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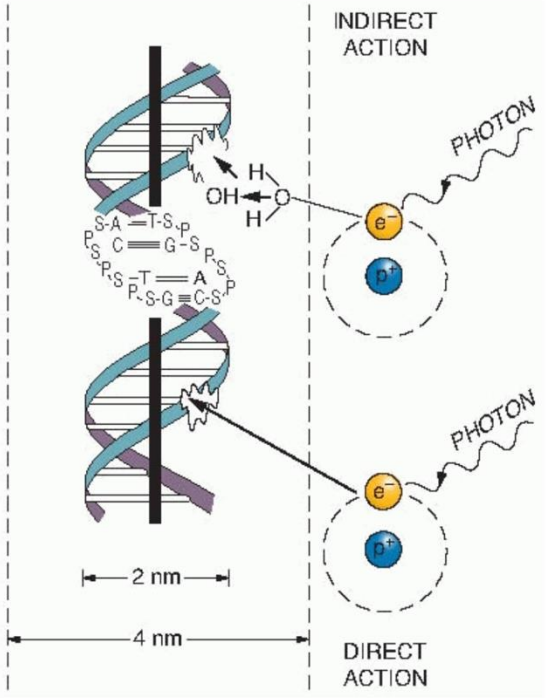
The Evolving Role of Precision Radiation Oncology Across the Prostate Cancer Continuum

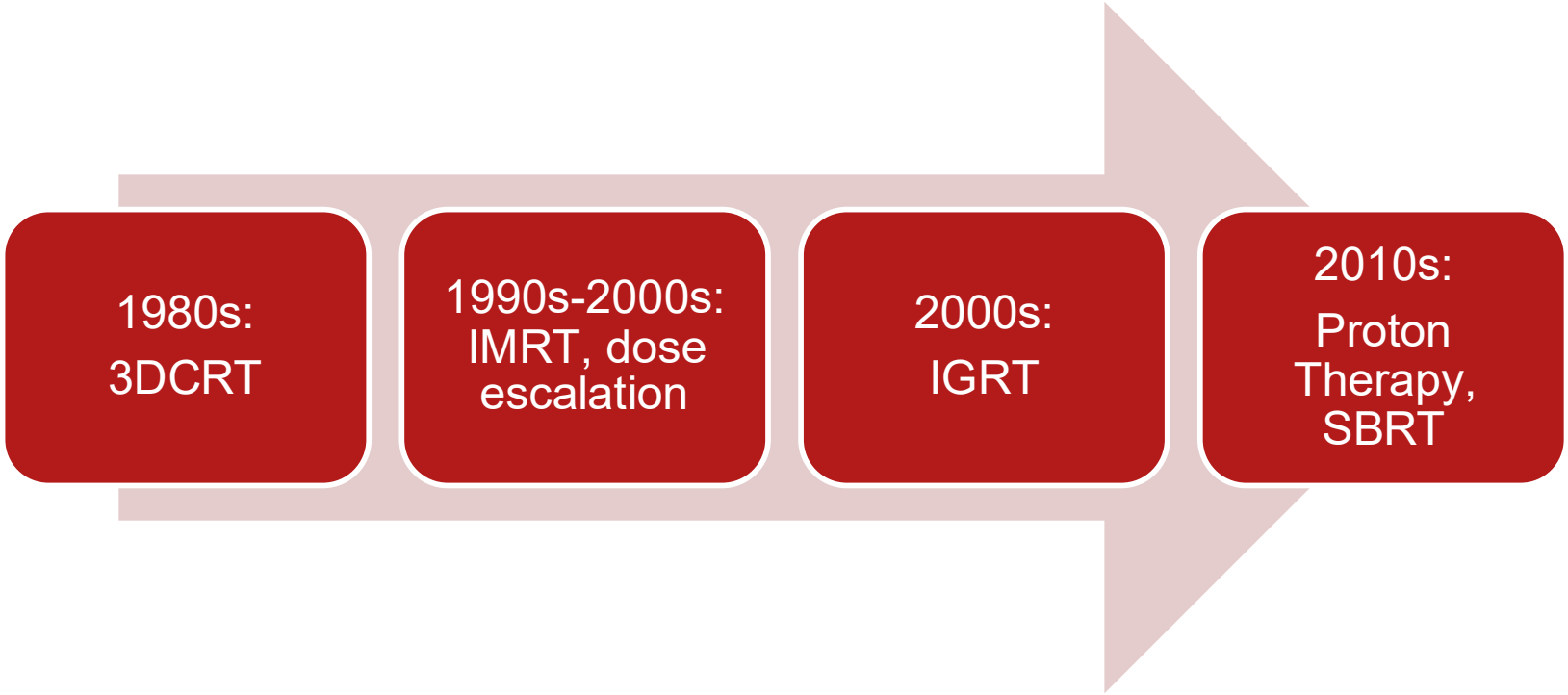
Emily S. Weg, MD
Director of Genitourinary Radiation Oncology
Assistant Professor, Department of Radiation Oncology
Weill Cornell Medicine / New York Presbyterian

What is radiation therapy?



$$\text{Therapeutic Ratio} = \frac{\text{Benefit}}{\text{Risk}}$$

What is radiation therapy for prostate cancer?



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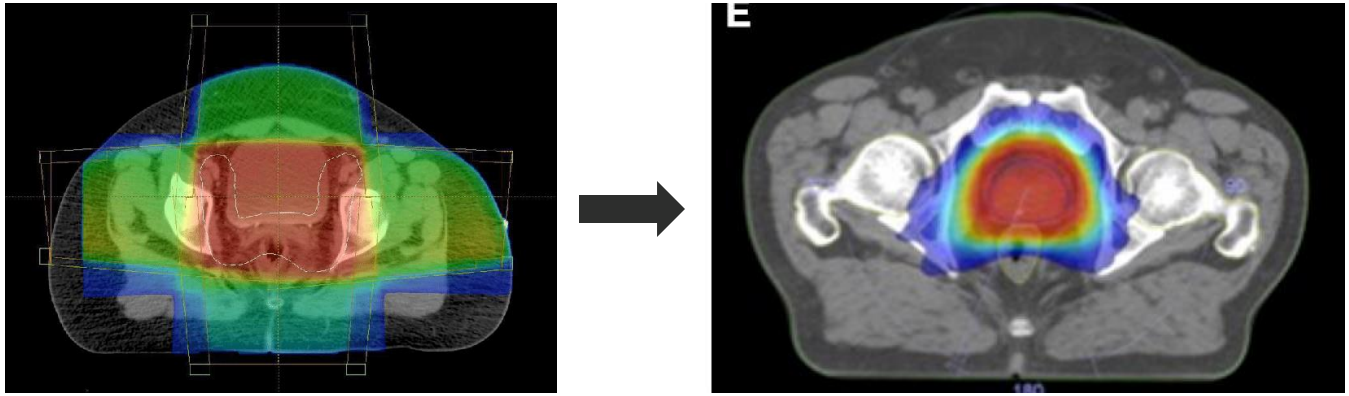
What is radiation therapy for prostate cancer?



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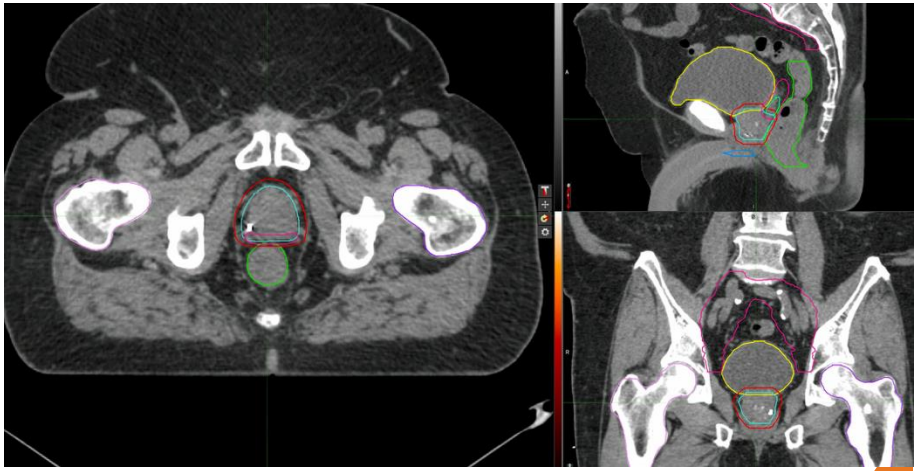
How is radiation used clinically?

- Definitive therapy for cancer
- Adjuvant therapy for cancer
- Palliative therapy for cancer
- Benign conditions

What do radiation oncologists do?

Consult → Simulation → Contour → Treatment plan → Treatment → Follow Up



Radiation for prostate cancer:

Radiation planning starts with contouring the target and avoidance structures

GTV = gross tumor volume

CTV = clinical target volume

PTV = planning target volume

ITV = internal target volume

OAR = organs at risk

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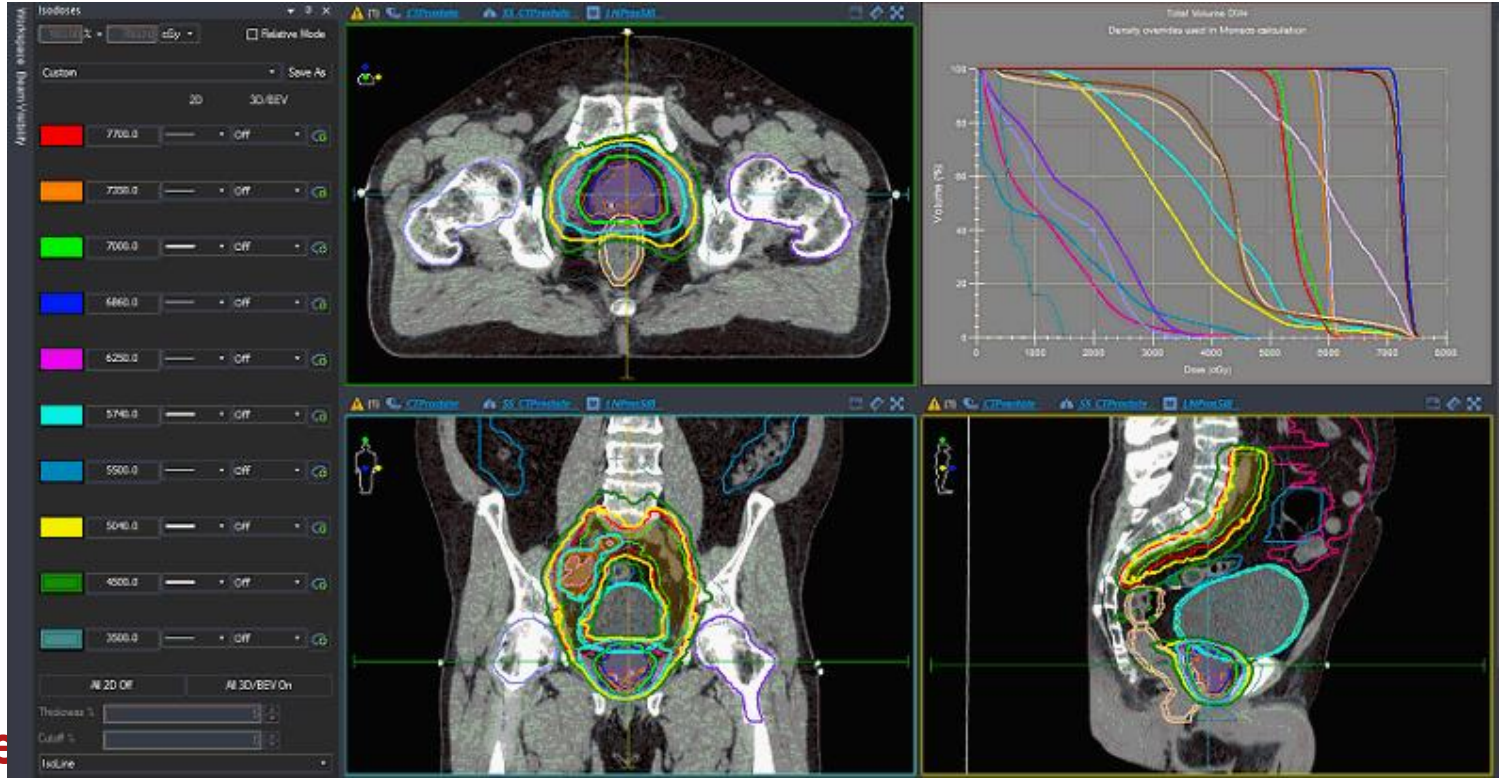
Radiation for prostate cancer: Radiation planning



