

Prostate Cancer Radiation Therapy



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Center for Multimodal Imaging and Genetics

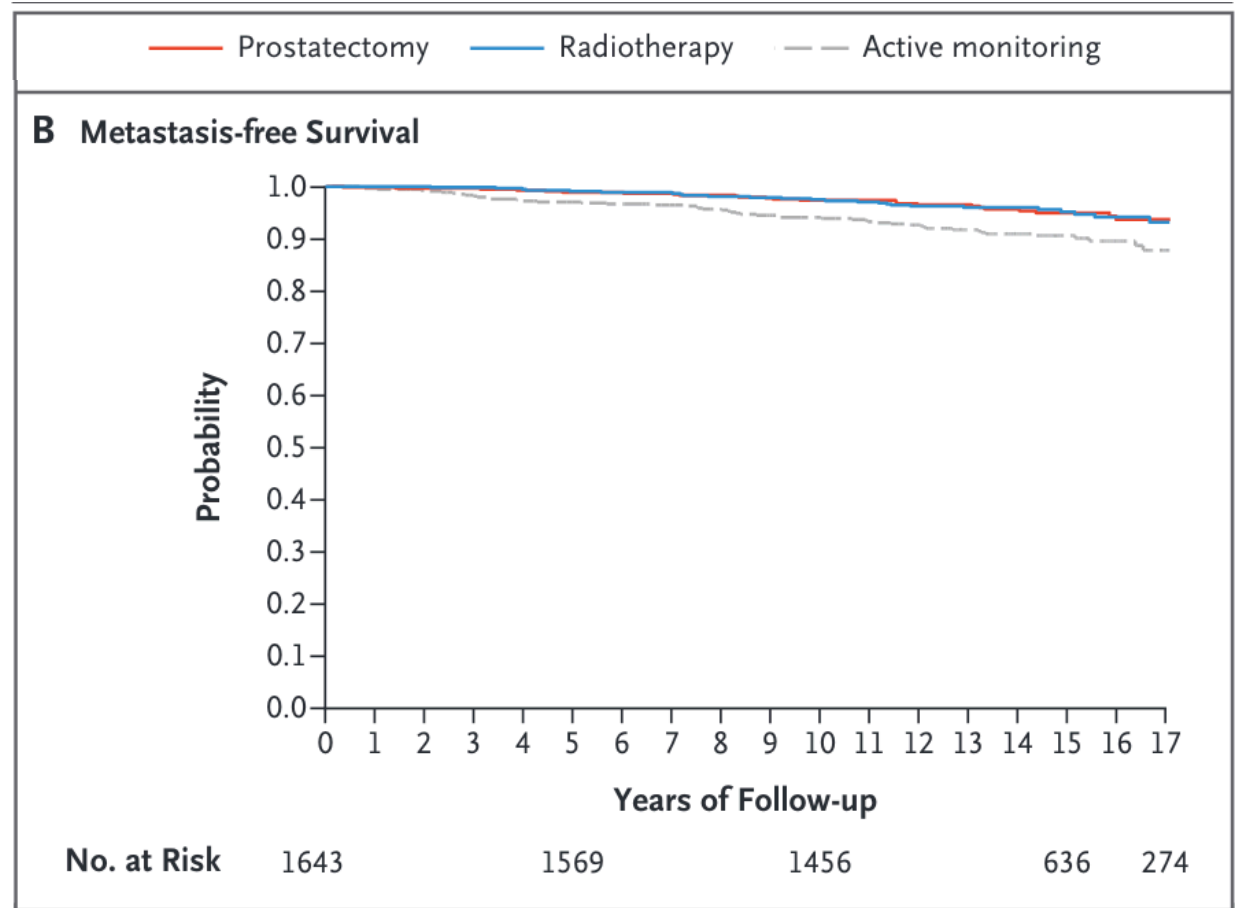
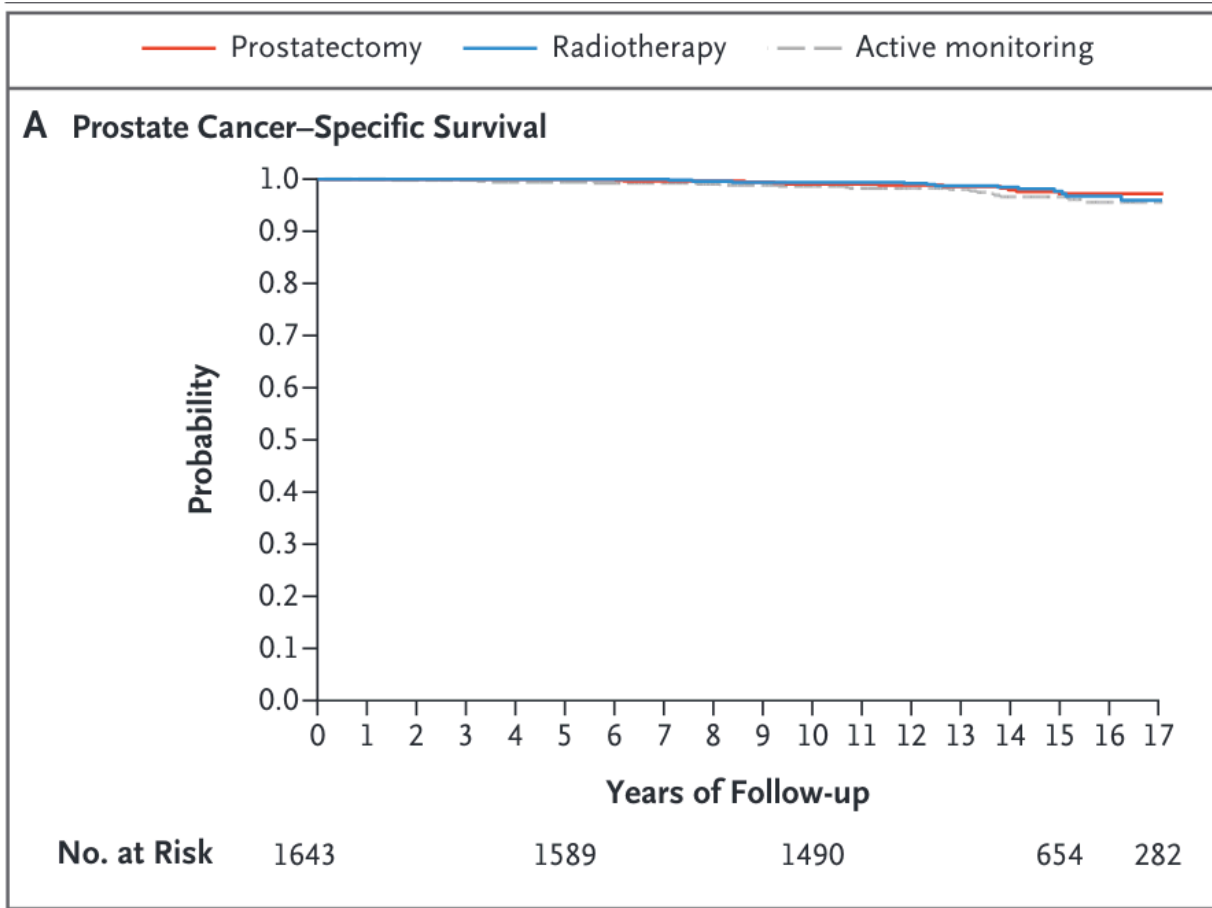
Center for Precision Radiation Medicine

