# The Role of Radiation Therapy Along the Continuum of Prostate Cancer

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MINNESOTA
SOCIETY OF CLINICAL ONCOLOGY

# Disclosures

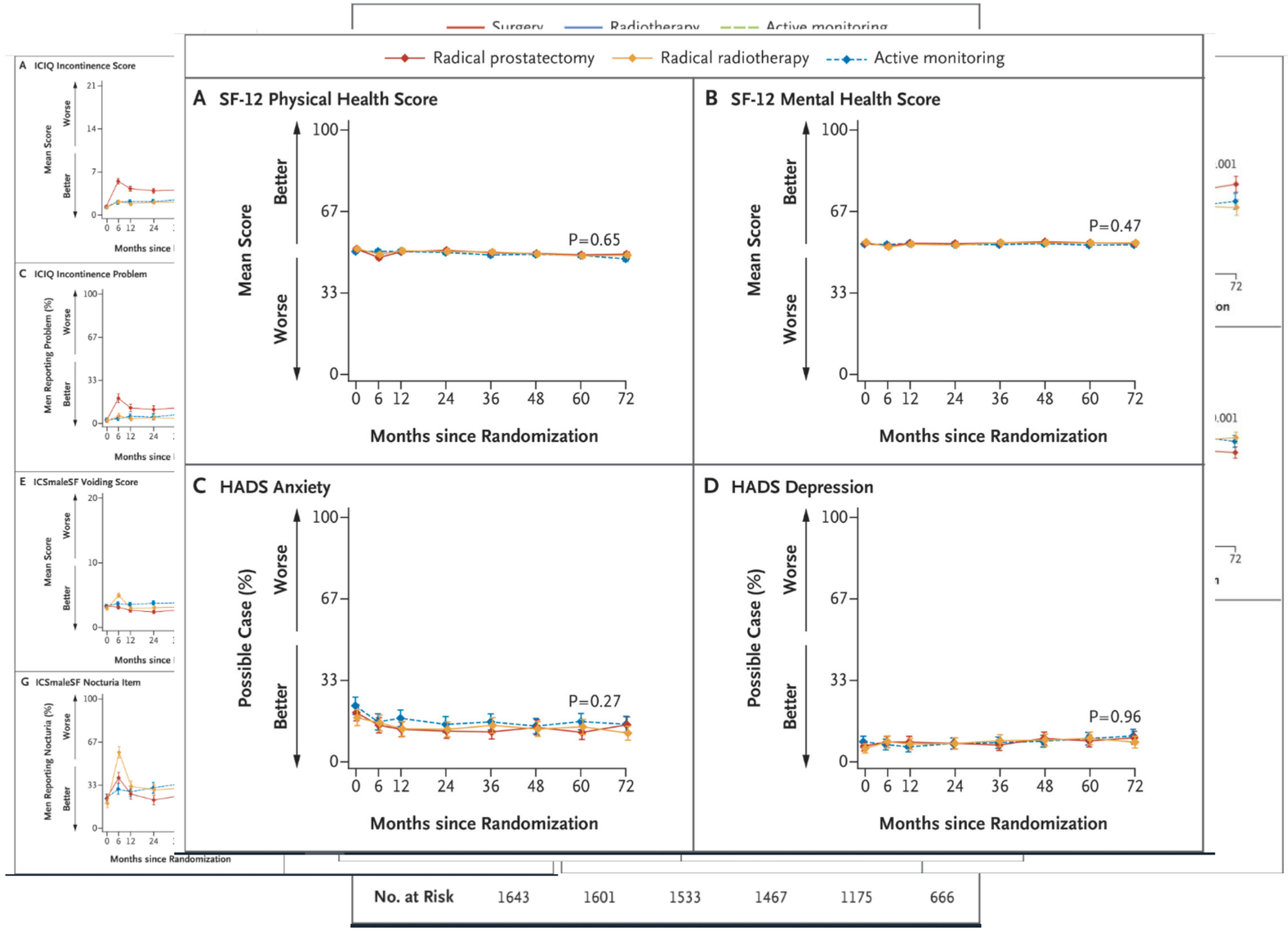
- Research Funding-Varian

# Overview

- Radiation therapy for localized prostate cancer
- Radiation Therapy in post-operative biochemically recurrent prostate cancer
- Radiation Therapy as treatment for oligometastatic prostate cancer
- Radiation Therapy's role in de novo, metastatic prostate cancer

# Radiation vs. Surgery for Localized Prostate Cancer

- PROTECT study randomized 1643 patients to active surveillance vs. radical prostatectomy vs. radiation therapy + androgen deprivation therapy
- Findings
  - No difference prostate cancer specific deaths between groups
  - More men developed metastases in the active surveillance group compared to RP and XRT groups
  - Definitive treatment had more upfront impact on bladder, bowel, and sexual QOL
  - Global measures regarding QOL were similar between groups
- Takeaways
  - There was NO difference in oncologic outcome between the surgery and radiation arms
  - QOL differences experienced by patient differ according to treatment modality
  - Patients with localized prostate cancer should receive counseled regarding BOTH modalities in order to facilitate informed decision making





Hamdy FC, et al. *NEJM* 2016; 375:1415-24.
Donovan JL, et al. *NEJM* 2016; 375:1425-37.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# Localized Prostate Cancer Topic 1: Radiation Modality Musings

- In 2022, multiple techniques are available to deliver therapeutic doses of radiation therapy for localized prostate cancer
- These include:
  - Photon (or X-ray) therapy
    - Intensity Modulated Radiation Therapy (IMRT) is the current standard of care
    - Widely available and most utilized
  - Proton Beam Therapy
    - Charged particle therapy available currently available at 40 centers in US
    - Has unique physical properties compared to photon therapy
  - Brachytherapy
    - Implantation of radiation sources directly into the prostate
    - Both temporary (High Dose Rate or HDR) and permanent (Low Dose Rate or LDR) brachytherapy treatments can be use for prostate cancer
  - Heavy Ion Therapy
    - Not available in US currently, but centers are active in Europe and Asia
    - Carbon Ion Therapy is mostly common amongst this group
    - Unclear role for prostate cancer moving forward

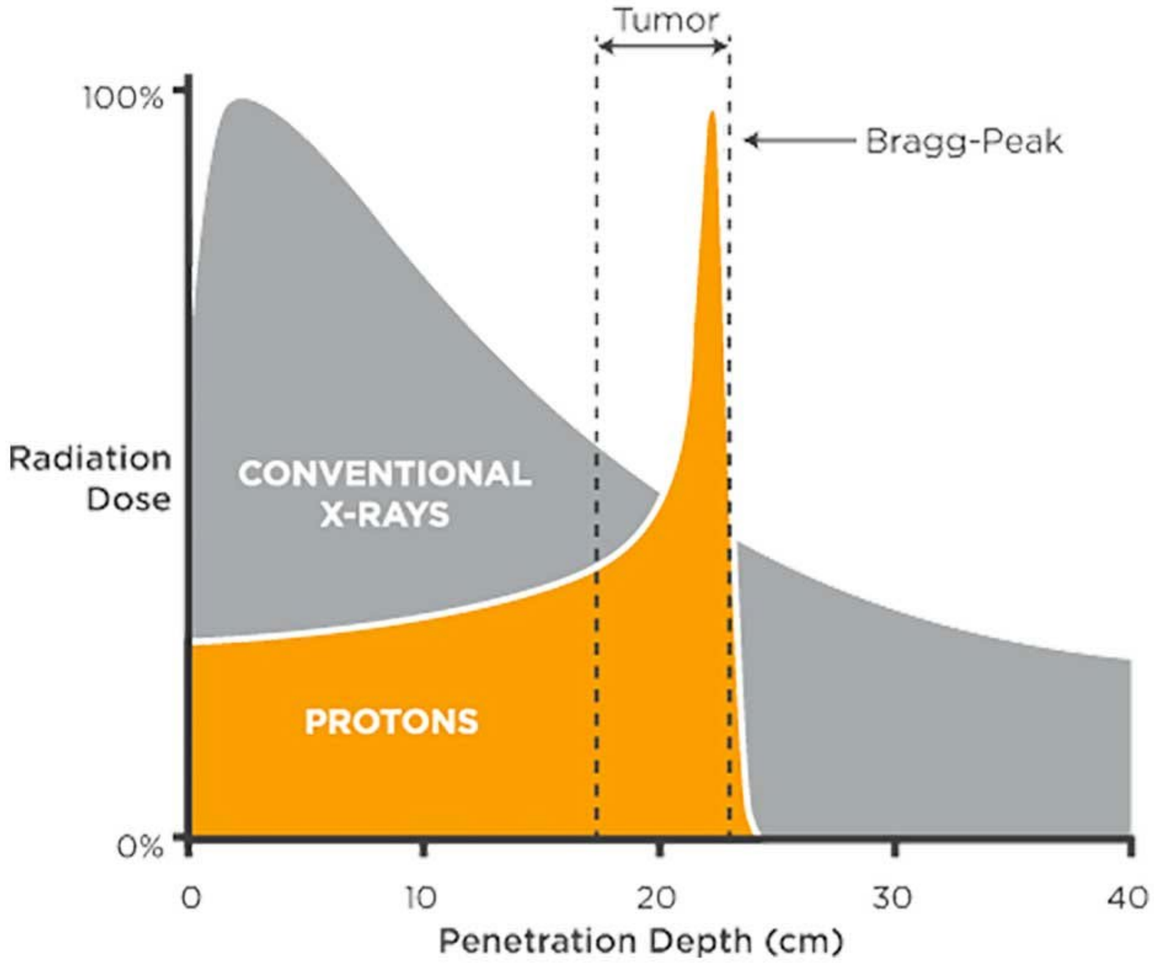
# Localized Prostate Cancer Topic 1: Radiation Modality Musings

- When it comes radiation dose and fractionation (dose per treatment) for patients receiving external beam treatments (i.e. photons or protons) the recent trends have supported shorter treatment courses
- SBRT (stereotactic body radiation therapy) is the fastest growing technique worldwide and use 5-7 treatments delivered over 10-20 days
- NCCN guidelines currently support multiple reasonable options across the risk spectrum

| Regimen | Preferred Dose/Fractionation | NCCN Risk Group (✓ indicates an appropriate regimen option if radiation therapy is given) | | | | | |
|---|---|---|---|---|---|---|---|
| | | Very Low and Low | Favorable Intermediate | Unfavorable Intermediate | High and Very High | Regional N1 | Low Volume M1[a] |
| **EBRT** | | | | | | | |
| Moderate Hypofractionation (Preferred) | 3 Gy x 20 fx<br>2.7 Gy x 26 fx<br>2.5 Gy x 28 fx | ✓ | ✓ | ✓ | ✓ | ✓ | |
| | 2.75 Gy x 20 fx | | | | | | ✓ |
| Conventional Fractionation | 1.8–2 Gy x 37–45 fx | ✓ | ✓ | ✓ | ✓ | ✓ | |
| Ultra-Hypofractionation | 7.25–8 Gy x 5 fx<br>6.1 Gy x 7 fx | ✓ | ✓ | ✓ | ✓ | | |
| | 6 Gy x 6 fx | | | | | | ✓ |
| **Brachytherapy Monotherapy** | | | | | | | |
| LDR<br>Iodine 125<br>Palladium 103<br>Cesium 131 | 145 Gy<br>125 Gy<br>115 Gy | ✓ | ✓ | | | | |
| HDR<br>Iridium-192 | 13.5 Gy x 2 implants<br>9.5 Gy BID x 2 implants | ✓ | ✓ | | | | |
| **EBRT and Brachytherapy (combined with 45–50.4 Gy x 25–28 fx or 37.5 Gy x 15 fx)** | | | | | | | |
| LDR<br>Iodine 125<br>Palladium 103<br>Cesium 131 | 110–115 Gy<br>90–100 Gy<br>85 Gy | | | ✓ | ✓ | | |
| HDR<br>Iridium-192 | 15 Gy x 1 fx<br>10.75 Gy x 2 fx | | | ✓ | ✓ | | |