Radiation for prostate cancer: Radiation planning

Priority	Dose	ROI/POI	Clinical goal	Value	Result	% outside
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Bladder	At most 15.00 % volume at 6000 cGy (RBE) dose	1.87 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Bladder	At most 20.00 % volume at 5700 cGy (RBE) dose	3.10 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Bladder	At most 25.00 % volume at 5400 cGy (RBE) dose	4.10 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Bladder	At most 35.00 % volume at 5100 cGy (RBE) dose	5.06 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Bladder	At most 50.00 % volume at 4800 cGy (RBE) dose	6.09 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	CTV_4800	At least 100.00 % volume at 4800 cGy (RBE) dose	100.00 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	CTV_6000	At least 100.00 % volume at 6000 cGy (RBE) dose	100.00 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	PenileBulb	At most 3900 cGy (RBE) average dose	1273 cGy (RBE)	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	PTV_4800	At least 95.00 % volume at 4800 cGy (RBE) dose	99.86 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	PTV_6000	At least 95.00 % volume at 6000 cGy (RBE) dose	97.00 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	PTV_6000	At most 6600 cGy (RBE) dose at 0.03 cm^3 volume	6164 cGy (RBE)	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Rectum	At most 11.00 cm^3 volume at 6000 cGy (RBE) dose	0.31 cm^3	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Rectum	At most 15.00 % volume at 5400 cGy (RBE) dose	6.15 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Rectum	At most 25.00 % volume at 5100 cGy (RBE) dose	8.33 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Rectum	At most 35.00 % volume at 4800 cGy (RBE) dose	12.27 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Rectum	At most 50.00 % volume at 4500 cGy (RBE) dose	15.40 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Rectum	At most 65.00 % volume at 2500 cGy (RBE) dose	40.73 %	✓	0 %
1	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Rectum	At most 70.00 % volume at 1400 cGy (RBE) dose	55.59 %	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Bladder	At most 5.00 % volume at 6000 cGy (RBE) dose	1.87 %	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Bladder	At most 25.00 % volume at 4800 cGy (RBE) dose	6.09 %	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Bladder	At most 55.00 % volume at 3000 cGy (RBE) dose	11.51 %	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Bowel_large	At most 5320 cGy (RBE) dose at 0.03 cm^3 volume	3924 cGy (RBE)	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Femur_Head_L	At most 50.00 % volume at 4200 cGy (RBE) dose	0.00 %	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Femur_Head_R	At most 50.00 % volume at 4200 cGy (RBE) dose	0.00 %	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	PenileBulb	At most 4200 cGy (RBE) average dose	1273 cGy (RBE)	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	PTV_4800	At least 95.00 % volume at 4800 cGy (RBE) dose	99.86 %	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	PTV_6000	At least 95.00 % volume at 5700 cGy (RBE) dose	99.70 %	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	PTV_6000	At most 6420 cGy (RBE) dose at 0.03 cm^3 volume	6164 cGy (RBE)	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Rectum	At most 1.00 % volume at 6000 cGy (RBE) dose	0.90 %	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Rectum	At most 35.00 % volume at 4800 cGy (RBE) dose	12.27 %	✓	0 %
2	Plan dose (RBE): Prostate6000_ESW (PlanCT_5.13.2021)	Rectum	At most 50.00 % volume at 3000 cGy (RBE) dose	35.48 %	✓	0 %

Radiation treatment on a linac

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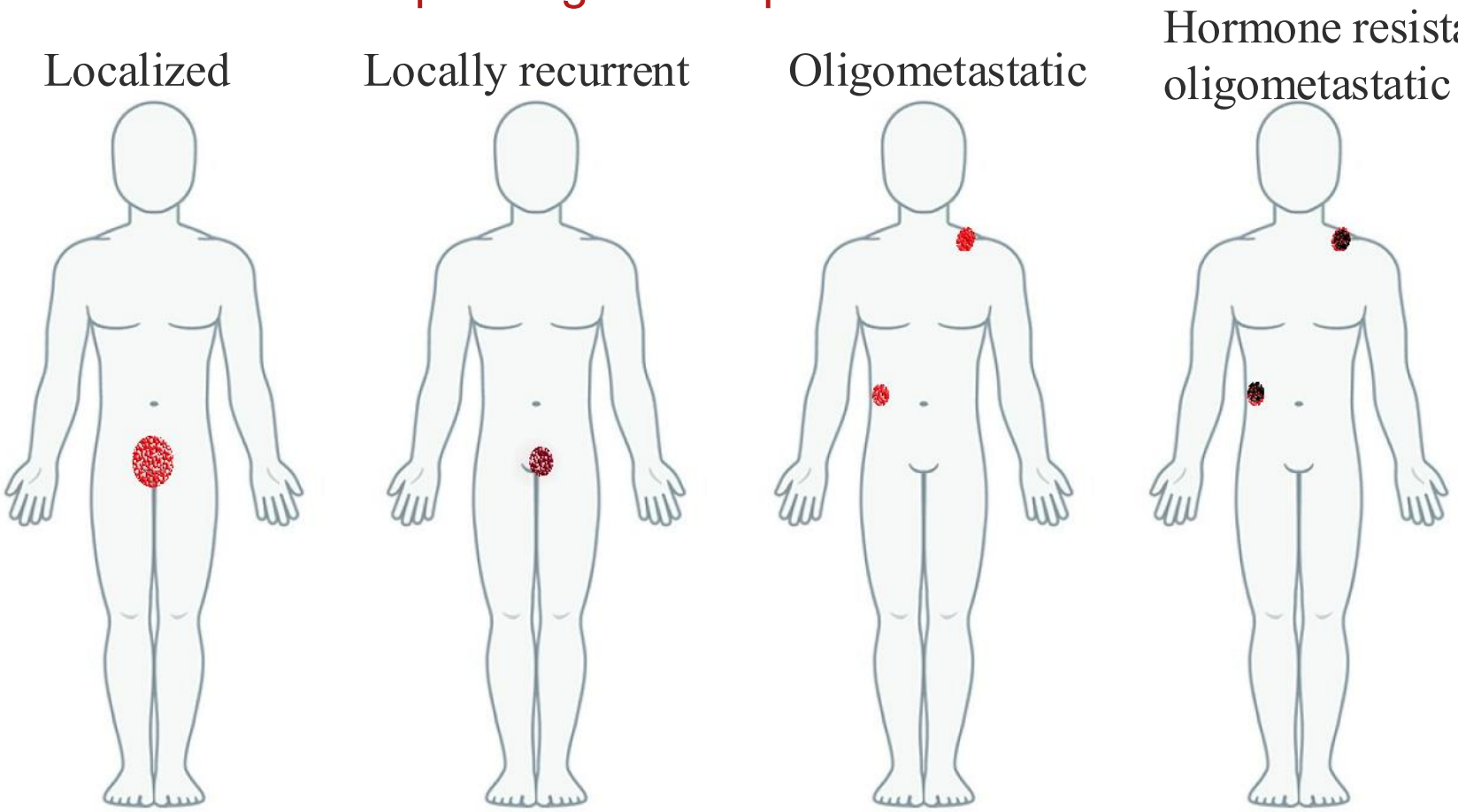
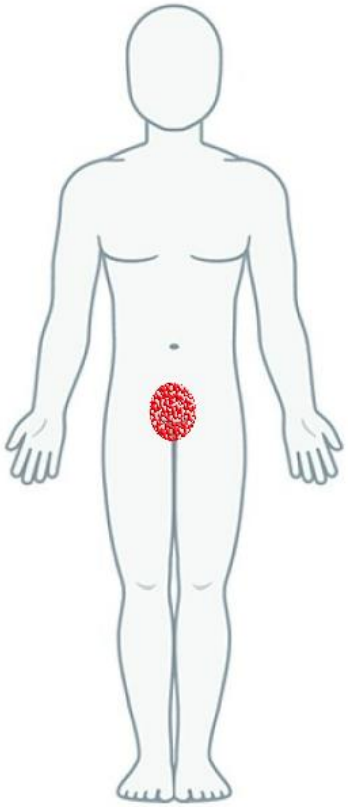
Role of radiation expanding across prostate cancer disease states

