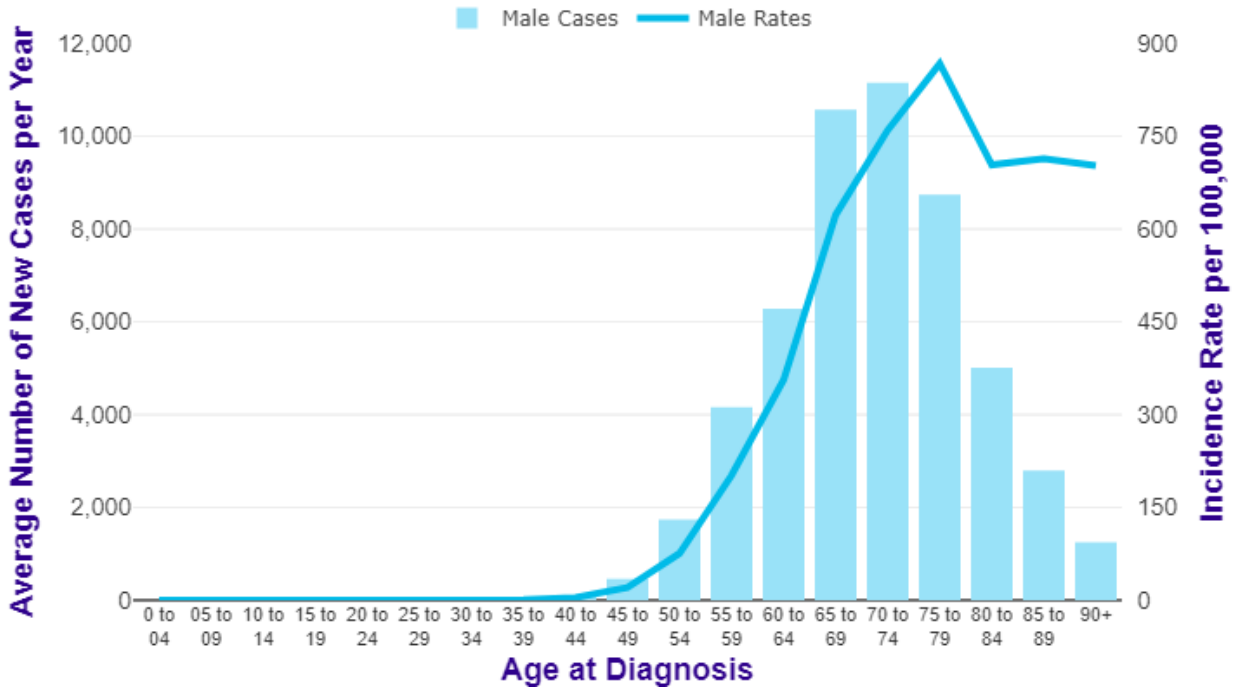
PROSTATE CANCER FACTS

- Most common mens cancer: >52000 new cases every year
- ~12000 deaths/yr
- ~48% diagnosed in early stage

TREATMENT OPTIONS:

- Surgery
- Brachytherapy
- External Beam Radiotherapy



Ideal Treatment: does it exist?

- ✓ Excellent Cure rates
- ✓ Minimal Toxicity
- ✓ High QOL
- ✓ Low Cost
- ✓ High patient satisfaction

Patient's FAQs

- My PSA
- Can I pee OK?
- Do I need a pad while going out?
- Can I still have erections
- Is my cancer cured/back?


OH FOR HEAVEN'S SAKE HONEY!...IT'S FOR YOUR OWN DAMN GOOD!
To UROLOGIST

BRACHYTHERAPY

vs.

