19th October 2024

Radiotherapy for Prostate Cancer : An Update

Presenters: Dr Jeremy de Leon

GenesisCare

Agenda

- Indications for Radiotherapy
  - How much radiotherapy
  - What to treat
- Use of ADT
- Advances in Radiotherapy Technology

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Indications for Radiotherapy

Management dependent on stage

Risk Group	Clinical/Pathologic Features (Staging, ST-1)		
Very low[j]	Has all of the following: • cT1c • Grade Group 1 • PSA <10 ng/mL • <3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core[k] • PSA density <0.15 ng/mL/g		
Low[j]	Has all of the following but does not qualify for very low risk: • cT1–cT2a • Grade Group 1 • PSA <10 ng/mL		
Intermediate[j]	Has all of the following: • No high-risk group features • No very-high-risk group features • Has one or more intermediate risk factors (IRFs): ▸ cT2b–cT2c ▸ Grade Group 2 or 3 ▸ PSA 10–20 ng/mL	Favorable intermediate	Has all of the following: • 1 IRF • Grade Group 1 or 2 • <50% biopsy cores positive (eg, <6 of 12 cores)[l]
		Unfavorable intermediate	Has one or more of the following: • 2 or 3 IRFs • Grade Group 3 • ≥ 50% biopsy cores positive (eg, ≥ 6 of 12 cores)[l]
High	Has no very-high-risk features and has exactly one high-risk feature: • cT3a OR • Grade Group 4 or Grade Group 5 OR • PSA >20 ng/mL		
Very high	Has at least one of the following: • cT3b–cT4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • >4 cores with Grade Group 4 or 5		

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Radiotherapy in the Curative Setting

Risk Group	Clinical/Pathologic Features (Staging, ST-1)		
Very low[j]	Has all of the following: • cT1c • Grade Group 1 • PSA <10 ng/mL • <3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core[k] • PSA density <0.15 ng/mL/g		
Low[j]	Has all of the following but does not qualify for very low risk: • cT1–cT2a • Grade Group 1 • PSA <10 ng/mL		
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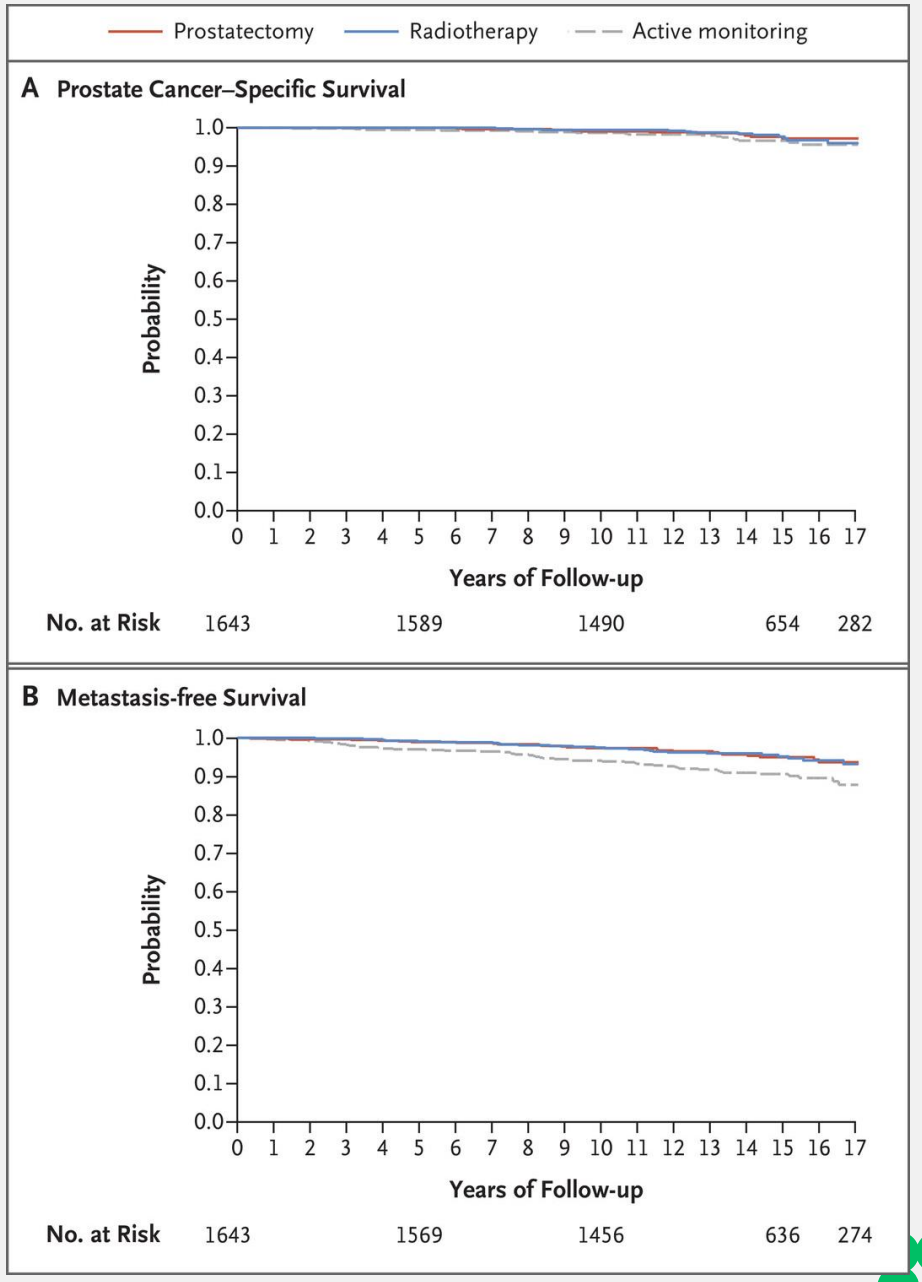
Very high	Has at least one of the following: • cT3b–cT4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • >4 cores with Grade Group 4 or 5		

- Primary treatment (*Definitive*)
- Following Surgery (*Salvage/ Adjuvant*)

Primary Treatment

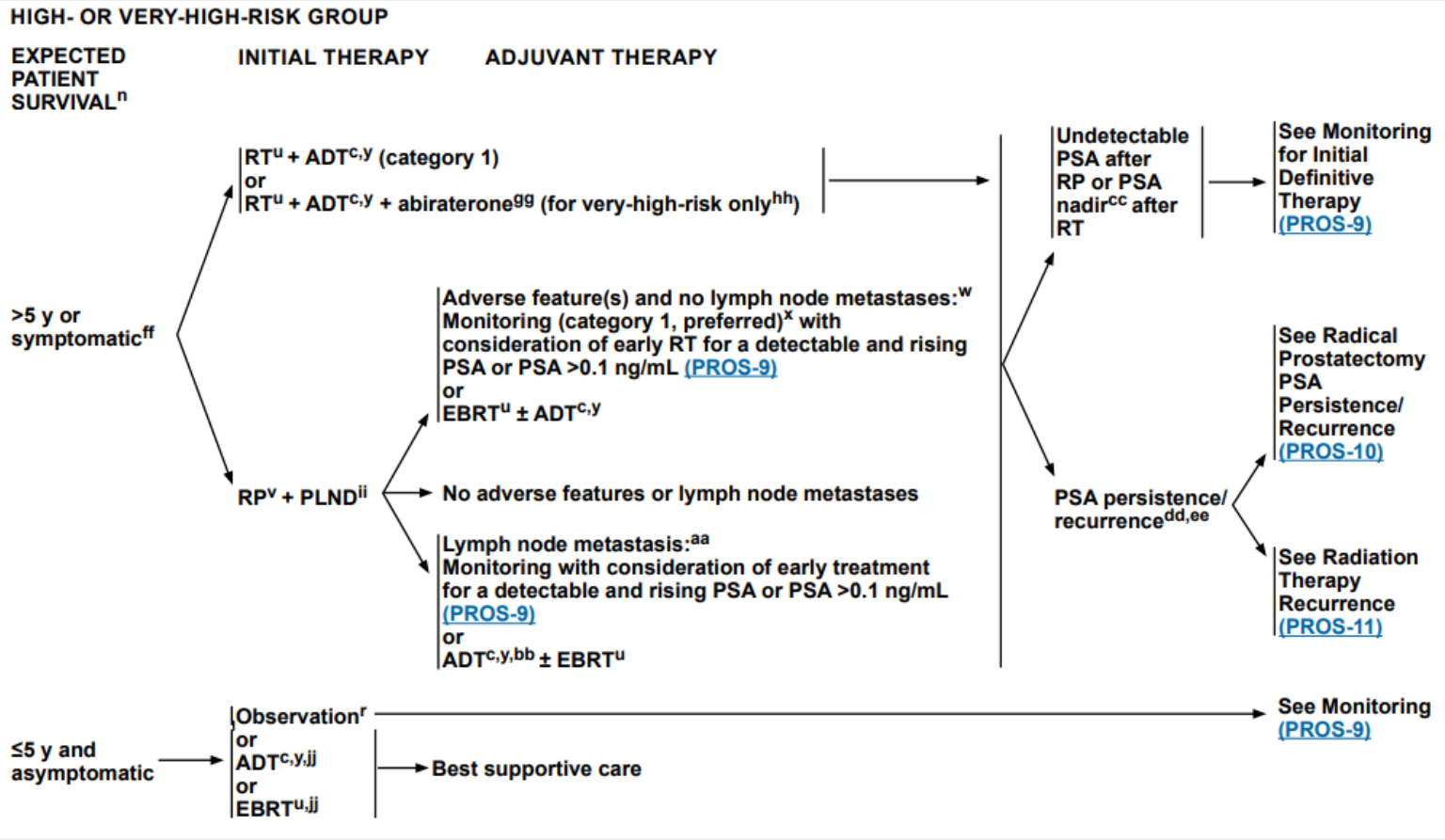
- Radiotherapy compared to Surgery
- Good evidence in the intermediate / low risk group
- Active monitoring
  - 54.8% required treatment by 10 years
  - 61% required treatment by 15 years



ProtecT Trial

Primary Treatment

- High Risk
  - No high quality RCT



available at www.sciencedirect.com
journal homepage: www.europeanurology.com
European Association of Urology
EUROPEAN UROLOGY

Original Article

Management of Patients with Advanced Prostate Cancer. Report from the 2024 Advanced Prostate Cancer Consensus Conference (APCCC)

Q4: In the majority of patients with very high-risk localised prostate cancer (NCCN definition) and NOT high-risk localised/locally advanced prostate cancer (STAMPEDE definition) N0 M0 on next-generation imaging, what is your recommended treatment?

No consensus.

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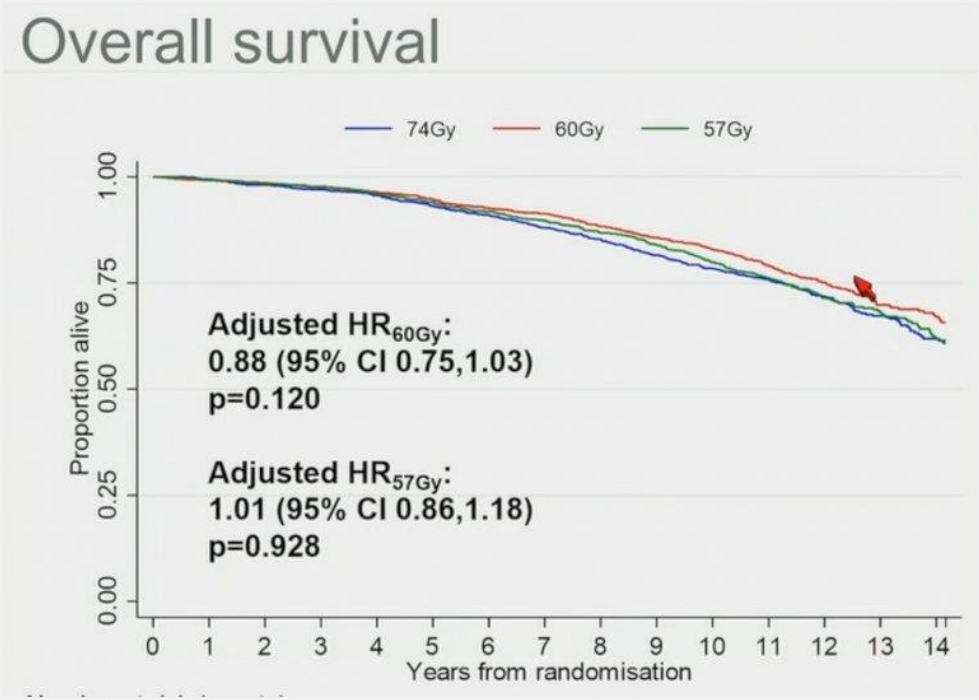
Number of fractions (treatment visits)