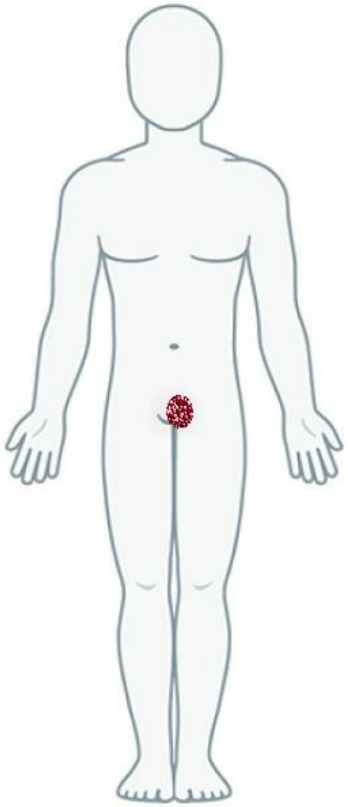


Role of radiation expanding across prostate cancer disease states

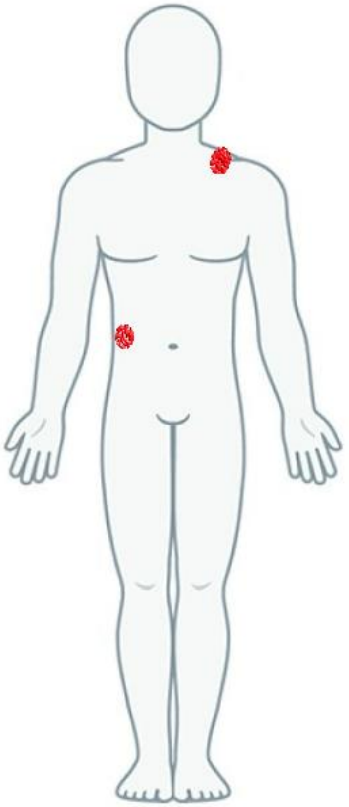
Localized



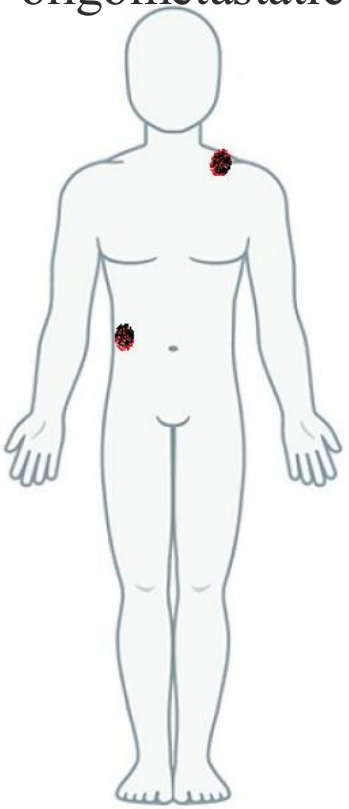
Locally recurrent



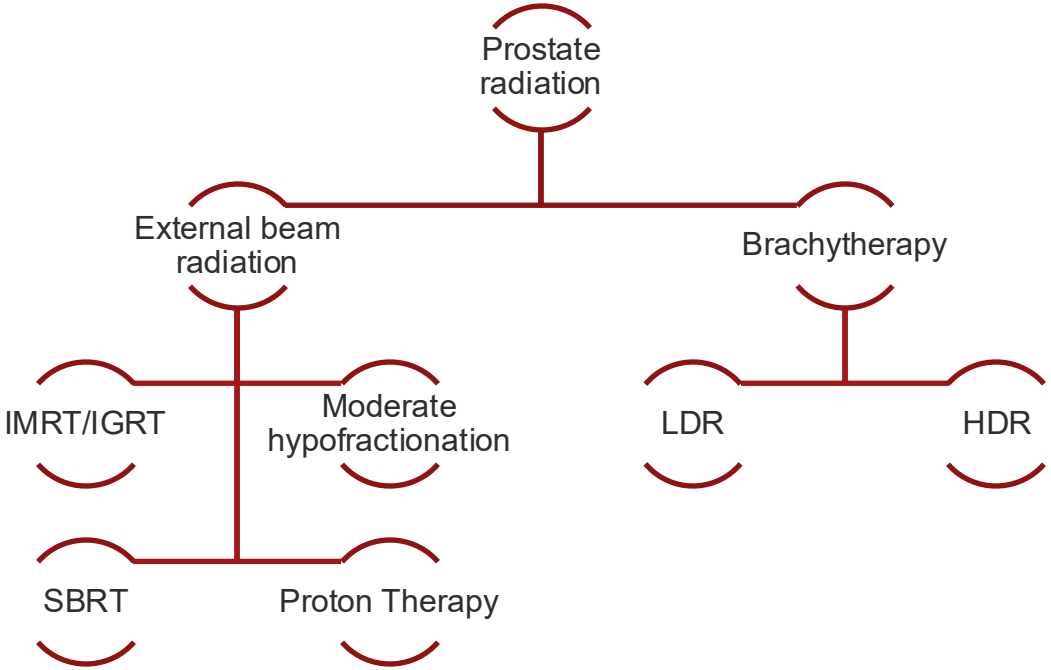
Oligometastatic



Hormone resistant oligometastatic



The landscape of radiation for LOCALIZED prostate cancer



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What is Stereotactic Body Radiation Therapy (SBRT)?

	Conventional fractionation	Moderate hypofractionation	SBRT
Dose	81Gy	70Gy	40Gy
Dose per fraction	1.8Gy	2.5Gy	8Gy
Fraction number	45	28	5

Why SBRT?

- Biology
- Socioeconomic
- Natural evolution

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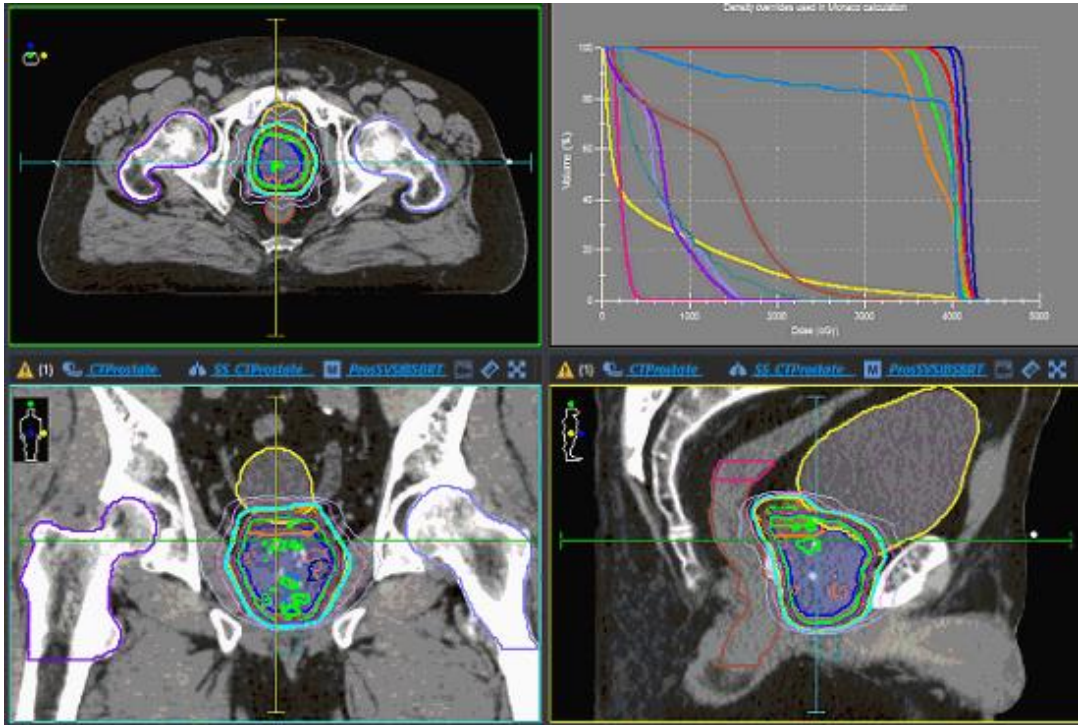
Stereotactic Body Radiation Therapy (SBRT): Precision matters

- High doses
- Small margins
- Extra image guided targeting
- Fiducial markers + rectal spacer
- Extra patient prep to minimize inter-fraction variations in internal anatomy



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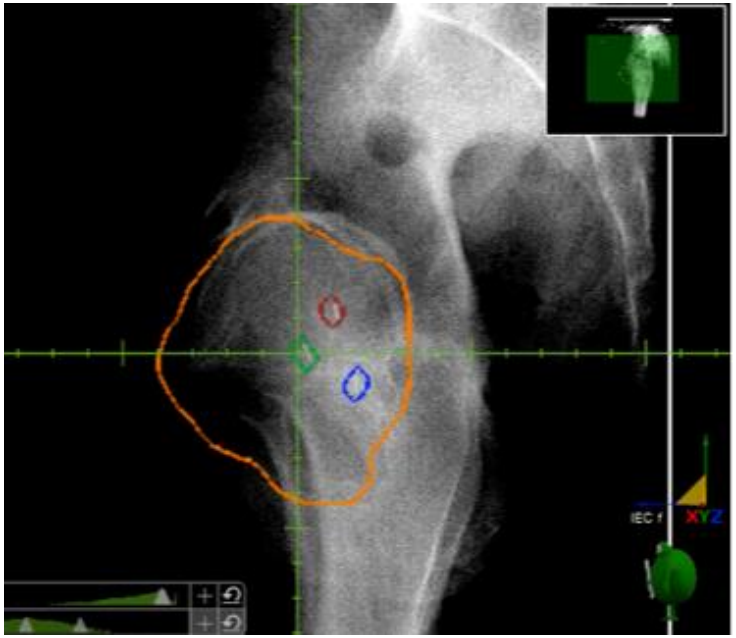
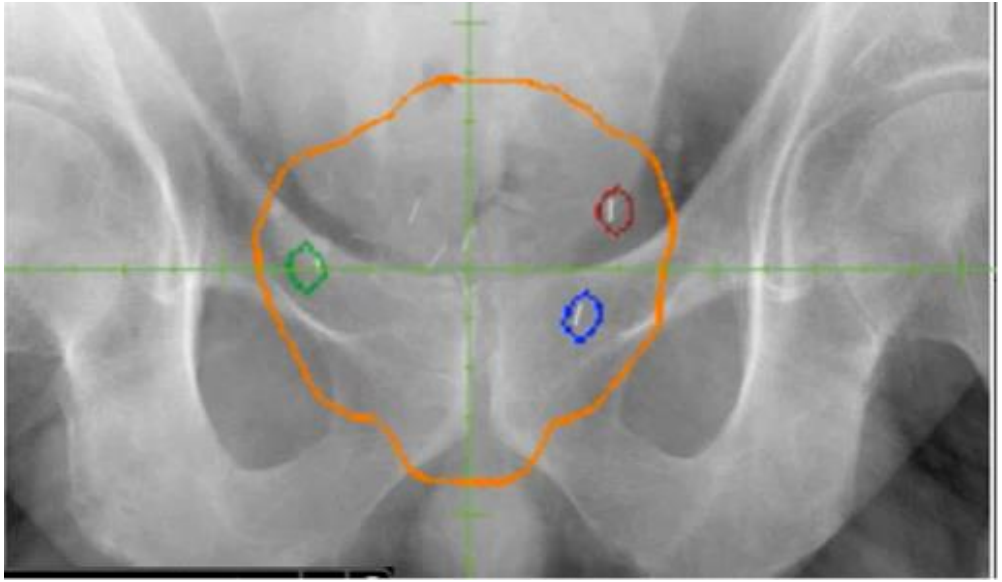
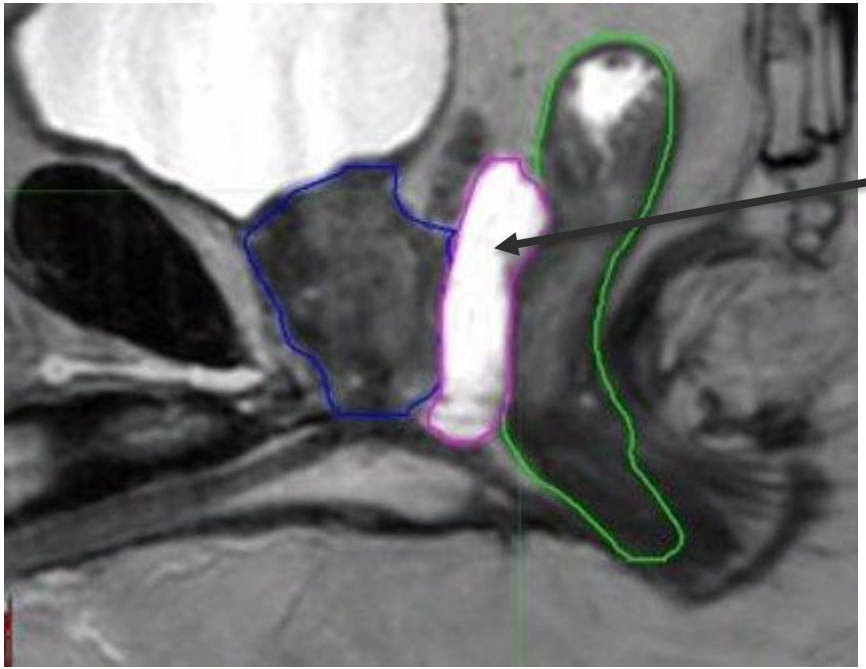
Fiducial Markers



