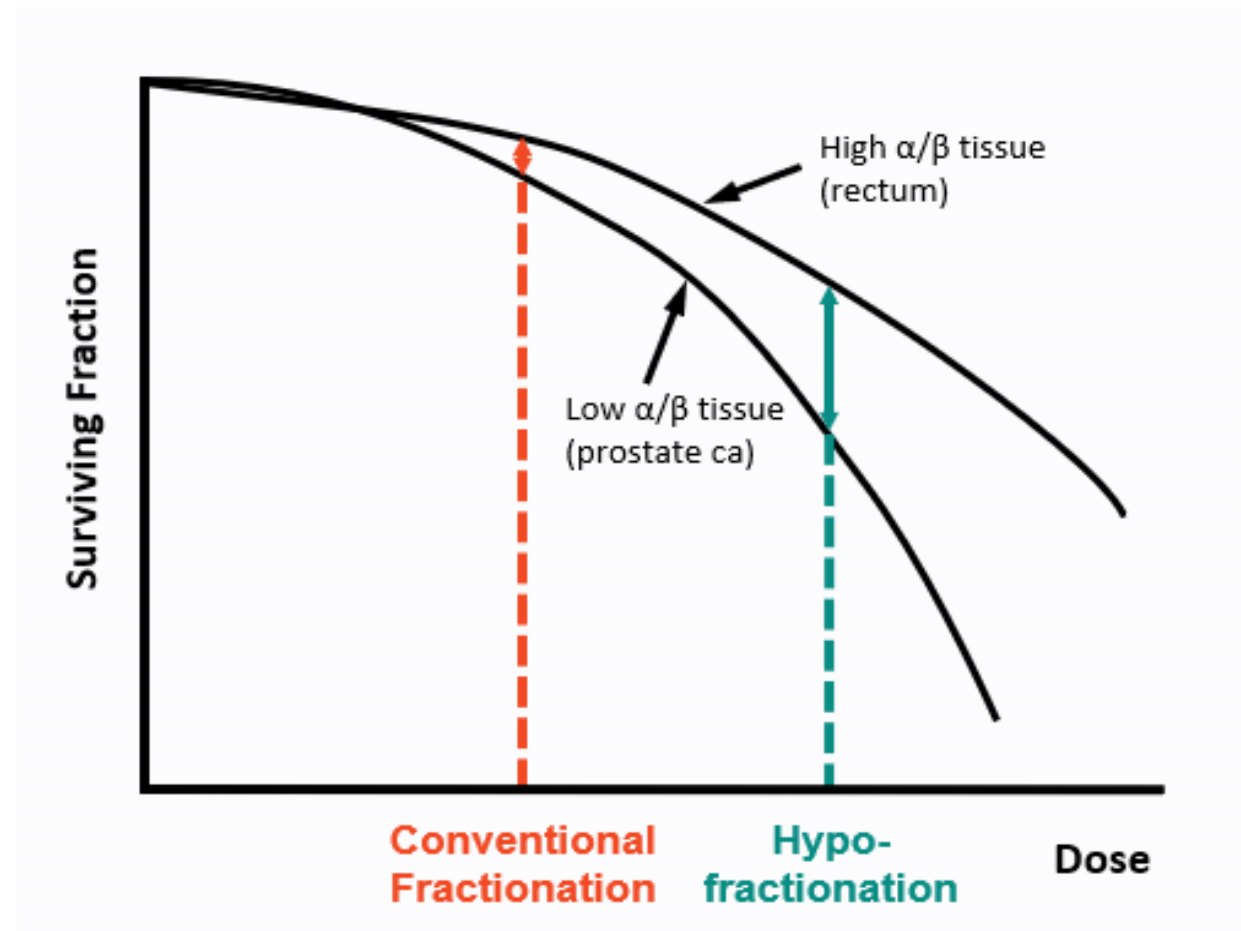
1 month



1.5 - 2 weeks

Why is hypofractionation (HF) important?