# Localized Prostate Cancer Topic 1: Radiation Modality Musings

## Proton Beam Therapy vs Photons (IMRT)

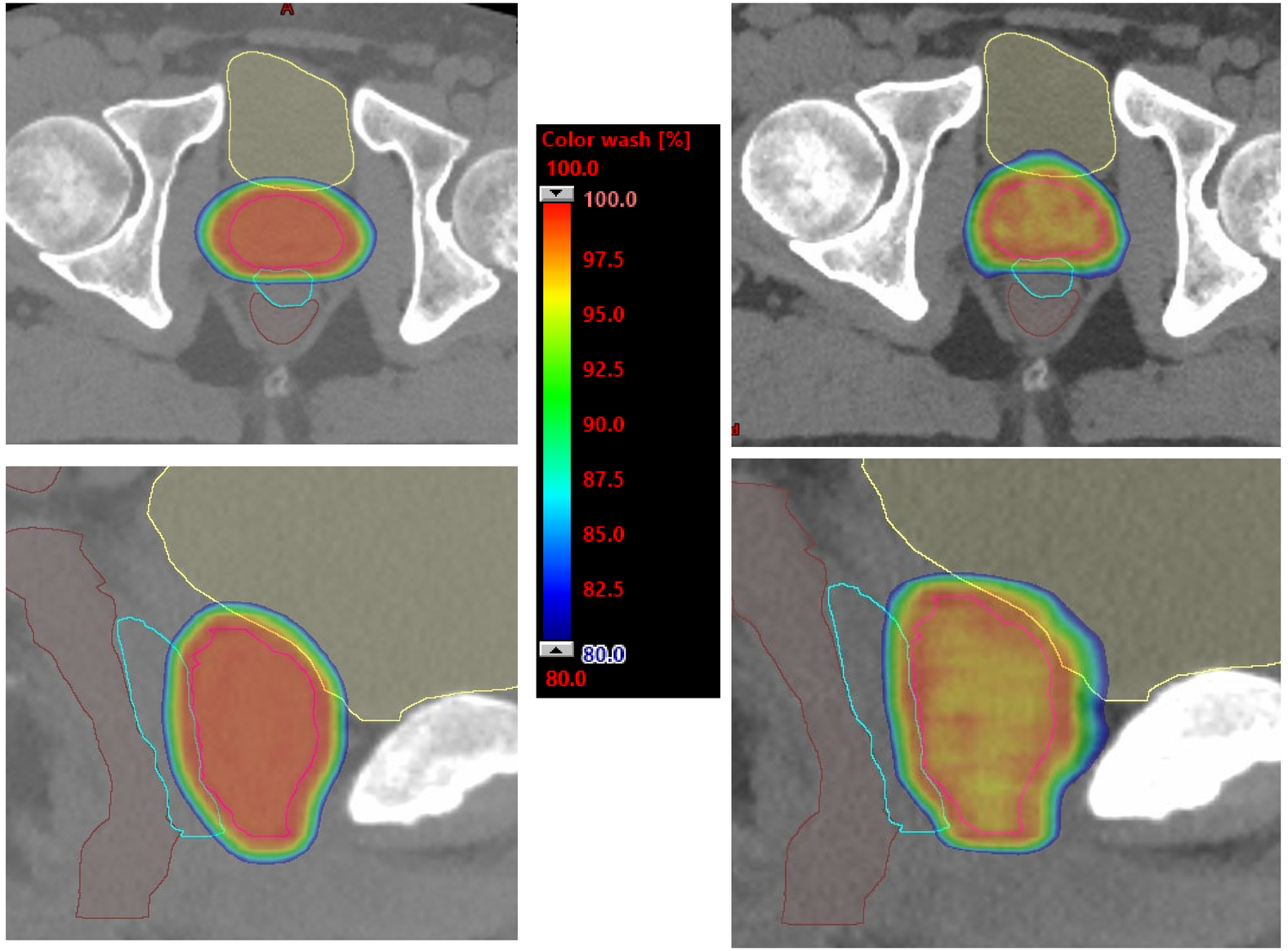


# Localized Prostate Cancer Topic 1: Radiation Modality Musings

## Proton Beam Therapy vs Photons (IMRT)

Protons

Photons (IMRT)



# Localized Prostate Cancer Topic 1: Radiation Modality Musings

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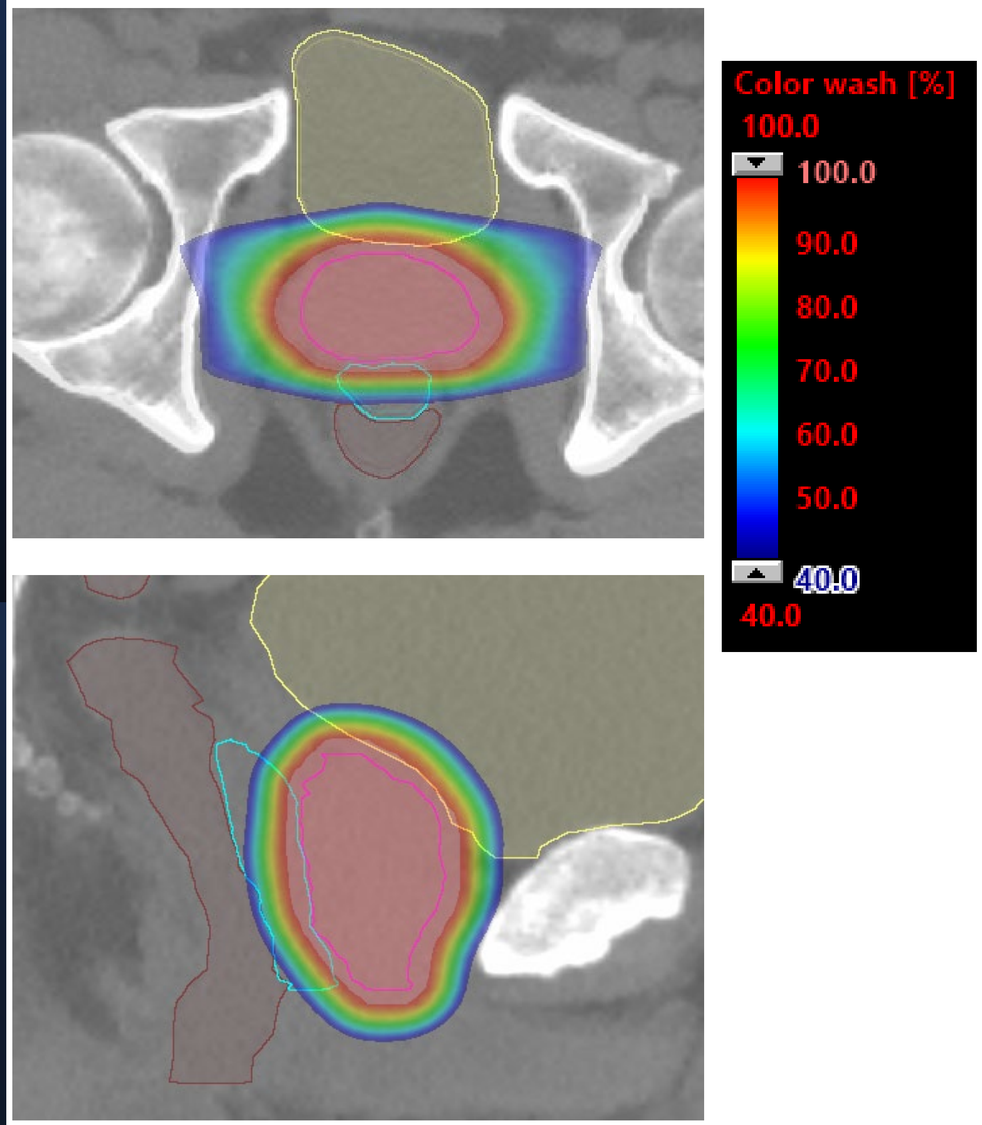

# Localized Prostate Cancer Topic 1: Radiation Modality Musings

## Proton Beam Therapy vs Photons (IMRT)

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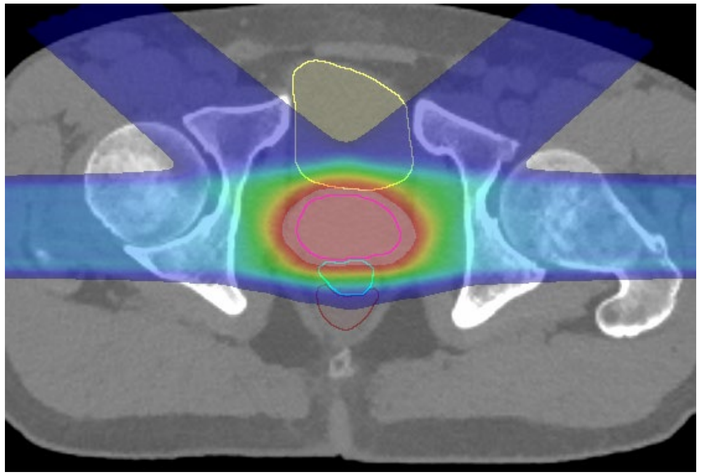
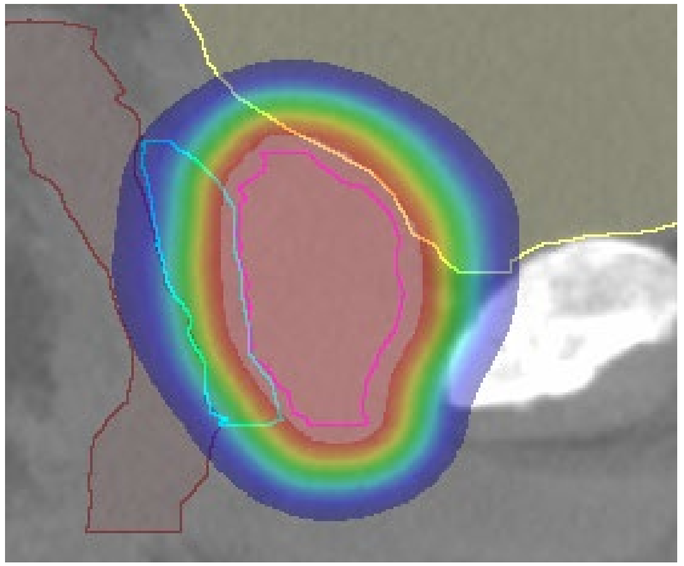
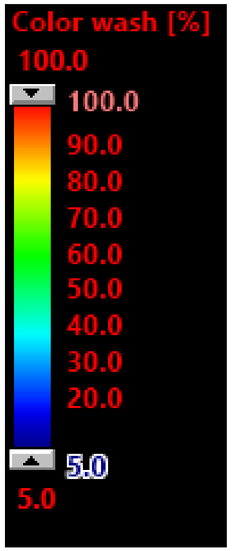
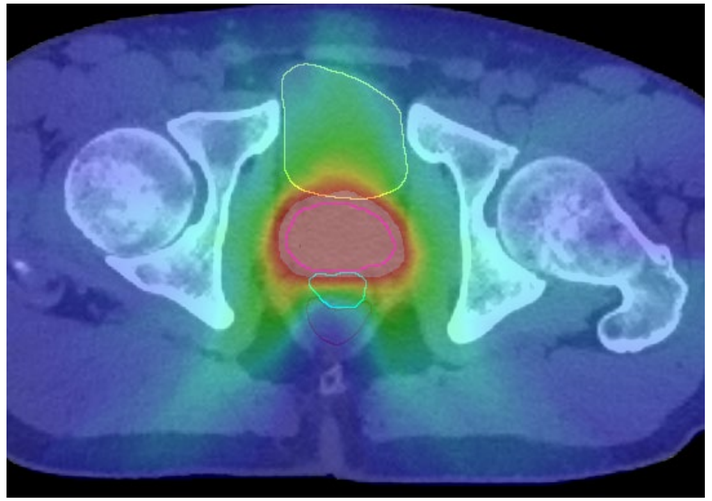
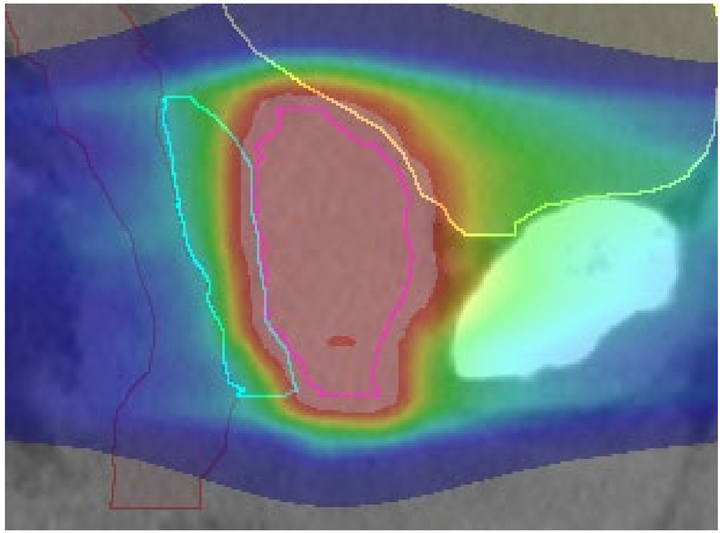