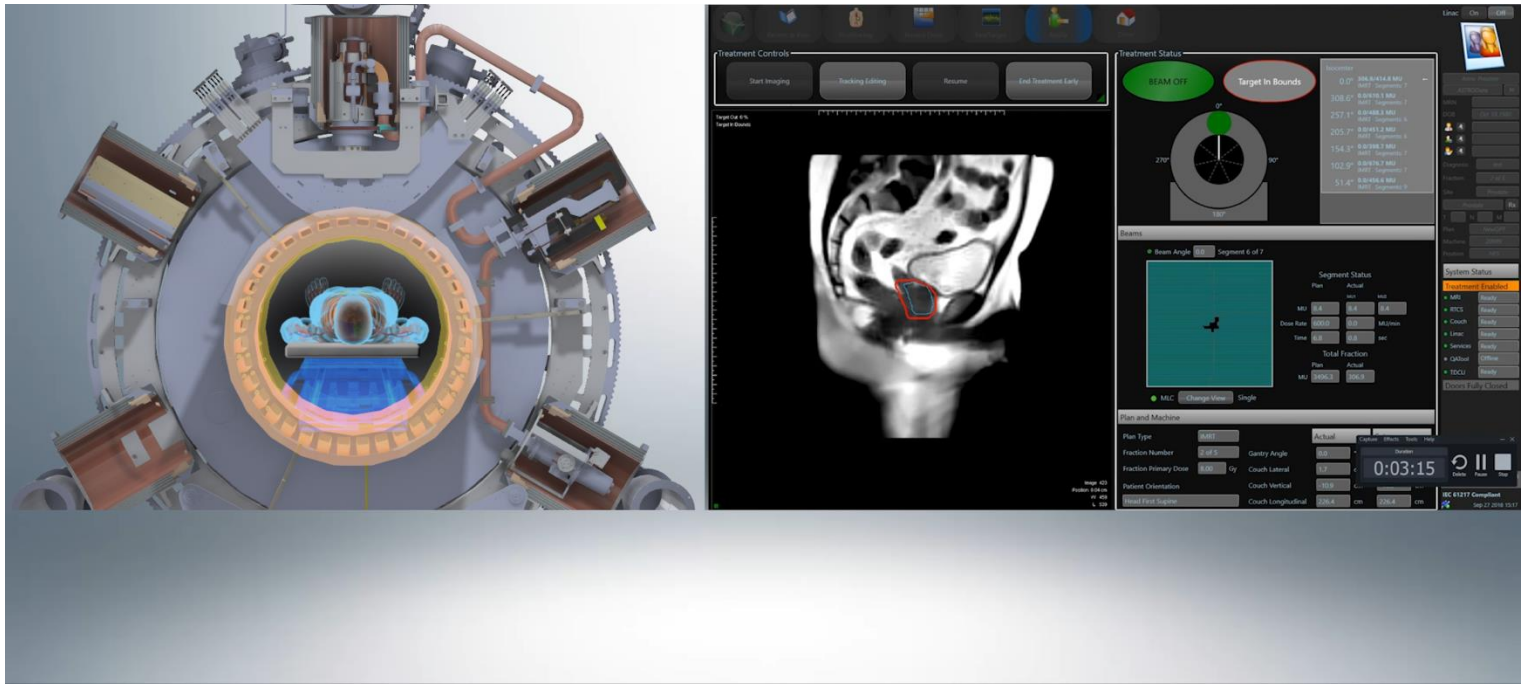


Rectal Hydrogel Spacer



Hydrogel Spacer creates about 1cm of distance between the prostate and rectum

SBRT on the MR Linac



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SBRT on the MR Linac

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SBRT on the MR Linac

JAMA Oncology

RCT: Magnetic Resonance Imaging–Guided vs Computed Tomography–Guided Stereotactic Body Radiotherapy for Prostate Cancer

POPULATION

156 Men

Men with clinically localized prostate adenocarcinoma receiving stereotactic body radiotherapy (SBRT)

Median age, 71 y

INTERVENTION

154 Participants randomized and analyzed

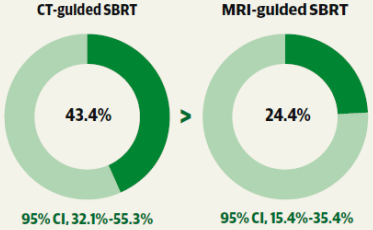
76 CT-guided SBRT
SBRT to the prostate using computed tomography (CT) guidance and a standard 4-mm planning margin

78 MRI-guided SBRT
SBRT to the prostate using magnetic resonance imaging (MRI) guidance with a 2-mm planning margin

FINDINGS

Incidence of acute grade ≥2 GU toxic effects was significantly lower with MRI-guided SBRT compared with CT-guided SBRT

Proportion with acute grade ≥2 GU toxic effects



P value for comparison = .01

LOCATION

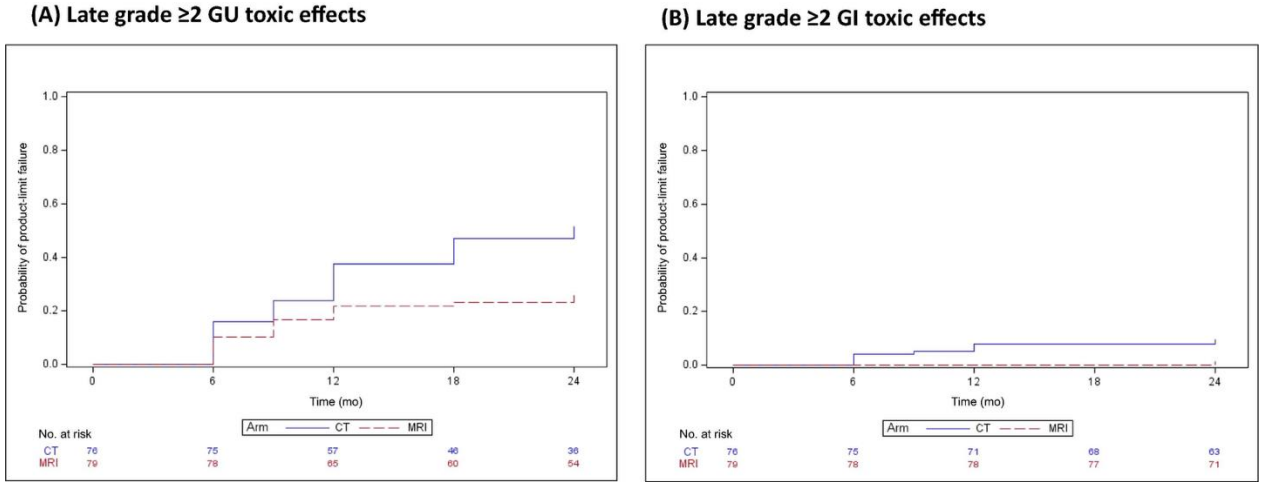
One large US medical center

PRIMARY OUTCOME

Incidence of acute grade ≥2 genitourinary (GU) toxic effects from the start of SBRT to ≤90 d post-SBRT, as measured by the Common Terminology Criteria for Adverse Events, version 4.03 scale

Kishan AU, Ma TM, Lamb JM, et al. Magnetic resonance imaging-guided vs computed tomography-guided stereotactic body radiotherapy for prostate cancer: the MIRAGE randomized clinical trial. *JAMA Oncol.* Published online January 12, 2023. doi:10.1001/jamaoncol.2022.6558

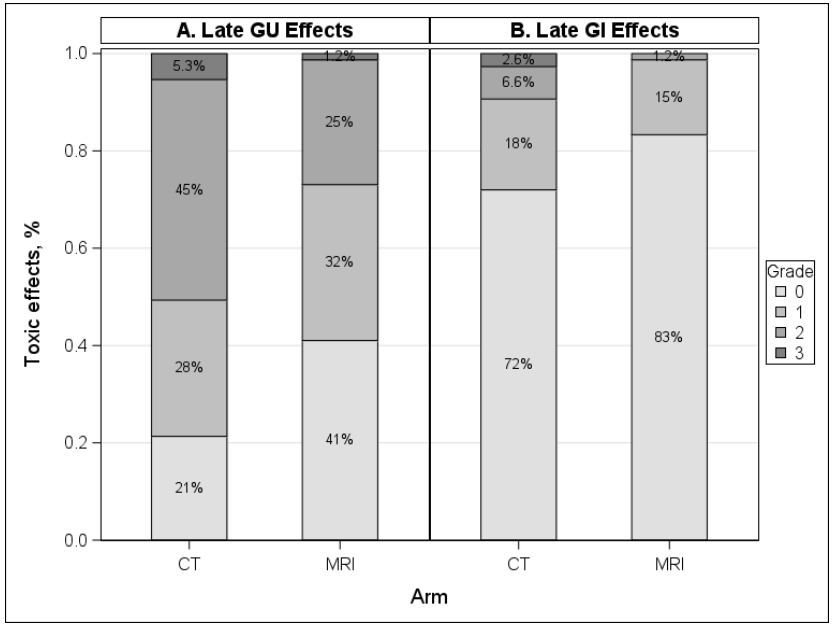
SBRT on the MR Linac: less 2-year toxicity



MR-guided SBRT associated with less 2-year G2+ GU (27% vs 51%, p=0.004) and GI tox (1.4% vs 9.5%, p=0.025)

Kishan et al, Eur Urol 2024.