University of California San Diego

ProtecT: Landmark clinical trial

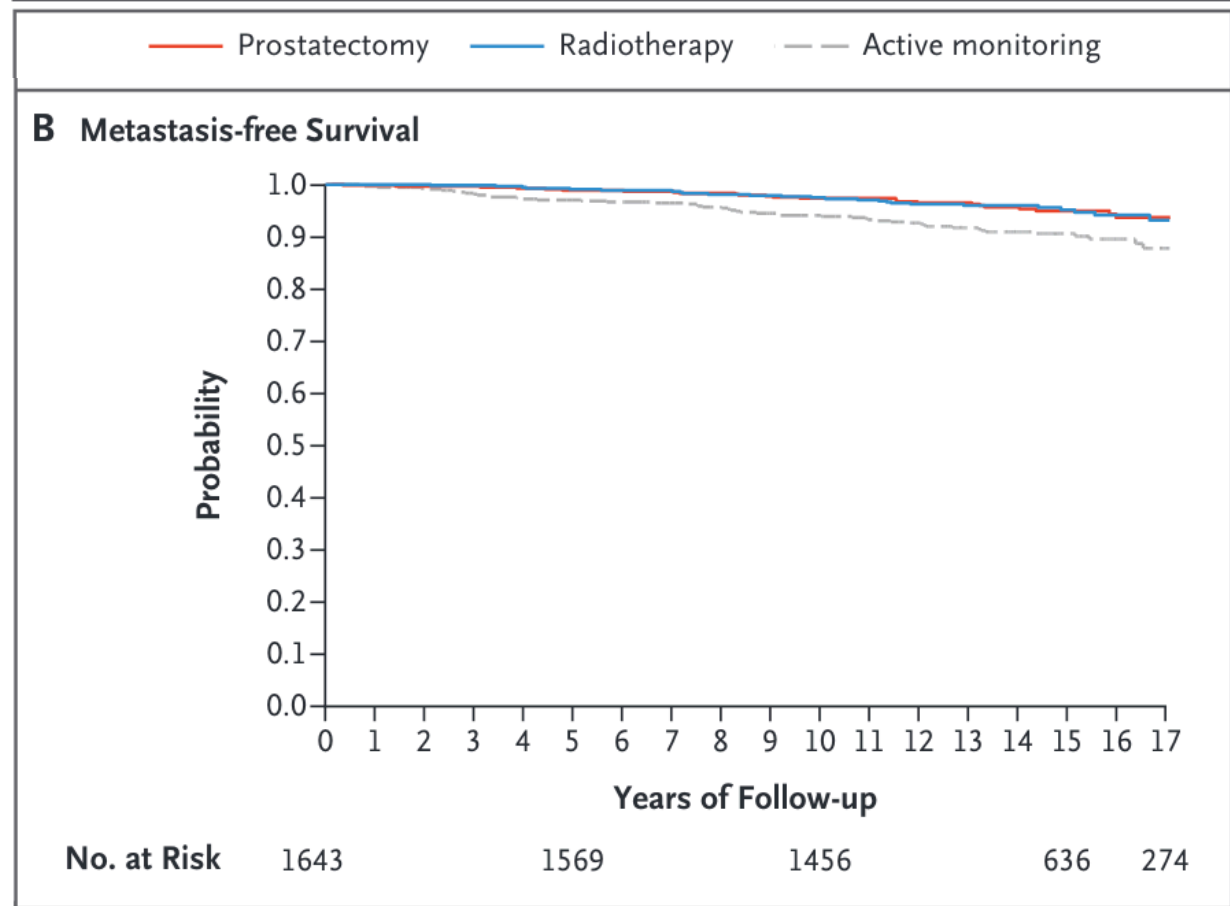
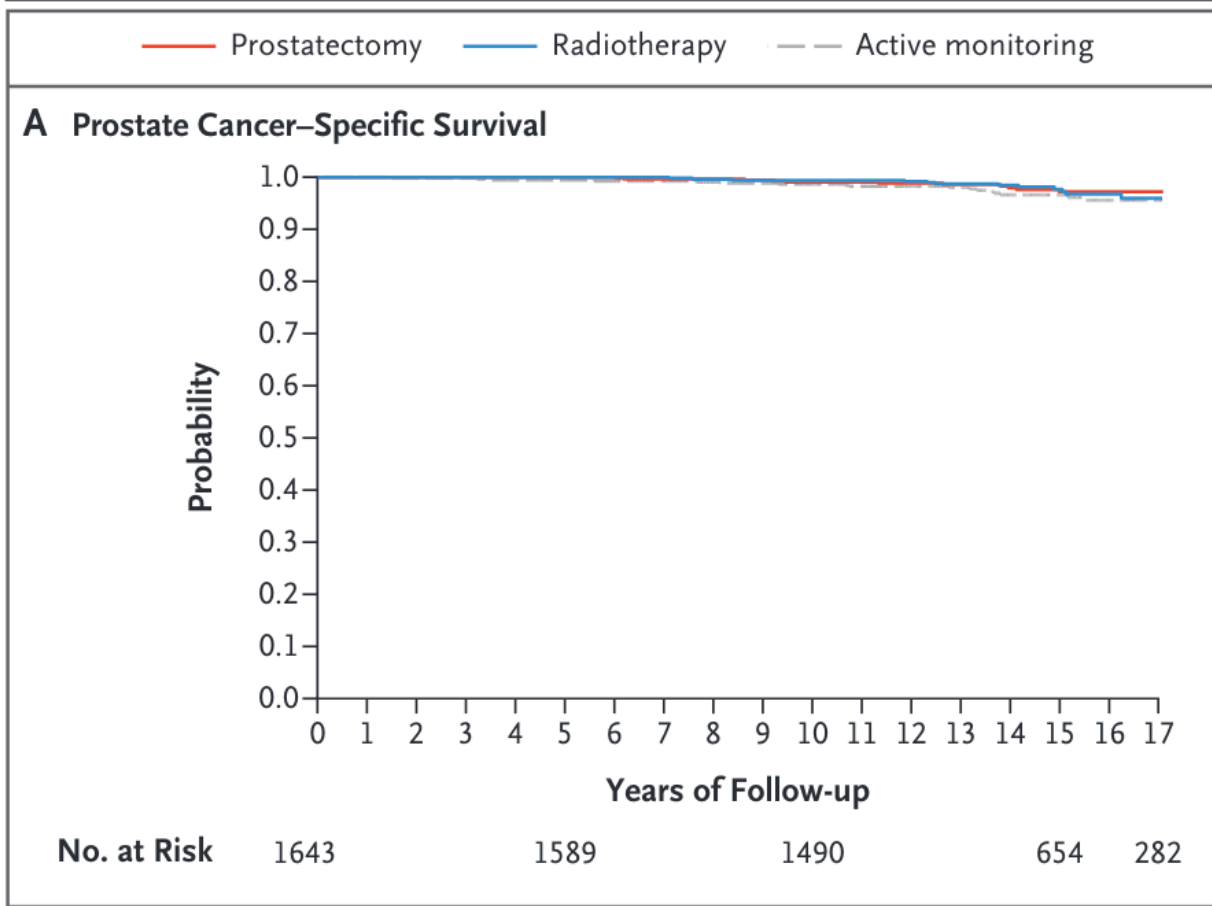
- Largest randomized trial comparing surgery and radiation
 - 1,643 patients randomized to one of 3 options:
 - Surgery / Radical prostatectomy
 - Radiation therapy with 3-6 months of hormone therapy (ADT)
 - Active monitoring – watch PSA, treat if concerning changes
 - Most patients had low risk or favorable-intermediate risk prostate cancer
- Patients enrolled from 1999 to 2009
 - Allows long-term results to be analyzed
 - Treatments have improved since then

Is Active Surveillance Safe?



- Yes, active surveillance is very safe for patients with low/favorable risk
- But must do **active** surveillance

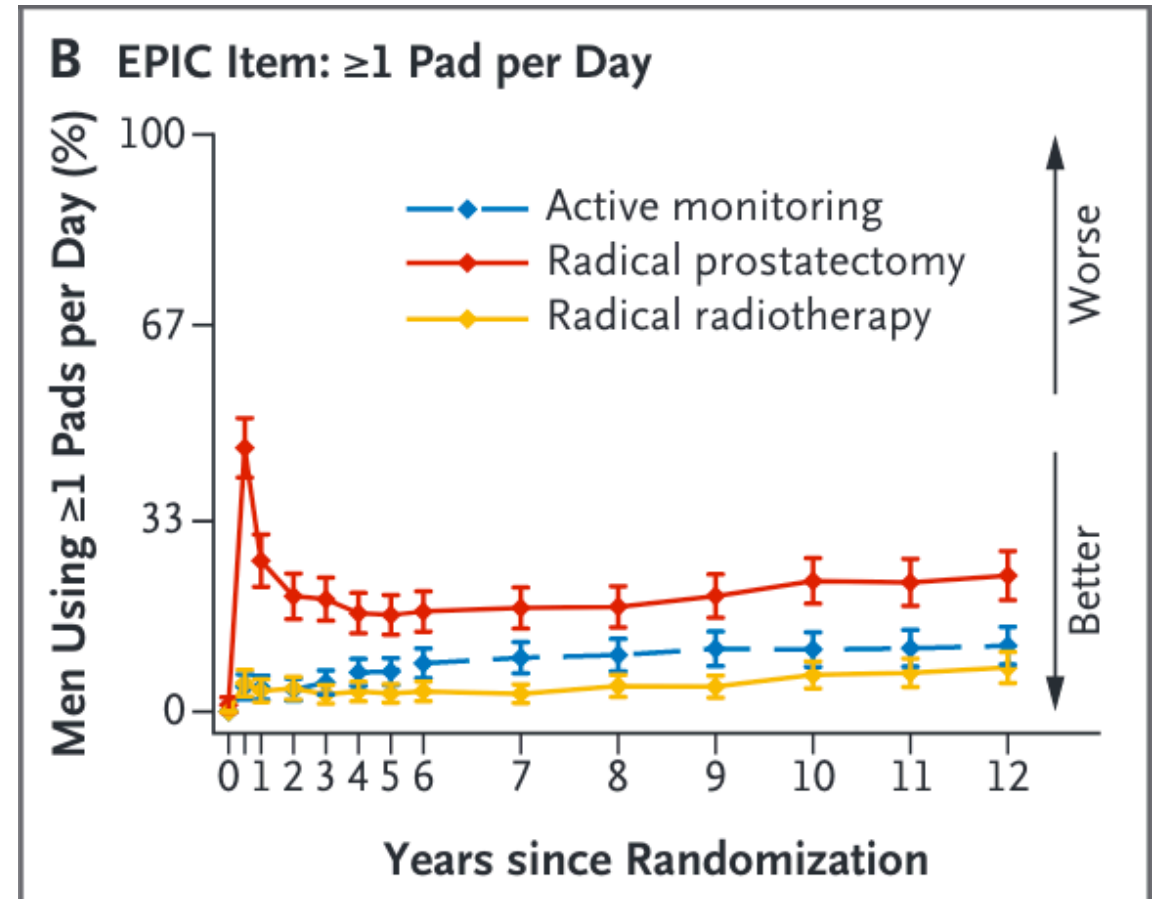
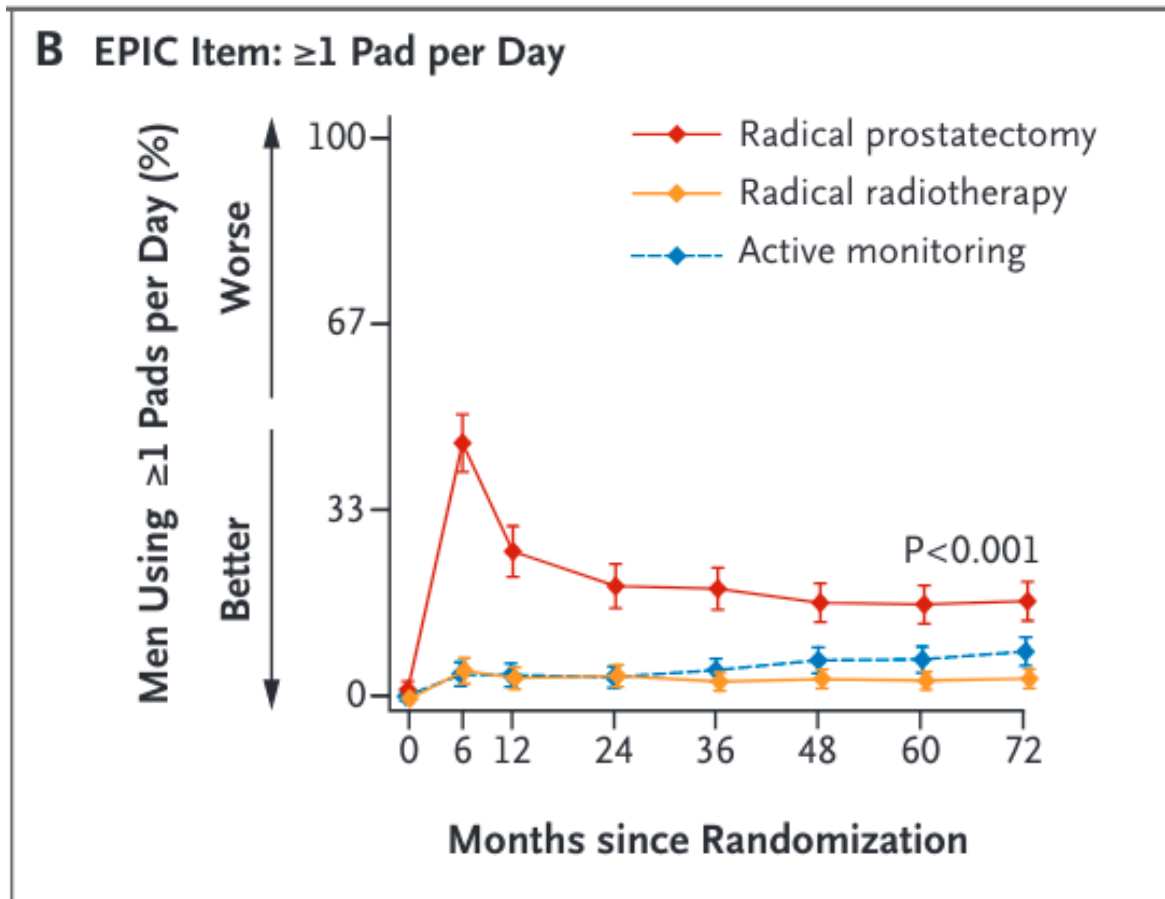
Which is better: prostatectomy or radiation therapy?