# Localized Prostate Cancer Topic 1: Radiation Modality Musings

# Photons (IMRT) vs Proton Beam Therapy

- Clinical Data
  - Prospective data are lacking
    - One randomized trial and one large, non-randomized trial will report in the next 2-3 years
    - Primary endpoints focus on toxicity/QOL
- Retrospective data are mixed, but suggest no significant advantage for protons (and possible detriment)

**Table 1** Current proton versus photon therapy comparative evidence for localized prostate cancer

| Study | Design | Source of data | Years | Toxicities: Protons compared to photons | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Acute | | | Late[a] | | |
| | | | | GU | GI | Sexual | GU | GI | Sexual |
| Kim 2011[50] | Database | SEER | 1992–2005 | NA | ↑ | NA | NA | ↑ | NA |
| Sheets 2012[51b] | Database | SEER | 2000–2009 | NA | NA | NA | = | ↑ | = |
| Yu 2012[48c] | Database | Medicare | 2008–2009 | ↓ | = | NA | = | = | NA |
| Pan 2018[52d] | Database | MarketScan | 2008–2015 | ↓ | = | ↓ | ↓ | ↑ | ↓ |
| Gray 2013[53e] | Non-randomized comparative | MGH PROST-QA Harvard-affiliated[f] | 2003–2008 | ↓/↑ | ↓/= | NA | = | = | NA |
| Hoppe 2014[56] | Non-randomized comparative | UF PROST-QA | 2003–2010 | = | =[g] | = | = | =[g] | = |
| Fang 2015[54] | Non-randomized comparative | University of Pennsylvania | 2010–2012 | = | = | NA | = | = | NA |

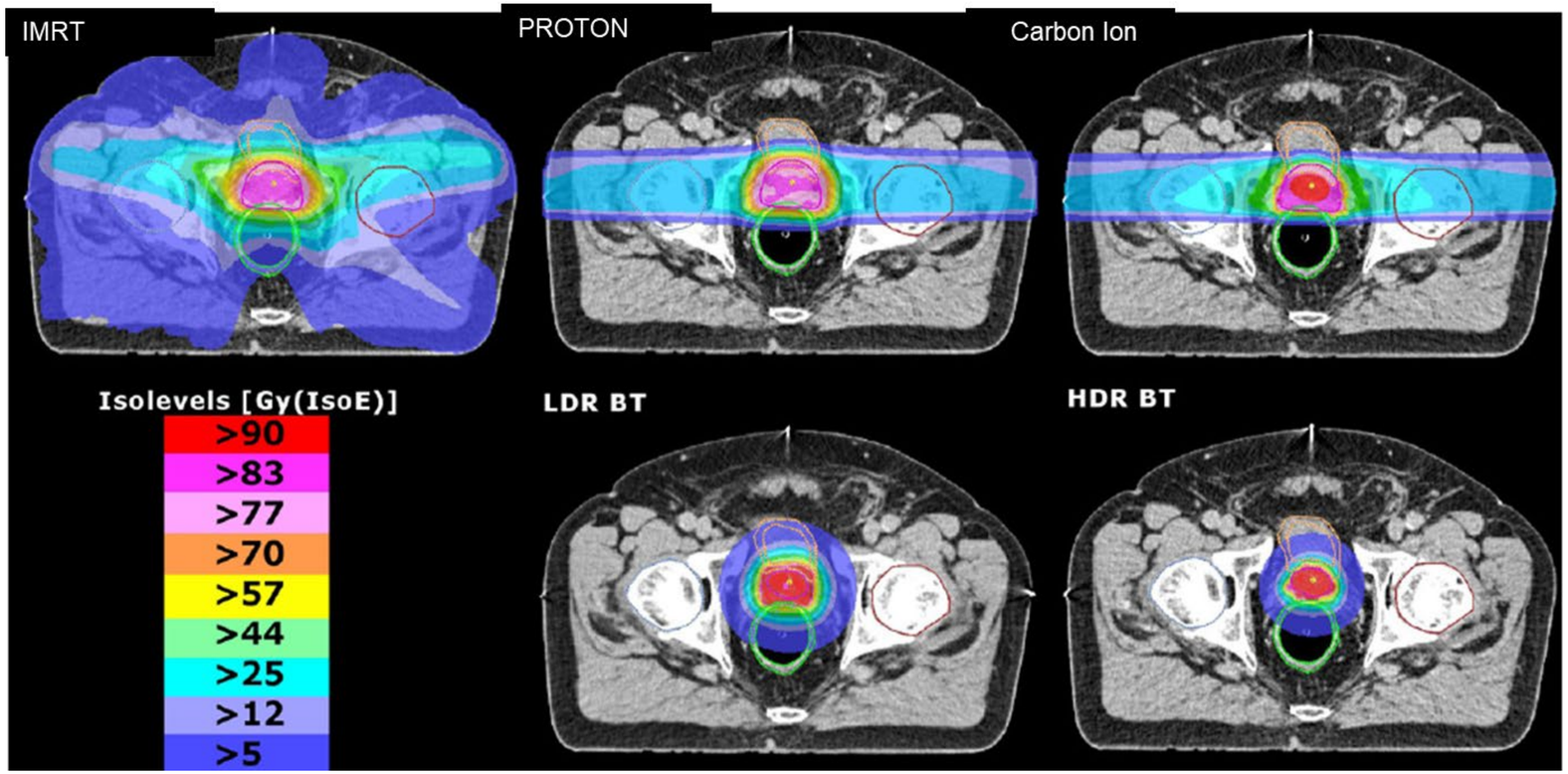
*SEER* Surveillance, Epidemiology, and End Results, *MGH* Massachusetts General Hospital, *PROST-QA* Prostate Cancer Outcomes and Satisfaction with Treatment Quality Assessment Consortium, *UF* University of Florida, *GI* Gastrointestinal, *GU* Genitourinary, *NA* not available

Kamran, SC, et al. *Prostate Cancer and Prostatic Diseases* 2019; 22:509-21

# Localized Prostate Cancer Topic 1: Radiation Modality Musings

## Let’s not forget about brachytherapy

- Brachytherapy allows superior dose conformality and normal tissue sparing compared to either IMRT or proton beam therapy
- Intraprostatic dose escalation from brachytherapy is superior to other techniques
- Brachytherapy is highly convenient and cost effective for patients, with treatment completed in 1-2 sessions

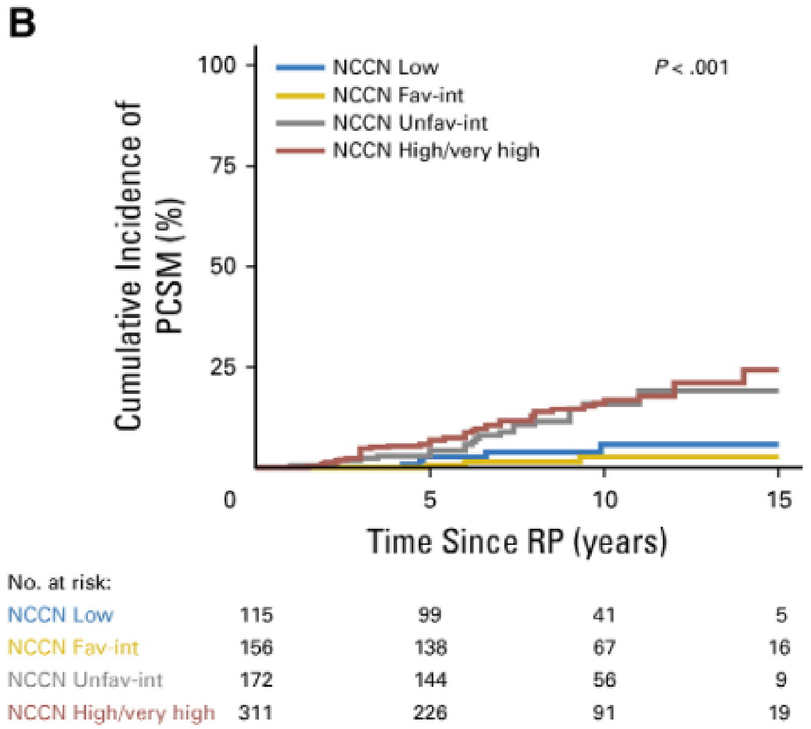



Georg et al. *IJROBP* 2013; 88:715-22

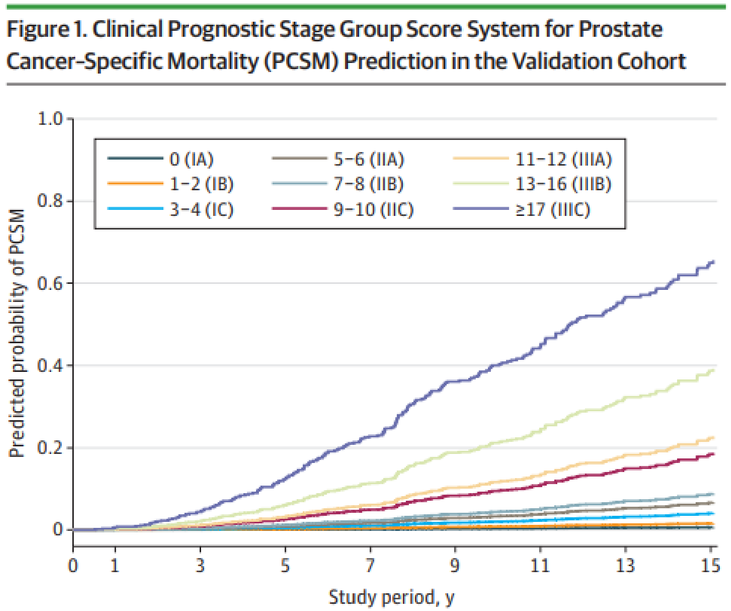
# Localized Prostate Cancer Topic 2: Systemic therapy in high risk patients

- Risk group categorization greatly influences prostate cancer specific mortality risk

## NCCN




## STAR-CAP

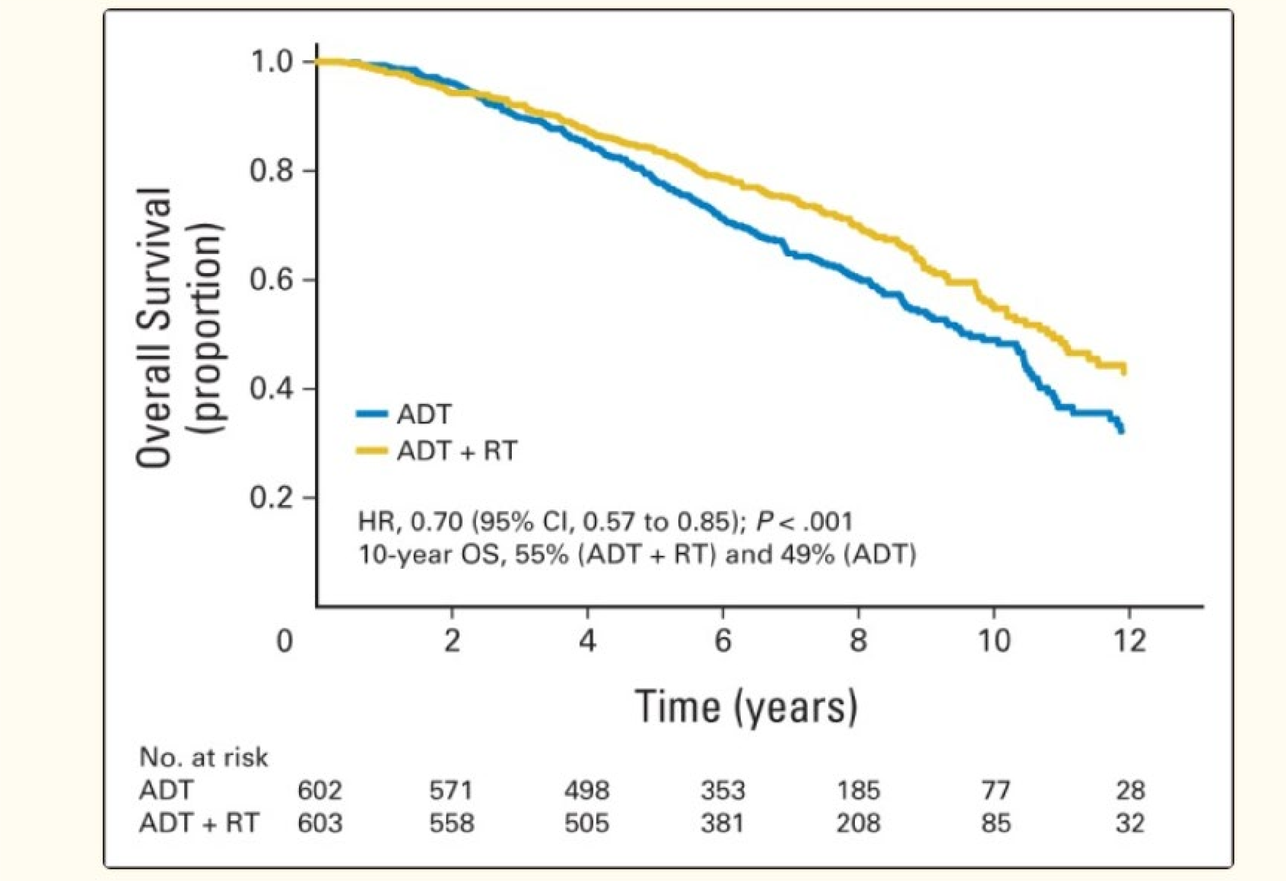




Spratt DE, et al. *JCO* 2018;36(6):581-90
Dess RT, et al. *JAMA Onc* 2020;6(12):1912-20