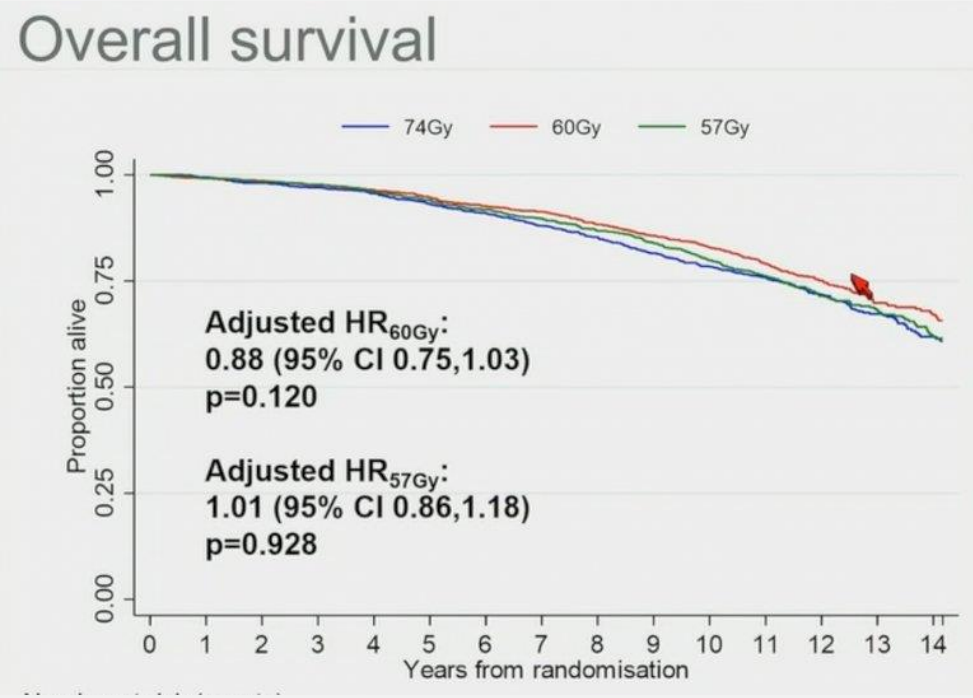
- Move to less number of visits
  - 20 visits standard in localised disease



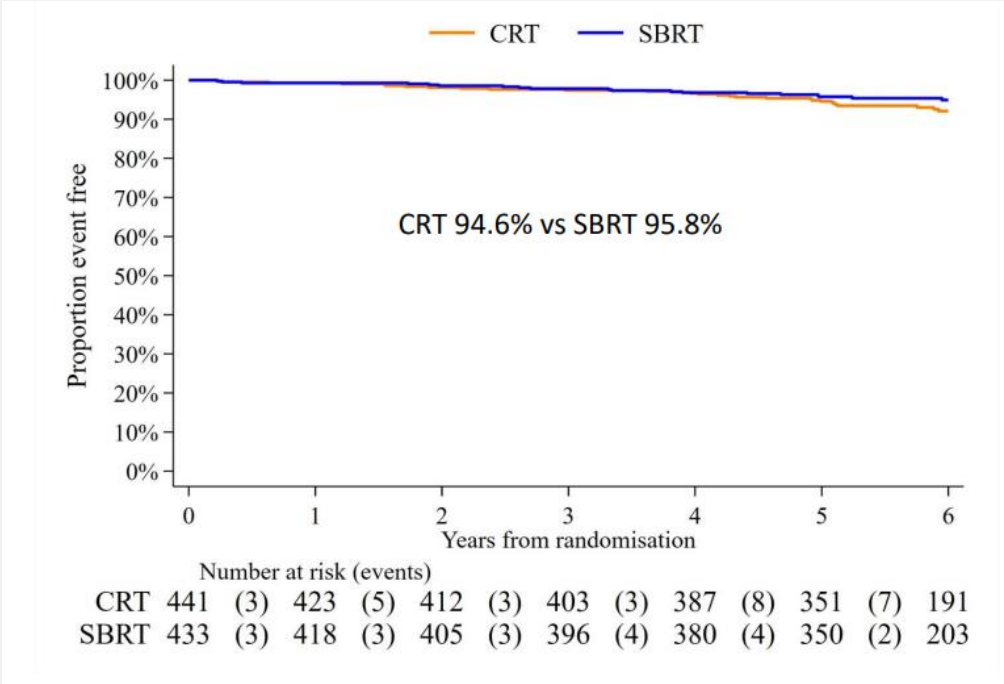
CHHiiP Trial

Number of fractions (treatment visits)

- Move to less number of visits
  - 20 visits standard in localised disease
  - 5 visits is quickly becoming 'standard'



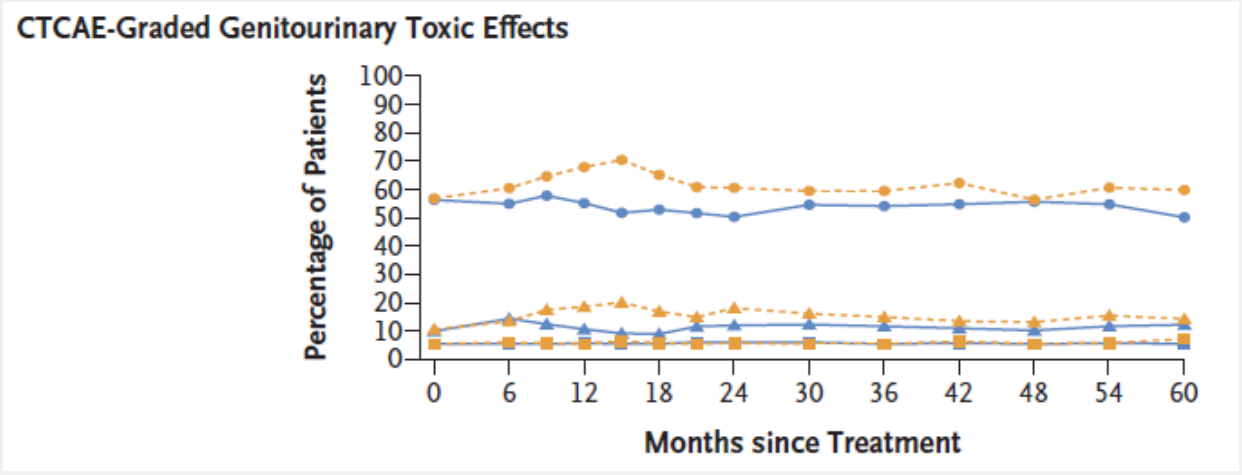
CHHiiP Trial

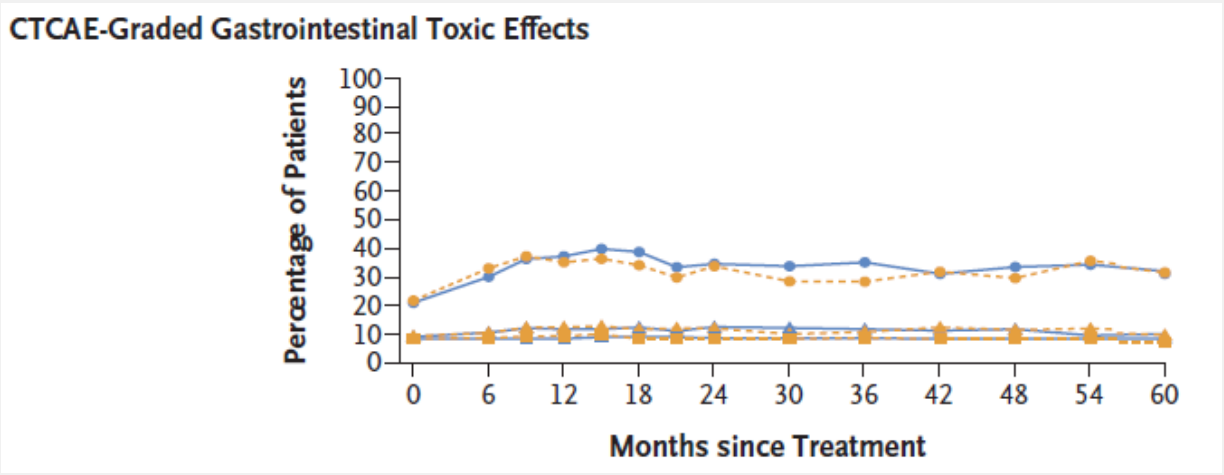


PACE B Trial
(5 year)

Number of fractions (treatment visits)

- Move to less number of visits
  - 20 visits standard in localised disease
  - 5 visits is quickly becoming 'standard'



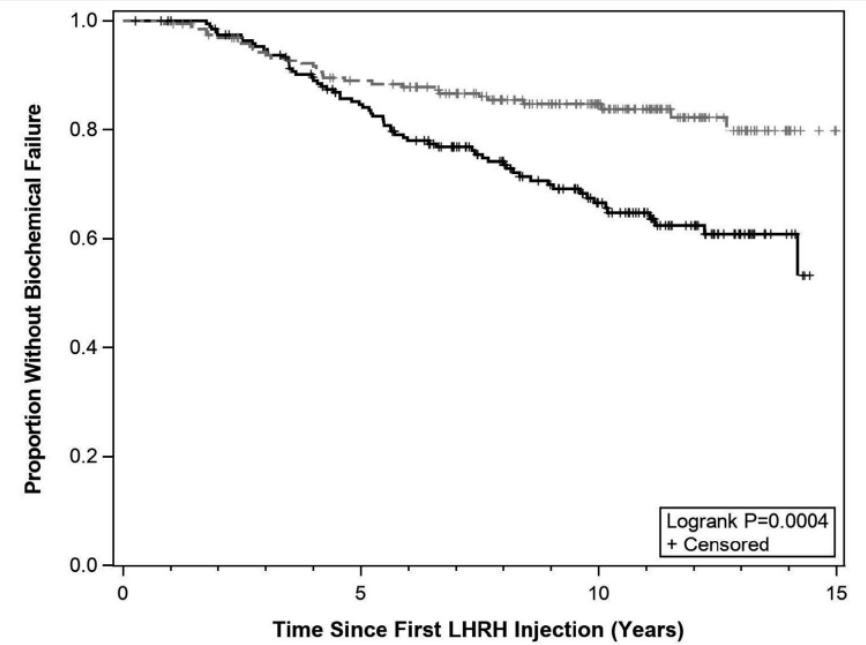


Stereotactic body radiotherapy: grade ≥1
Stereotactic body radiotherapy: grade ≥2
Stereotactic body radiotherapy: grade ≥3
Control radiotherapy: grade ≥1
Control radiotherapy: grade ≥2
Control radiotherapy: grade ≥3

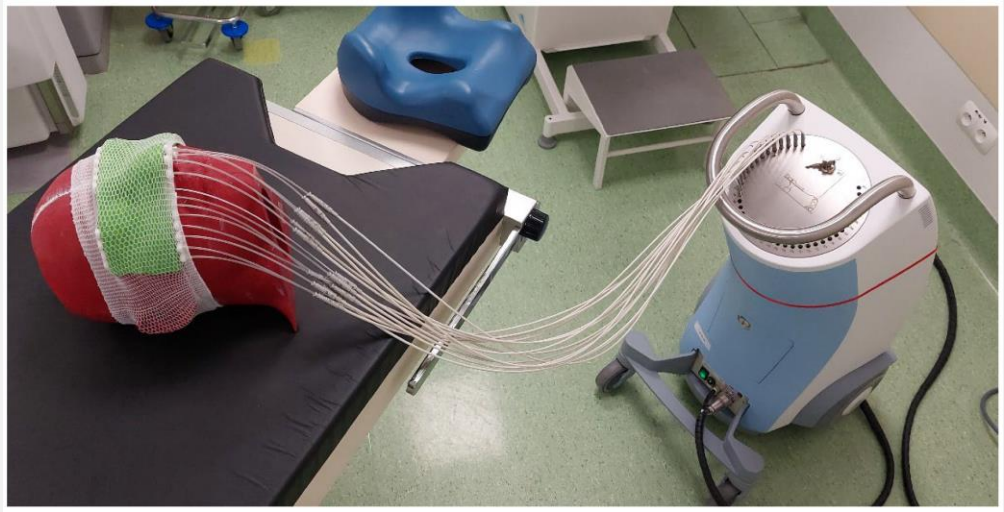
PACE B Trial (2024)

Escalate dose

- More radiation = Higher chance of cell death
- Higher risk disease



ASCENDE RT (10 year data)