SABR

- **Brachytherapy**
  - day case procedure
  - a time-tested technique
  - has excellent, proven outcomes
  - very long follow-up

- **Stereotactic Ablative radiation therapy**
  - shortened treatment duration
  - potential radiobiological advantage
  - interest increased over the past decade

The Debaters

Proponent of SABR

Dr Julia Murray
Consultant Clinical Oncologist
The Royal Marsden NHS Foundation Trust

Defender for Brachytherapy

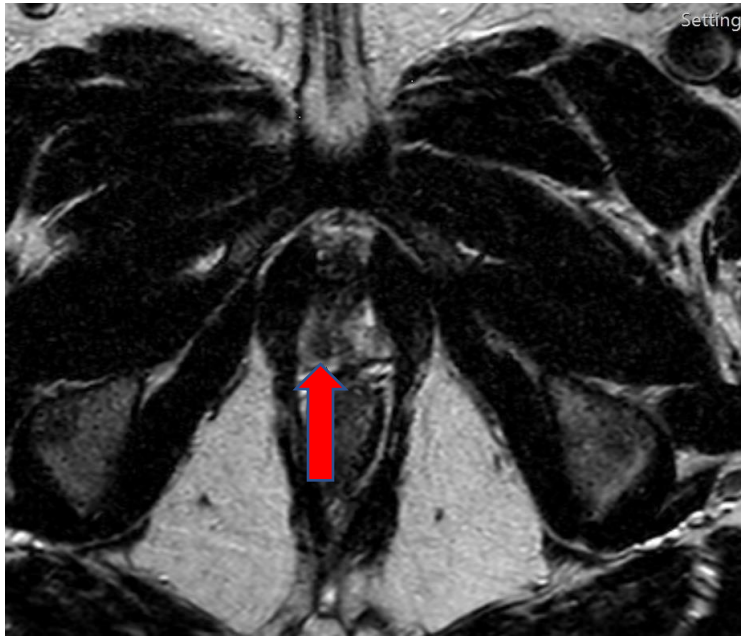
Professor Ann Henry
Consultant Clinical Oncologist
The Leeds Teaching Hospitals NHS Trust

Case-1

Post -TURP

- 70yr old, PS=0-1
- Co-incidental finding of < 5% , Gl 3+3=6 GG1 on TURP 6/12 previously
- Good urinary function now
- Post TURP MRI – Right posterior medial apical lesion
- Post TURP PSA 2.5
- Post TURP prostate biopsies ¼ cores right posterior involved with Gl3+4=7, GG2, 9mm involvement
- Keen on active treatment and wants to maintain sexual function