- **Both highly effective.** No difference in cancer outcomes for low/favorable-risk
- If surgery for higher risk cancer, may need radiation after (worse side effects)
- If radiation for higher risk cancer, may need longer duration of hormone therapy

Side effects from surgery vs. radiation

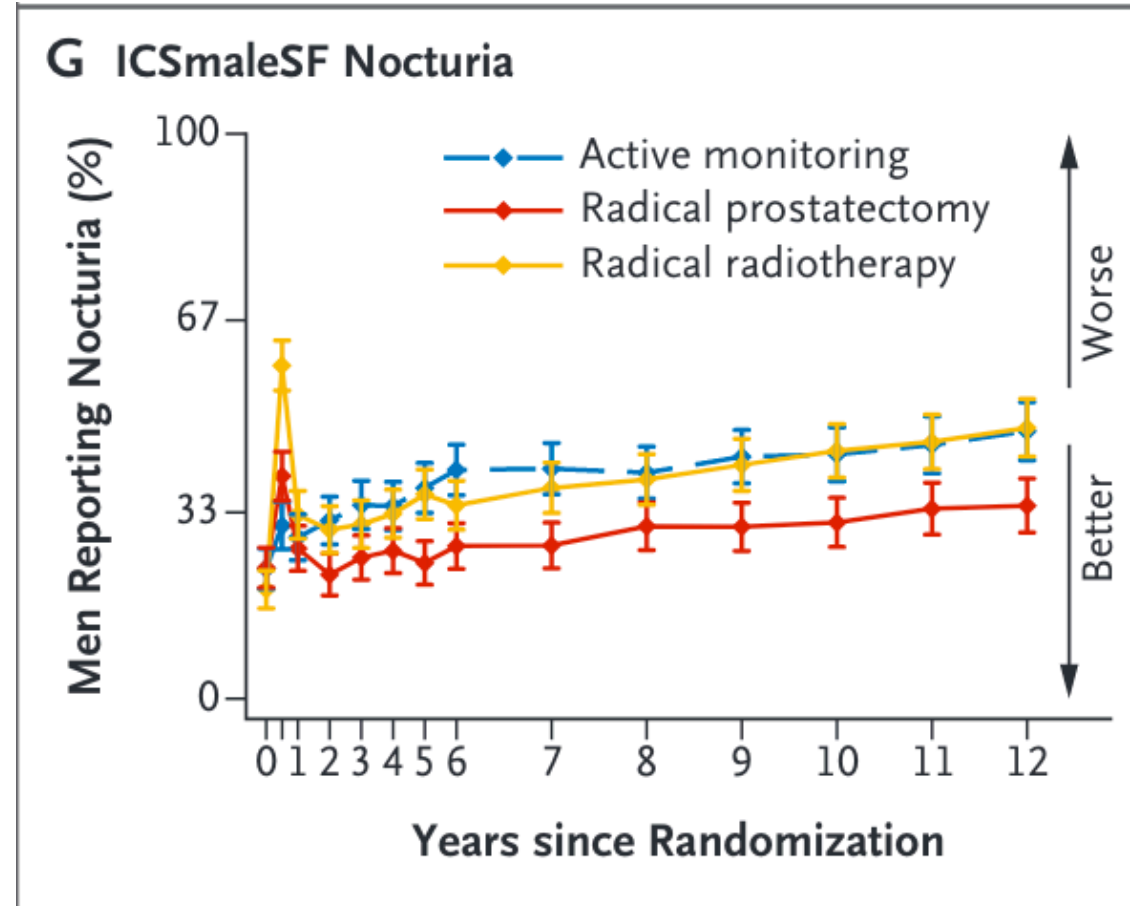
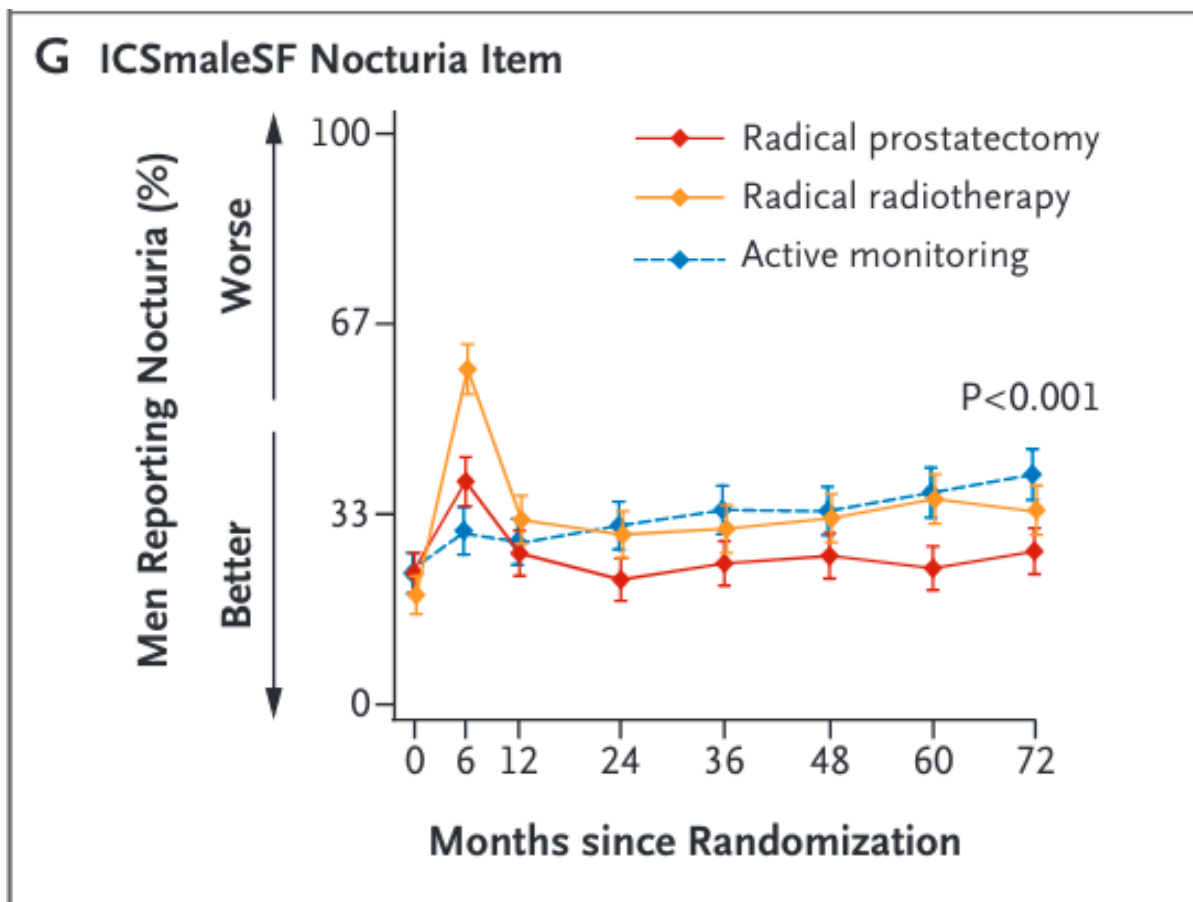
Urinary incontinence: need to **wear a pad** because you leak urine



- More likely to need a pad for urine leakage after surgery

Side effects from surgery vs. radiation

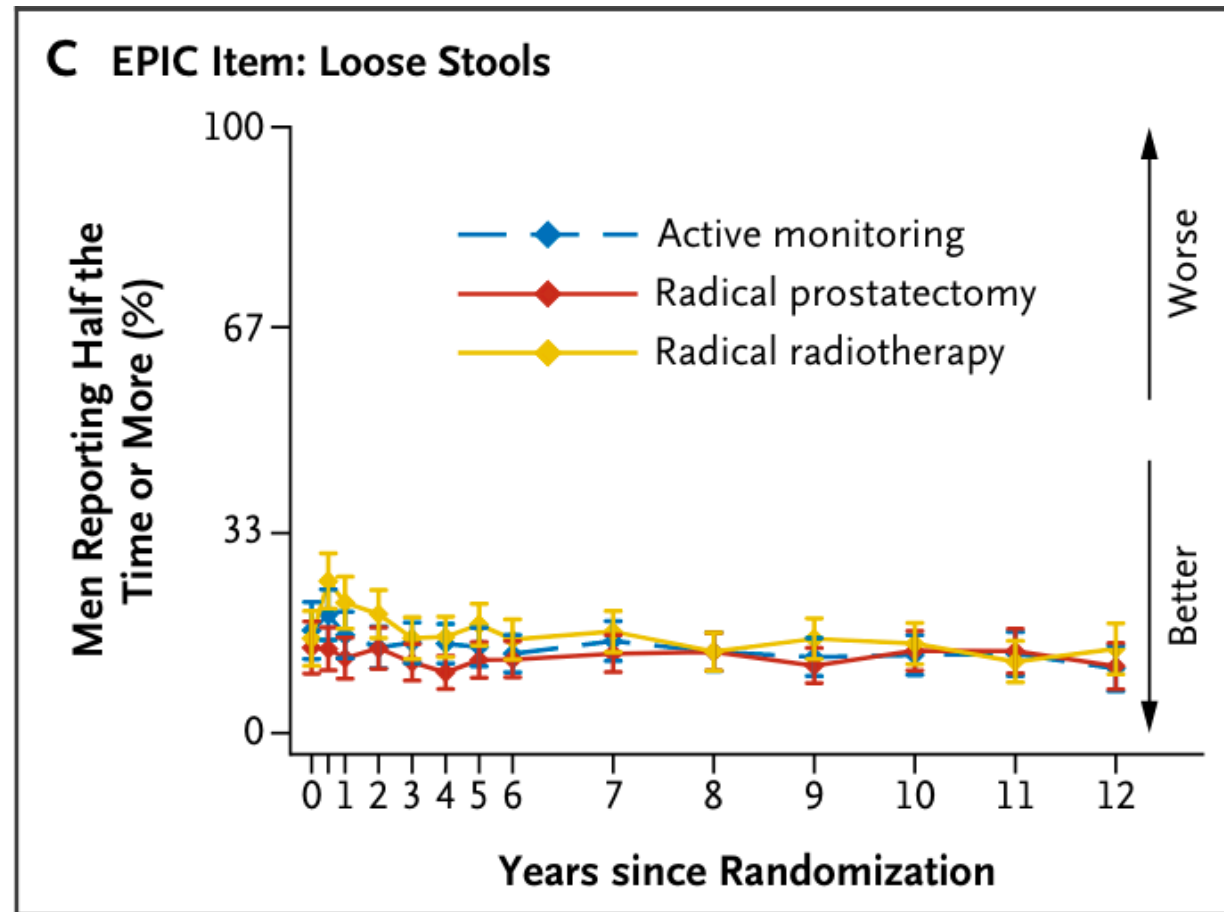
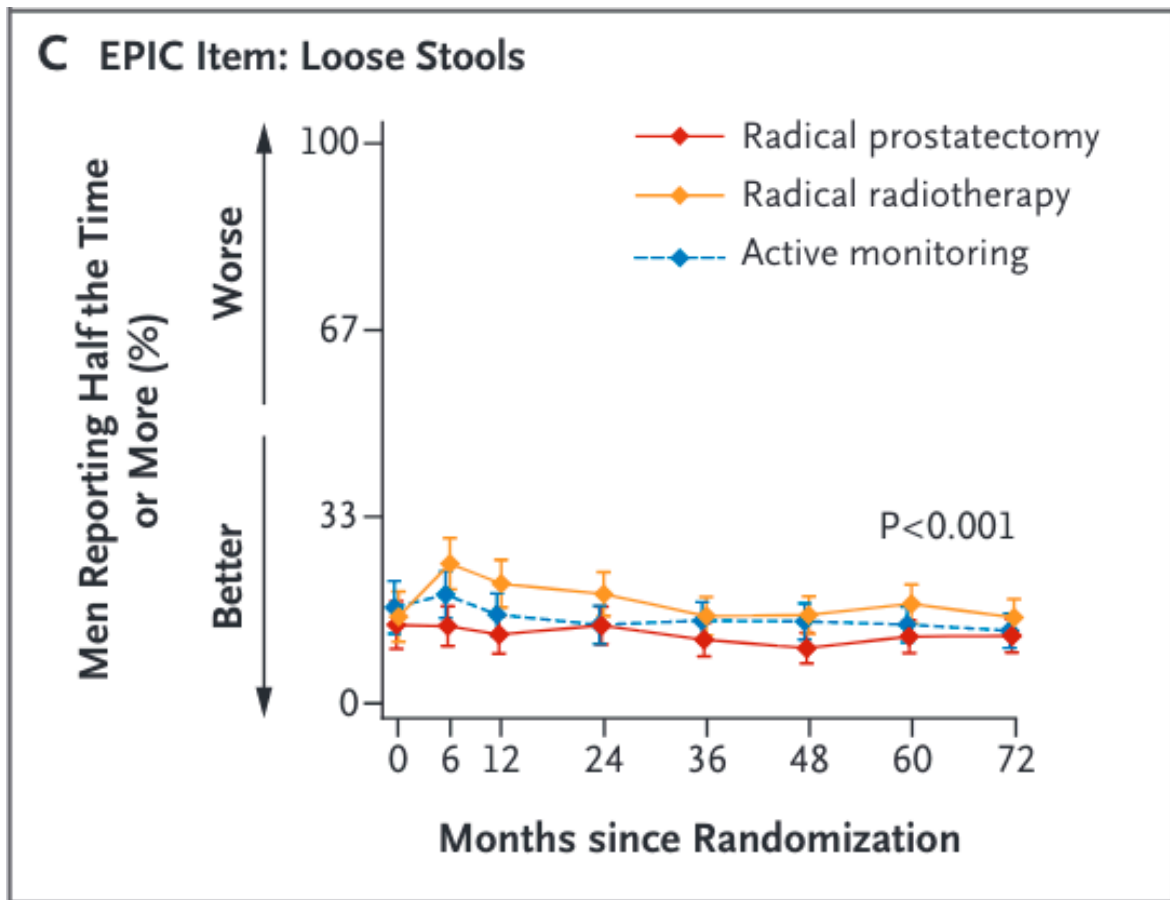
Nocturia: **waking up at night** (≥ 2 times) to urinate