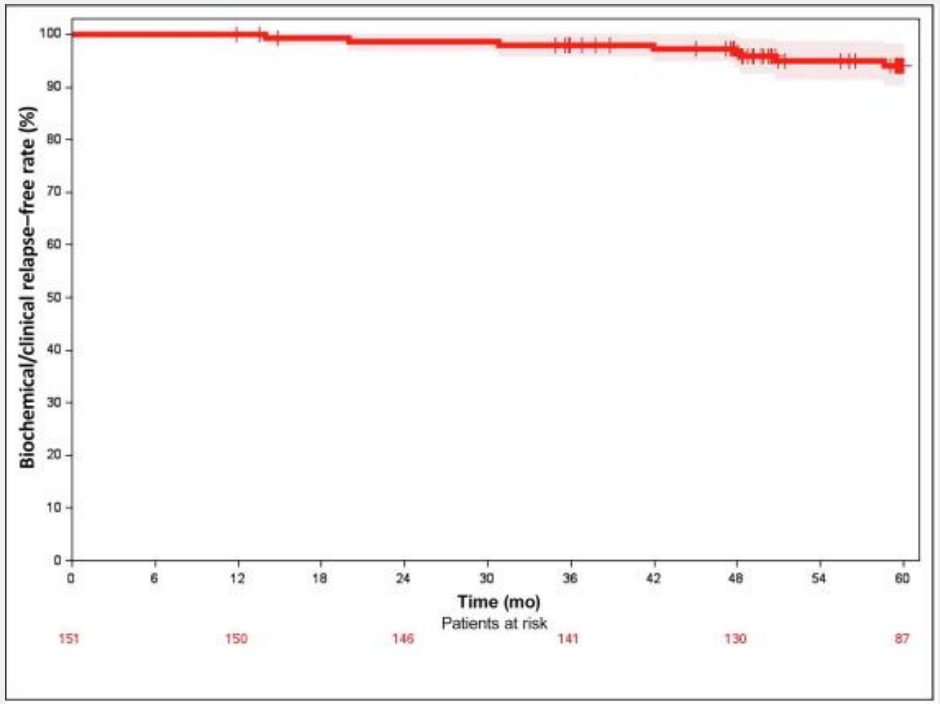


https://www.mdpi.com/2075-4426/12/9/1432

https://www.elekta.com/products/brachytherapy/

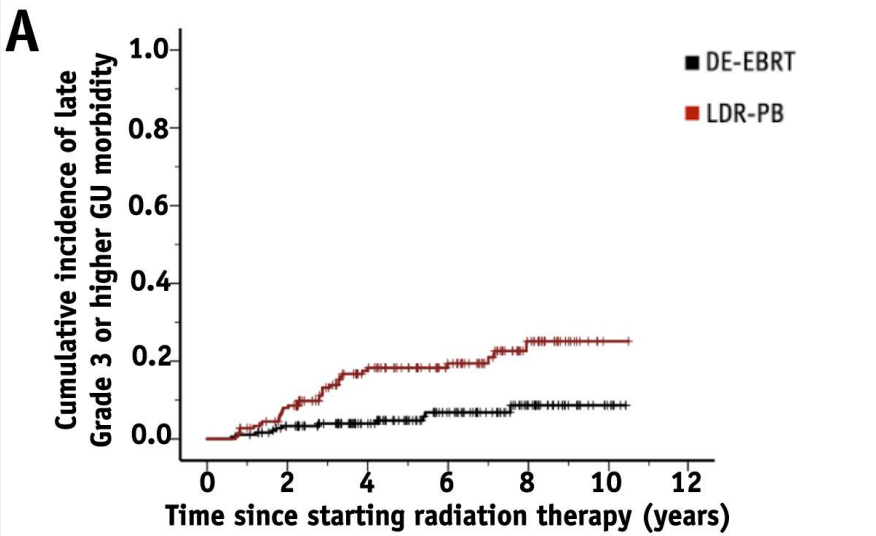
Escalate dose

- Non invasive option
  - Mimic brachytherapy doses

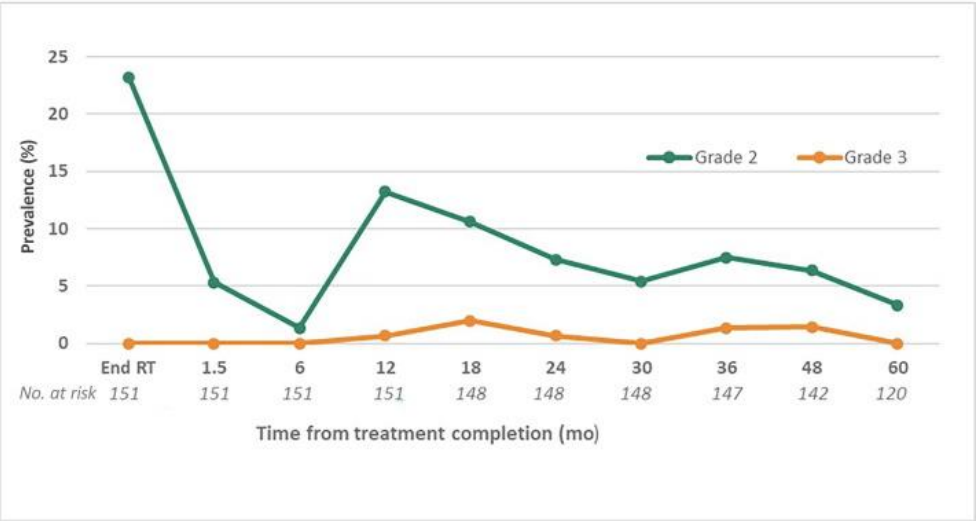


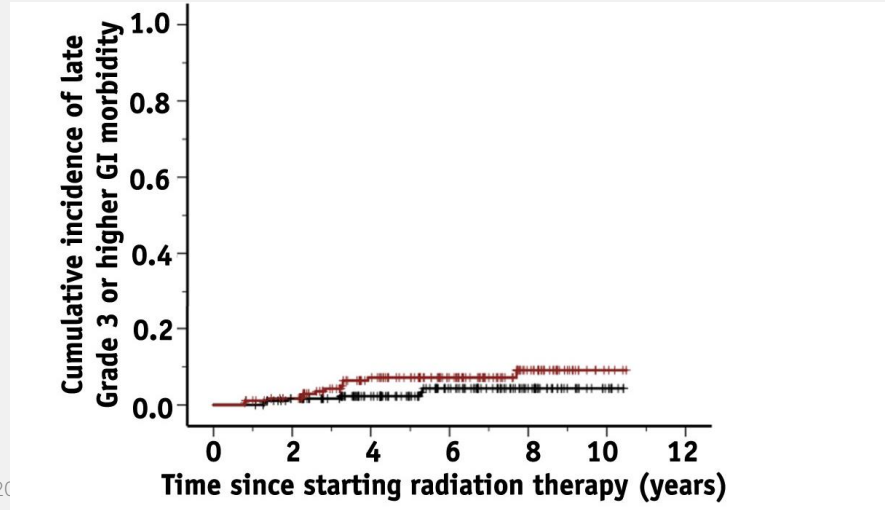
PROMETHEUS (5 year)

Escalate dose



GU





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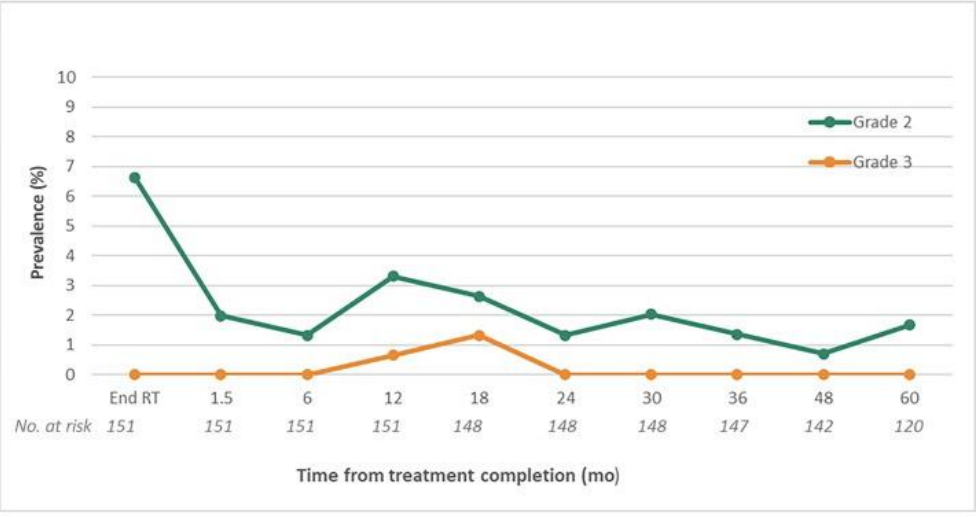
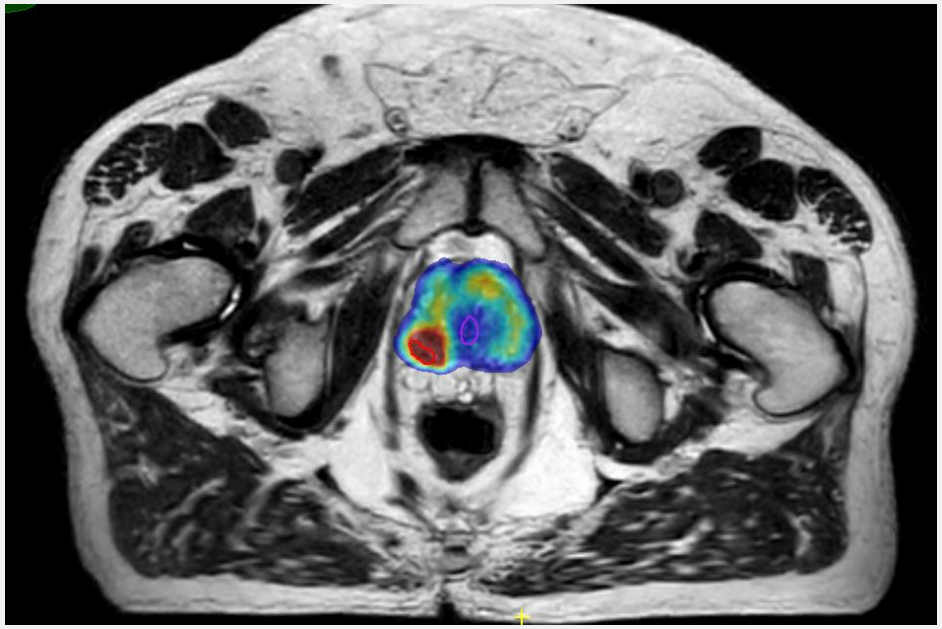
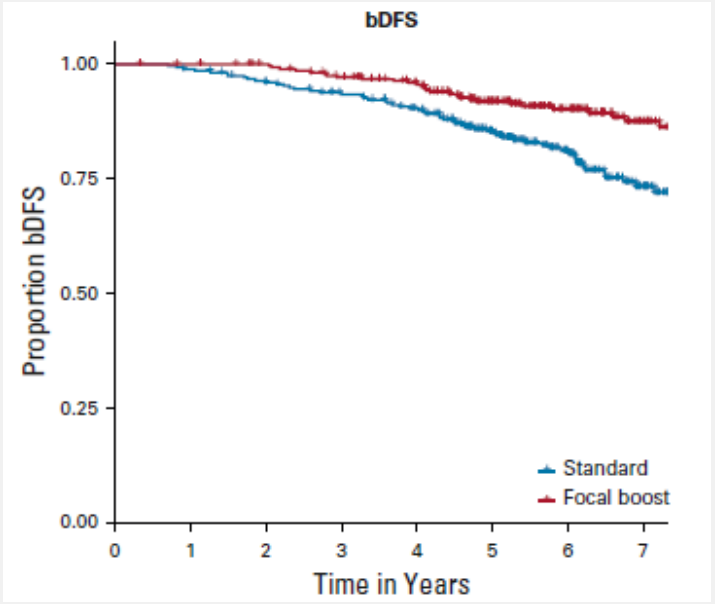


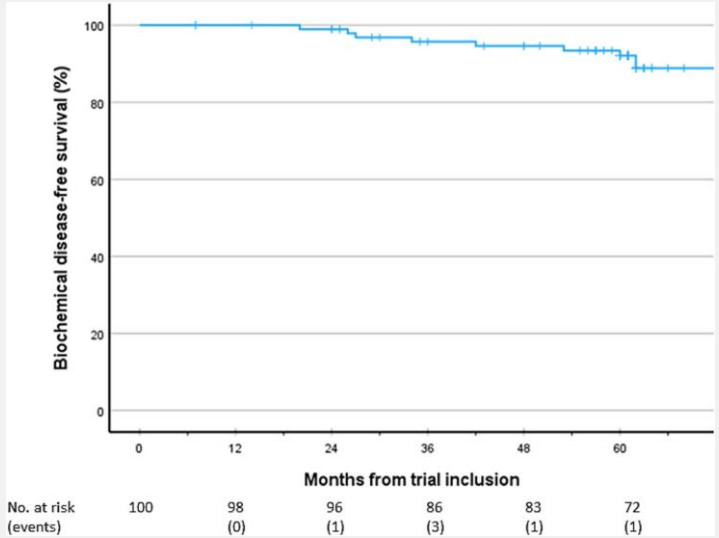
DiL : Escalate dose only to tumour

- Focused dose escalation
- Improved imaging
- Comprehensive and targeting biopsy





FLAME

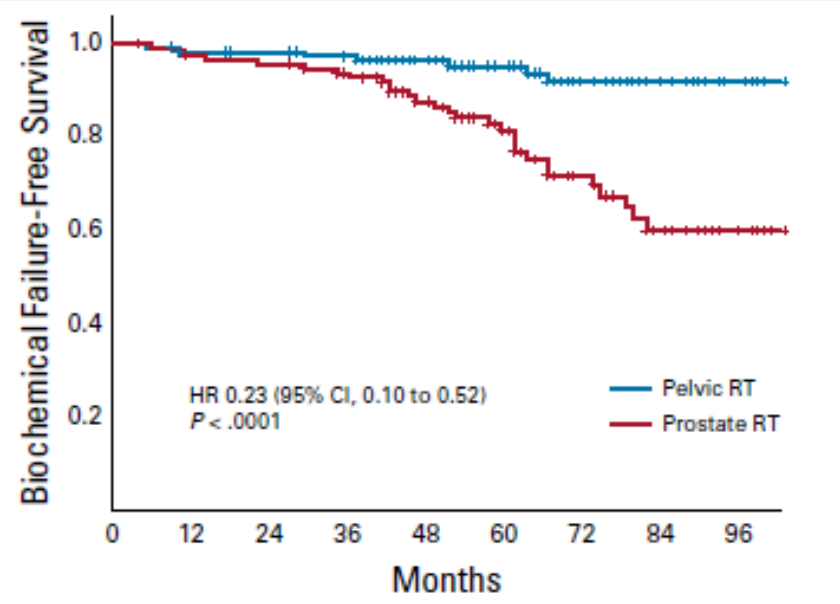


HypoFLAME

Areas to Treat

- Considerations if need to treat more than just the prostate
  - High risk prostate cancer
  - Positive lymph nodes detected on imaging