# Localized Prostate Cancer Topic 2: Systemic therapy in high risk patients

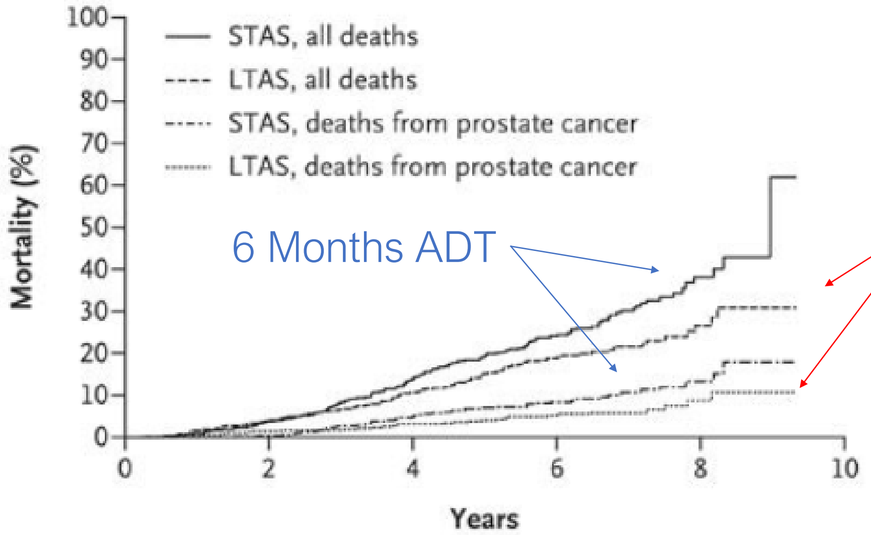
- What can influence PCSM in high risk, non-metastatic prostate cancer patients?
  - Randomized data have shown-
    - **Adding XRT to long-term ADT improves survival**




Mason MD, et al. JCO 2015;33(19):2143-50.

# Localized Prostate Cancer Topic 2: Systemic therapy in high-risk patients

- What can influence PCSM in high risk, non-metastatic prostate cancer patients?
  - Randomized data have shown-
    - **Adding long-term ADT to XRT improves overall survival**

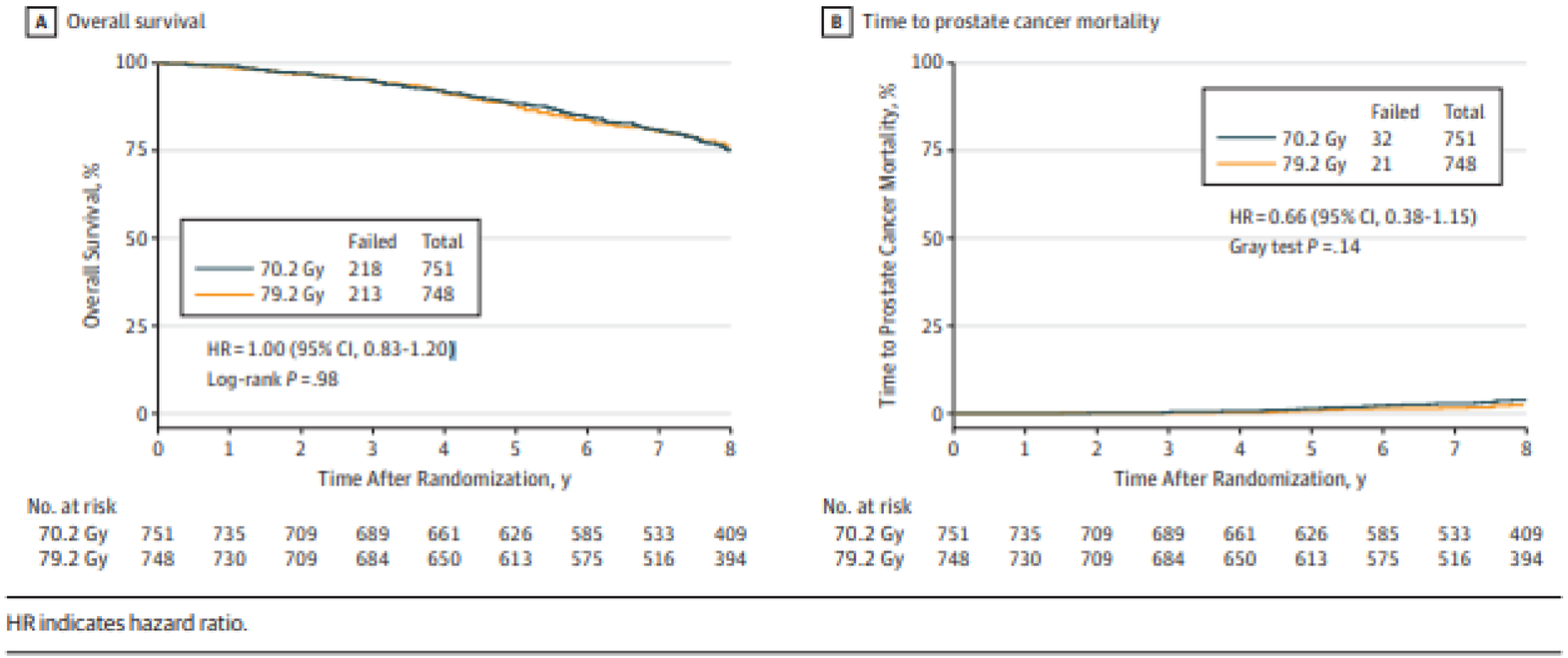



| No. at Risk | | | | | | No. of Events |
|---|---|---|---|---|---|---|
| STAS, all deaths | 483 | 454 | 388 | 231 | 43 | 132 |
| LTAS, all deaths | 487 | 454 | 407 | 249 | 50 | 98 |
| STAS, deaths from prostate cancer | 483 | 454 | 388 | 231 | 43 | 47 |
| LTAS, deaths from prostate cancer | 487 | 454 | 407 | 249 | 50 | 29 |

Bollla M, et al. *NEJM* 2009;360:2516-27.

# Localized Prostate Cancer Topic 2: Systemic therapy in high risk patients

- What can influence PCSM in high risk, non-metastatic prostate cancer patients?
  - Randomized data have shown-
    - **Radiation dose escalation DOES NOT improve survival**




HR indicates hazard ratio.

Michalski JM, et al. *JAMA Onc* 2018;4(6)

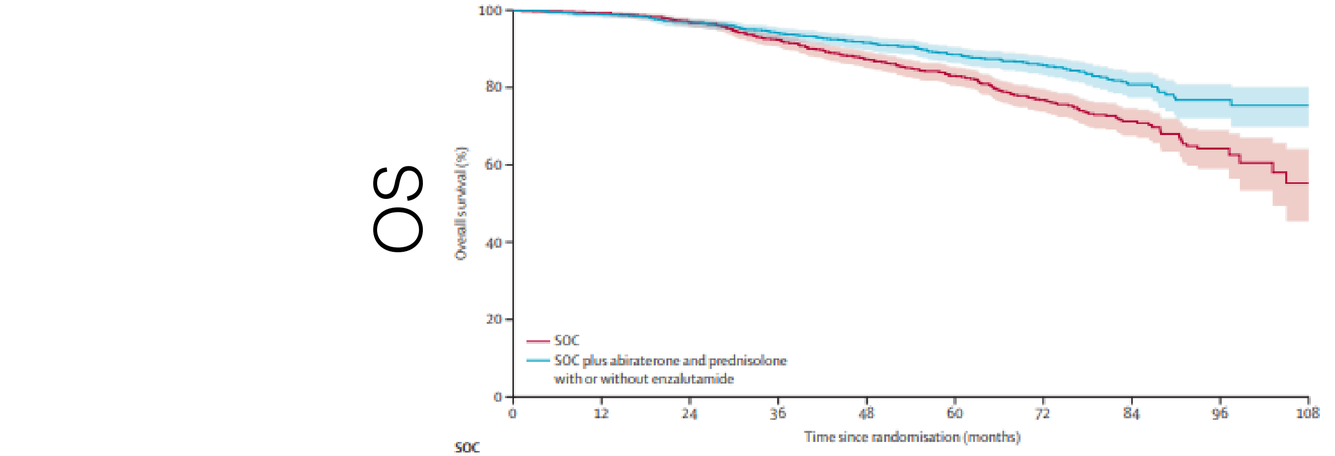
# Localized Prostate Cancer Topic 2: Systemic therapy in high risk patients

**Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol**

Attard G, et al. Lancet 2022;399:447-60.

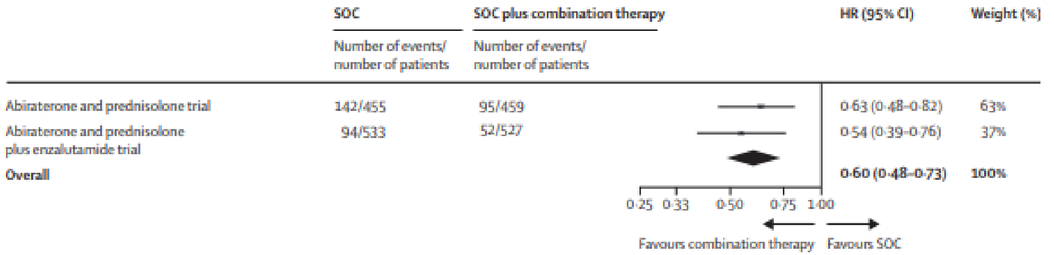
- **STAMPEDE Strikes Again!**
- 1974 men with non-metastatic very high risk prostate cancer randomly assigned to XRT + ADT (3 years) vs XRT + ADT + abiraterone (2 years)
- Very High Risk required at least TWO of:
  - T3/T4 tumor
  - Grade Group 4-5 (Gleason 8-10)
  - PSA ≥ 40 ng/ml

OS




| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **SOC** | | | | | | | | | | |
| At risk | 988 | 974 | 947 | 901 | 837 | 610 | 368 | 200 | 63 | 10 |
| Censored | 0 | 8 | 11 | 14 | 28 | 216 | 421 | 568 | 693 | 742 |
| Event | 0 | 6 | 30 | 73 | 123 | 162 | 199 | 220 | 232 | 236 |
| **SOC plus combination therapy** | | | | | | | | | | |
| At risk | 986 | 956 | 928 | 899 | 861 | 645 | 386 | 205 | 74 | 16 |
| Censored | 0 | 21 | 29 | 32 | 46 | 234 | 477 | 641 | 766 | 823 |
| Event | 0 | 9 | 29 | 55 | 79 | 107 | 123 | 140 | 146 | 147 |

**B**



# Localized Prostate Cancer Topic 2: Systemic therapy in high risk patients

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Four Penn Center
1600 JFK BLVD Suite 1020
Philadelphia, PA 19103
Nrgoncology.org