- Nocturia common during radiation therapy
- In the long term, nocturia is less common after surgery than after radiation

Side effects from surgery vs. radiation

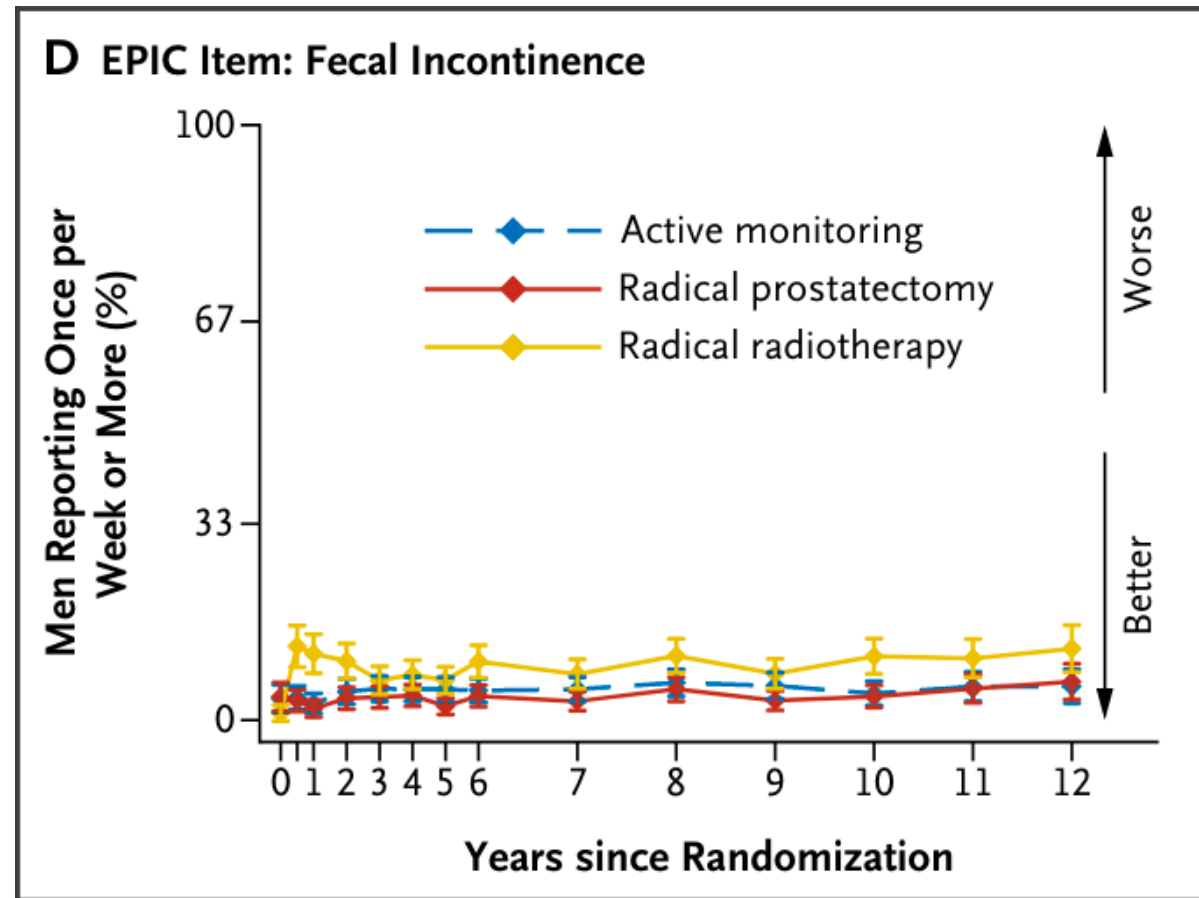
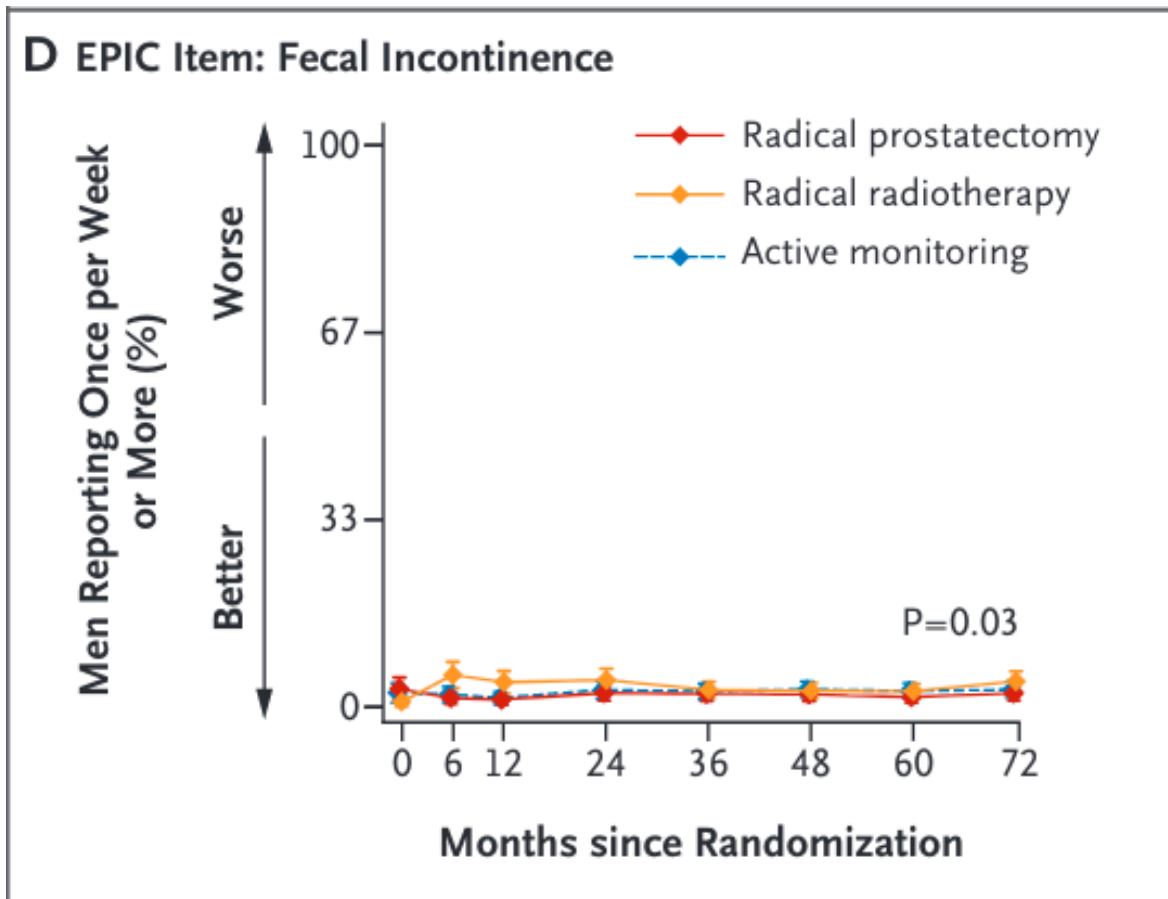
Loose stools



- Loose stools somewhat common during radiation
- Some men may continue to have loose stools for a year or more after radiation