- Selecting the appropriate patient



POPRT

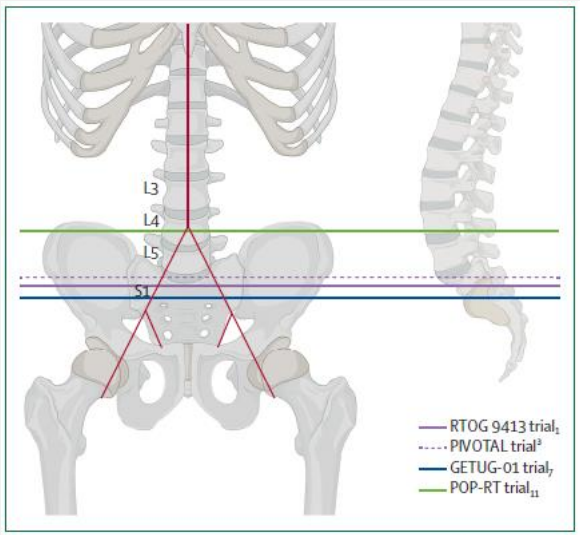
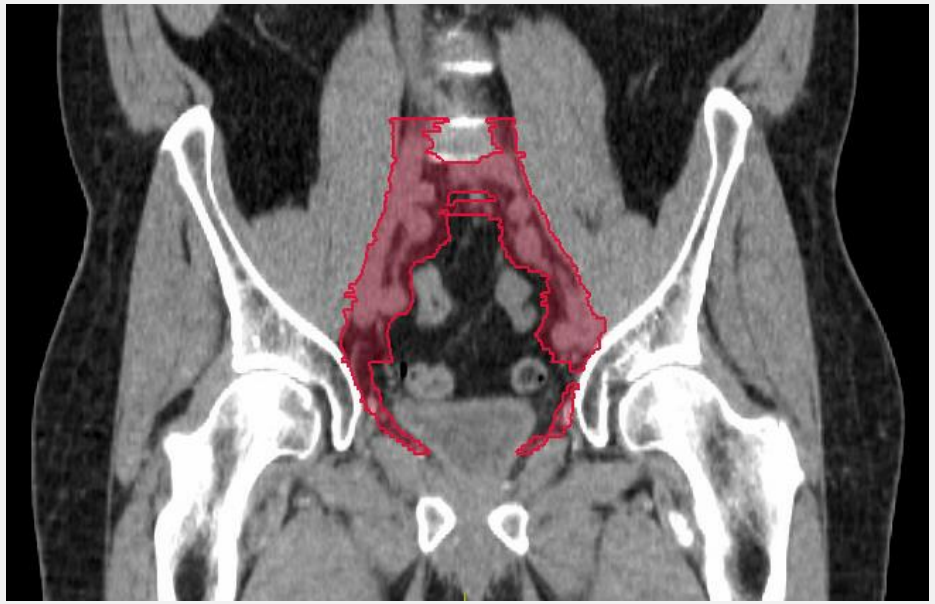
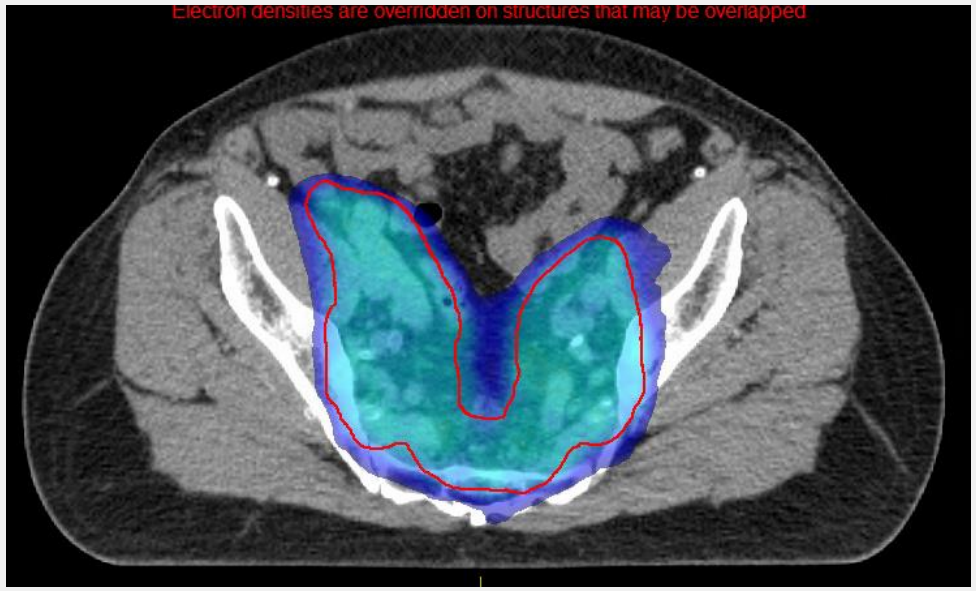
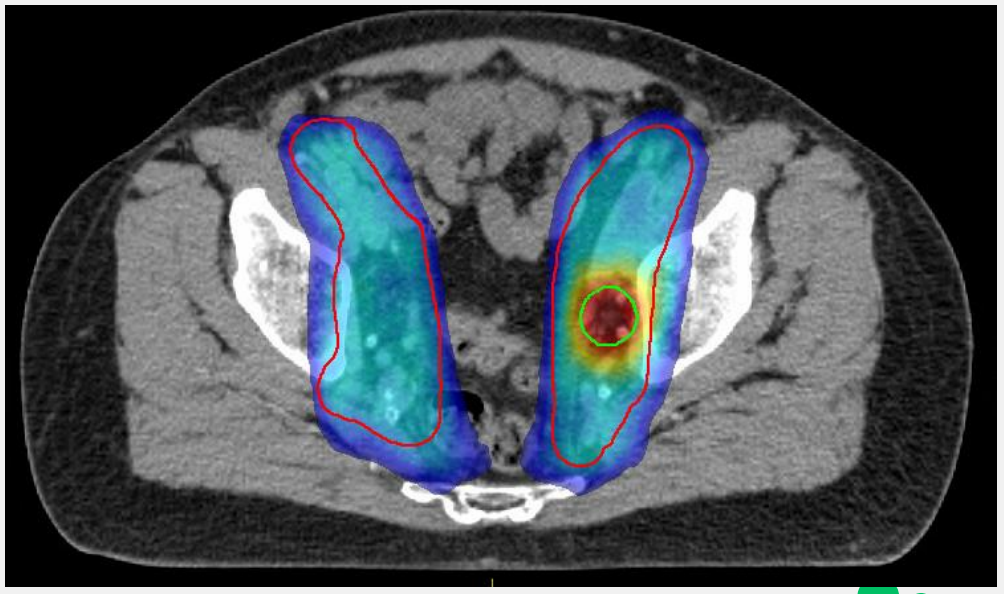


Figure 1: **Comparison of radiation treatment upper borders in different randomised trials**
Figure created with BioRender. Upper borders of the pelvic treatment fields used in different trials. The arterial vasculature of the abdomen and pelvis depicted in relation to the bony anatomy (red). Exact description of the respective upper borders is shown in table 2.





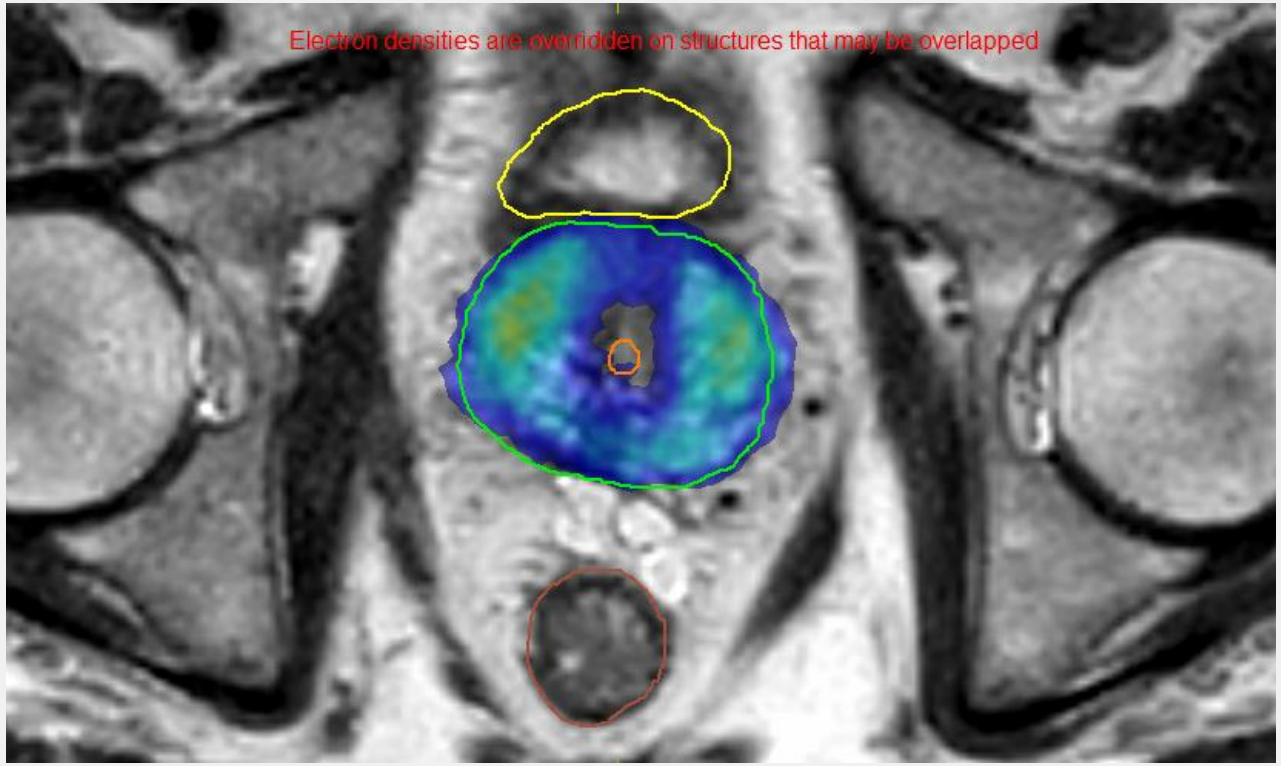


Side Effects

Patient Reported

- 9.3% patients reported moderate urinary bother at 10 years
  - Need for operative procedure <1%

- 7.6% patients reported moderate bowel bother at 10 years
  - 10% needed scope for investigation



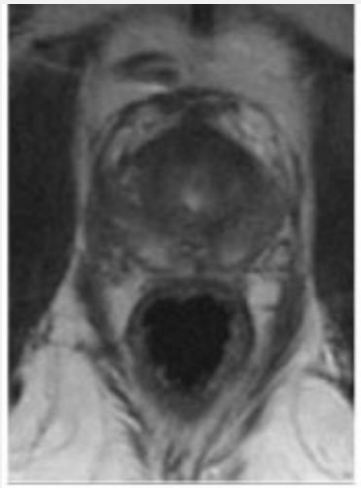
Side Effects

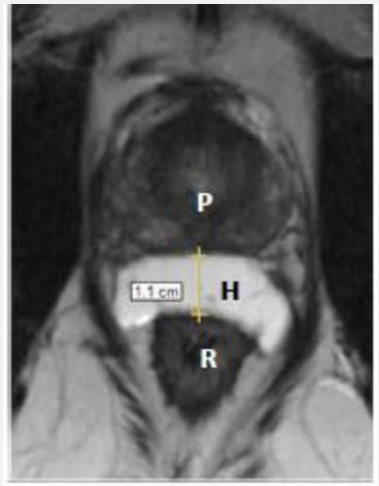
Patient Reported

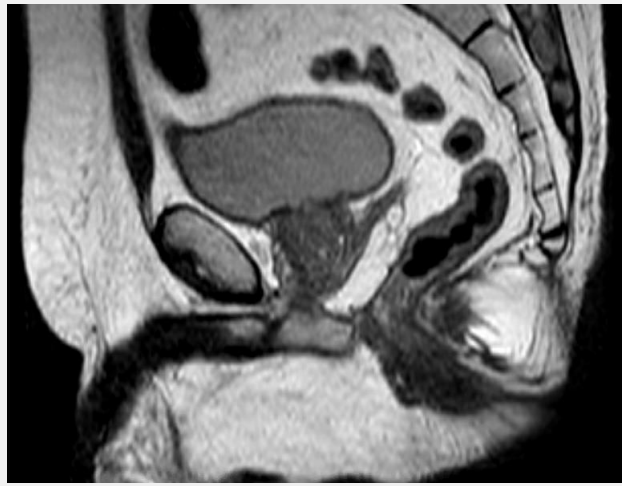
- 9.3% patients reported moderate urinary bother at 10 years
  - Need for operative procedure <1%
- 7.6% patients reported moderate bowel bother at 10 years
  - 10% needed scope for investigation

Reducing rectal toxicity

- Rectal Spacing
- 77% reduction in significant toxicity







Harvey M; Comprehensive review of the use of hydrogel spacers prior to radiation therapy for prostate cancer. BJU Int. 2023 Mar;131(3):280-287

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Androgen Deprivation Therapy

Androgen Deprivation Therapy

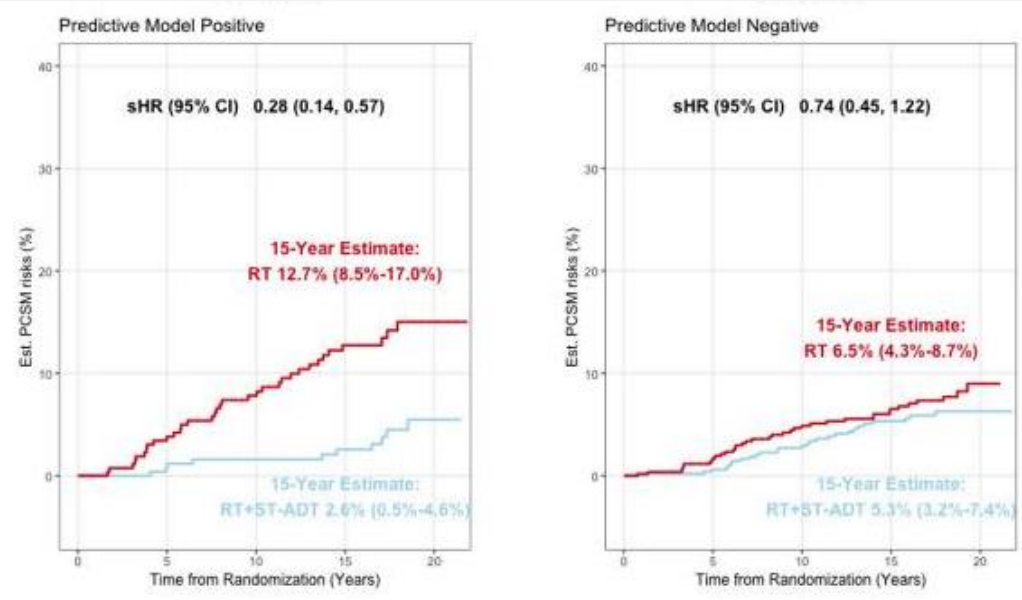
- Selected patient
  - High risk patients
  - Select intermediate risk patients