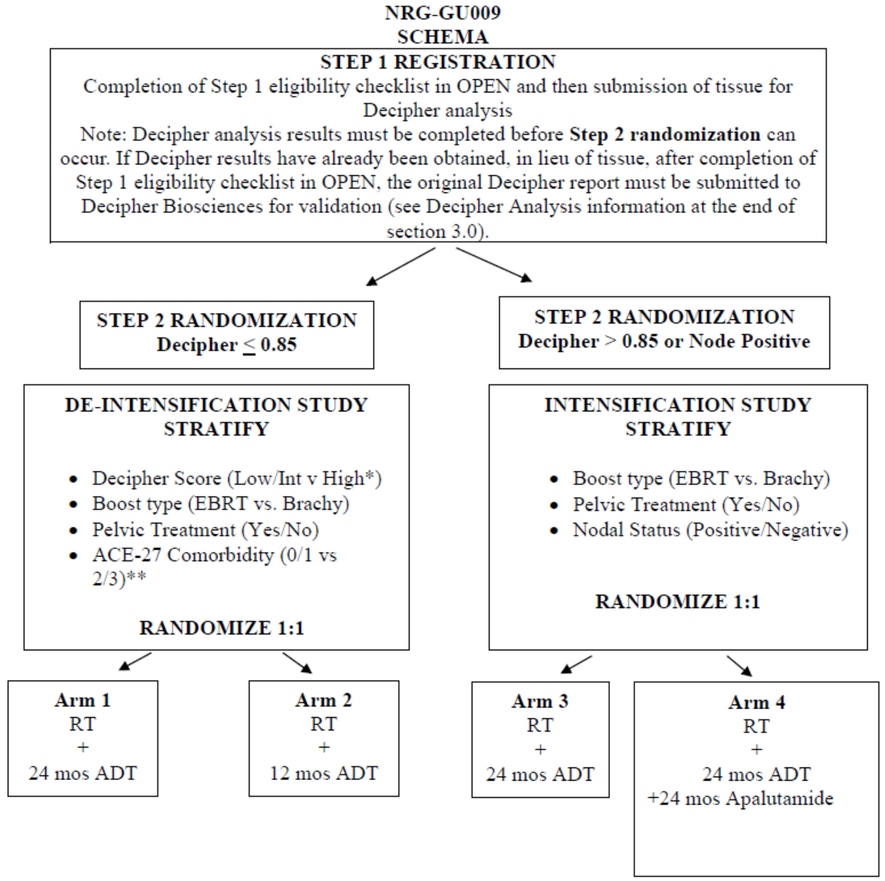
**NRG-GU009**: PARALLEL PHASE III RANDOMIZED TRIALS FOR HIGH RISK PROSTATE CANCER EVALUATING DE-INTENSIFICATION FOR LOWER GENOMIC RISK AND INTENSIFICATION OF CONCURRENT THERAPY FOR HIGHER GENOMIC RISK WITH RADIATION (PREDICT-RT*)

**Prostate RNA Expression/Decipher To Individualize Concurrent Therapy with Radiation*

**ClinicalTrials.gov Identifier NCT# 04513717**
**NCI Version Date: (September 24, 2021)**

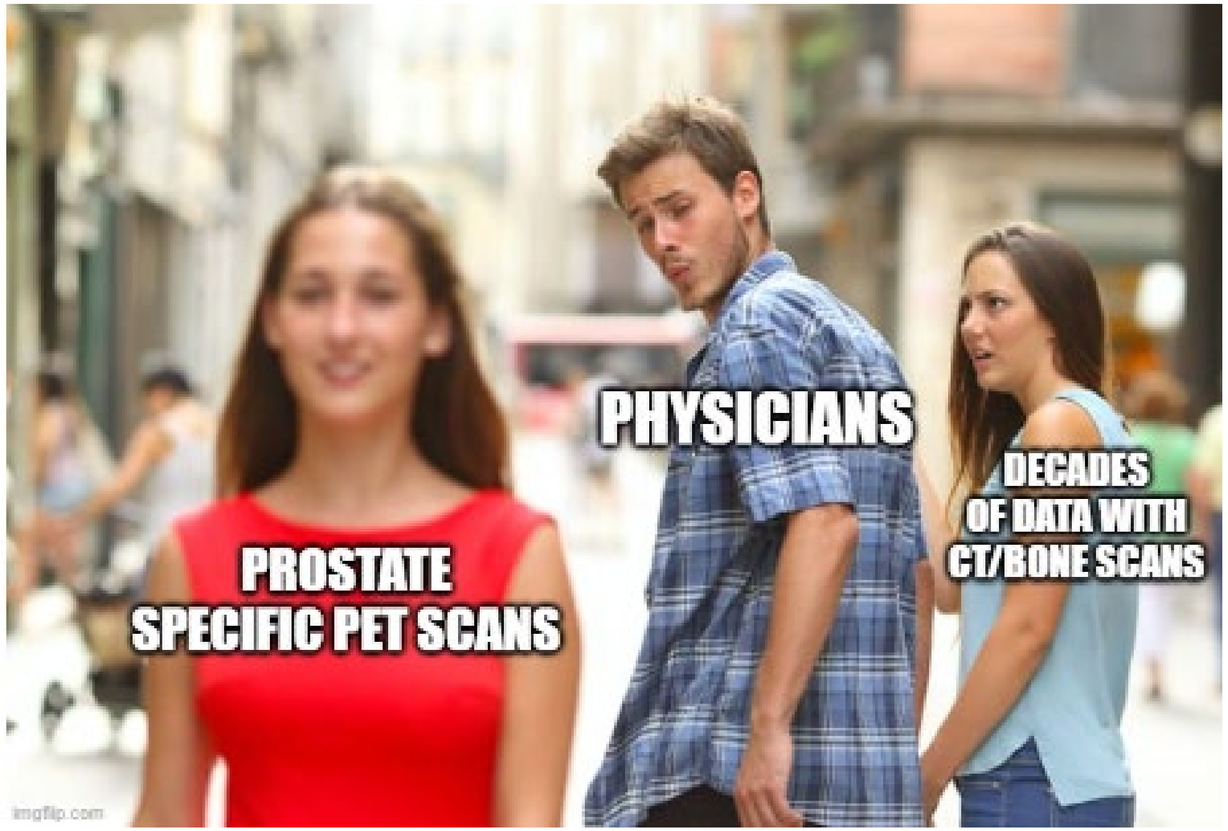
**Principal Investigator:**
Paul Nguyen, MD
Dana-Farber/Brigham and Women's
Radiation Oncology
75 Francis St
Boston, MA

- **Does STAMPEDE data translate to standard NCCN high risk patients?**
- **Do ALL high risk patients need treatment escalation or can some have similar outcomes with less intense ADT?**
- **Prospective studies are underway to determine if systemic therapy can be personalized**



# Recurrent Prostate Cancer

- **Management of biochemically recurrent/progressive prostate is a rapidly evolving field**
- **The development of novel PET imaging has allowed earlier anatomical localization of disease sites**
- **Enthusiasm for metastasis-directed therapy has grown simultaneously, but what is its real role in clinical care?**



# Recurrent Prostate Cancer Topic 1: Initial Biochemical Recurrence after Prostatectomy

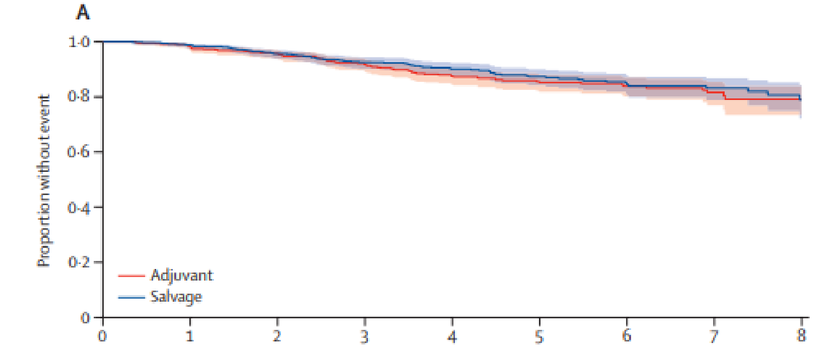
**Timing of radiotherapy after radical prostatectomy (RADICALS-RT): a randomised, controlled phase 3 trial**

*Christopher C Parker, Noel W Clarke, Adrian D Cook, Howard G Kynaston, Peter Meidahl Petersen, Charles Catton, William Cross, John Logue, Wendy Parulekar, Heather Payne, Rajendra Persad, Holly Pickering, Fred Saad, Juliette Anderson, Amit Bahl, David Bottomley, Klaus Brasso, Rohit Chahal, Peter W Cooke, Ben Eddy, Stephanie Gibbs, Chee Goh, Sandeep Gujral, Catherine Heath, Alastair Henderson, Ramasamy Jaganathan, Henrik Jakobsen, Nicholas D James, Subramanian Kanaga Sundaram, Kathryn Lees, Jason Lester, Henriette Lindberg, Julian Money-Kyrle, Stephen Morris, Joe O'Sullivan, Peter Ostler, Lisa Owen, Prashant Patel, Alvan Pope, Richard Popert, Rakesh Raman, Martin Andreas Røder, Ian Sayers, Matthew Simms, Jim Wilson, Anjali Zarkar, Mahesh K B Parmar, Matthew R Sydes*

Lancet 2020; 396: 1413–21

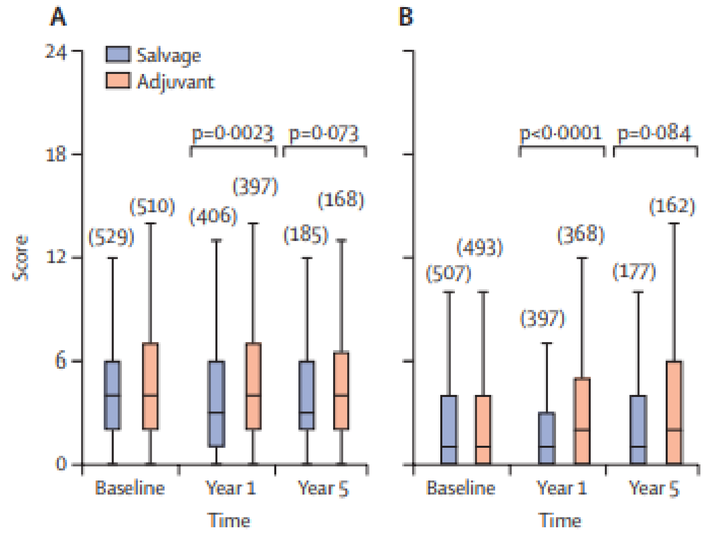
- Data supporting meaningful improvements in patient outcomes following radiation therapy to the prostate fossa +/- pelvic lymph nodes are plentiful
- Recent randomized trials have shown that **adjuvant** radiation therapy for those with high-risk features (pT3/pT4, + margins) provides **no oncologic advantage** over **early salvage** radiation therapy but does **increase toxicity**

## Biochemical PFS




## PRO (higher scores are worse)

Urinary Bowel



# Recurrent Prostate Cancer Topic 1: Initial Biochemical Recurrence after Prostatectomy

VOLUME 34 · NUMBER 32 · NOVEMBER 10, 2016

JOURNAL OF CLINICAL ONCOLOGY

Improved Metastasis-Free and Survival Outcomes With Early Salvage Radiotherapy in Men With Detectable Prostate-Specific Antigen After Prostatectomy for Prostate Cancer

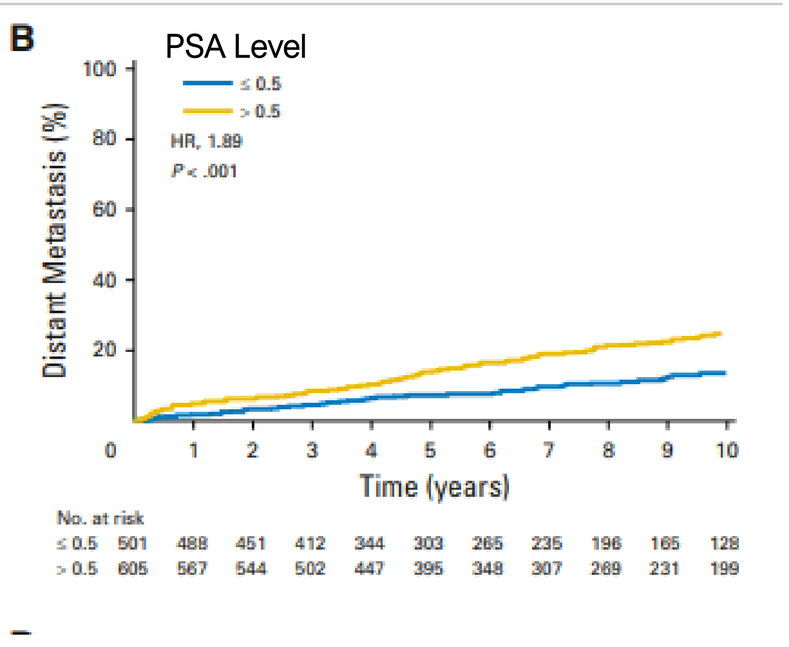
*Bradley J. Stish, Thomas M. Pisansky, William S. Harmsen, Brian J. Davis, Katherine S. Tzou, Richard Choo, and Steven J. Buskirk*