Side effects from surgery vs. radiation

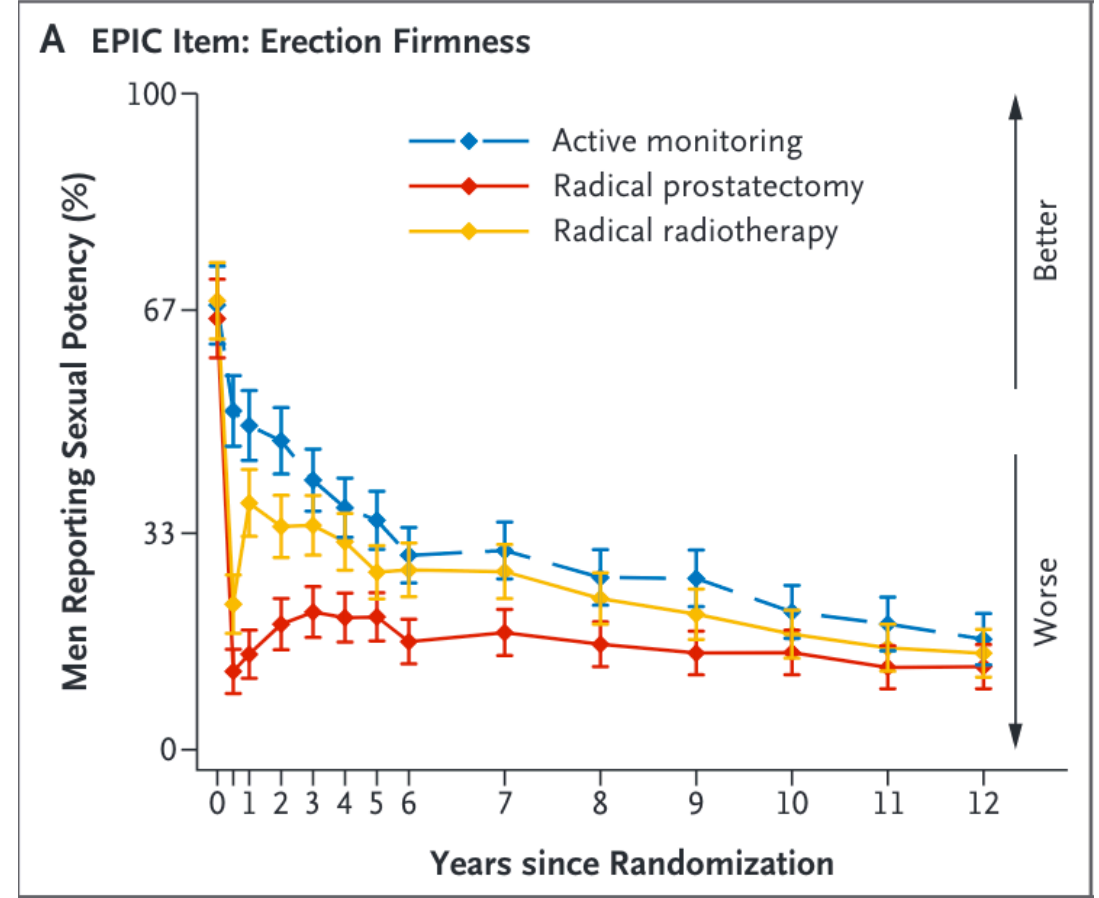
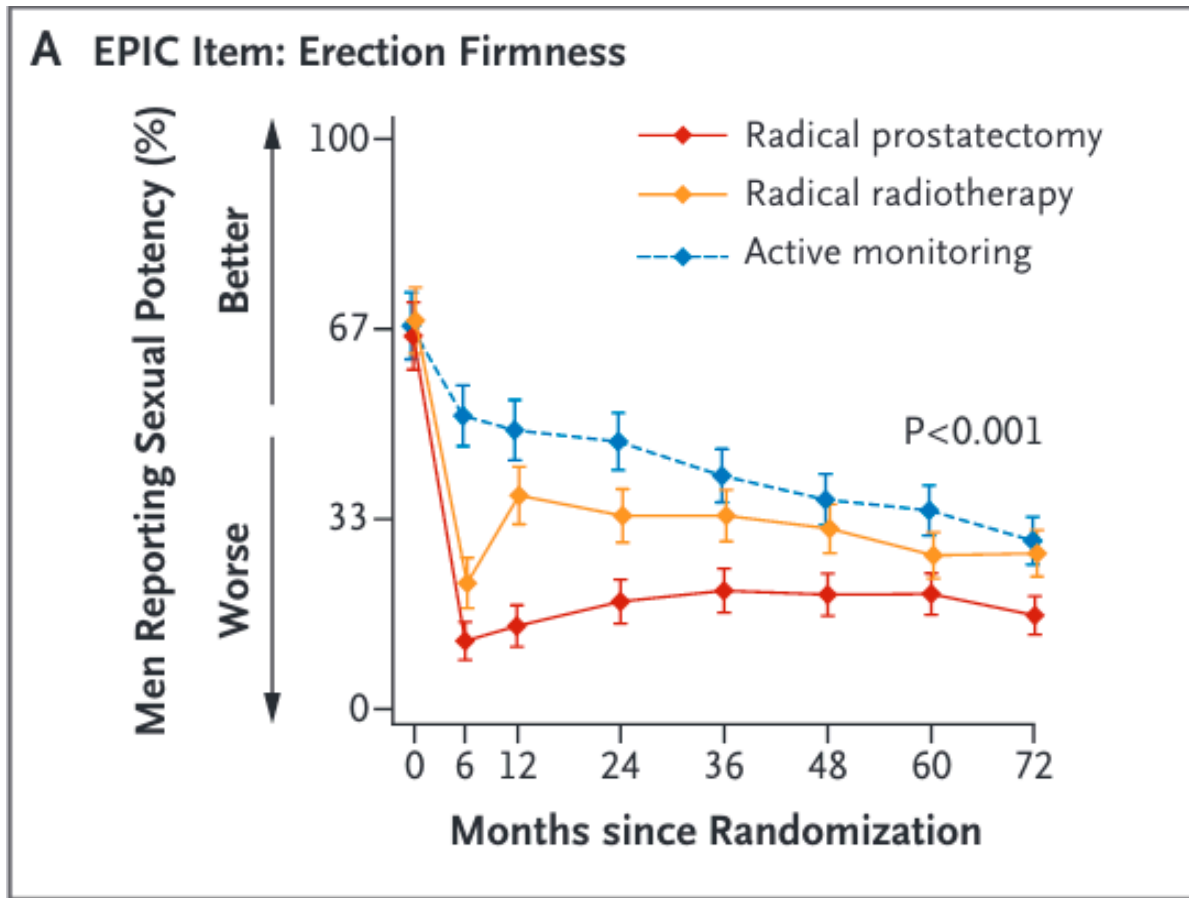
Fecal incontinence: **fecal leakage** ≥ 1 time per week



- Fecal incontinence uncommon overall but more common after radiation
- Modern radiation substantially reduces dose to rectum (IGRT, IMRT, +/-spacer)

Side effects from surgery vs. radiation

Erections firm enough for intercourse



- Few men have firm erections during treatment and recovery
- Sexual function better preserved after radiation than after surgery

Advanced radiation therapy for prostate cancer

- IMRT = intensity modulated radiation therapy
 - Shape the radiation dose to the target
- IGRT = image guided radiation therapy
 - Scan patient every day before treatment to ensure accurate targeting
- Focal radiation boost
 - Increase dose to the tumor visible on MRI

Focal radiation boost for prostate cancer

Journal of Clinical Oncology®

original reports

Focal Boost to the Intraprostatic Tumor in External Beam Radiotherapy for Patients With Localized Prostate Cancer: Results From the FLAME Randomized Phase III Trial

Linda G. W. Kerkmeijer, MD, PhD^{1,2}; Veerle H. Groen, MD¹; Floris J. Pos, MD, PhD³; Karin Haustermans, MD, PhD⁴; Evelyn M. Monninkhof, PhD⁵; Robert Jan Smeenk, MD, PhD²; Martina Kunze-Busch, PhD²; Johannes C. J. de Boer, PhD¹; Jochem van der Voort van Zijp, MD, PhD¹; Marco van Vulpen, MD, PhD⁶; Cédric Draulans, MD, PhD⁴; Laura van den Bergh, MD, PhD⁷; Sofie Isebaert, PhD⁴; and Uulke A. van der Heide, PhD³

- Randomized trial:
 - Treat whole prostate the same or ‘boost’ dose to the visible tumor
 - (Patients had intermediate- or high-risk cancer)

Focal radiation boost for prostate cancer

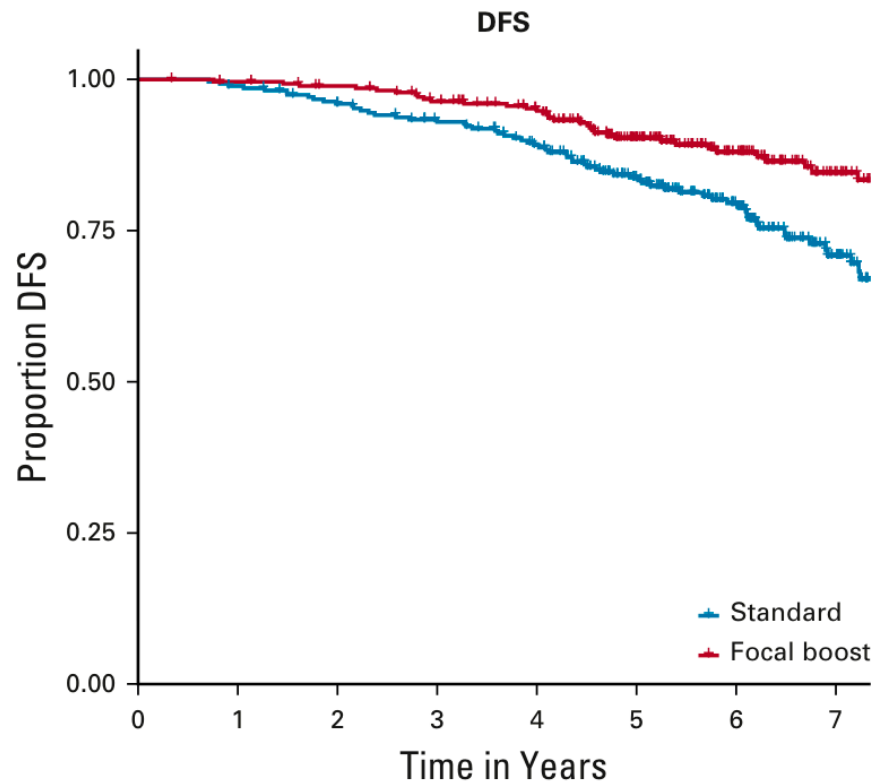


Table 2 – Cox per-protocol regression analysis for local failure and regional + distant metastatic failure

	Adjusted HR (95% CI) ^a	p value
Local failure	0.33 (0.14–0.80)	0.01
Regional + distant metastatic failure	0.56 (0.34–0.91)	0.02