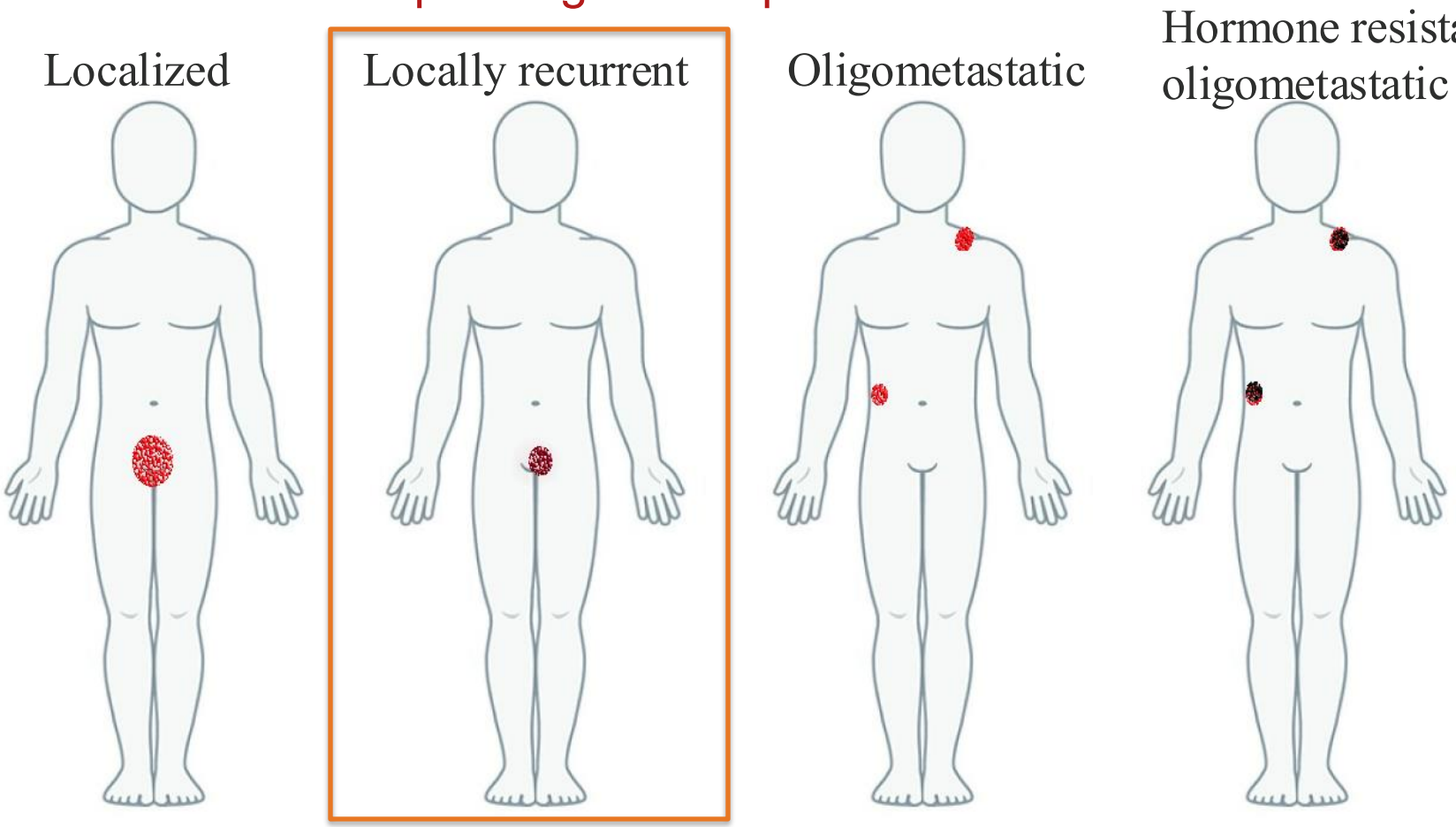
SBRT on the MR Linac: only 1% G3 tox



MR-guided SBRT associated with less late GU and GI toxicity

Kishan et al, Eur Urol 2024.

Role of radiation expanding across prostate cancer disease states



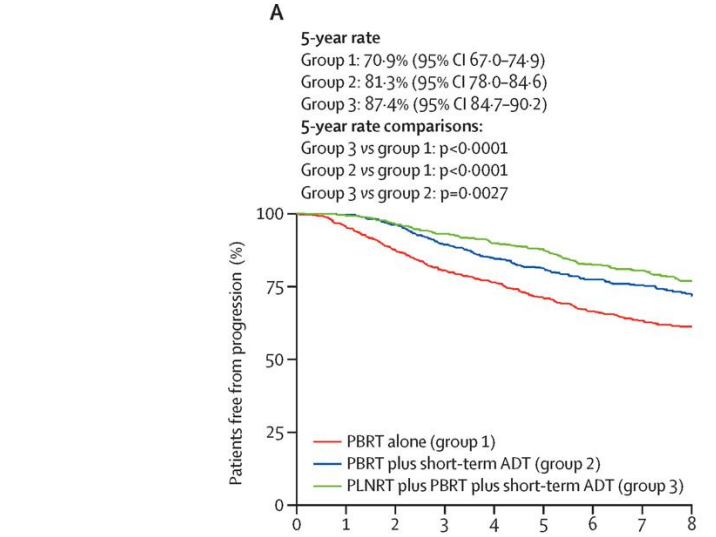
PSA recurrence following prostatectomy

Outcomes are improving!

- ultrasensitive PSA detection
- earlier interventions
- better diagnostics with PSMA PET

Outcomes after modern techniques for post-operative salvage radiation therapy: RTOG 0534 / SPPORT Trial (Pollack et al, The Lancet 2022)

- Phase III RCT with 3 arms: salvage RT to the prostate bed alone +/- ADT x4-6 months +/- elective pelvic nodal irradiation
- 1800 patients enrolled
- 5 year freedom from progression was 71% vs 81% vs **87%**



Number at risk (number censored)

PBRT alone (group 1)	564 (0)	506 (33)	449 (49)	403 (59)	371 (71)	333 (83)	290 (106)	234 (149)	180 (196)
PBRT plus short-term ADT (group 2)	578 (0)	555 (20)	524 (32)	480 (40)	440 (55)	401 (77)	341 (118)	273 (178)	193 (247)
PLNRT plus PBRT plus short-term ADT (group 3)	574 (0)	559 (11)	536 (17)	511 (24)	484 (34)	459 (46)	396 (83)	324 (146)	250 (207)

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PSA recurrence following prostatectomy

Quality of life post treatment is improving!

- More thoughtful use of ADT

Local recurrence following **radiation**

Can you reirradiate?

How should intra-prostatic failures after RT be managed?

Table 3 – Covariate-adjusted meta-regression comparing efficacy and toxicity between salvage modalities and radical prostatectomy

	2-yr RFS	5-yr RFS	Severe GU toxicity	Severe GI toxicity
Radical prostatectomy				
Adjusted percent[a] (95% CI)	72% (66–78%)	53% (46%–59%)	21% (16%–26%)	1.5% (0.4%–3.2%)
Odds ratio (95% CI)	1.0	1.0	NA	NA
p value	Reference	Reference	Reference	Reference
R^2 (%)	0.0	0.0	0.0	0.0
Cryotherapy				
Adjusted percent[a] (95% CI)	66% (59–72%)	57% (49–65%)	15% (8–23%)	0.9% (0.3–1.8%)
Odds ratio (95% CI)	0.74 (0.49–1.12)	1.20 (0.80–1.79)	NA	NA
p value	0.2	0.4	0.2	0.5
R^2 (%)	25	0.0	8.2	27
HIFU				
Adjusted percent[a] (95% CI)	52% (45%–59%)	46% (37%–55%)	23% (17%–30%)	0.8% (0.1%–2.1%)
Odds ratio (95% CI)	0.42 (0.28–0.64)	0.76 (0.48–1.21)	NA	NA
p value	**<0.001**	0.2	0.5	0.4
R^2 (%)	0.0	41	15	22
SBRT				
Adjusted percent[a] (95% CI)	58% (46–69%)	56% (37–73%)	5.6% (1.4–12%)	0.0% (0.0–1.2%)
Odds ratio (95% CI)	0.52 (0.30–0.93)	1.13 (0.50–2.58)	NA	NA
p value	0.03	0.8	**<0.001**	0.07
R^2 (%)	55	4.2	0.00	0.0
HDR				
Adjusted percent[a] (95% CI)	77% (69–83%)	58% (52–64%)	9.6% (6.0–13.9%)	0.0% (0.0–0.3%)
Odds ratio (95% CI)	1.26 (0.77–2.09)	1.25 (0.88–1.78)	NA	NA
p value	0.4	0.2	**0.002**	**0.003**
R^2 (%)	0.0	91	0.0	0.0
LDR				
Adjusted percent[a] (95% CI)	79% (72–85%)	53% (43–63%)	9.1% (5.2–14%)	2.1% (0.6–4.0%)
Odds ratio (95% CI)	1.49 (0.89–2.50)	1.02 (0.63–1.67)	–	–
p value	0.13	0.9	**0.001**	0.6
R^2 (%)	4.3	5.2	12	20%

CI = confidence interval; GI = gastrointestinal; GU = genitourinary; HDR = high-dose-rate brachytherapy; HIFU = high-intensity focused ultrasound; LDR = low-dose-rate brachytherapy; NA = not available; RFS = recurrence-free survival; SBRT = stereotactic body radiotherapy.
Significant p-values after Bonferroni correction appear in bold.
[a] Back-transformed regression coefficients for ease of interpretation.

"MASTER" Meta-analysis of local salvage therapies after RT (Valle et al, Eur Urol 2021)

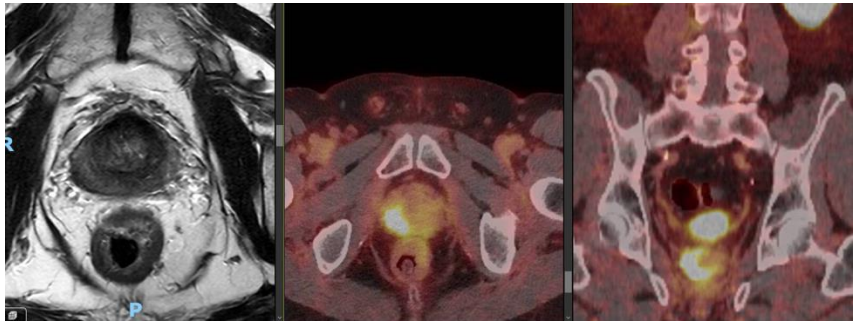
N=261 with SBRT

NCCN 2025 guidelines are the first to include SBRT as an option for reirradiation in this setting