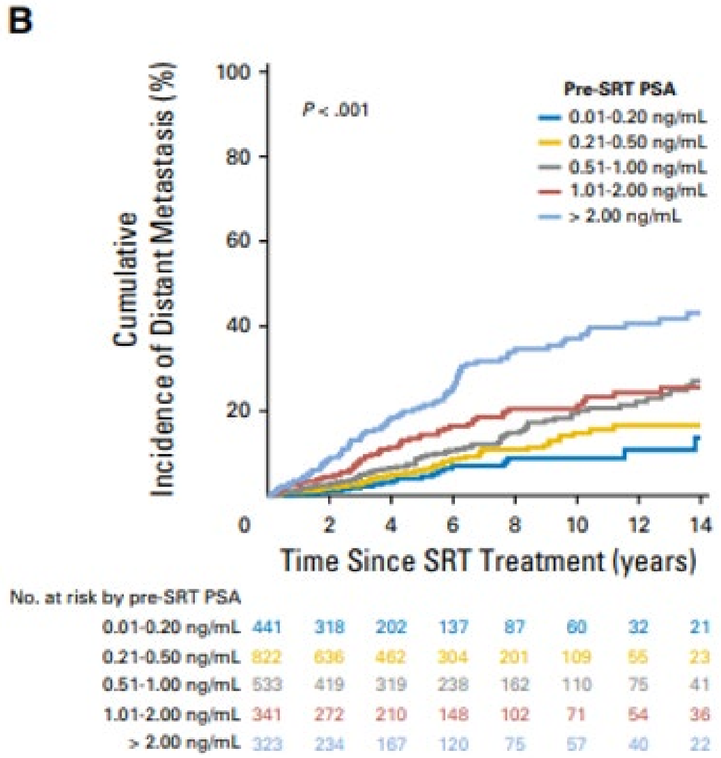
Contemporary Update of a Multi-Institutional Predictive Nomogram for Salvage Radiotherapy After Radical Prostatectomy

*Rahul D. Tendulkar, Shree Agrawal, Tianming Gao, Jason A. Efstathiou, Thomas M. Pisansky, Jeff M. Michalski, Bridget F. Koontz, Daniel A. Hamstra, Felix Y. Feng, Stanley L. Liauw, Matthew C. Abramowitz, Alan Pollack, Mitchell S. Anscher, Drew Moghanaki, Robert B. Den, Kevin L. Stephans, Anthony L. Zietman, W. Robert Lee, Michael W. Kattan, and Andrew J. Stephenson*

VOLUME 34 · NUMBER 30 · OCTOBER 20, 2016

- Data supporting meaningful improvements in patient outcomes following radiation therapy to the prostate fossa +/- pelvic lymph nodes are plentiful
- Early salvage radiation (pre-radiotherapy PSA <0.5 ng/ml) significantly improves outcomes compared to “Late” salvage radiation



# Recurrent Prostate Cancer Topic 1: Initial Biochemical Recurrence after Prostatectomy

- Data supporting meaningful improvements in patient outcomes following radiation therapy to the prostate fossa +/- pelvic lymph nodes are plentiful
- PSMA PET is a useful tool for initial biochemical recurrence
  - Waiting to invoke salvage RT until local recurrence is **NOT** yet standard of care and may jeopardize outcomes
    - Recall PET resolution is limited to around 4 mm
    - Salvage XRT works **BEST** in **PET negative** patients!

**3-Year Freedom from Progression After $^{68}$Ga-PSMA PET/CT–Triaged Management in Men with Biochemical Recurrence After Radical Prostatectomy: Results of a Prospective Multicenter Trial**

Louise Emmett[1,2], Reuben Tang[1,3], Rohan Nandurkar[2], George Hruby[4,5], Paul Roach[6,7], Jo Anne Watts[8,9], Thomas Cusick[3], Andrew Kneebone[4,7], Bao Ho[1], Lyn Chan[1], Pim J. van Leeuwen[10], Matthijs J. Scheltema[3,11], Andrew Nguyen[1], Charlotte Yin[6], Andrew Scott[12,13], Colin Tang[14], Michael McCarthy[15], Karen Fullard[1], Matthew Roberts[16,17], Roslyn Francis[9,15], and Phillip Stricker[2,7,18]

THE JOURNAL OF NUCLEAR MEDICINE • Vol. 61 • No. 6 • June 2020

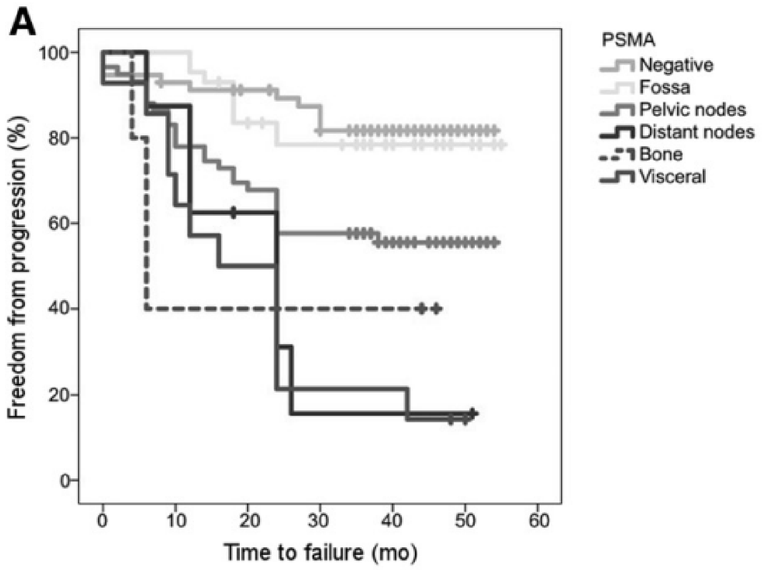



**TABLE 3**
PSMA PET Result Stratified by Increasing PSA Level

| PSA (ng/mL) | PSMA PET-negative | PSMA PET-positive | Overall |
|---|---|---|---|
| <0.2 | 41 (49.4%) | 42 (50.6%) | 83 |
| 0.2–0.5 | 36 (34.9%) | 67 (65.1%) | 103 |
| 0.51–0.99 | 9 (27.3%) | 24 (72.7%) | 33 |
| 1.0–5.0 | 4 (9.8%)) | 37 (90.2%) | 41 |
| Total | 90 (34.6%) | 170 (65.4%) | 260 |

# Recurrent Prostate Cancer Topic 1: Initial Biochemical Recurrence after Prostatectomy

- Data supporting meaningful improvements in patient outcomes following radiation therapy to the prostate fossa +/- pelvic lymph nodes are plentiful
- PSMA is a useful tool for initial biochemical recurrence
  - Be VERY CAREFUL to carefully evaluate small rib lesions on PSMA PET as false positives are common
  - True determination of rib lesions (biopsy confirmation or positivity on another imaging modality) can be challenging.
  - Consider pre-test probability and sometimes empiric treatment is reasonable

*BJU Int* 2020; **126:** 396–401 doi:10.1111/bju.15152

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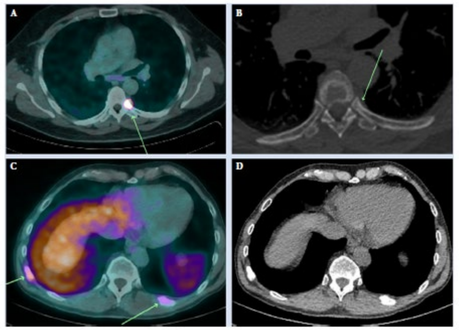
**Original Article**

**Solitary rib lesions showing prostate-specific membrane antigen (PSMA) uptake in pre-treatment staging $^{68}$Ga-PSMA-11 positron emission tomography scans for men with prostate cancer: benign or malignant?**

Michael Y. Chen[1,2], Anthony Franklin[1,2], John Yaxley[1,2], Troy Gianduzzo[1,2], Rhiannon McBean[1], David Wong[1], Annaleis Tatkovic[1], Louise McEwan[1], James Walters[1] and Boon Kua[1]

[1]*Wesley Hospital, Brisbane, Qld, Australia, and* [2]*School of Medicine, University of Queensland, Brisbane, Qld, Australia*




Benign PSMA-avid solitary rib lesions

In all, 61 men (98.4%) with solitary rib lesions on pre-treatment $^{68}$Ga-PSMA PET/CT scans satisfied the criteria for benign lesions (Table 2). Follow-up $^{68}$Ga-PSMA PET/CT scans were not routinely performed and only three patients had follow-up $^{68}$Ga-PSMA PET/CT scans due to clinical suspicion.

# Recurrent Prostate Cancer Topic 2: Oligometastatic Disease

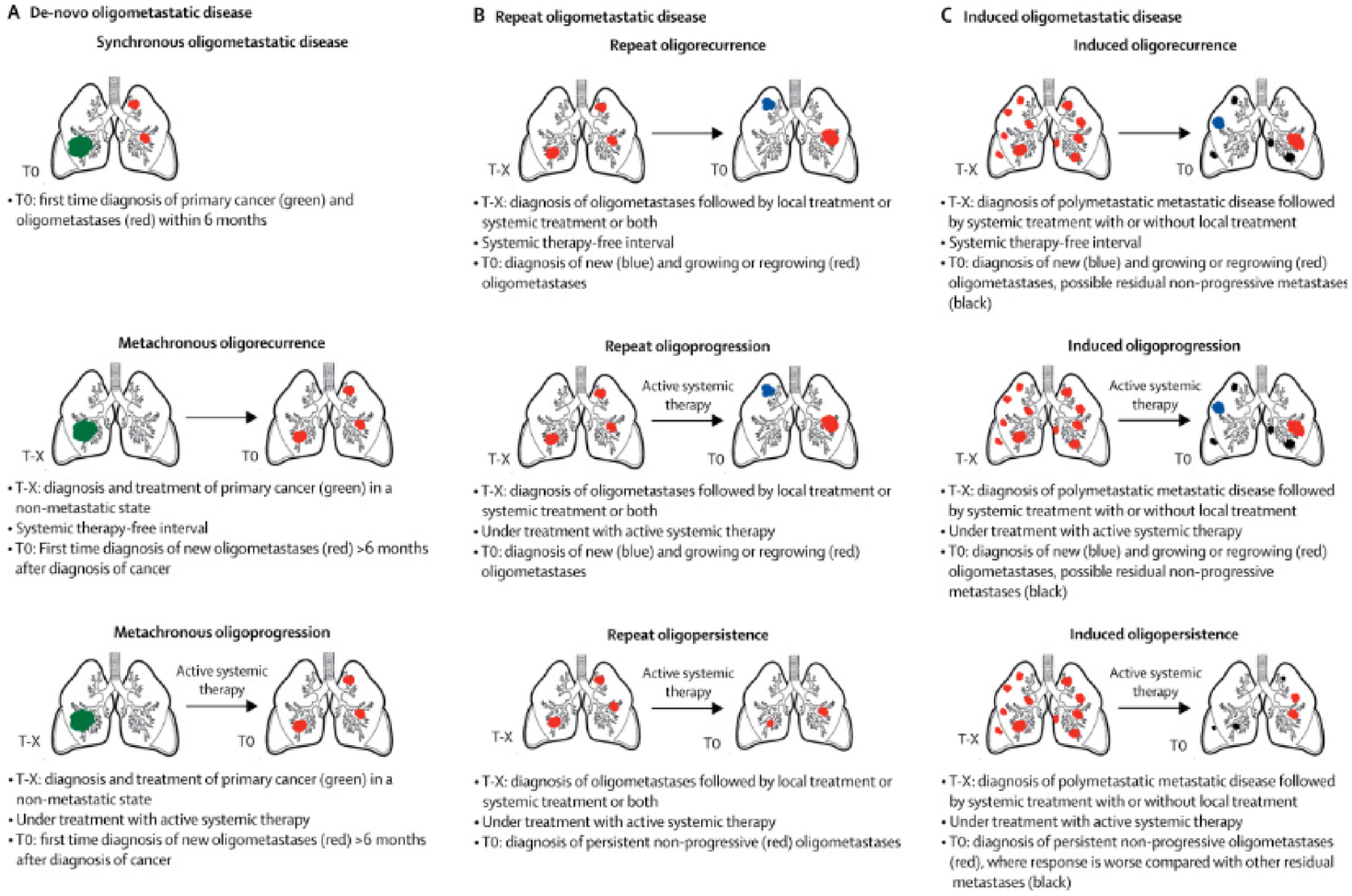
THE LANCET
Oncology
Volume 21, Issue 1, January 2020, Pages e18-e28