Brachy or SABR

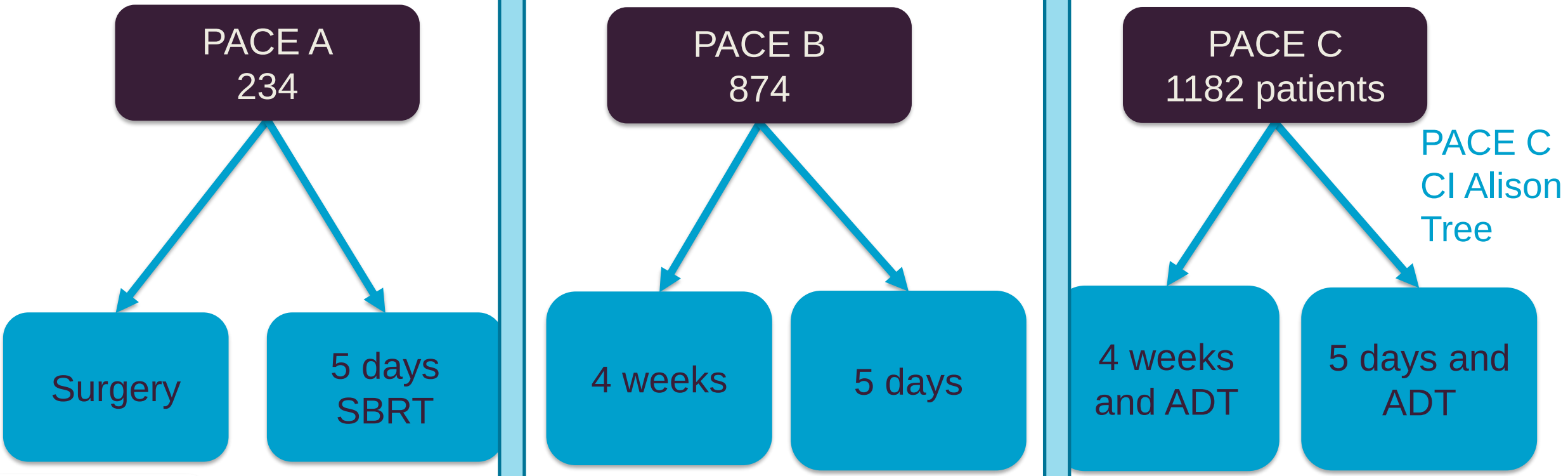


Initial Audience Vote for Case-1

Proponent of SABR

Dr Julia Murray

The PACE umbrella
Localised prostate cancer
CI Dr Nick van As



PACE C
CI Alison
Tree

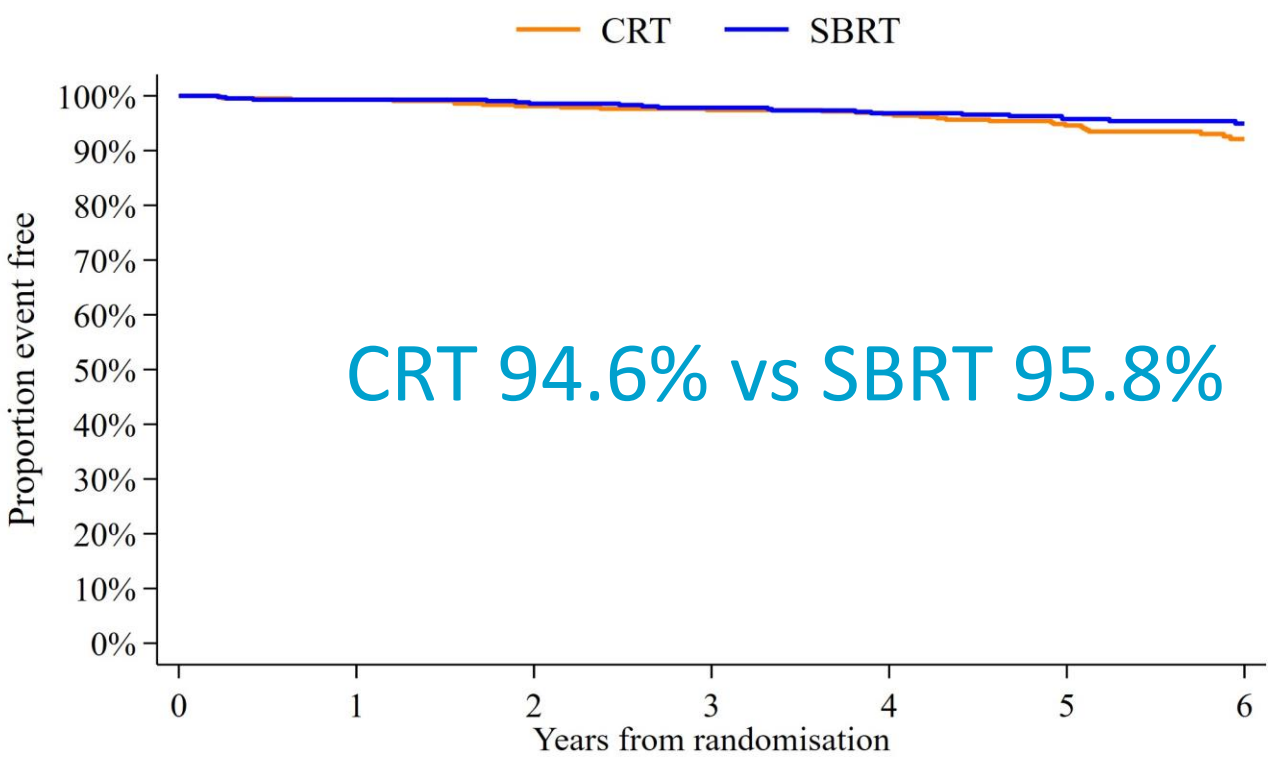
varian

The ROYAL MARSDEN
NHS Foundation Trust

ICR The Institute of Cancer Research

ACCURAY

Biochemical/clinical failure



CRT 94.6% vs SBRT 95.8%

874 men with localised PCa
- T1c -T2c
- Gleason ≤ 3+4
- PSA ≤ 20

- MRI Staged
- No ADT

>90% patients intermediate risk, 82% Gleason 3+4, 31% PSA >10 ng/ml

van As et al, ASTRO 2023

What about side effects?