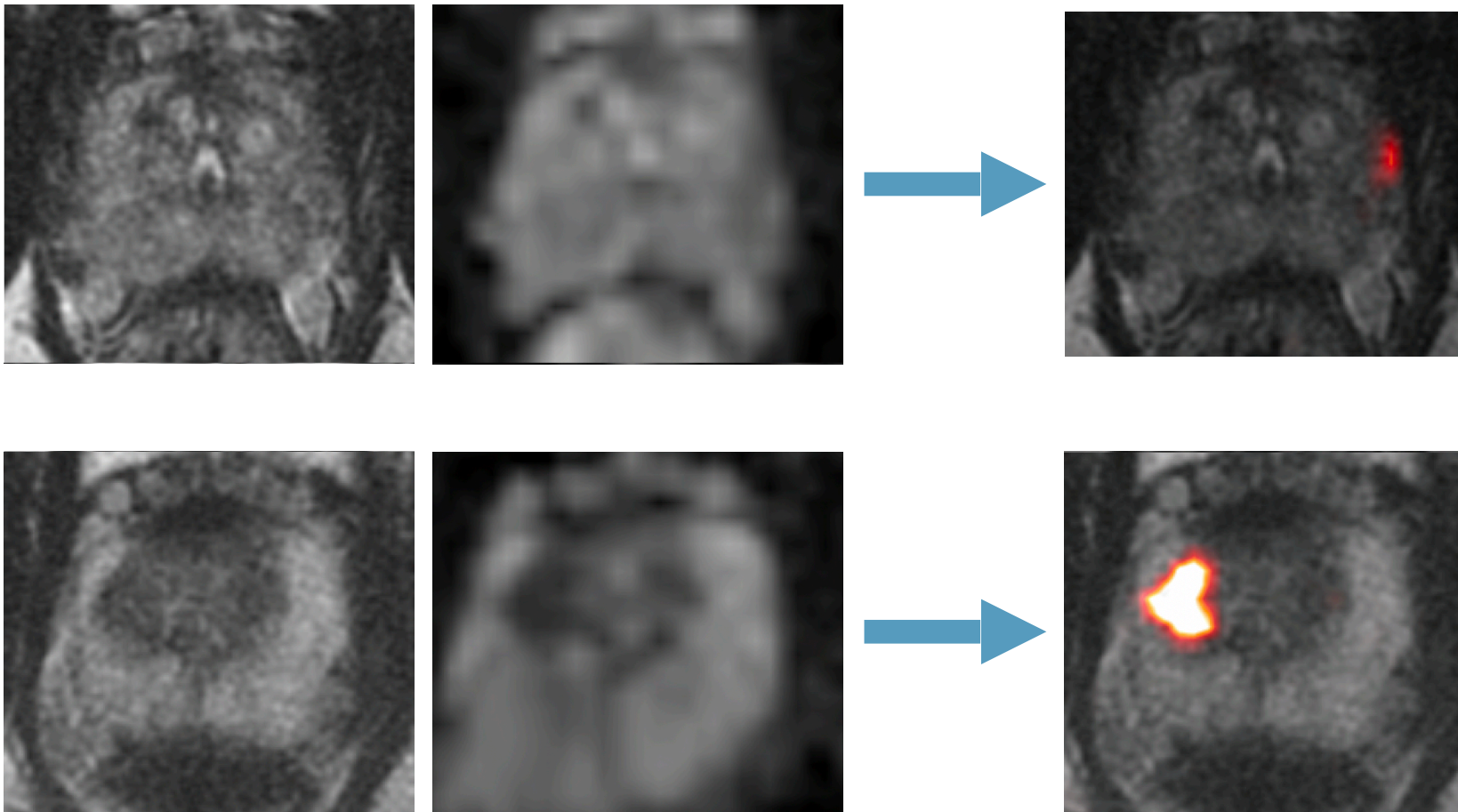
CI = confidence interval; HR = hazard ratio.
^a Adjusted for center, age (in years), hormonal treatment duration (in months), timing of hormonal treatment (neoadjuvant vs adjuvant), T stage, initial prostate-specific antigen (in ng/ml), and Gleason score.

- Focal boost group had:
 - **67% less cancer recurrence** in the prostate
 - **44% less cancer metastasis**
 - No increase in toxicity (only boosted as could be safely achieved)

Fewer metastases / recurrences without increased toxicity

- Every patient should get this, right?
- We conducted a survey of radiation oncologists in 2022-2023
 - Two years after FLAME trial results published
 - Over 250 radiation oncologists participated
 - Conclusion: overwhelming **majority of patients not getting** focal boost
- Why not?
 - Lack of access to high-quality MRI
 - Cannot see tumor target
 - Difficult to align MRI and CT scans for treatment planning

Focal radiation boost for prostate cancer



- Advanced MRI for prostate cancer: Restriction Spectrum Imaging (RSI)
 - Improve accuracy of prostate MRI for diagnosis and treatment
 - Multiple completed and active studies led by Dr. Seibert at UC San Diego

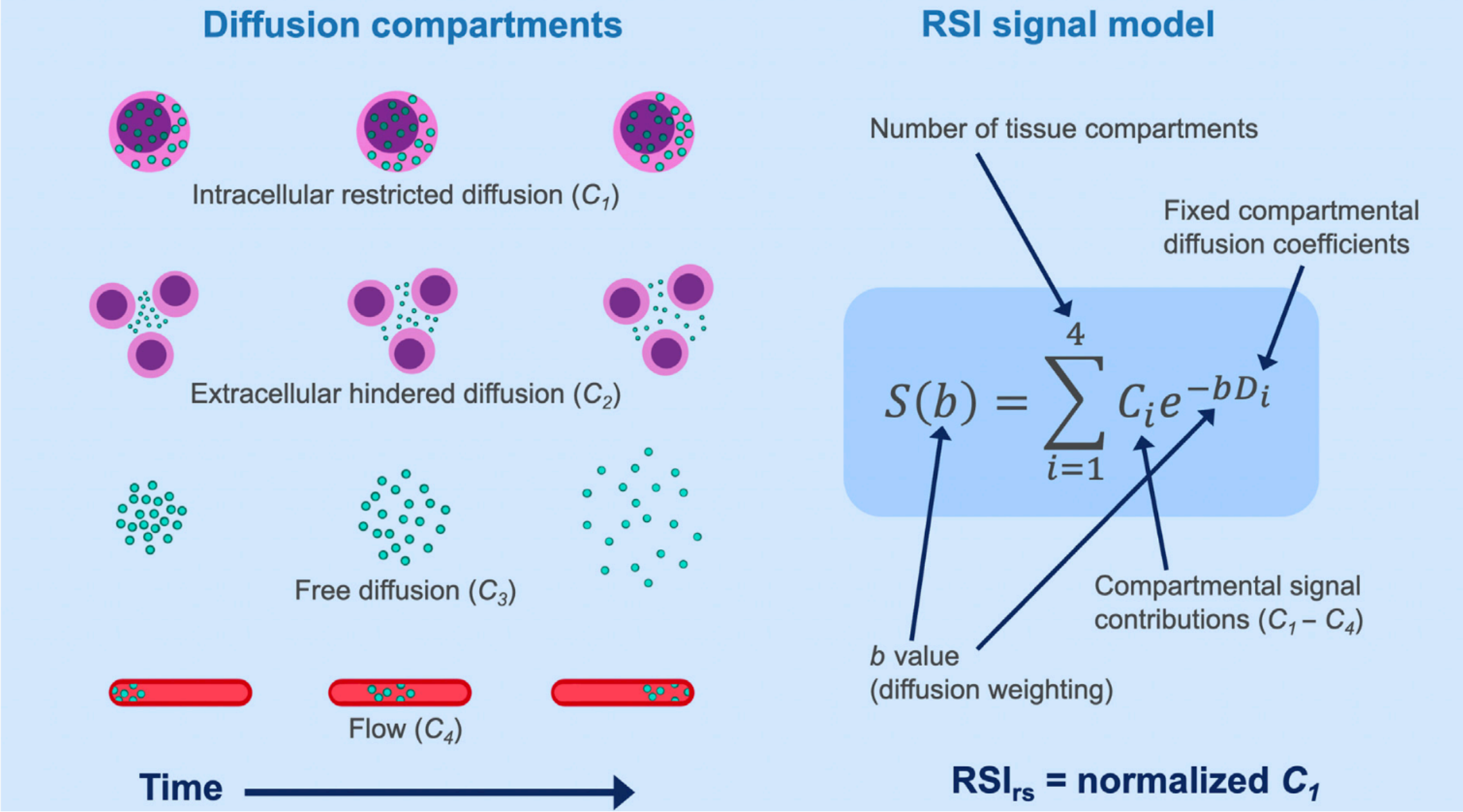
A major focus of Dr. Seibert's research team:

More accurate radiation therapy for patients
with prostate cancer everywhere

Focal RT boost is better for patients ... what's the catch?

- You can't aim at what you can't see
 - Radiation oncologists need to learn to **reliably** identify the boost target
- Advanced MRI can help
 - RSIs: Restriction Spectrum Imaging restriction score

RSI: Advanced MRI for cancer detection



Can advanced MRI (RSIrs) improve tumor targeting?

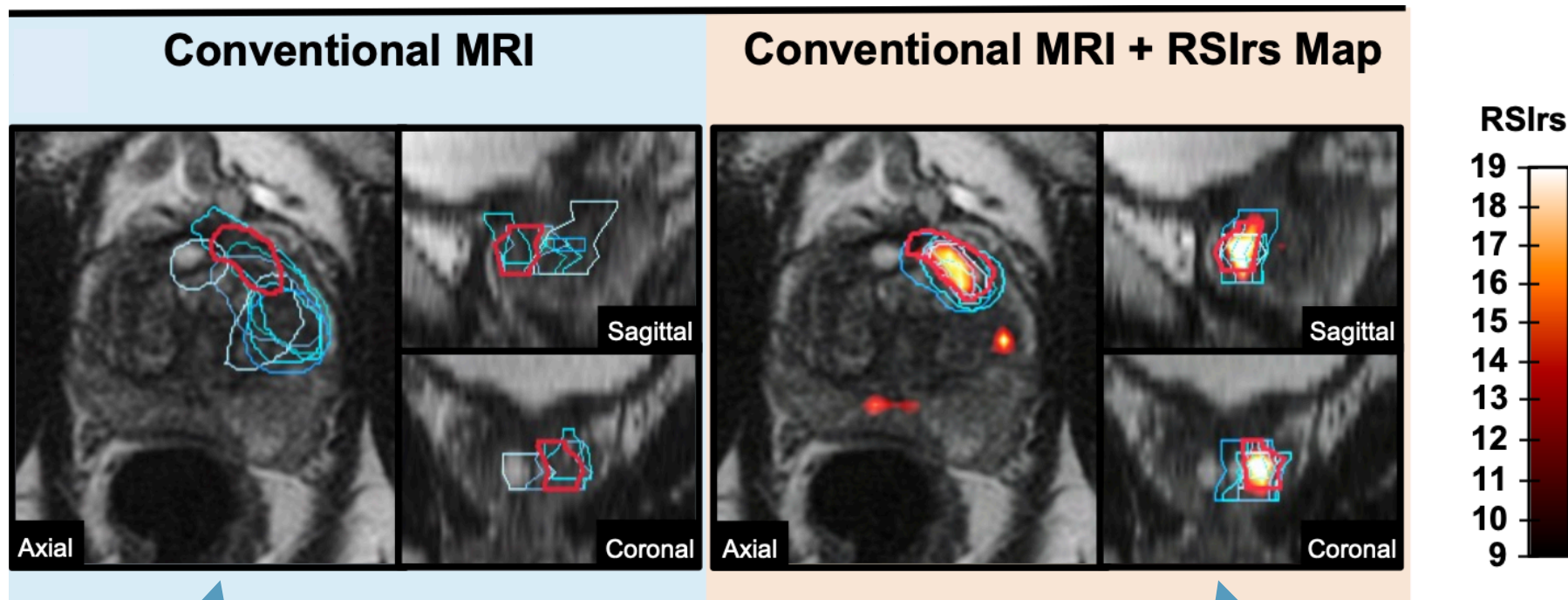
- We ran a study. 44 radiation oncologists participated
 - They were given prostate MRI images
 - They were told where the tumor was (in words)
 - They attempted to circle the tumor for focal RT boost
- Sometimes, they were only given conventional MRI
- And sometimes, they were also given RSIrs maps

Can advanced MRI (RSIs) improve tumor targeting?