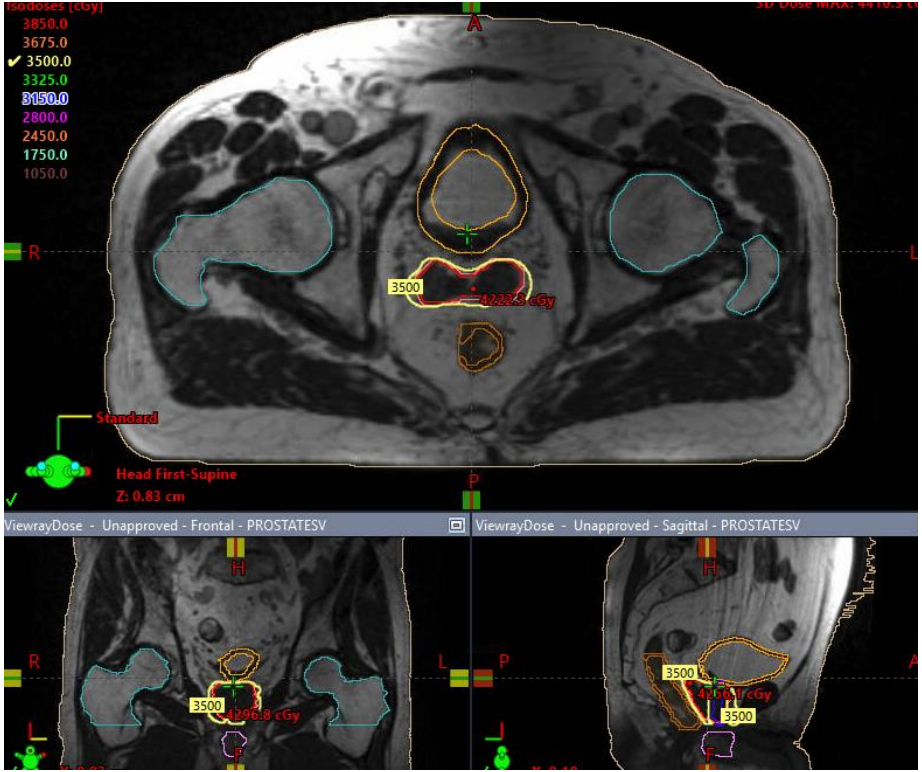
Case for local recurrence after RT

- 75M with PC diagnosed 2013
- Radiation to 81Gy / 45 fx completed 2/2014
- slowly rising PSA to 7.3, PSA DT >2 years
- MR and PSMA PET c/w local recurrence Biopsy demonstrates Gleason 3+4

- Plan: salvage re-RT with SBRT on MR linac



Salvage re-RT with MRgSBRT



PSA went from 7.3 to 1.3 at his first 3-month follow up

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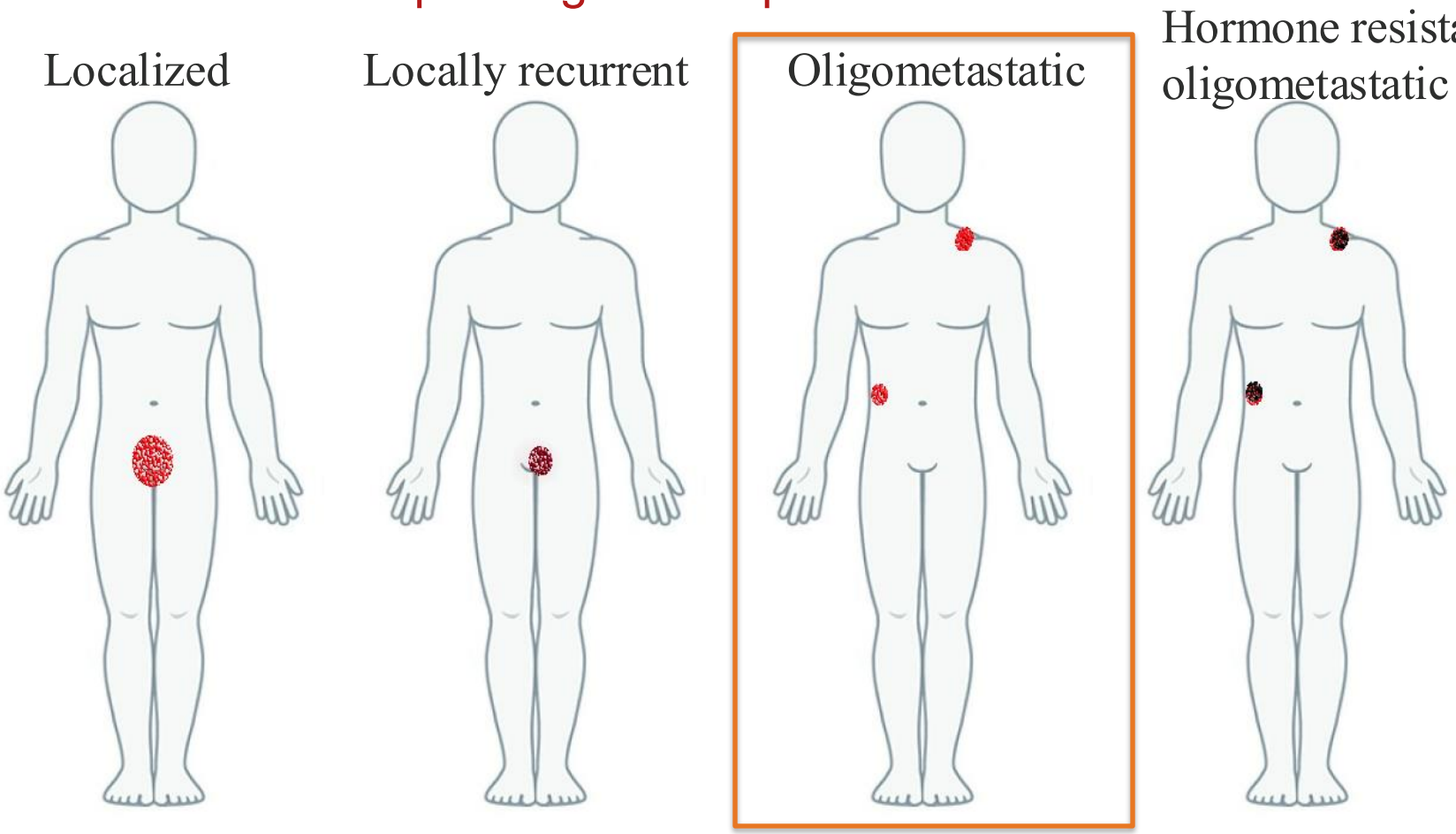
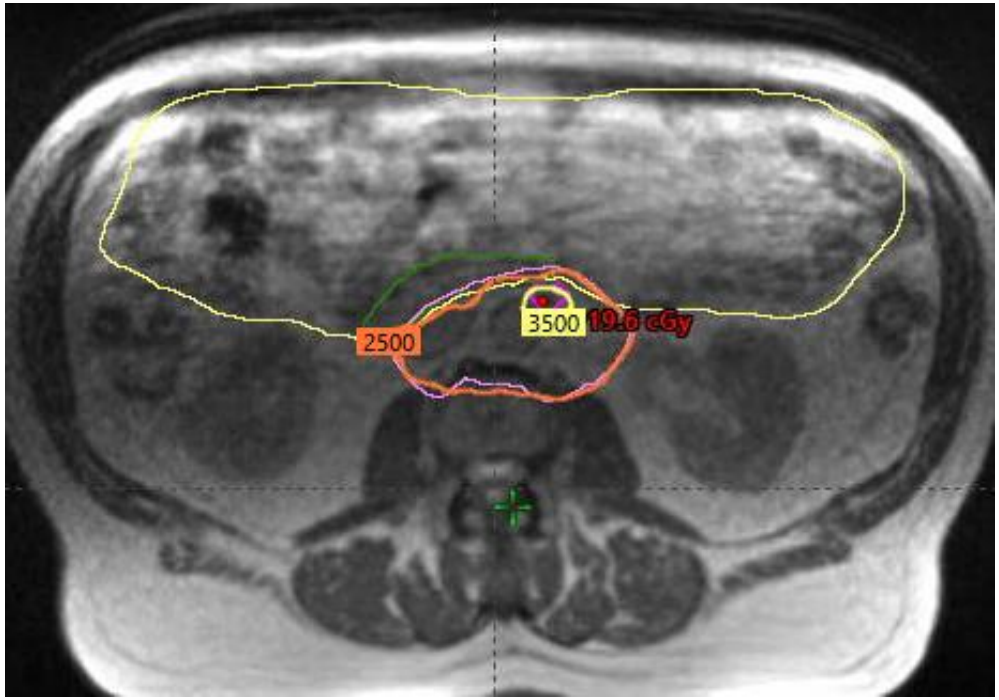
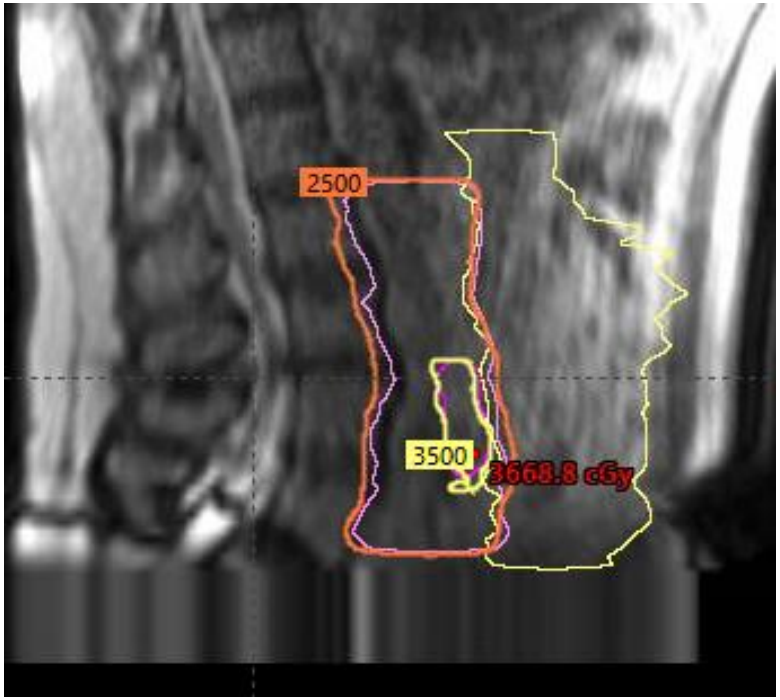
Role of radiation expanding across prostate cancer disease states



Metastasis-directed stereotactic body radiation therapy for **oligorecurrent disease**





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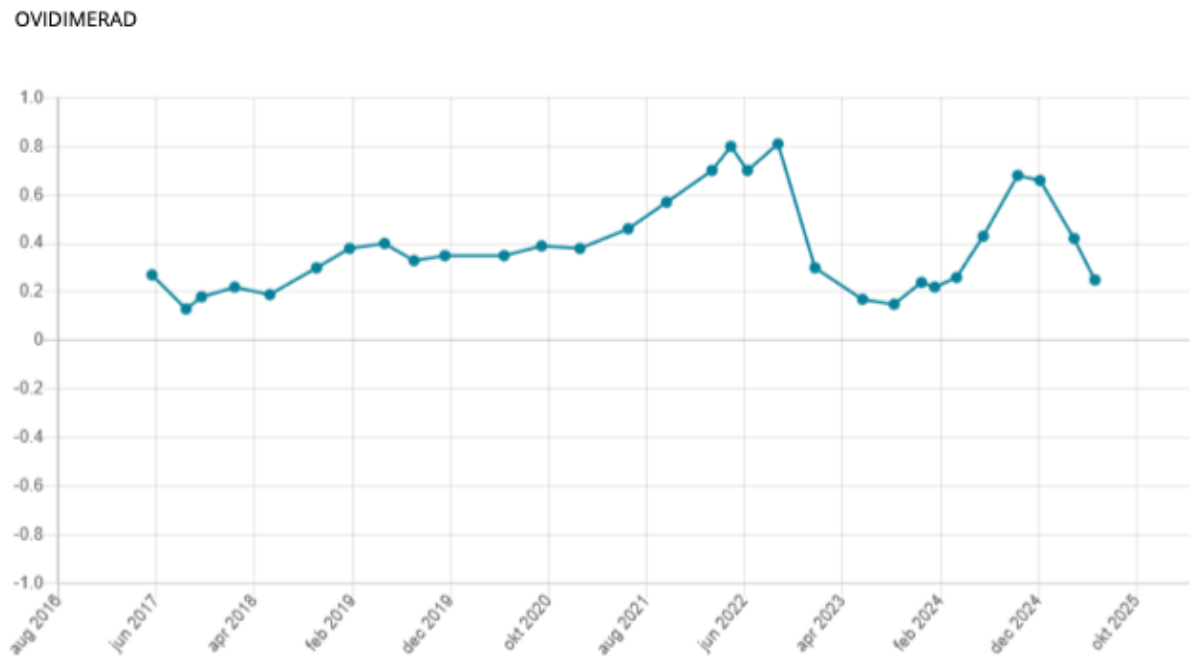
Metastasis-directed stereotactic body radiation therapy for **oligorecurrent disease**