- High risk (MARCAP analysis)
  - Improves overall survival : 7.7% at 10 years
  - 18 – 21 months
  - Adjuvant ADT most important

Androgen Deprivation Therapy :

Intermediate Risk

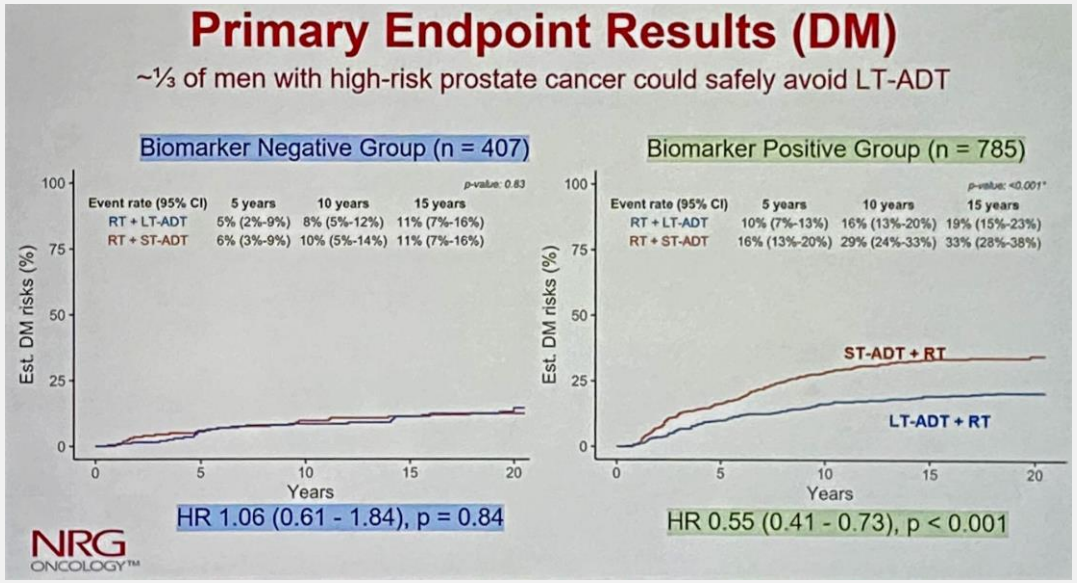
- Benefit of ADT
  - Part of treatment guidelines
  - Available*



Spratt DE et al; Artificial Intelligence Predictive Model for Hormone Therapy Use in Prostate Cancer.

High Risk

- Short term versus Long term



ASCO 2022

Salvage/ Adjuvant Radiotherapy

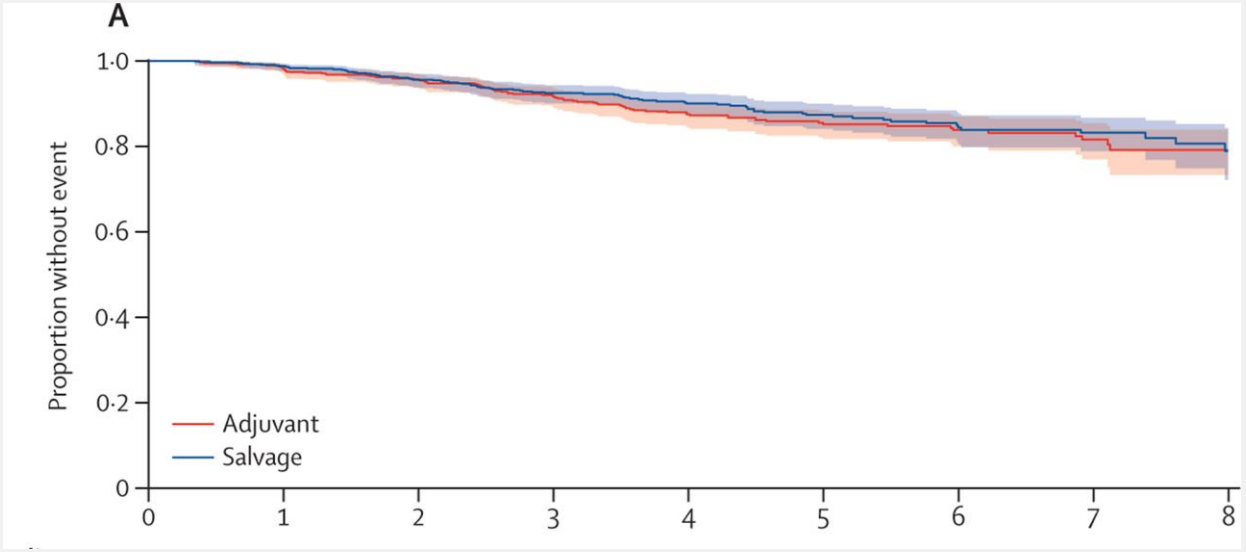
Salvage/ Adjuvant Radiotherapy

- PSA doesn't have to be zero
  - Low Intermediate Risk PSA >= 0.2
  - High Risk PSA >= 0.1

- Not all people need further treatment

	EAU Low Risk BCR	EAU High Risk BCR
After RP	PSA-DT > 1 yr AND pathological ISUP grade group < 4	PSA-DT ≤ 1 yr OR pathological ISUP grade group 4–5

Salvage/ Adjuvant Radiotherapy : Lower risk



RADICALS

- Approx 60% avoid radiotherapy

Salvage/ Adjuvant Radiotherapy : Higher risk

- Lower PSA = Improved outcome

TABLE 3. AHR for ACM When sRT(t) is Delivered Above the Prespecified PSA Cutpoint After RP Compared With PSA Levels at or Below the PSA Cutpoint

PSA Cutpoint in ng/mL	No. of Men	No. of Deaths	No. of PC Deaths	AHR (95% CI)	P
>0.10	2,897	179	55	0.88 (0.56 to 1.36)	.55
≤0.10	336	23	8		
>0.15	2,579	164	53	1.11 (0.77 to 1.58)	.58
≤0.15	654	38	10		
>0.20	2,190	150	50	1.28 (0.93 to 1.76)	.14
≤0.20	1,043	52	13		
>0.25	1,677	134	45	1.49 (1.11 to 2.00)	.008
≤0.25	1,556	68	18		
>0.30	1,362	117	39	1.45 (1.09 to 1.92)	.01
≤0.30	1,871	85	24		
>0.35	1,167	105	36	1.46 (1.10 to 1.94)	.008
≤0.35	2,066	97	27		
>0.40	985	97	32	1.58 (1.19 to 2.09)	.001
≤0.40	2,248	105	31		
>0.45	864	89	29	1.53 (1.16 to 2.04)	.003
≤0.45	2,369	113	34		
>0.50	737	79	27	1.61 (1.21 to 2.14)	.001
≤0.50	2,496	123	36		

Abbreviations: (t), time dependent; ACM, all-cause mortality; AHR, adjusted hazard ratio; ng/mL, nanograms/milliliter; PC, prostate cancer; PSA, prostate-specific antigen; RP, radical prostatectomy.

Tilki D,. Prostate-Specific Antigen Level at the Time of Salvage Therapy After Radical Prostatectomy for Prostate Cancer and the Risk of Death. J Clin Oncol. 2023 May 1;41(13):2428-2435

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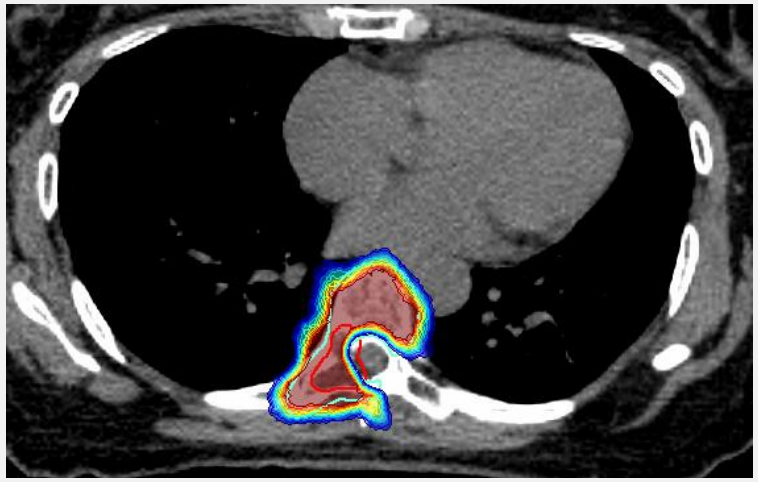
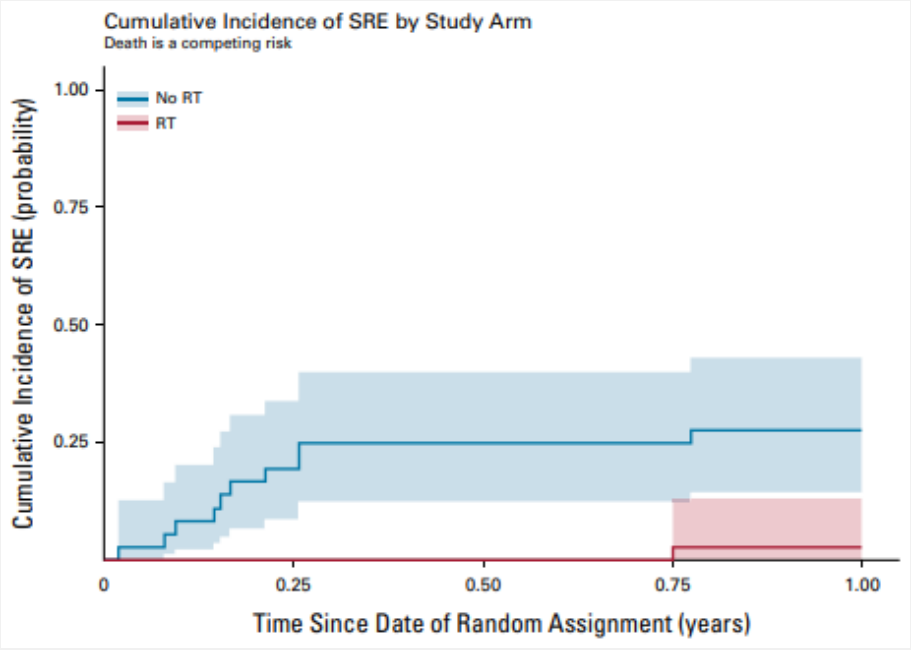
Metastatic Setting

Metastatic Setting

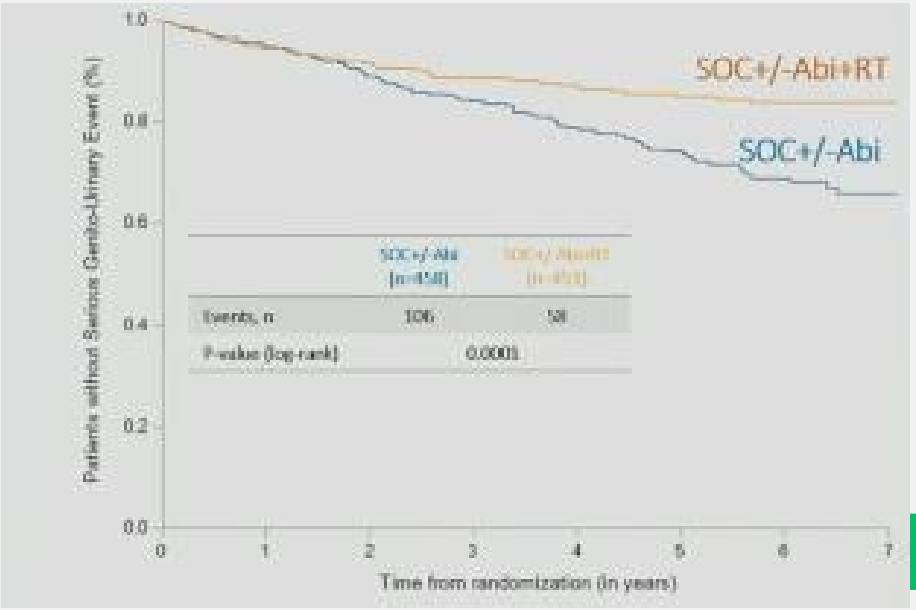
- Symptomatic
  - Pain
  - Bleeding

- Prophylactically
  - Significant reduction in
    - Major skeletal events
    - Urinary toxicity