- Results without RSIs:
 - **18% of all attempts were complete misses** (0% overlap with tumor)
 - **91% of doctors completely missed at least one tumor**
 - **On average (median), each doctor completely missed 3 tumors**
 - (Average number of targets/attempts per participant = 18)
- But with RSIs:
 - **Complete misses dropped from 18% to 2%, overall**
 - **Doctors completely missing a tumor dropped from 91% to 30%**
 - **Complete misses per doctor went from 3 tumors to zero tumors**

Example 1:

- Expert radiologists outlined the **tumor in red**
- Radiation oncologists' **attempts** to outline the tumor are shown in **shades of blue**

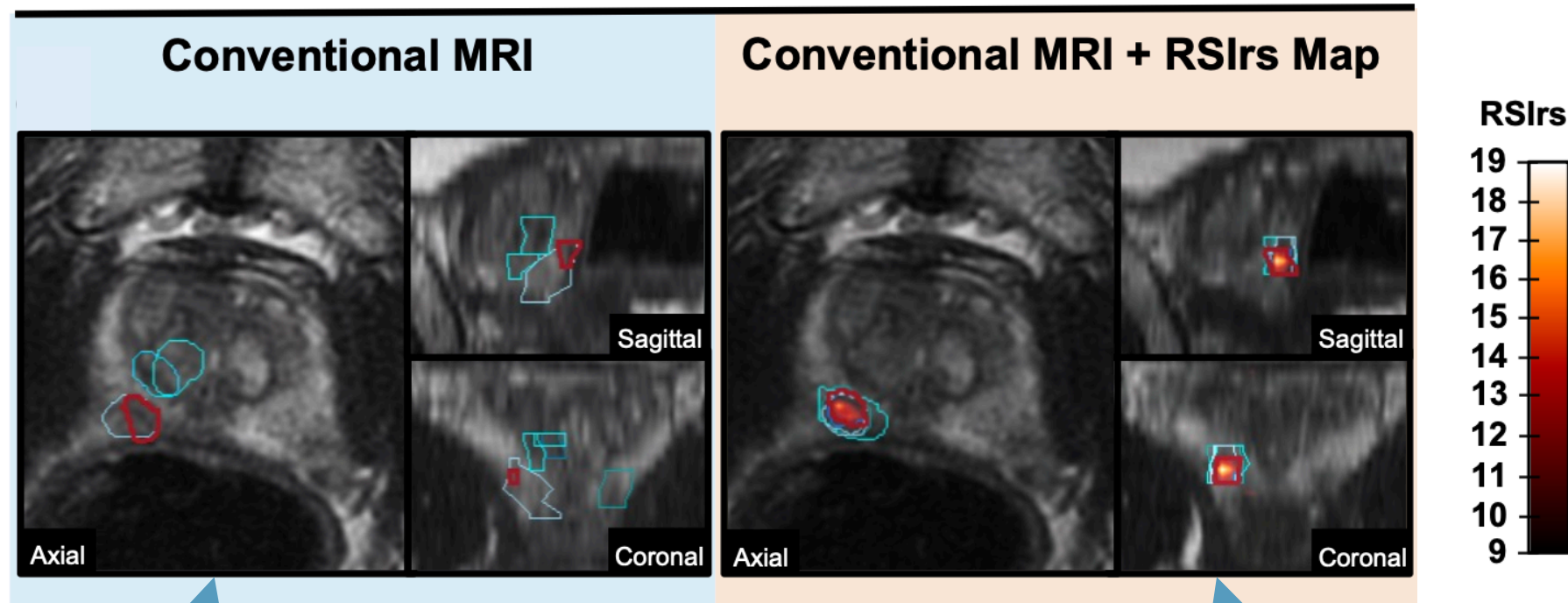


With only conventional MRI, many oncologists struggled to find the tumor

With RSIs maps, these same oncologists each correctly outlined the tumor target

Example 2:

- Expert radiologists outlined the **tumor** in **red**
- Radiation oncologists' **attempts** to outline the tumor are shown in **shades of blue**

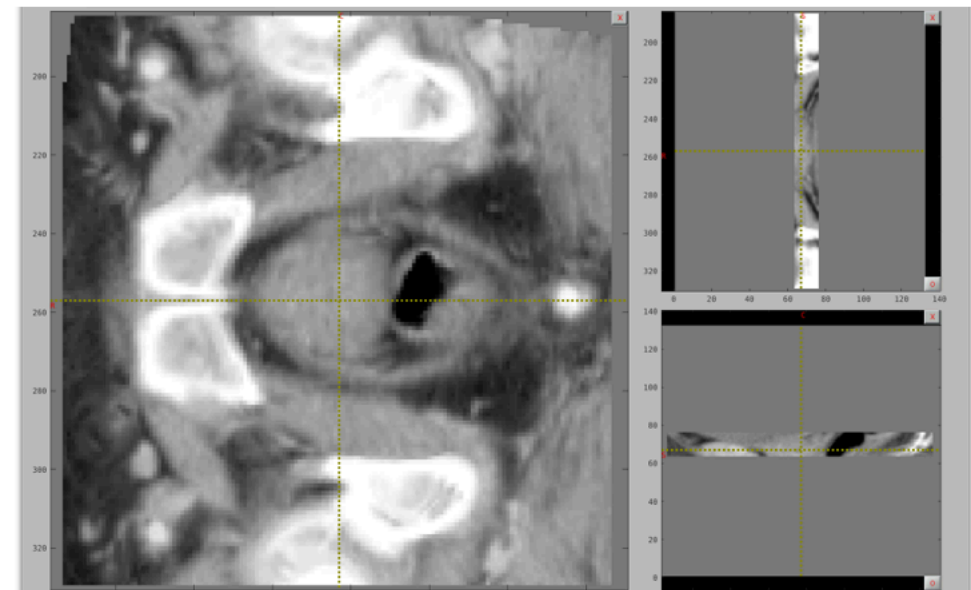
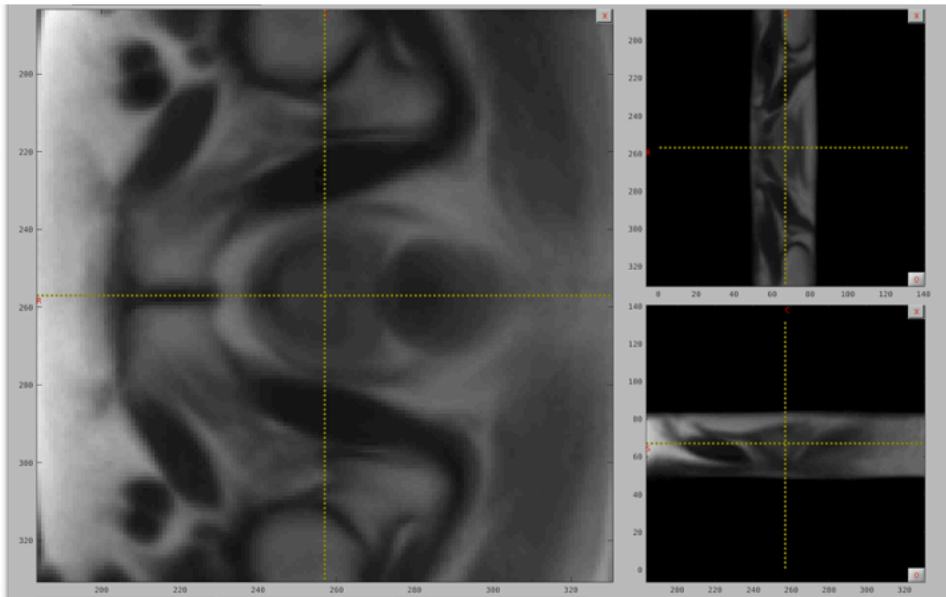


With only conventional MRI, many oncologists struggled to find the tumor

With RSIs maps, these same oncologists each correctly outlined the tumor target

Improved alignment of MRI and CT scans

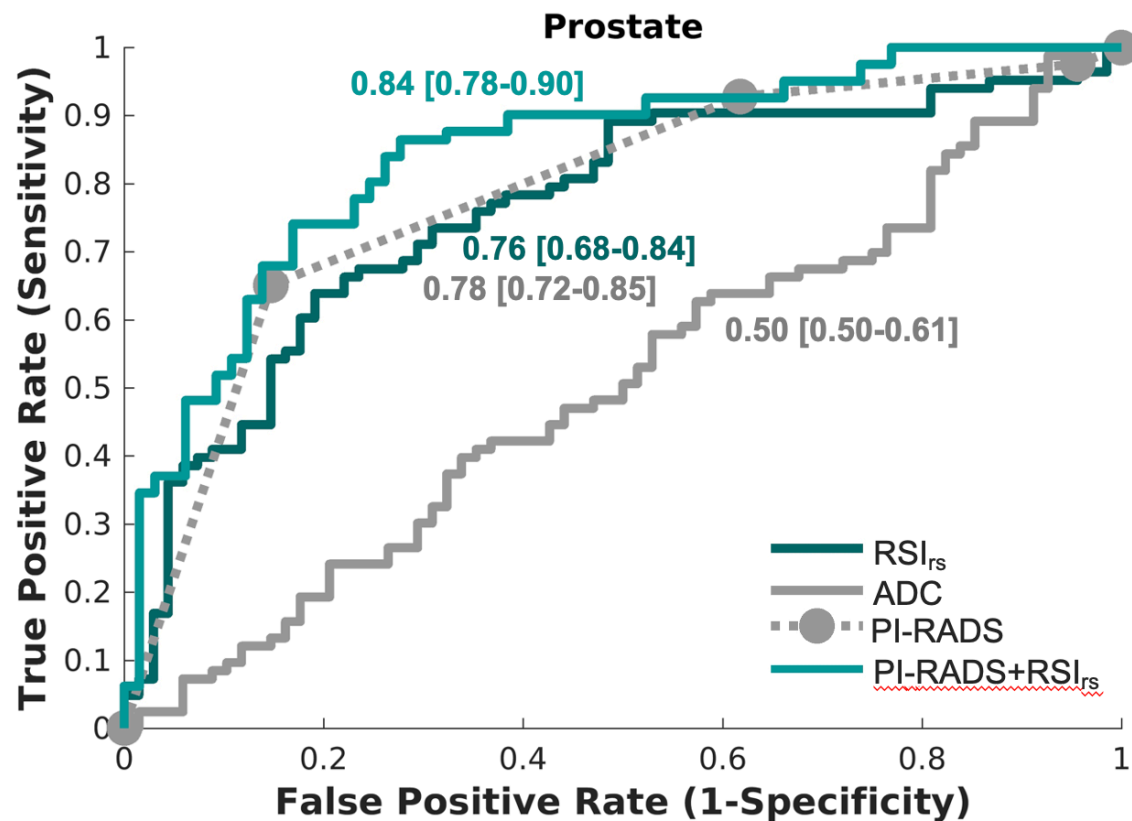
- Tumor only visible on MRI, but CT scan used for radiation planning
 - Solution 1: Atlas-based multi-modal registration
 - Solution 2: MRI-only planning (create synthetic CT scan from MRI scan)