- **Favorable radiobiology:** rationale low proliferation rate cancer, α/β lower than surrounding tissues ($\alpha/\beta \sim 1.5$) so hypofractionated radiation should yield similar LC without more toxicity



Salvage SBRT

- Low / intermediate grade
- Biopsy Proof of recurrent disease (timing of biopsy)
- Staging
- PSA and PSADT (< 10, > 12 months)
- Performance Status
- Prior radiotherapy dose

Salvage SBRT



Salvage SBRT

Reirradiation for isolated local recurrence of prostate cancer

- European Institute of Oncology, Milan, Italy– 64 patients 2009 – 2016
- 45 prostate, 19 prostate bed
- 59 external beam (4 IMRT), 4 brachytherapy
- 25 – 30 Gy in 5 fractions, 1 10 Gy x 2, 1 12 Gy x 2
- 2 yr. bRFS 40%, clinical progression free survival 53%
- Late toxicity in 62 patients, only 1 Grade 3 GU event

Salvage SBRT

Salvage Robotic SBRT for local Prostate Cancer Recurrence

- Cancer Oscar Lambret – 23 patients 2011 – 2014
- 19 external beam, 4 brachytherapy
- 10 extra capsular invasion
- 14 received androgen ablation
- 36 Gy in 6 fractions
- 2 yr. DFS 54%
- 2 pts. with Grade 3 GU, 2 grade 2 GU

Salvage SBRT

Salvage Robotic SBRT for local Prostate Cancer Recurrence

- University of Florence, Italy – 50 patients, 2012 - 2016
- F¹⁸ – Choline PET, MRI
- All external beam , 11 received androgen ablation
- 30 patients had high risk disease
- 30 Gy in 5 fractions

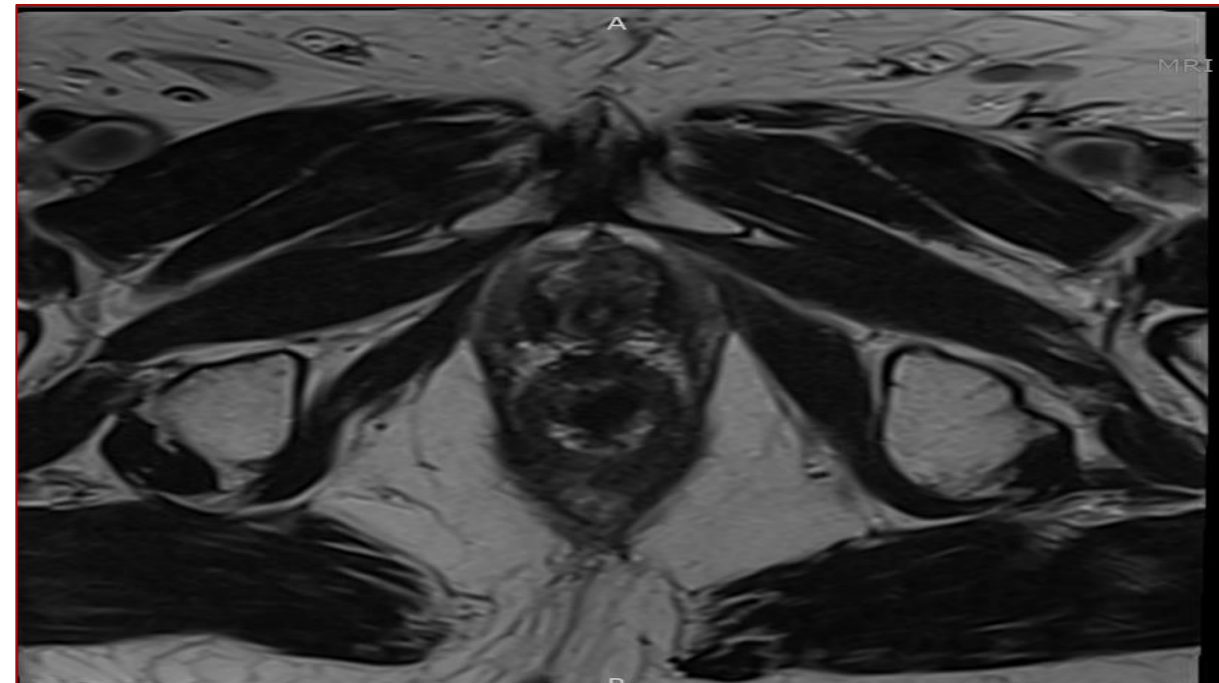
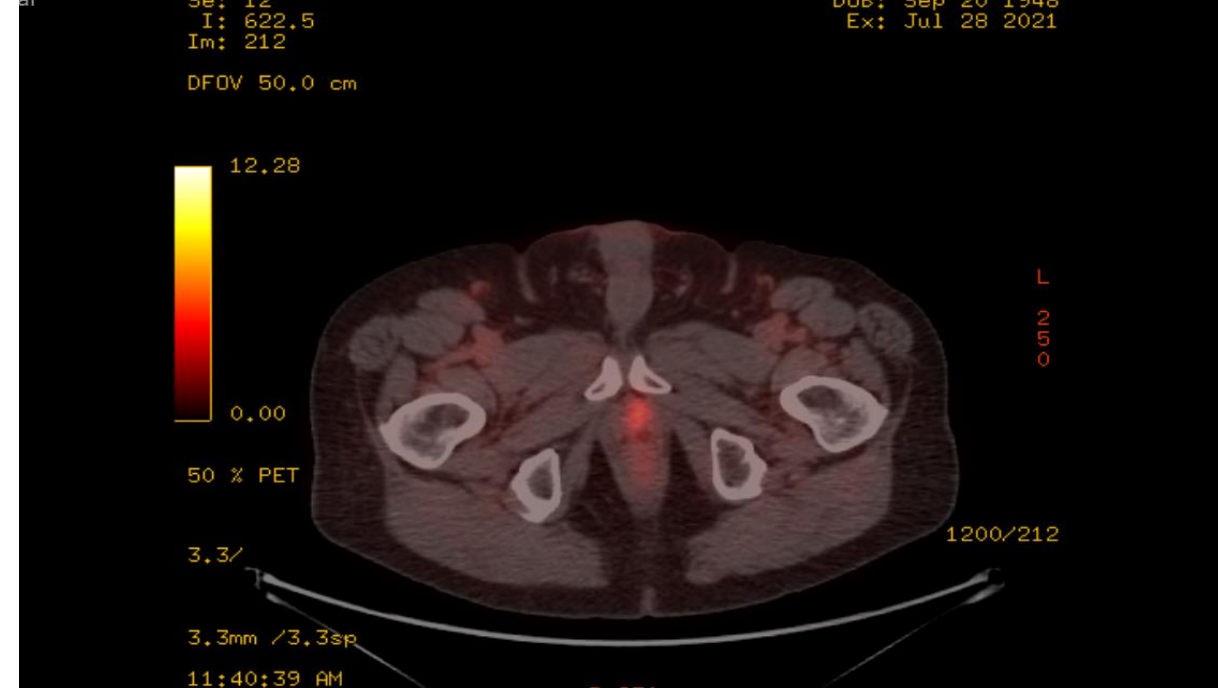
Salvage SBRT