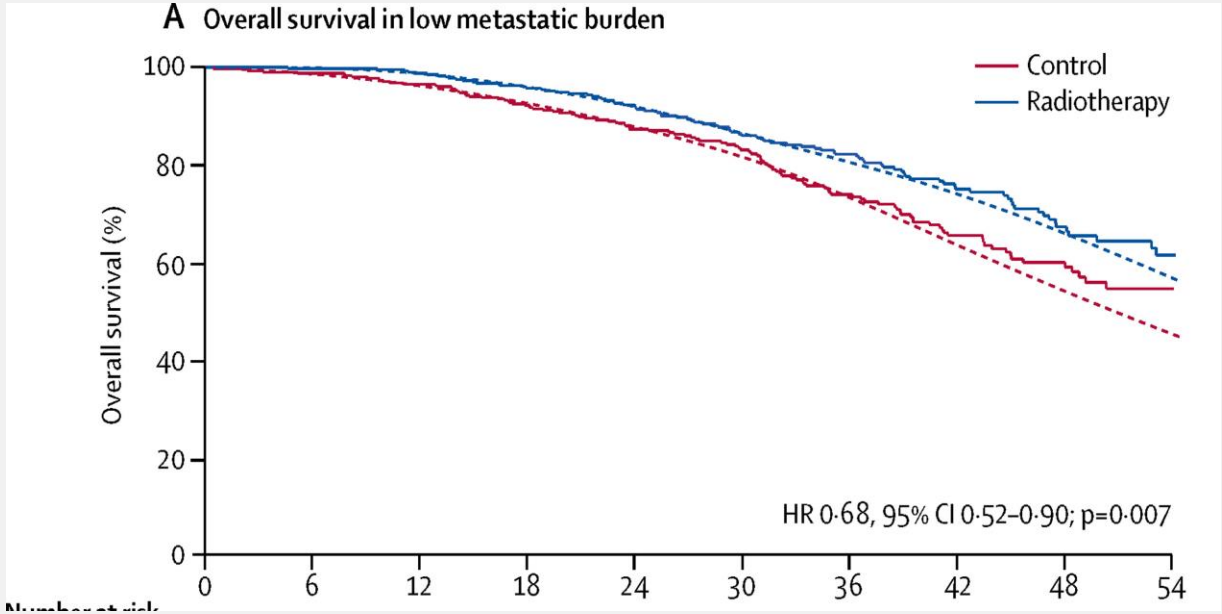
Prophylactic Radiation Therapy Versus Standard of Care for Patients With High-Risk Asymptomatic Bone Metastases:



ASCO 2023:PEACE -1

Metastatic Setting

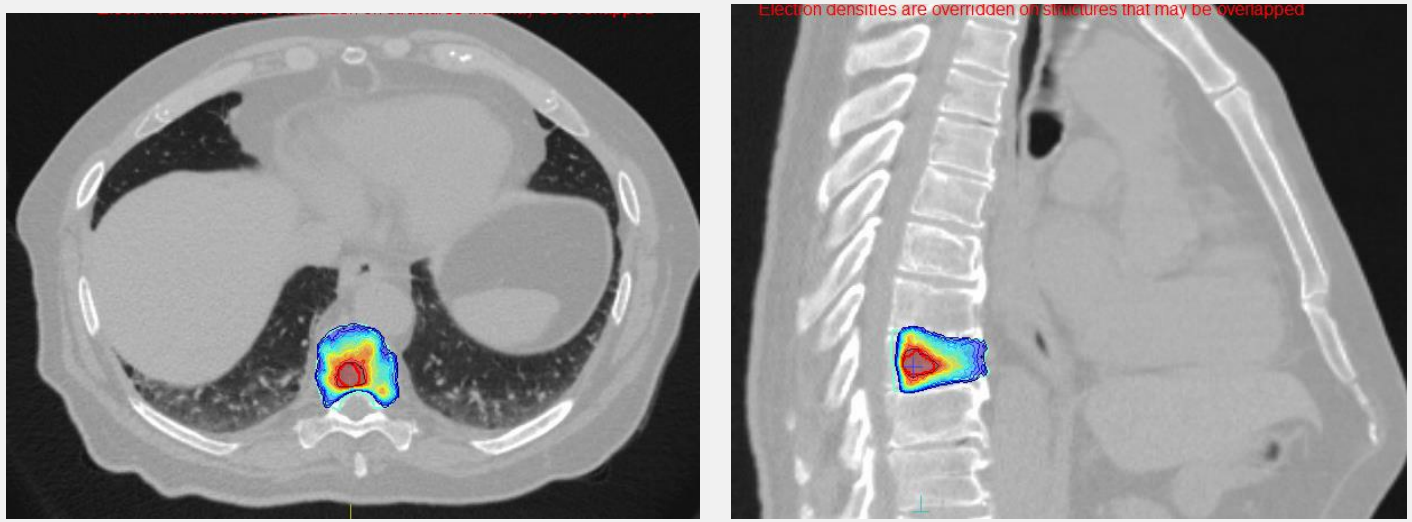
- Treating the prostate alone in metastatic disease
- "Conventional" staging
- Select patients



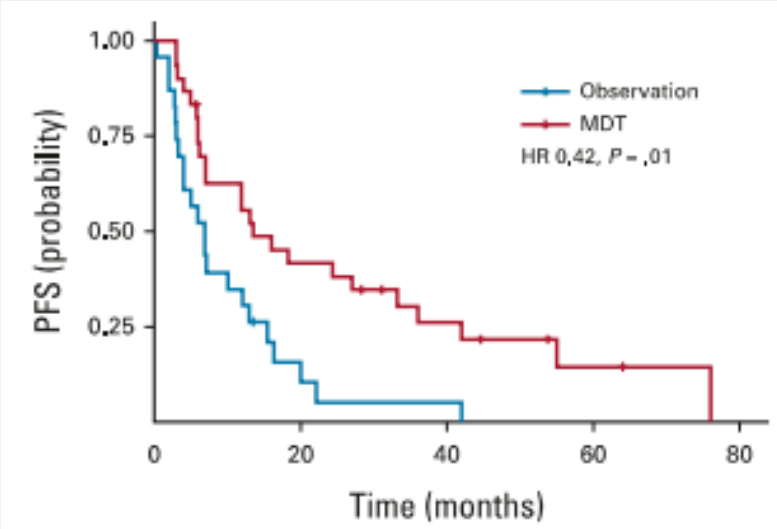
Stampede

Metastatic Setting

- Oligometastatic
  - Low number of metastatic sites
  - Stereotactic/ Ablative radiotherapy to sites

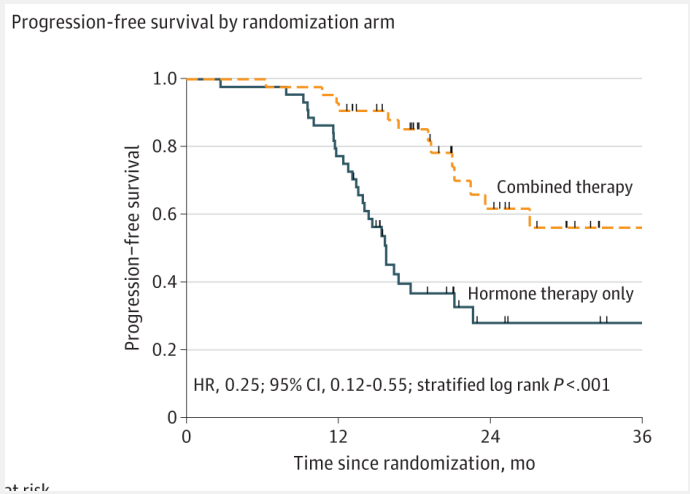


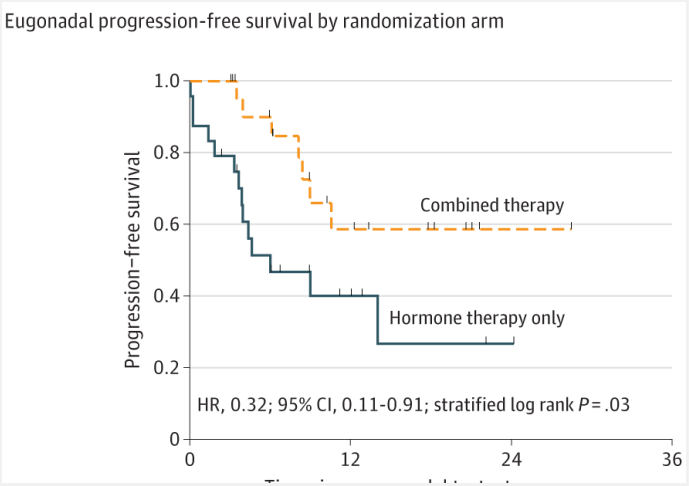
- Delay ADT



STOMP and ORIOLE

- Prolong time off ADT
  - Maintain testosterone level longer





EXTEND trial

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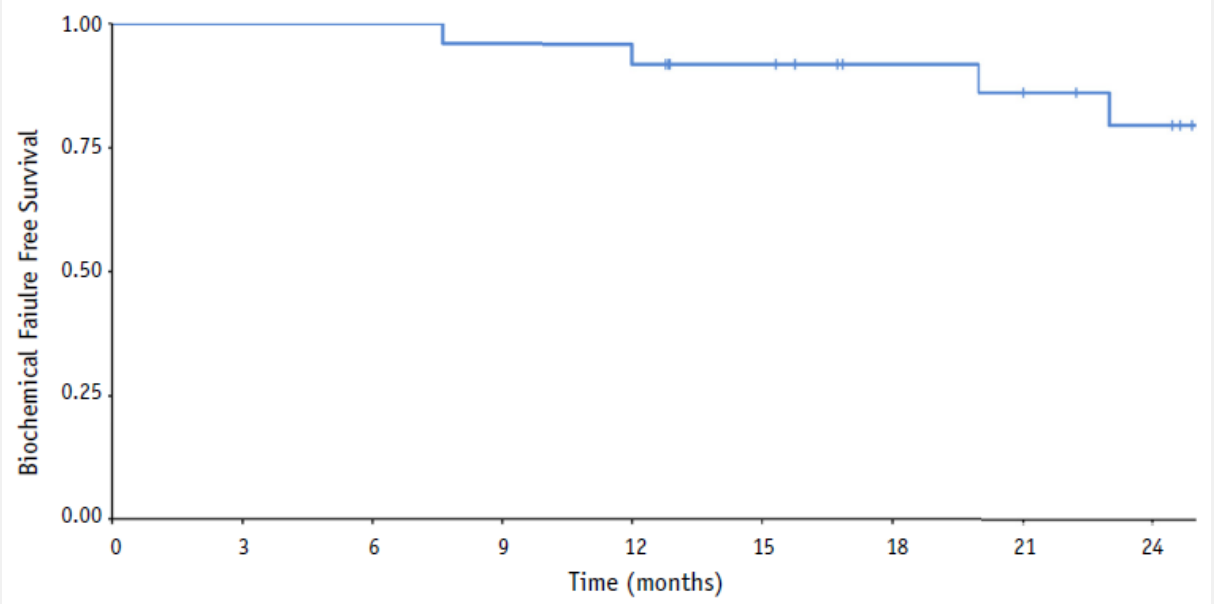
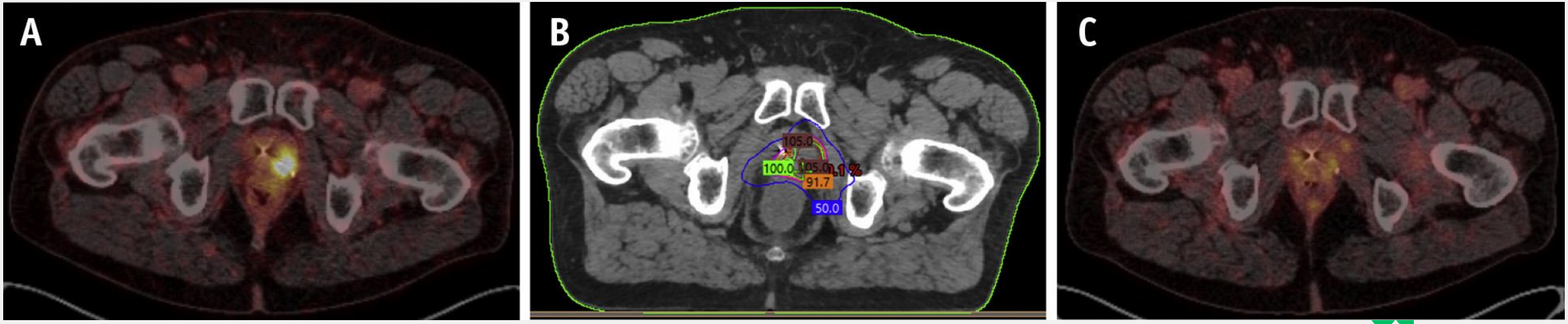
Local Failure

- Radiotherapy as an options for local failure





Bergamin S; Interim Results of a Prospective Prostate-Specific Membrane Antigen-Directed Focal Stereotactic Reirradiation Trial for Locally Recurrent Prostate Cancer. Int J Radiat Oncol Biol Phys. 2020 Dec 1;108(5):1172-1178.