Review

## Characterisation and classification of oligometastatic disease: a European Society for Radiotherapy and Oncology and European Organisation for Research and Treatment of Cancer consensus recommendation

Prof Matthias Guckenberger MD [a], Prof Yolande Lievens PhD [b], Angelique B Bouma MD [c], Laurence Collette PhD [c], Andre Dekker PhD [d], Prof Nandita M deSouza FRCR [f], Prof Anne-Marie C Dingemans PhD [e, g], Beatrice Fournier PhD [c], Coen Hurkmans PhD [h], Prof Frédéric E Lecouvet PhD [i], Prof Icro Meattini MD [j, k], Alejandra Méndez Romero PhD [l], Prof Umberto Ricardi MD [m], Nicola S Russell PhD [n], Daniel H Schanne MD [a], Prof Marta Scorsetti MD [o], Prof Bertrand Tombal PhD [p], Prof Dirk Verellen PhD [q] ... Prof Piet Ost PhD [b]

- **Definitions are important (and evolving)**



# Recurrent Prostate Cancer Topic 2: Oligometastatic Disease (recurrent)

- **STOMP and ORIOLE were two prostate-specific studies of MDT in patients with oligometastatic prostate cancer**
- **Both showed that MDT could delay progression and initiation of ADT**
- **However, the benefit of MDT with regards to more definitive oncologic outcomes remains to be proven**

VOLUME 36 · NUMBER 5 · FEBRUARY 10, 2018

JOURNAL OF CLINICAL ONCOLOGY

Surveillance or Metastasis-Directed Therapy for Oligometastatic Prostate Cancer Recurrence: A Prospective, Randomized, Multicenter Phase II Trial

*Piet Ost, Dries Reynders, Karel Decaestecker, Valérie Fonteyne, Nicolaas Lumen, Aurélie De Bruycker, Bieke Lambert, Louke Delrue, Renée Bultijnck, Tom Claeys, Els Goetghebeur, Geert Villeirs, Kathia De Man, Filip Ameye, Ignace Billiet, Steven Joniau, Friedl Vanhaverbeke, and Gert De Meerleer*

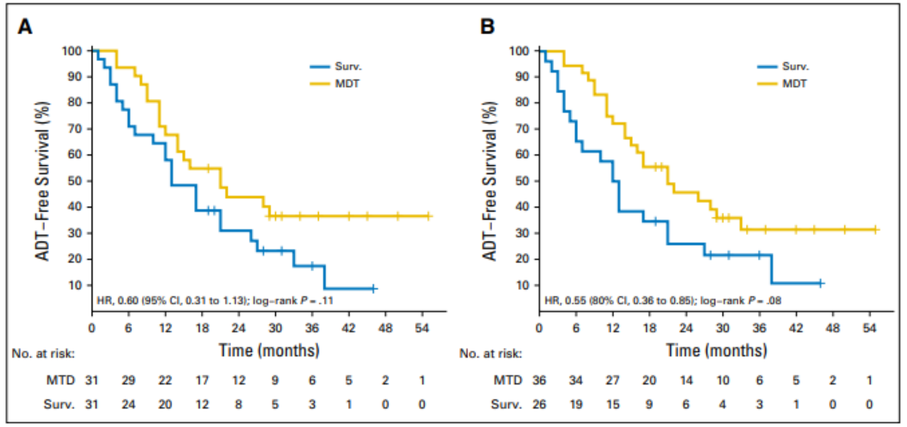


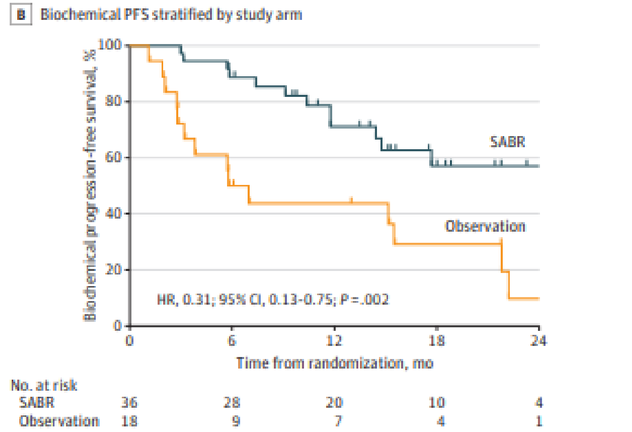

**Fig 2.** Kaplan-Meier plot comparing androgen deprivation therapy (ADT)–free survival of surveillance versus metastasis-directed therapy (MDT) for (A) the intention-to-treat analysis and (B) the per-protocol analysis. HR, hazard ratio; Surv., surveillance.

*JAMA Oncol.* 2020;6(5):650-659. doi:10.1001/jamaoncol.2020.0147

**JAMA Oncology** | Original Investigation

Outcomes of Observation vs Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer
The ORIOLE Phase 2 Randomized Clinical Trial

Ryan Phillips, MD, PhD; William Yue Shi, BS; Matthew Deek, MD; Noura Radwan, MD; Su Jin Lim, ScM; Emmanuel S. Antonarakis, MD; Steven P. Rowe, MD, PhD; Ashley E. Ross, MD, PhD; Michael A. Gorin, MD; Curtiland Deville, MD; Stephen C. Greco, MD; Hailun Wang, PhD; Samuel R. Denmeade, MD; Channing J. Paller, MD; Shirl Dipasquale, MS, RN; Theodore L. DeWeese, MD; Daniel Y. Song, MD; Hao Wang, PhD; Michael A. Carducci, MD; Kenneth J. Pienta, MD; Martin G. Pomper, MD, PhD; Adam P. Dicker, MD, PhD; Mario A. Eisenberger, MD; Ash A. Alizadeh, MD, PhD; Maximilian Diehn, MD, PhD; Phuoc T. Tran, MD, PhD



# Recurrent Prostate Cancer Topic 2: Oligometastatic Disease (recurrent)

NRG ONCOLOGY
*Advancing Research. Improving Lives.™*

NRG Oncology
Four Penn Center
1600 JFK BLVD Suite 1020
Philadelphia, PA 19103
Nrgoncology.org

**NRG-GU011**: A PHASE II DOUBLE-BLINDED, PLACEBO-CONTROLLED TRIAL OF **PRO**STATE OLIGO**MET**ASTATIC RADIOT**HE**RAPY WITH OR WITHOUT **AN**DROGEN DEPRIVATION THERAPY IN OLIGOMETASTATIC PROSTATE CANCER (NRG PROMETHEAN)

**ClinicalTrials.gov Identifier NCT# 05053152**
**NCI Version Date: (March 15, 2022)**

**Principal Investigator:**
Bridget Koontz, MD
GenesisCare
28595 Orchard Lake Road
Suite 110
Farmington Hills, MI
919-451-5525
bridget.koontz@usa.genesiscare.com

- **We must be aware that there really is no standard of care defined for biochemically recurrent, oligometastatic prostate cancer detected by PET imaging**
- **Thus, equipoise exists to evaluate the role of MDT in lieu of ADT in these patients**
- **Current NCCN guideline endorse MDT as an option for patient with oligometastatic prostate cancer**

**NRG-GU011**
**SCHEMA**

Recurrent Oligometastatic Prostate Cancer (detected by PET) after RT to Prostate or Radical Prostatectomy +/- Post-Operative Radiotherapy

**STRATIFY**

- Extrapelvic node(s) only vs Bone +/- node(s) [pelvic/extrapelvic]
- PSA Doubling Time <12 mos vs ≥ 12mos
- Fluciclovine PET vs PSMA PET

**RANDOMIZE***

↓ ↓

**Arm 1**
SABR + blinded placebo** for 6 months

**Arm 2**
SABR + blinded relugolix** for 6 months

# Recurrent Prostate Cancer Topic 3: Oligometastatic Disease (progressive)

ELSEVIER

European Urology Oncology

Volume 4, Issue 3, June 2021, Pages 447-455

## Metastasis-directed Therapy Prolongs Efficacy of Systemic Therapy and Improves Clinical Outcomes in Oligoprogressive Castration-resistant Prostate Cancer

Matthew P. Deek [a, †], Kekoa Taparra [b, †], Ryan Phillips [a], Pedro Isaacsson Velho [c], Robert W. Gao [b], Curtiland Deville [a], Daniel Y. Song [a], Stephen Greco [a], Michael Carducci [c], Mario Eisenberger [c], Theodore L. DeWeese [a], Samuel Denmeade [c], Kenneth Pienta [c], Channing J. Paller [c], Emmanuel S. Antonarakis [c], Kenneth R. Olivier [b], Sean S. Park [b], Phuoc T. Tran [a, c, d], Bradley J. Stish [b]

- **Metastasis-directed therapy can be a powerful tool to allow patients on stable systemic therapy to continue on their current regimen by treating 1-3 sites of progressive disease**
- **This retrospective analysis of CRPC shows that MDT compared to a change in systemic therapy improve PSA failure and distant metastasis-free survival**

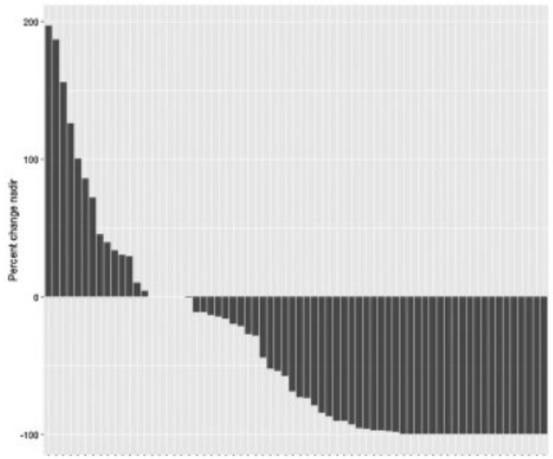
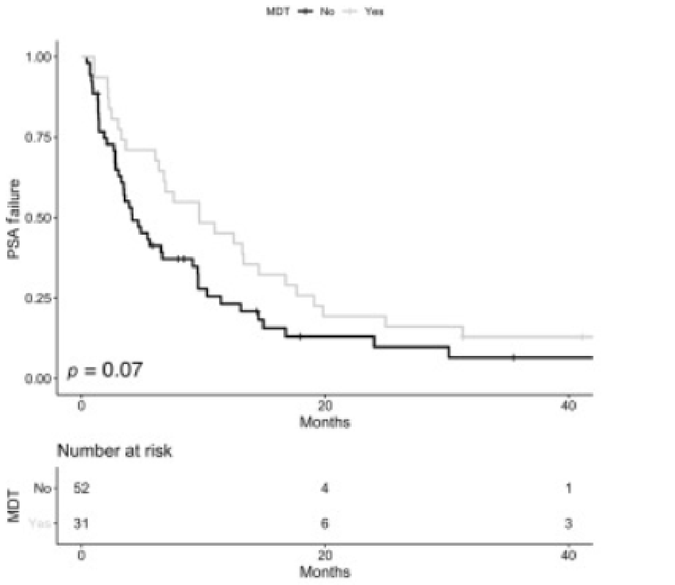



Fig. 1. Waterfall plot of PSA change following radiation therapy. PSA = prostate-specific antigen.