Other ongoing projects in the Seibert Lab

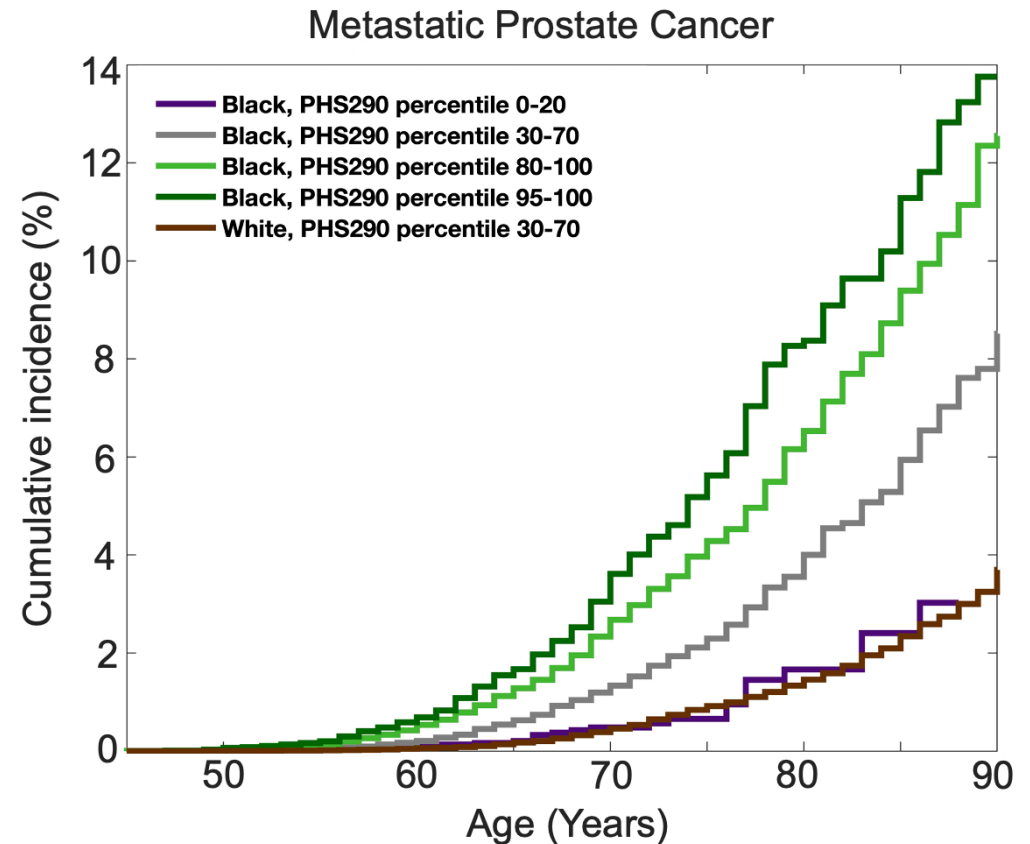
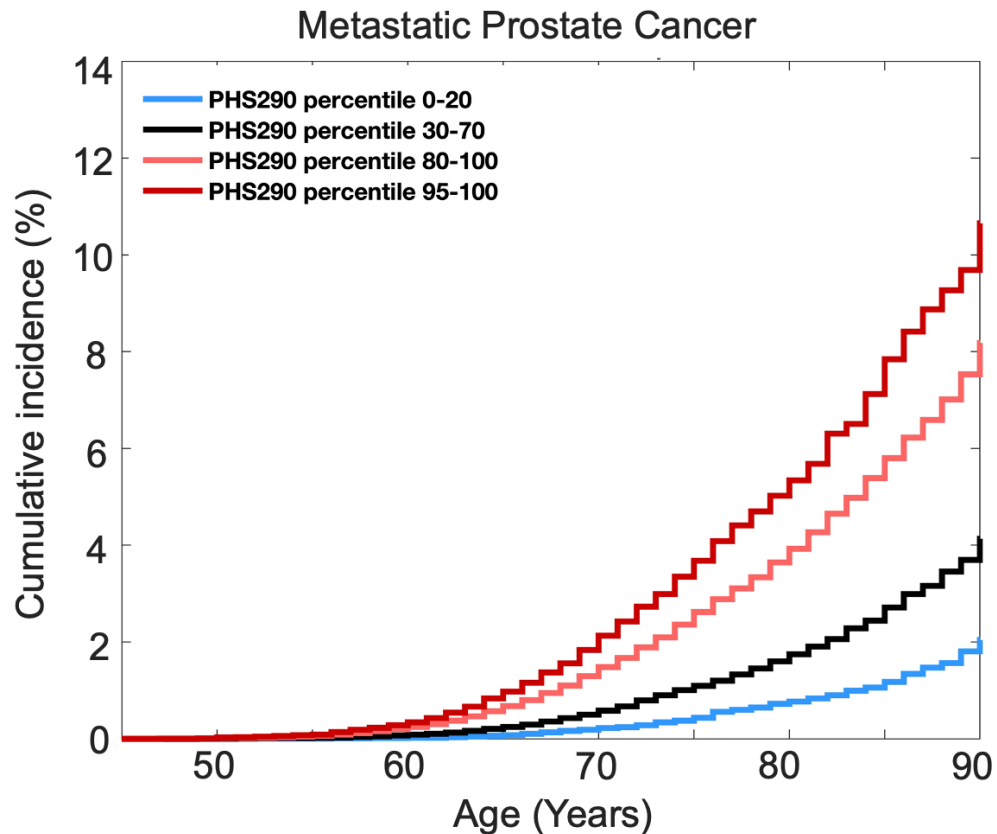
Predict need for biopsy with quantitative MRI (RSIrs)

- RSIrs makes radiologists' predictions more accurate
 - Clinical trial designed and led by Dr. Seibert to start in 2023
 - Participating centers: Harvard, Cambridge, Cornell, UCSF, UC San Diego



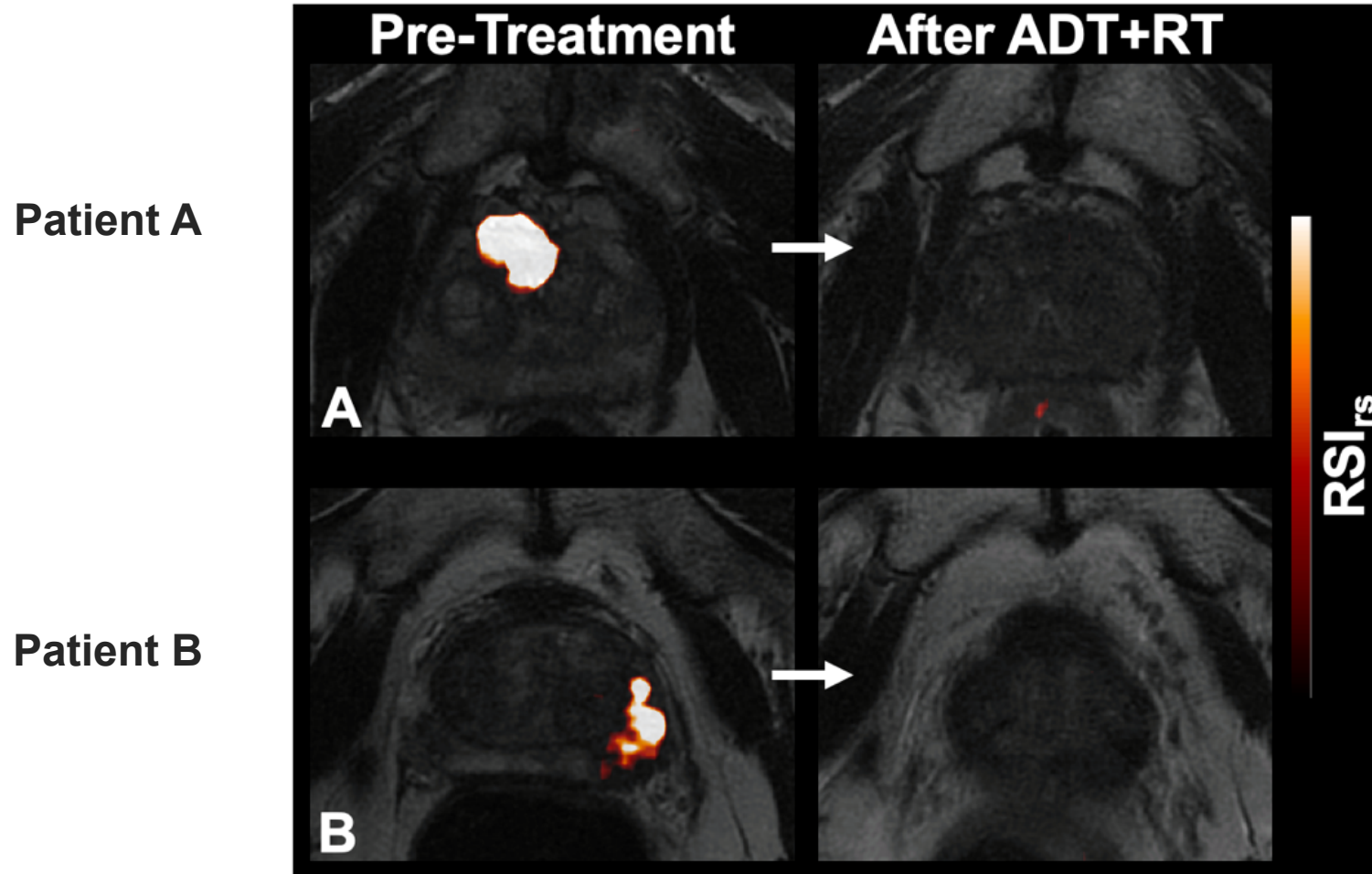
Use genetics to predict lifetime prostate cancer risk

- We developed a genetic score (PHS290)
 - Associated with risk of metastatic and fatal prostate cancer
 - Combine genetics and race or ancestry to predict overall risk



Measure treatment response with advanced MRI (RSIrs)

- Measure tumor response to radiation and hormone therapy (ADT)
 - Clinical trial designed and led by Dr. Seibert is ongoing



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CUREBOUND



UNIVERSITY OF CALIFORNIA
RESEARCH INITIATIVES
Cancer Research Coordinating Committee

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