Salvage Robotic SBRT for local Prostate Cancer Recurrence

- 1 year bRFS 80%
- Decreased with high grade

Toxicity	Grade 1	Grade 2	Grade 3
Acute bladder toxicity	9	1	1 *
Late bladder toxicity	9	3	1 †
Acute rectal toxicity	4	0	0
Late rectal toxicity	1	2	0

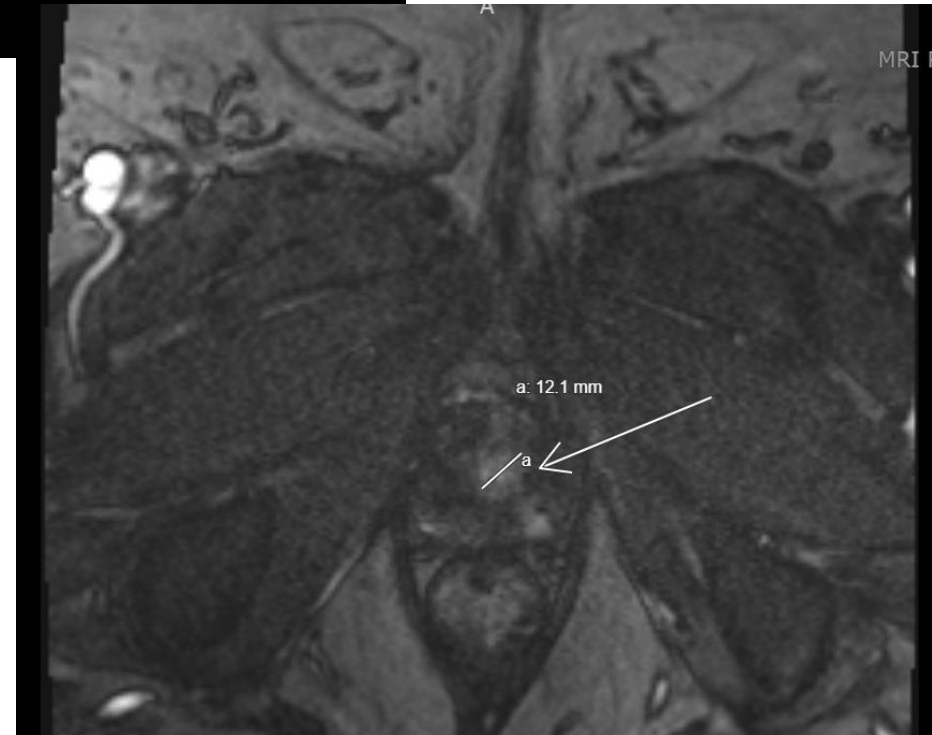
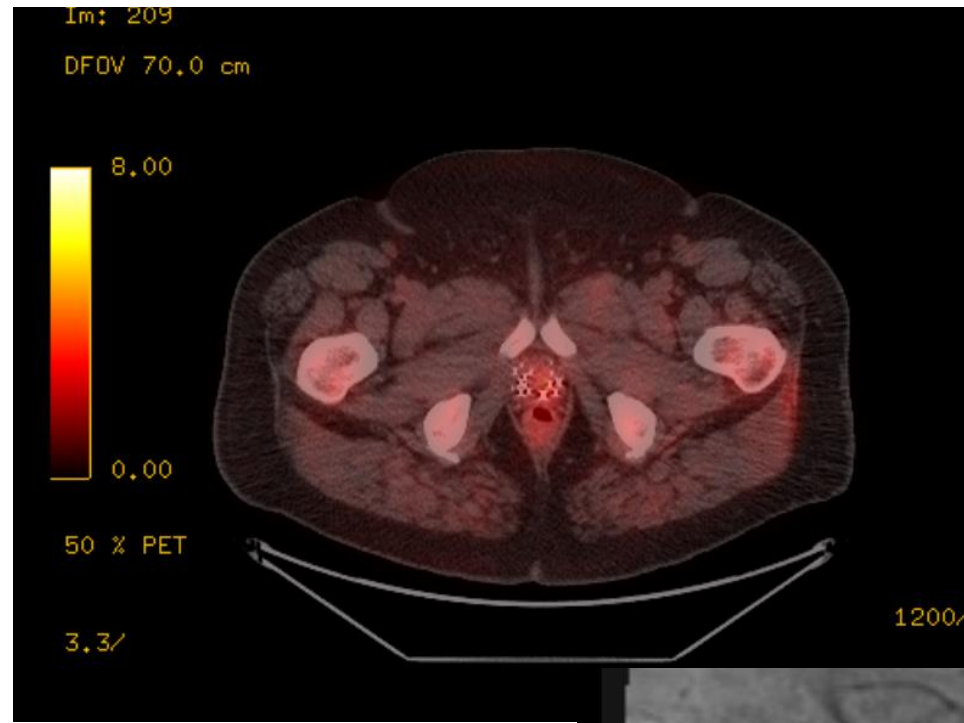
74 yo s/p RALP in 2015,
T3a, Gleason (4+3), neg.
margins. Post op PSA
0.8 ng/ml. XRT 68.4
Prostate
Bed. PSA nadir 0.03
ng/ml. Repeat PSA in
June of 2021
returned 0.82 ng/ml.
Axumin uptake in
prostate bed
MRI 11 x 11 mm mass



6 months lurpron , 36.25
Gy in 5 fractions, No
significant Late Grade 2
urgency PSA < 0.01
ng/ml



67 yo, PSA 5.5, Gleason 6 s/p brachytherapy 2004 NED until August of 2021, PSA 1.4 ng/ml Axumin mild uptake in gland. MRI 14 cc prostate with early contrast enhancement with Lt. central gland. Biopsy Gleason (4+4)



Lupron injection given
SBRT prostate, seminal
vesicles and nodes 36.25
Gy in 5 fractions, 25 Gy
nodes Acute Grade 2
GU and GI