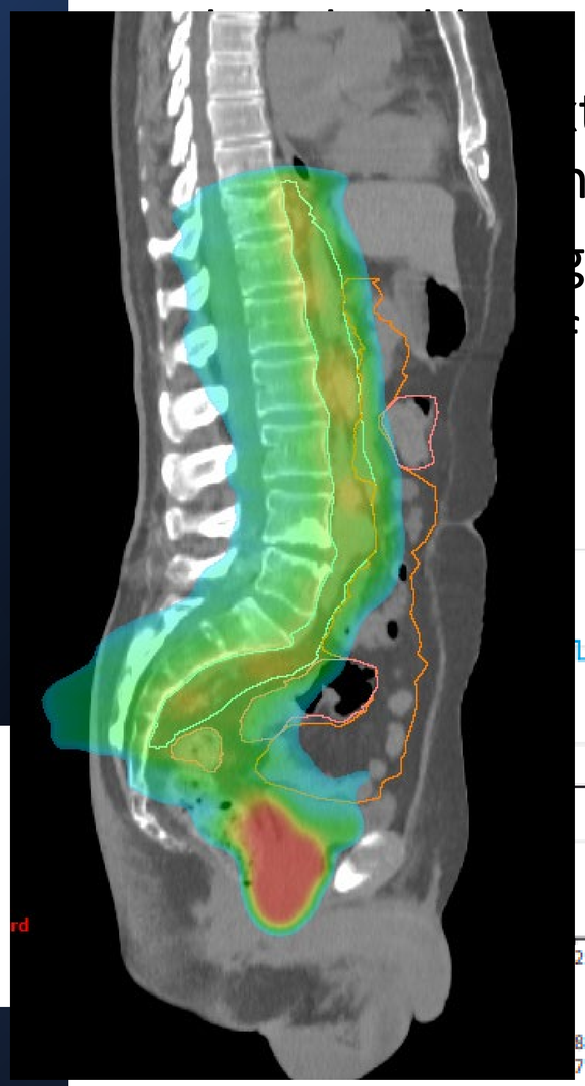
# De Novo Metastatic Prostate Cancer: N1 and M1a

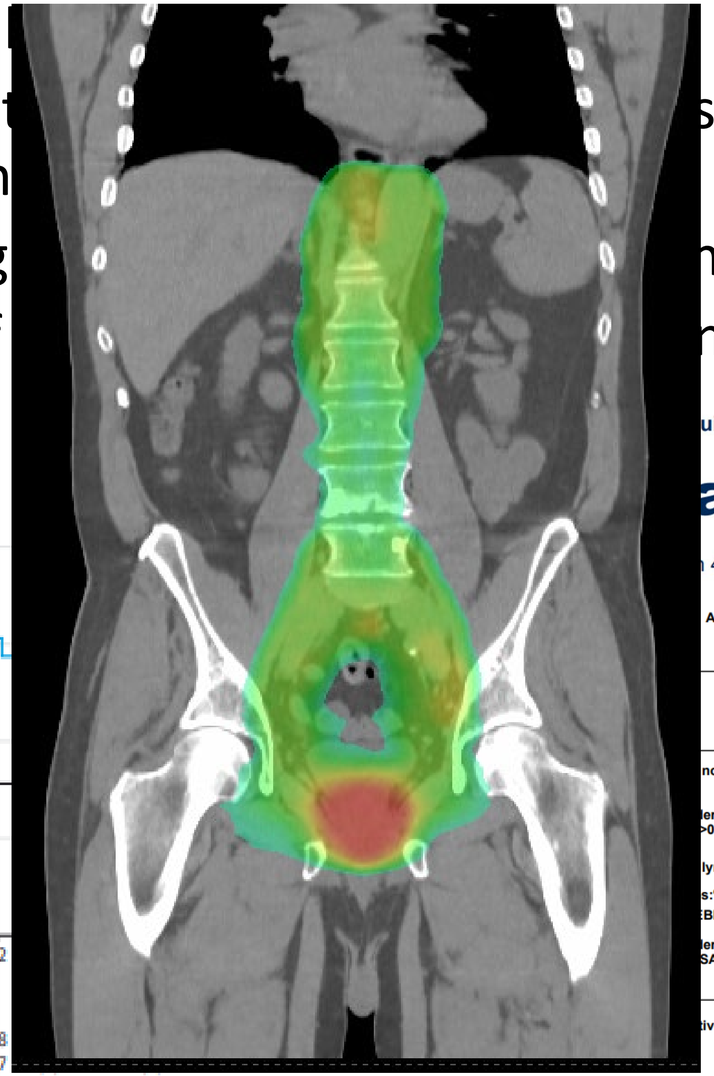
- In patients with clinical N1 (and some with M1a) prostate cancer, radiation is an important component of treatment

s is generally

n ASIR

nable





Original Investigation

**Failure-Free Survival and Radiotherapy in Patients With Newly Diagnosed Nonmetastatic Prostate Cancer**
Data From Patients in the Control Arm of the STAMPEDE Trial

Nicholas D. James, BSc, MBBS, PhD, FRCP, FRCR; Melissa R. Spears, MSc, BSc; Noel W. Clarke, MBBS, FRCS(Eng), ChM(Manch), FRCS(Urol); David P. Dearnaley, MA, MB, BChir, MD, FRCP, FRC; Malcolm D. Mason, MD, FRCP, FRCR, FSB; Christopher C. Parker, BA, BM, BChir, MD; Alastair W. S. Ritchie, MD, FRCSEd; J. Martin Russell, BSc, MB, ChB, MRCP(UK), FRCR, FRCPSG; Francesca Schiavone, PhD; Gerhardt Attard, MD, PhD; Johann S. de Bono, MBChB, MSc, PhD, FRCP, FMedSci; Alison Birtle, MB, BS, MRCP, FRCR, MD; Daniel S. Engeler, MD; Tony Elliott, BSc, MSc, PhD, MBChB, MRCP, FRCR; David Matheson, BSc, PGCE, DipEd, MEd, PhD, FRSA, FHEA; Joe O'Sullivan, MD, FRCR, FFRRCSI, FRCPI; Delia Pudney, MBChB; Narayanan Srihari, MB, BS; Jan Wallace, MB, ChB, FRCR; Jim Barber, MA, DM, FRCR, MRCP; Isabel Syndikus, MD; Mahesh K. B. Parmar, DPhil, MSc, BSc; Matthew R. Sydes, MSc, CStat; for the STAMPEDE Investigators

JAMA Oncology March 2016 Volume 2, Number 3

uidelines in Oncology (NCCN Guidelines®)

ate Cancer

4.2022 — May 10, 2022

ADJUVANT THERAPY

Undetectable PSA after RP or PSA nadir[z] after RT → See Monitoring (PROS-9)

no lymph node metastases:[r,s]

eration of early RT for a detectable >0.1 ng/mL (See PROS-9)

lymph node metastases

s:[cc]

EBRT[o] (category 2B)

eration of early treatment for a SA or PSA >0.1 ng/mL (See PROS-9)

PSA persistence/ recurrence[aa,bb] → See Radical Prostatectomy PSA Persistence/ Recurrence (PROS-10); See Radiation Therapy Recurrence (PROS-11)

tive care

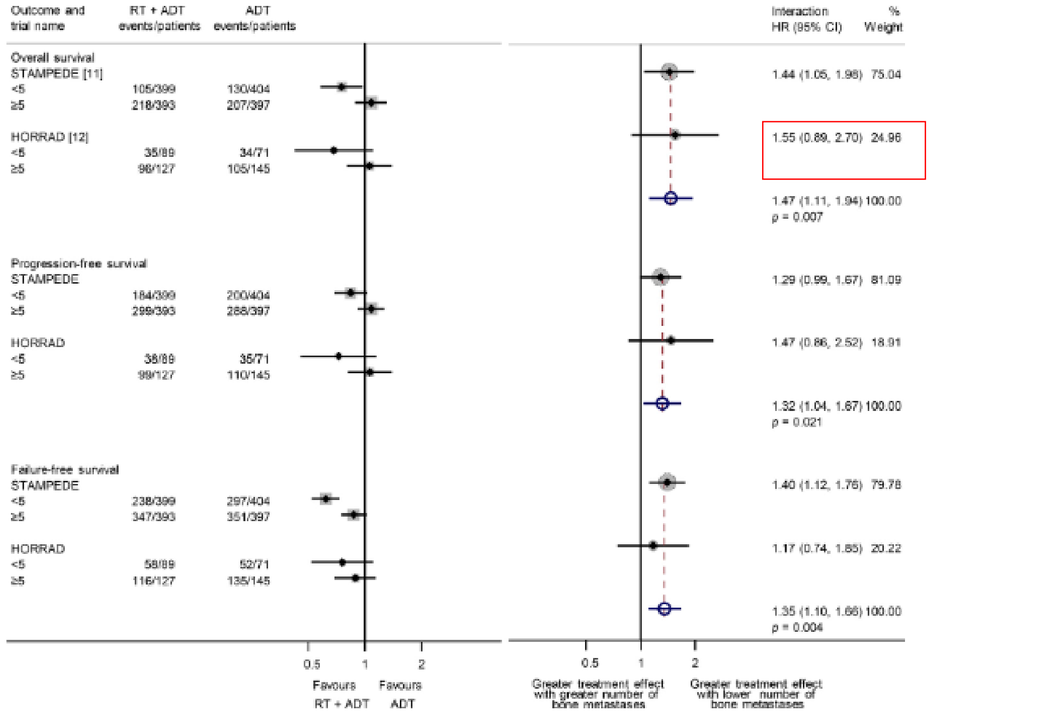
# De Novo Metastatic Prostate Cancer: M1

**Prostate Radiotherapy for Metastatic Hormone-sensitive Prostate Cancer: A STOPCAP Systematic Review and Meta-analysis**

*Sarah Burdett[a,*], Liselotte M. Boevé[b,c,†], Fiona C. Ingleby[d,†], David J. Fisher[a], Larysa H. Rydzewska[a], Claire L. Vale[a], George van Andel[c], Noel W. Clarke[e], Maarten C. Hulshof[f], Nicholas D. James[g], Christopher C. Parker[h], Mahesh K. Parmar[d], Christopher J. Sweeney[i], Matthew R. Sydes[d], Bertrand Tombal[j], Paul C. Verhagen[k], Jayne F. Tierney[a], the STOPCAP M1 Radiotherapy Collaborators*

EUROPEAN UROLOGY 76 (2019) 115–124

- HORRAD and STAMPEDE Arm H results pooled
  - These both included newly diagnosed M1 Pca
  - Arms were ADT vs ADT + RT to prostate
- Overall survival in **entire cohort** no different between ADT and ADT+RT
- Interaction of RT was assessed by disease volume.
  - < 5 metastases vs ≥ 5 metastases
  - **Overall survival** significantly improved with RT
  - 3 year OS=77% vs 70%



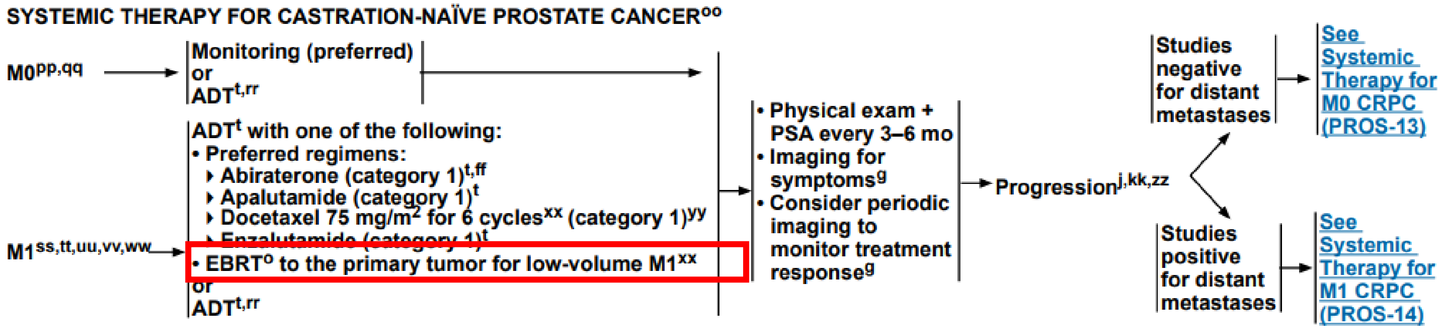
# De Novo Metastatic Prostate Cancer: M1

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

**Prostate Cancer**

Version 4.2022 — May 10, 2022

- Thus, XRT to the primary is listed in NCCN guidelines as a recommendation for low volume M1 patients




- However, many questions remain:
  - Does this benefit remain when more intensive systemic therapy regimens are employed?
  - These studies utilized CT/Bone scan staging, what do we do in the PSMA PET era?
  - Should we consider metastasis-directed therapy in conjunction with prostate only radiation?

# Conclusions

- Radiation therapy is an excellent option for most men with localized prostate cancer
  - Current data support multiple techniques with similar long-term outcomes
- There appears to be a role for escalated systemic therapy in some men with high-risk prostate cancer receiving XRT
  - Personalization may be possible, although studies are pending
- Radiation plays an important, and potentially curative, role in initial biochemical recurrence after radical prostatectomy
  - Evolving technology may prove to guide patient selection, but this remains outside the current standard of care
- Current data support prostate radiation therapy in patients with newly diagnosed low volume M+ prostate cancer
  - Future studies will help further define the place of radiotherapy in this rapidly evolving landscape