Advanced Technology

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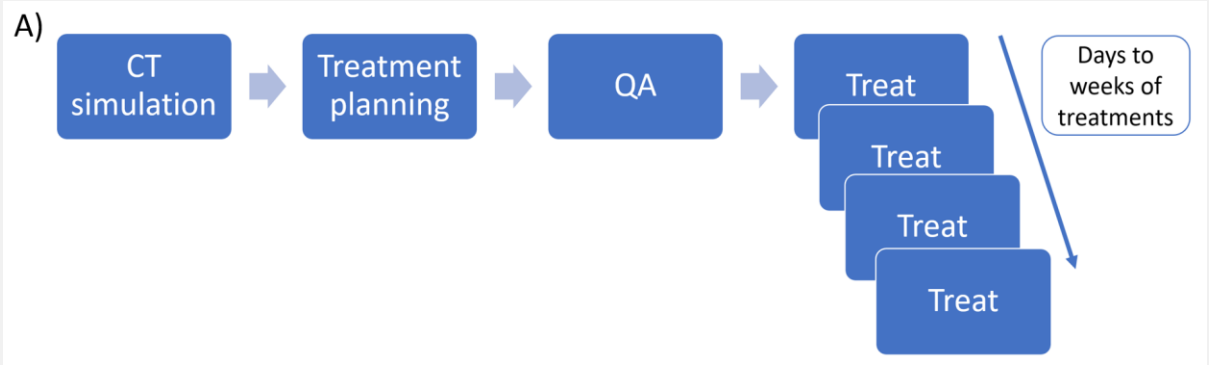
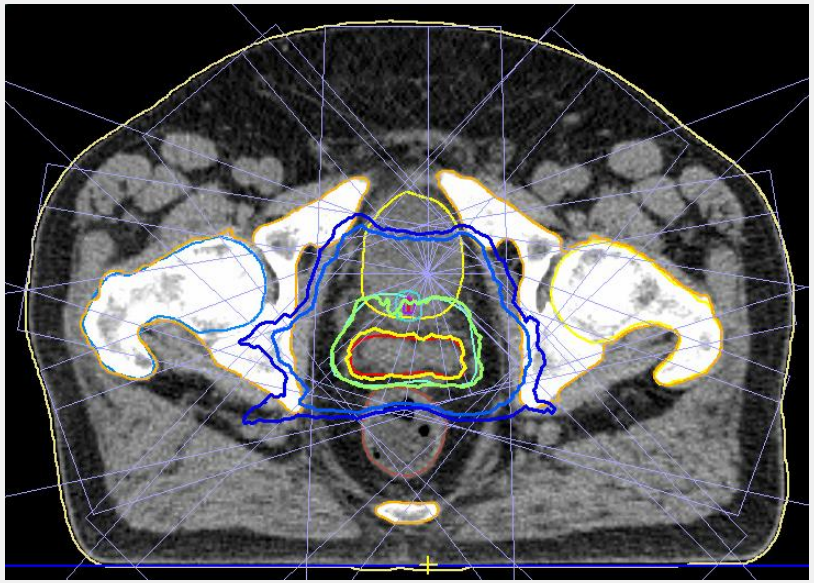
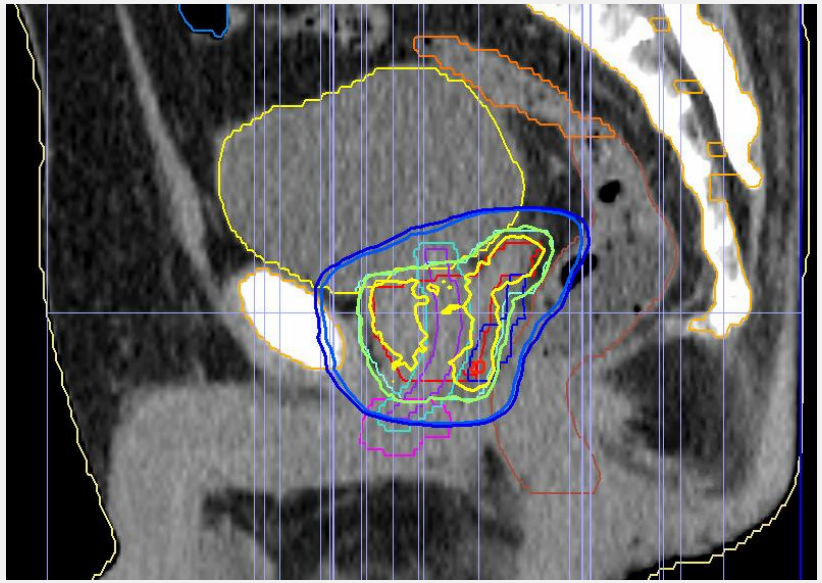
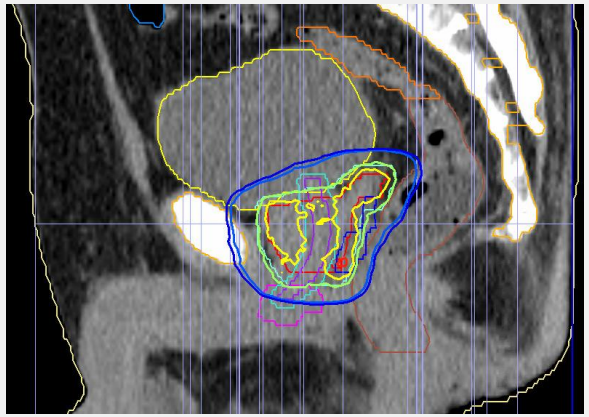
Advanced Technology

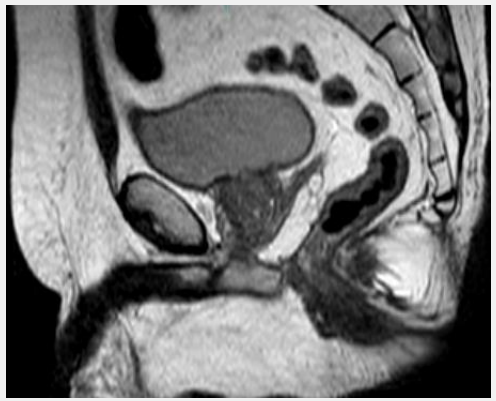




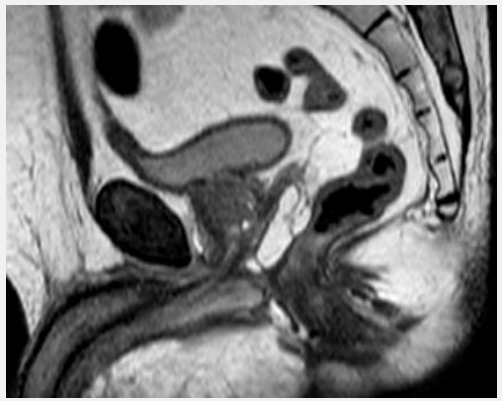


Advanced Technology



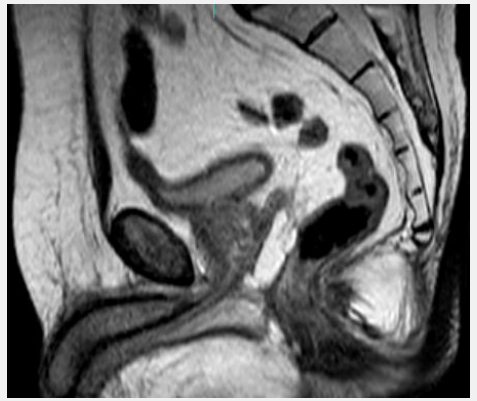


Treatment 1



Treatment 2

Treatment 3



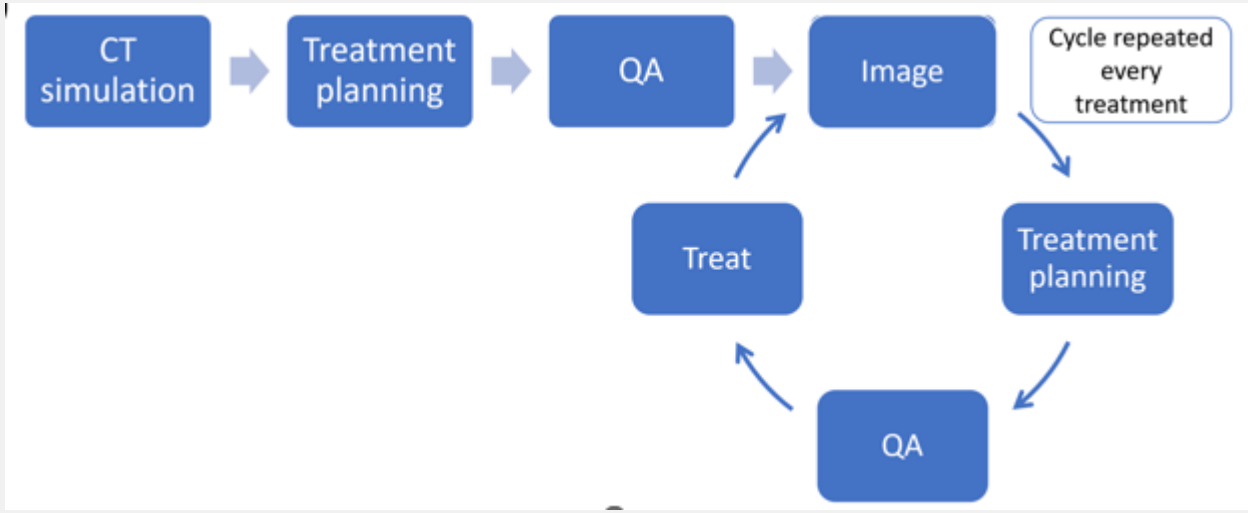
Treatment 4

Treatment 5

GenesisCare

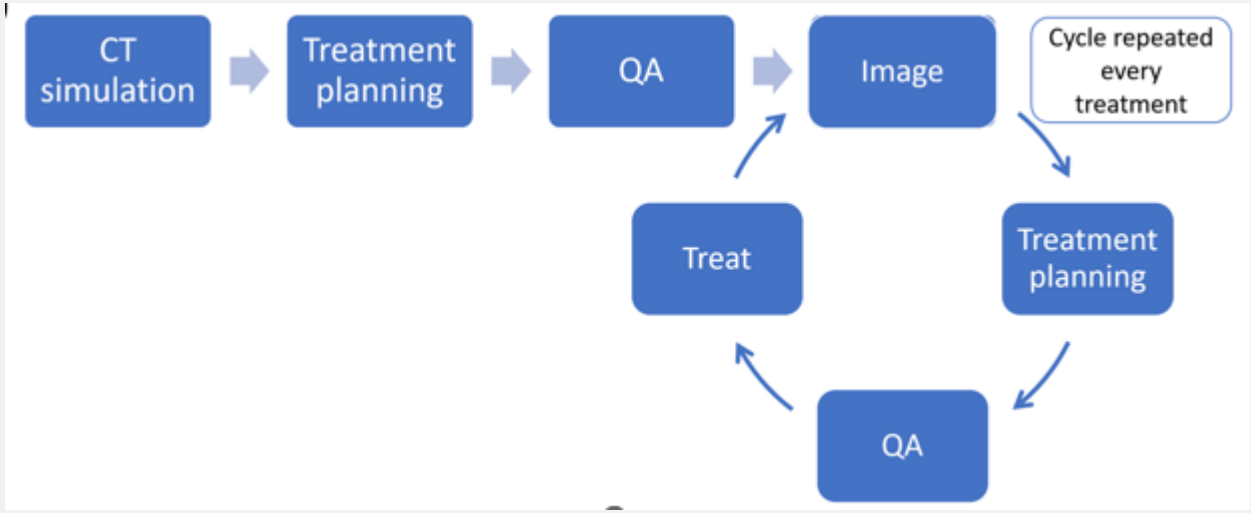
Advanced Technology

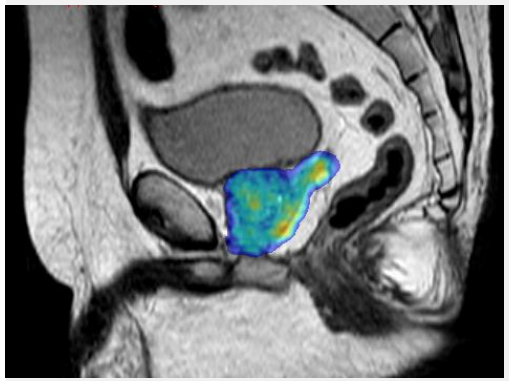
- Adaptive Treatment



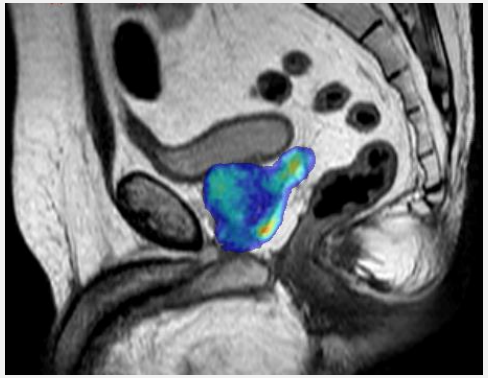
Advanced Technology

- Adaptive Treatment

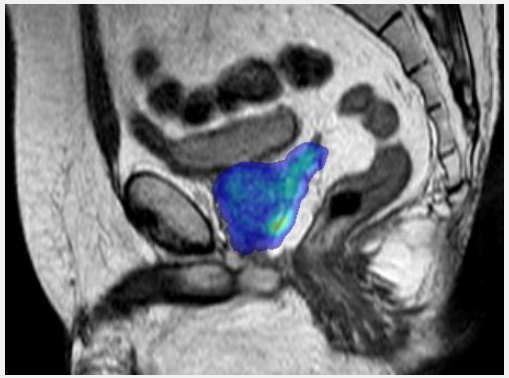




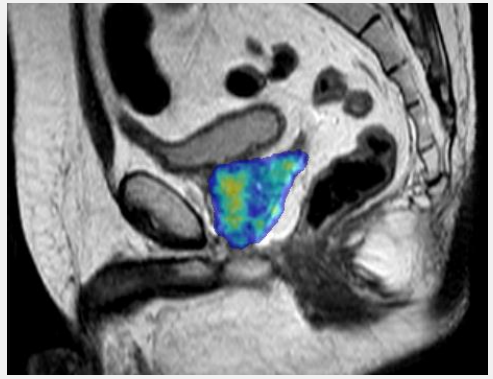
Treatment 1



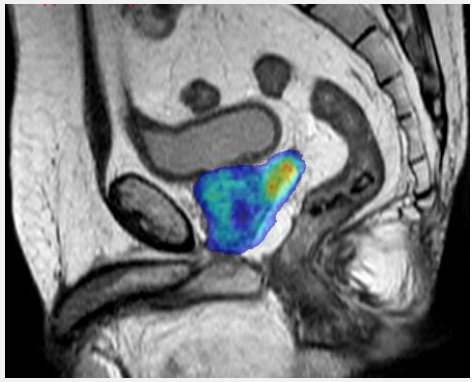
Treatment 2



Treatment 3



Treatment 4



Treatment 5

GenesisCare

MRI Linac

Benefits in Prostate Cancer Treatment

- Real time monitoring

Improved Toxicity with MRI Guided

- Approximately halves short term toxicity

- Acute grade 2+ GU toxicity
  - MR guided : 16%
  - Non MR Guided : 28%

- Acute grade 2+ GI toxicity
  - MR guided : 4%
  - Non MR Guided : 9%

Leeman JE. Acute toxicity comparison of magnetic resonance-guided adaptive versus fiducial or computed tomography-guided non-adaptive prostate stereotactic body radiotherapy: A systematic review and meta-analysis. Cancer. 2023 Oct 1;129(19):3044-3052