P—PSA



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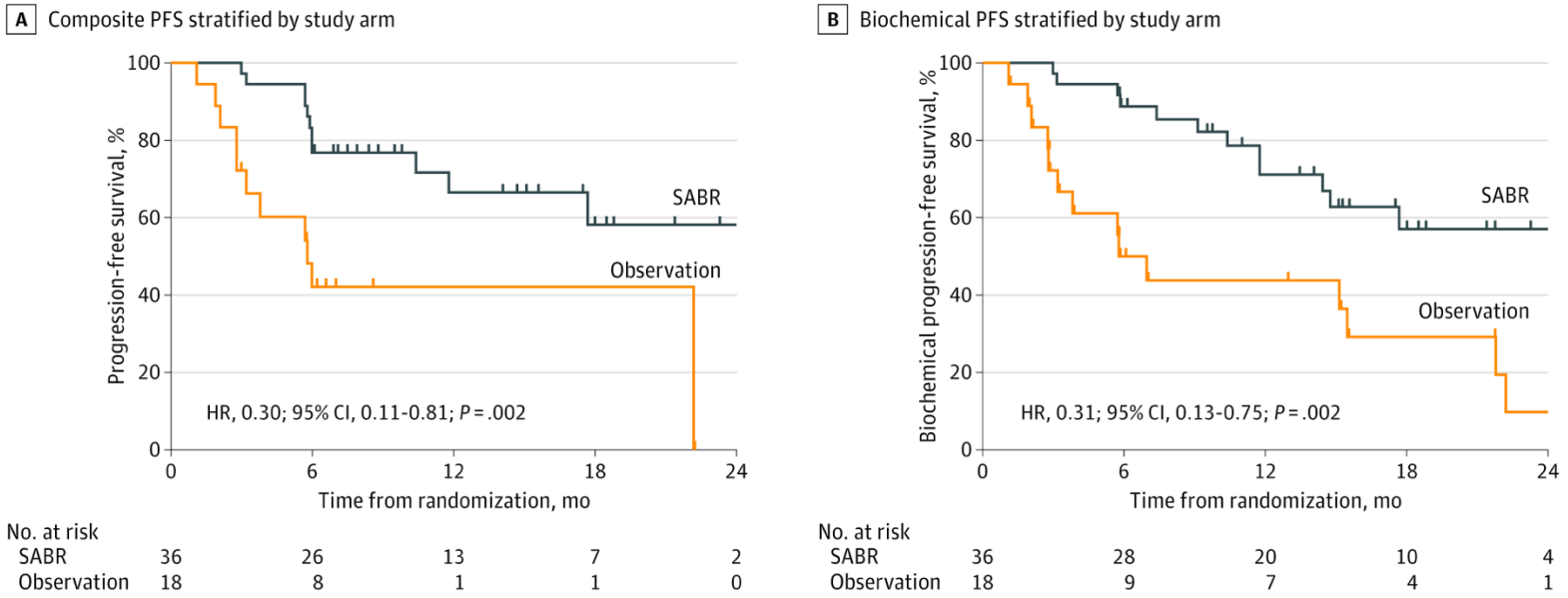
Oligometastasis-directed SBRT improves outcomes: ORIOLE study



6-month PFS was 80% with SBRT vs 40% on observation.
Median PFS was 6 months on observation vs not reached with SBRT.

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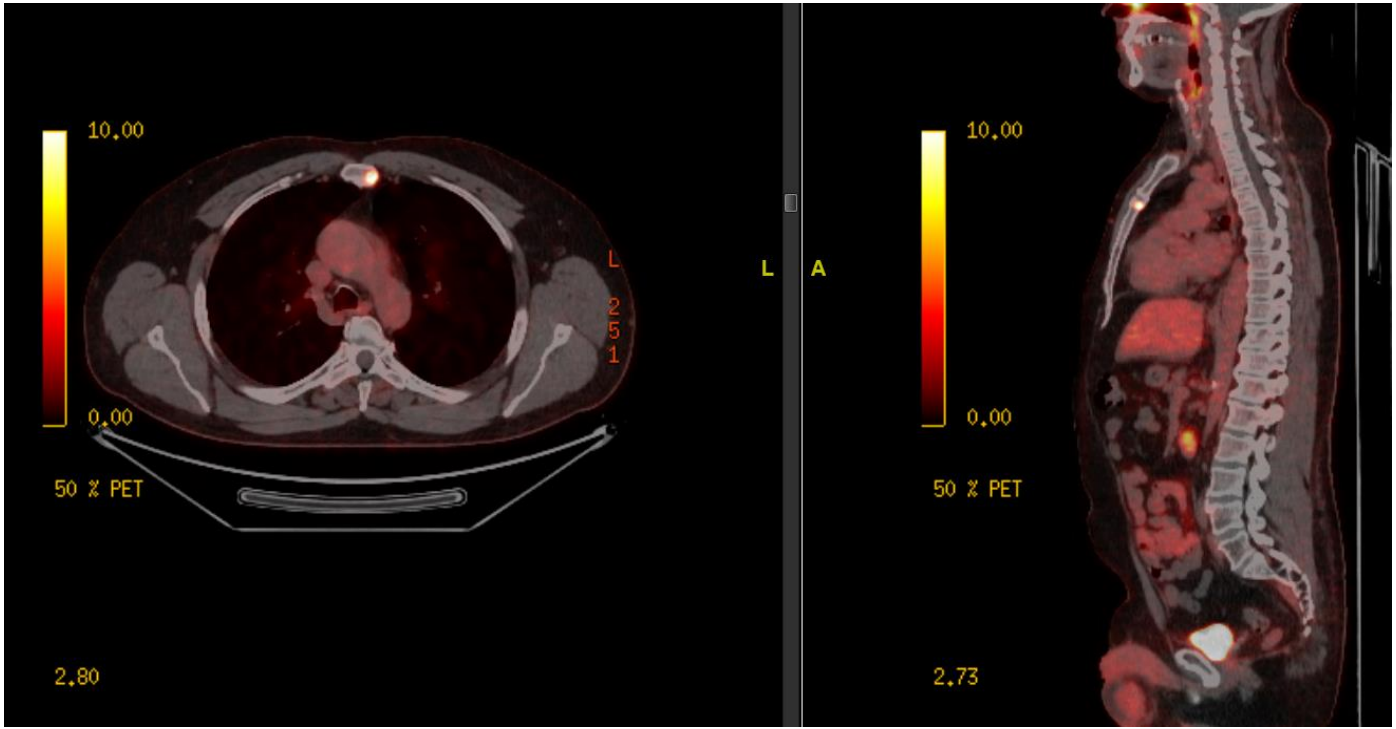
Phillips et al, JAMA Onc 2020.

Case 2: Metastasis-directed SBRT



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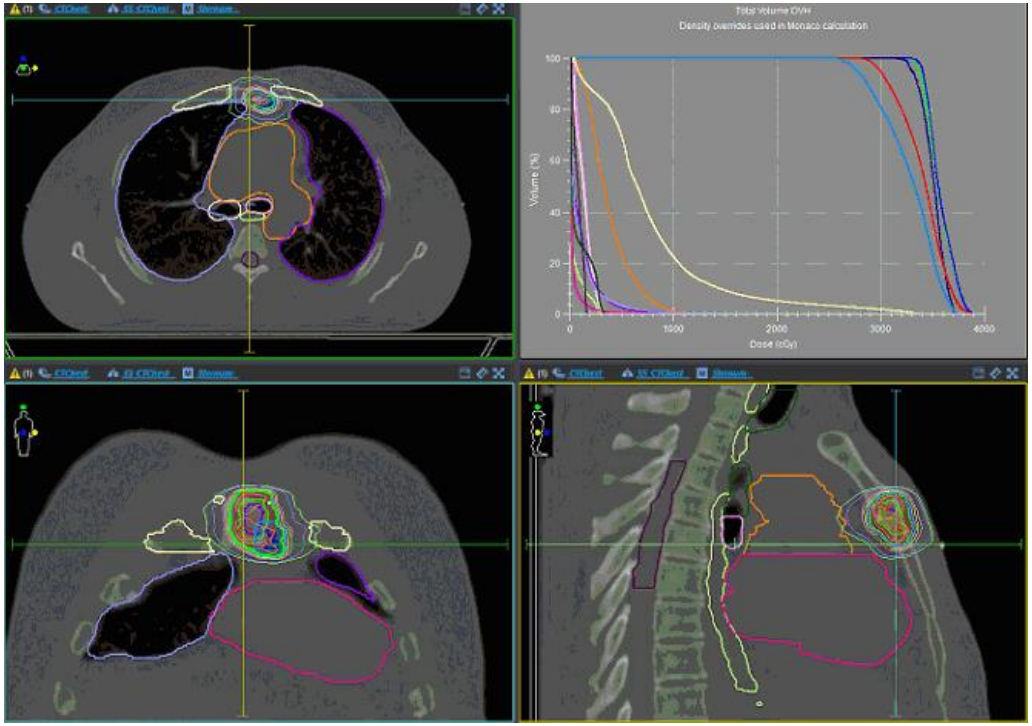
Case 2: Metastasis-directed SBRT to the sternum