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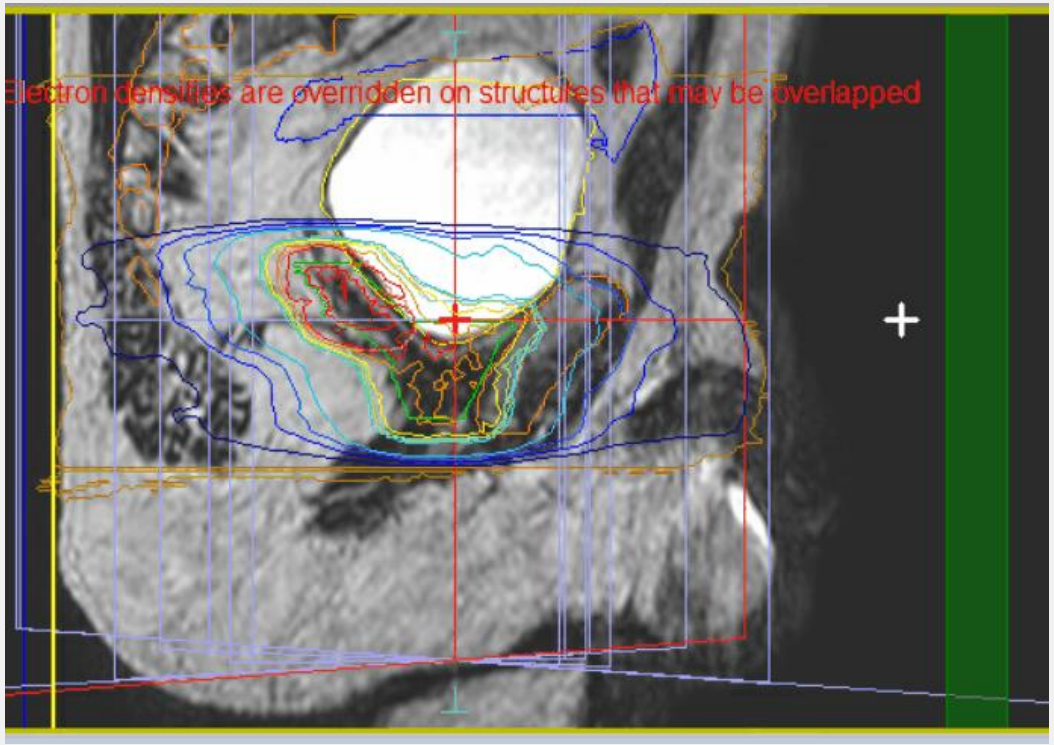
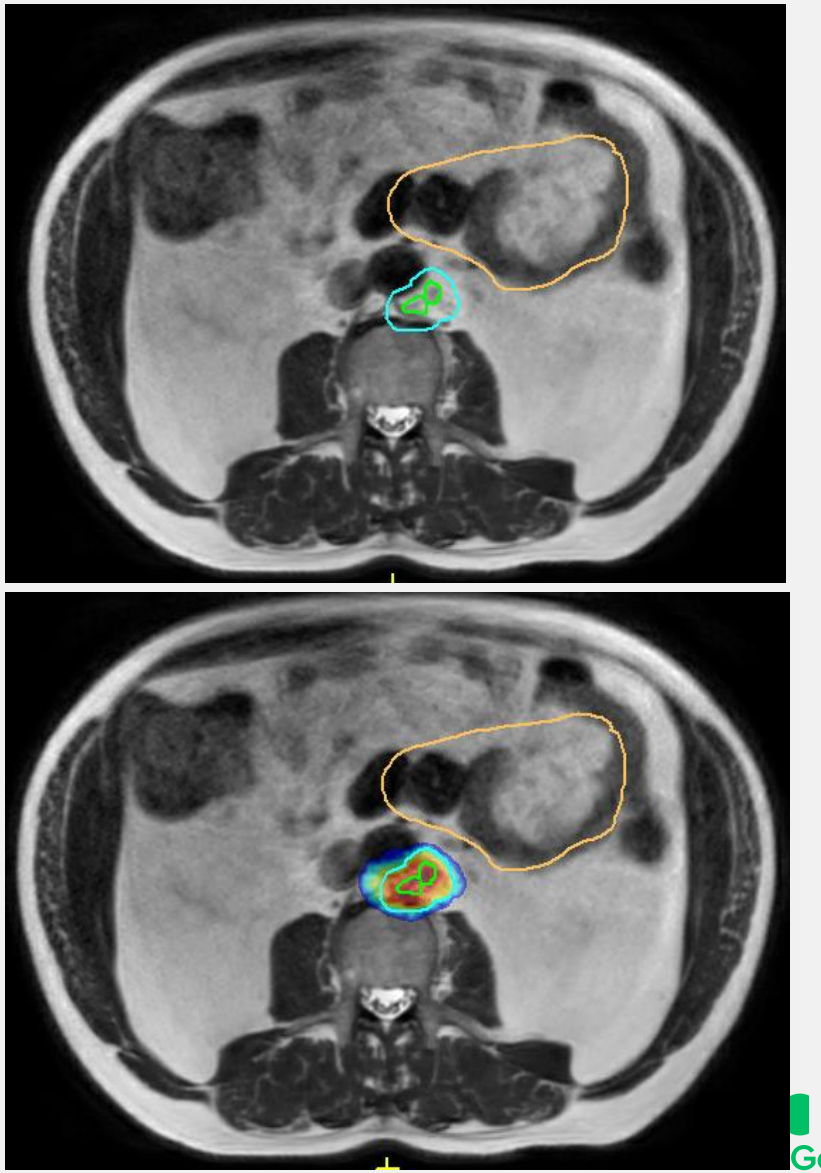
Benefits in Prostate Cancer Treatment





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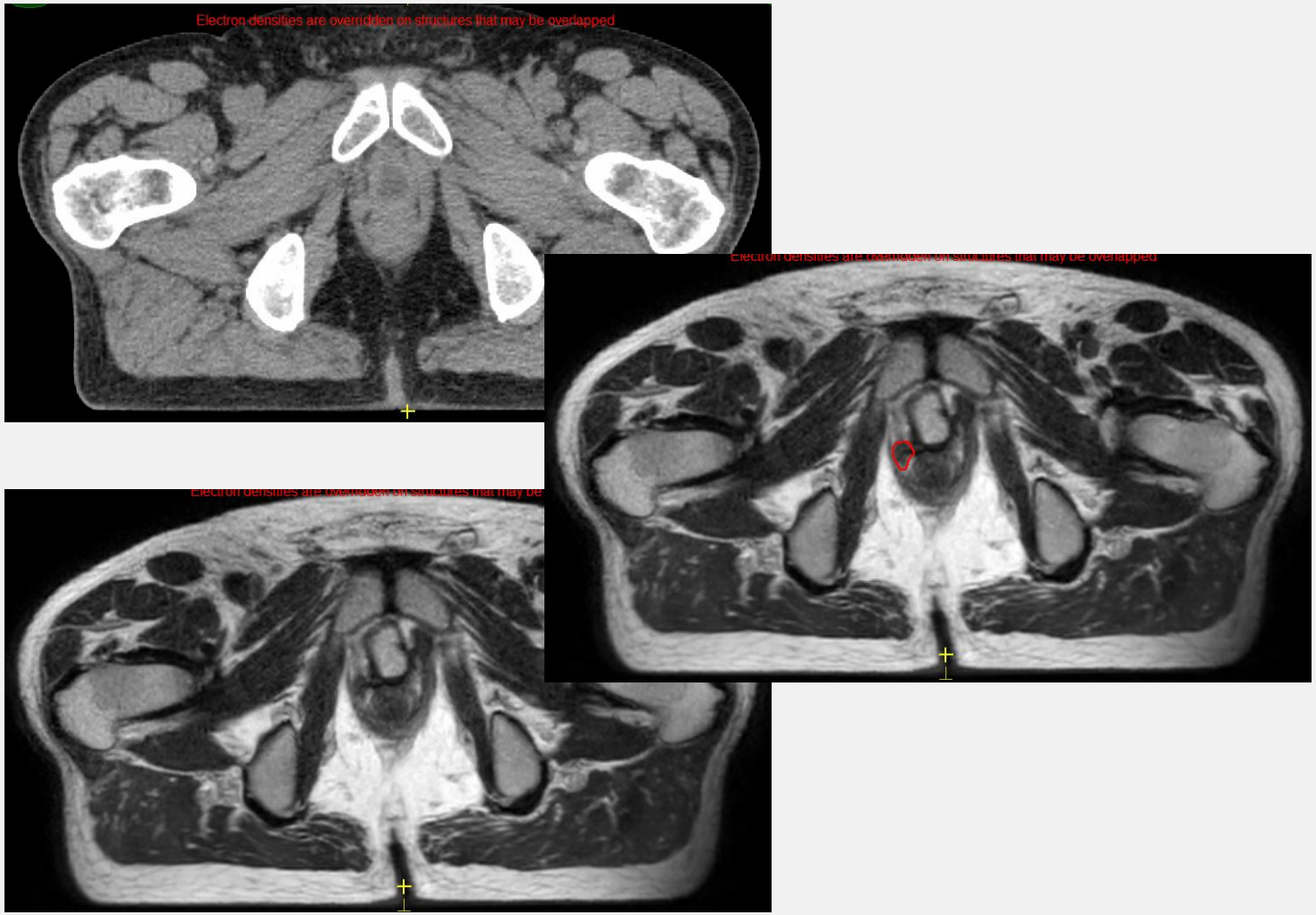
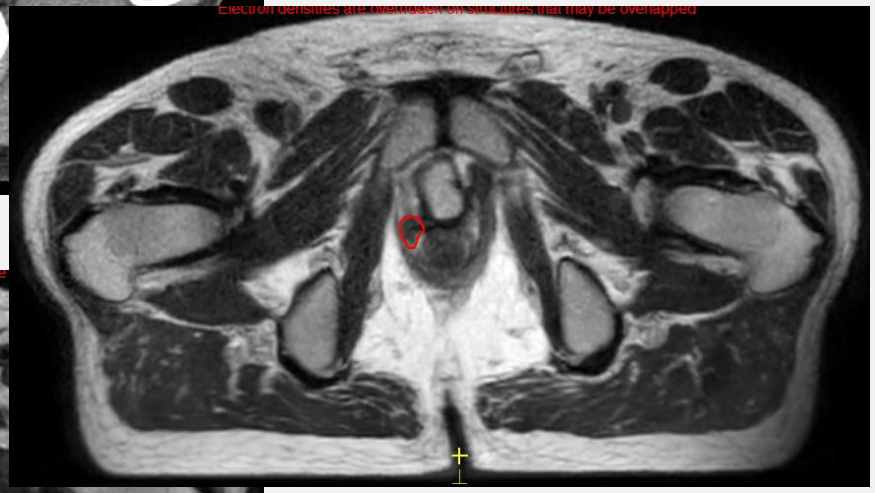
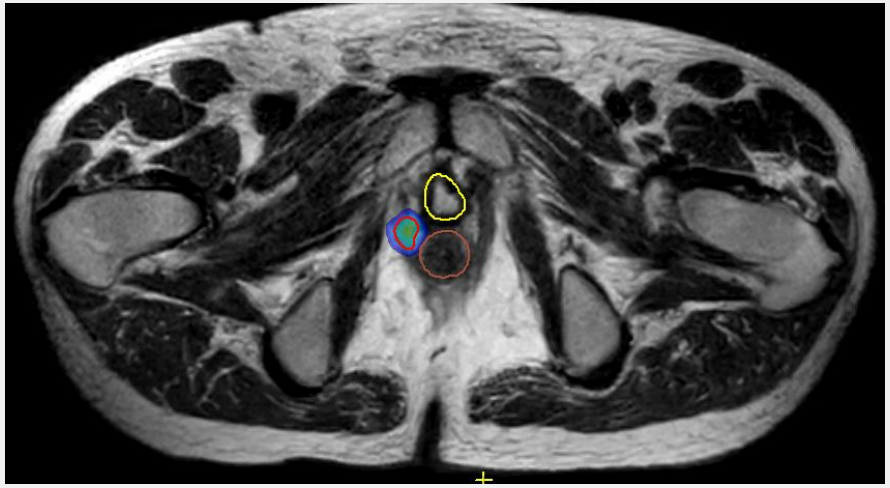
Benefits in Prostate Cancer Treatment

Benefits in Prostate Cancer Treatment



Benefits in Prostate Cancer Treatment





Summary

- Radiotherapy is a curative option
- Reducing number of treatments becoming the norm
- Higher doses to the tumour (DiL) improves outcome
- Treat the whole pelvis in select patients
- ADT improves outcome
  - Improved ability to determine who benefits most
- Increasing role of Radiotherapy in metastatic disease
- Advanced techniques such as MRI Guided

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