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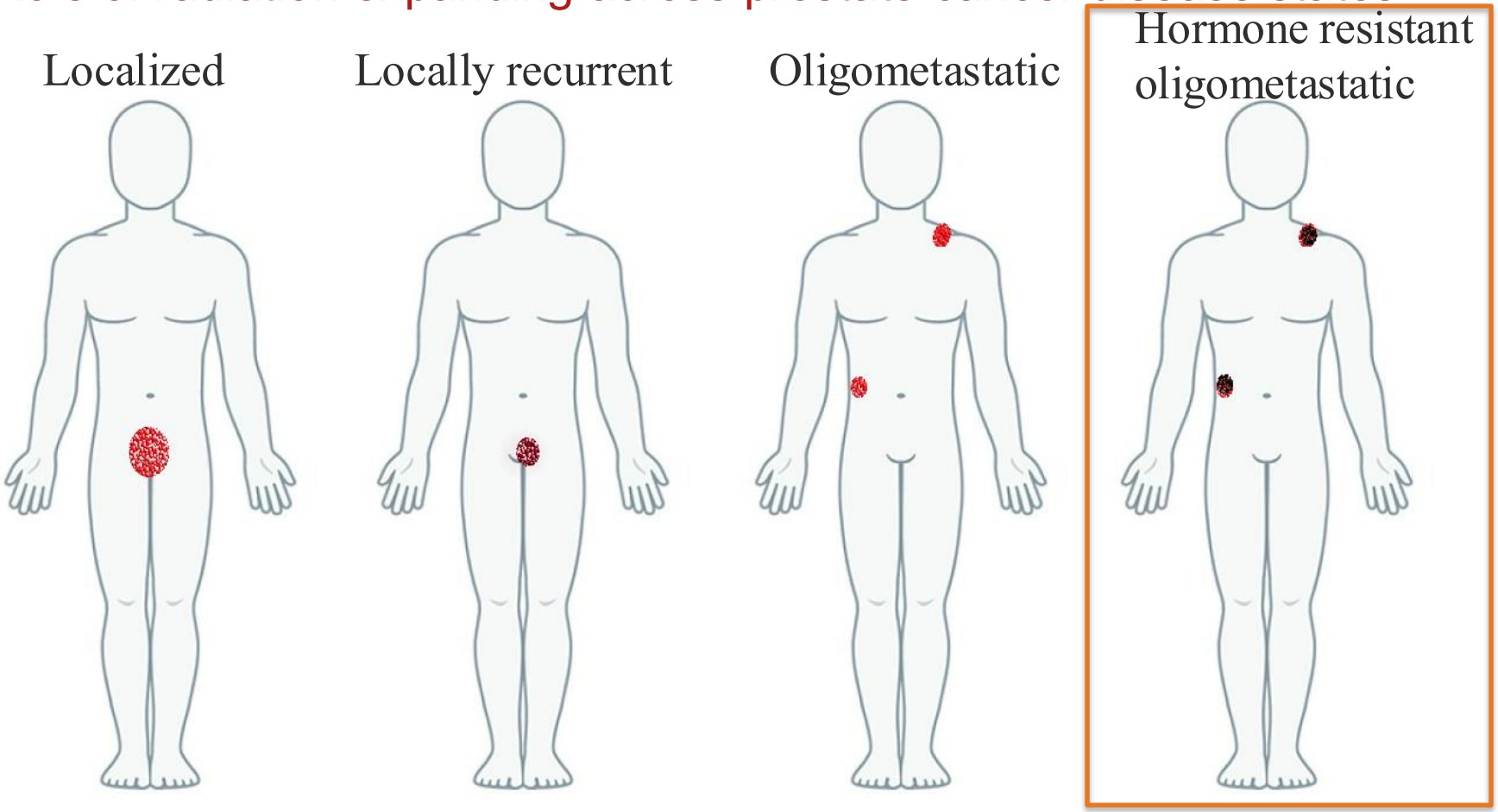
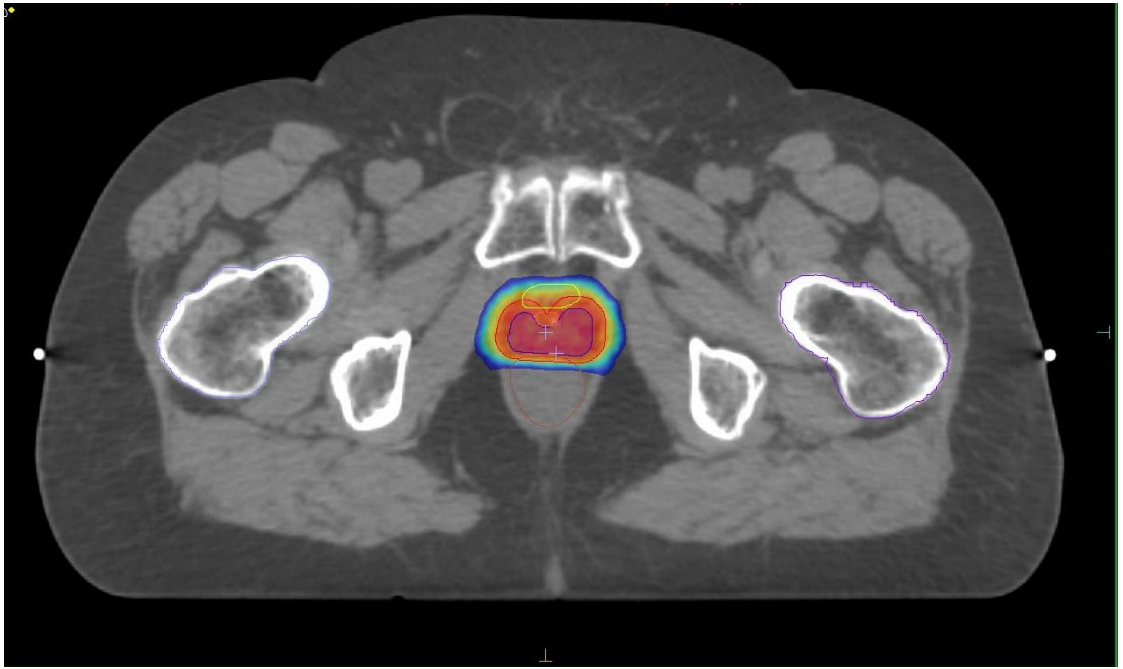
Role of radiation expanding across prostate cancer disease states



Stereotactic body radiation therapy for hormone resistant disease

- Man in his 70s, diagnosed with de novo MPC in 2010
- Treated with long-term ADT
- Developed early CRPC, with single site of progression in the prostate
- Referred for SBRT



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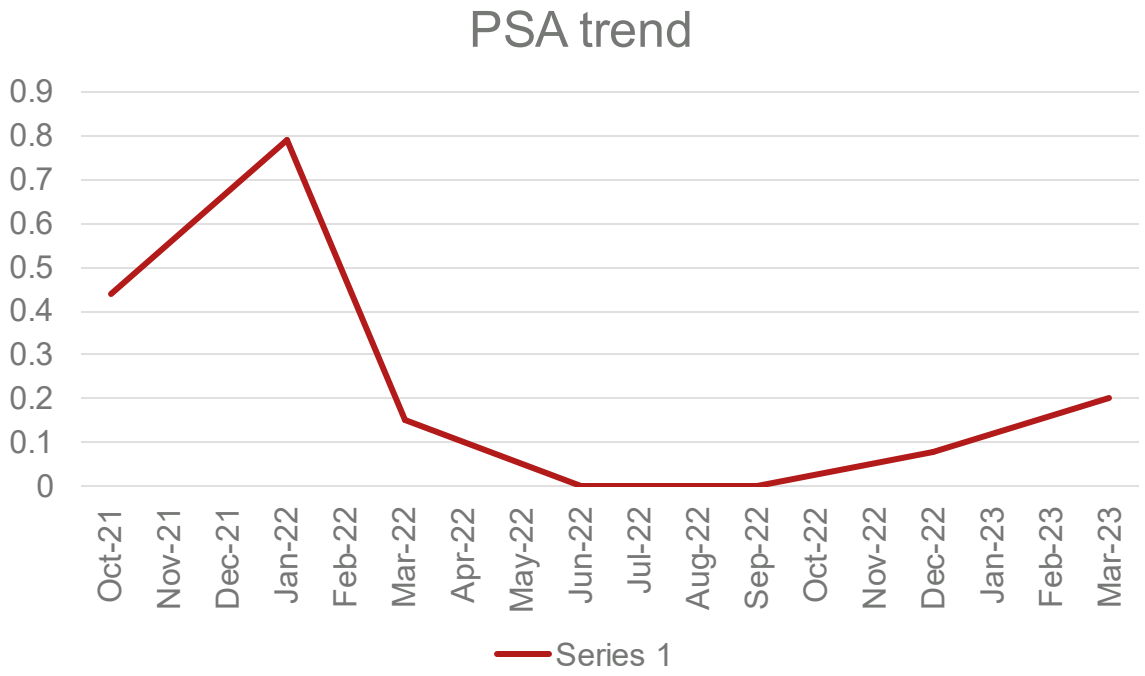
Stereotactic body radiation therapy for hormone resistant disease



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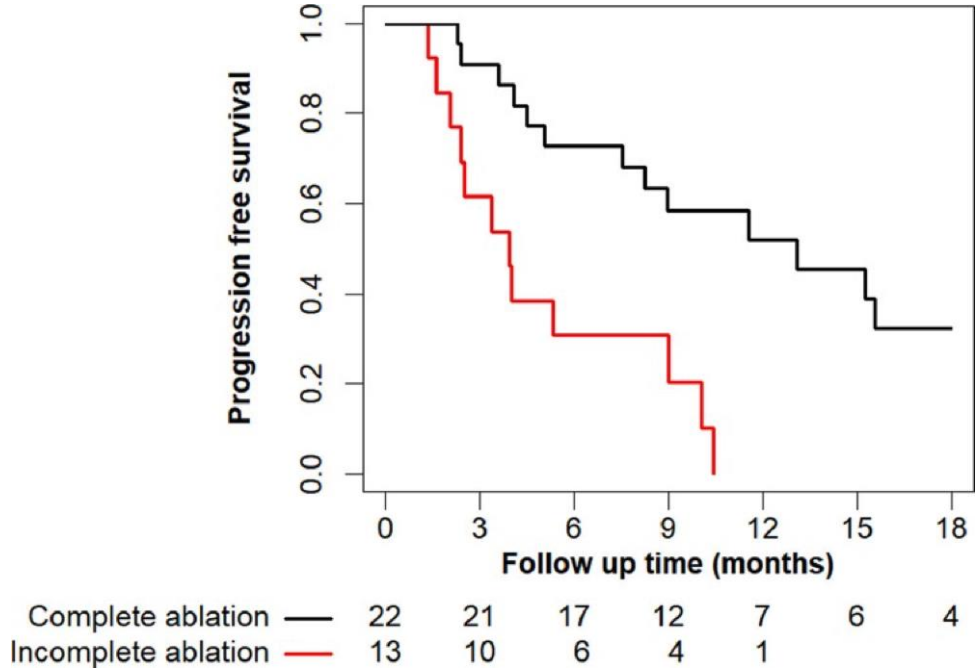
SBRT for **oligoprogressive** hormone resistant disease improves progression free survival



Brennan et al, *Advanced in Rad Onc 2021.*

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In Sum:

Localized disease

- Many different radiation tools to help individualize treatment
- MRgSBRT is a promising new technology

Locally recurrent

- Post-operative salvage therapy is improving with earlier interventions
- Post-radiation salvage therapy with MRgSBRT can yield promising outcomes

Oligorecurrent hormone sensitive

- Metastasis directed therapy can yield meaningful PFS benefit with minimal side effects

Oligoprogressive hormone resistant

- Metastasis directed therapy can yield meaningful PSA response with minimal side effects

Questions?

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