2142 men
10 single or multi-institutional
Phase 2 trials
Median FU 6.9 years

JAMA Network Open™

Original Investigation | Oncology

Long-term Outcomes of Stereotactic Body Radiotherapy for Low-Risk and Intermediate-Risk Prostate Cancer

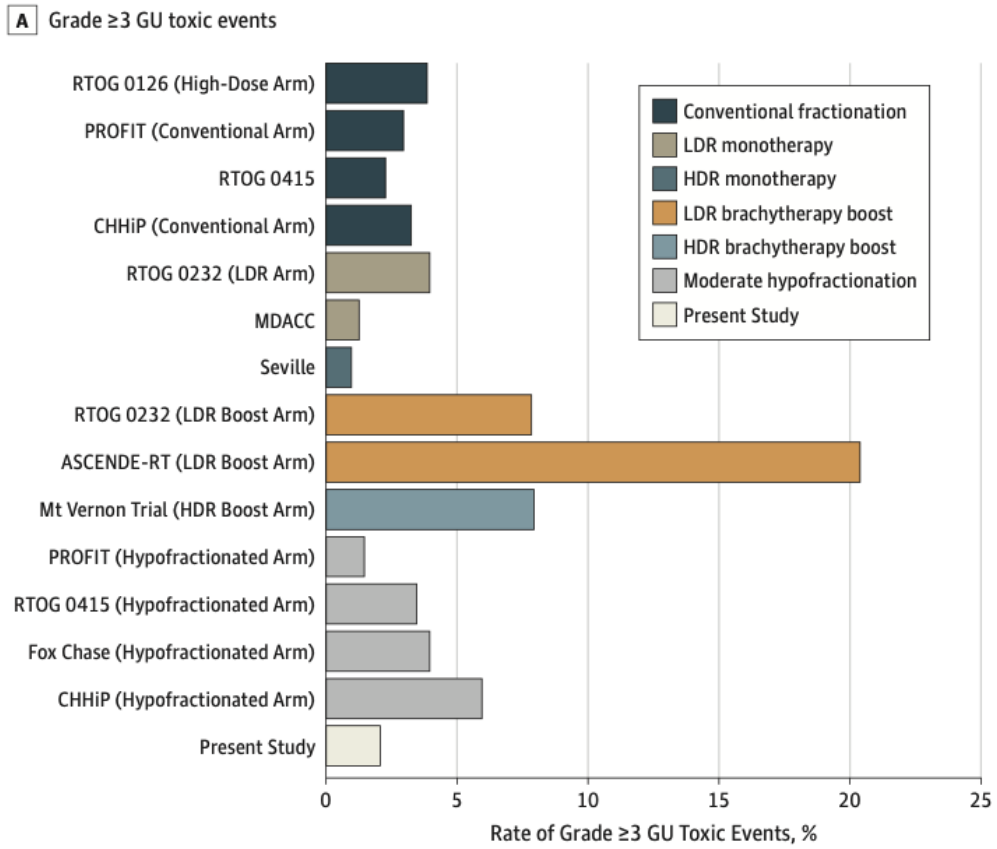
Amar U. Kishan, MD; Audrey Dang, MD; Alan J. Katz, MD, JD; Constantine A. Mantz, MD; Sean P. Collins, MD, PhD; Nima Aghdam, MD; Fang-I Chu, PhD; Irving D. Kaplan, MD; Limor Appelbaum, MD; Donald B. Fuller, MD; Robert M. Meier, MD; D. Andrew Loblaw, MD; Patrick Cheung, MD; Huong T. Pham, MD; Narek Shaverdian, MD; Naomi Jiang, MD; Ye Yuan, MD, PhD; Hilary Bagshaw, MD; Nicolas Prionas, MD, PhD; Mark K. Buyyounouski, MD, MS; Daniel E. Spratt, MD; Patrick W. Linson, MD; Robert L. Hong, MD; Nicholas G. Nickols, MD, PhD; Michael L. Steinberg, MD; Patrick A. Kupelian, MD; Christopher R. King, MD, PhD

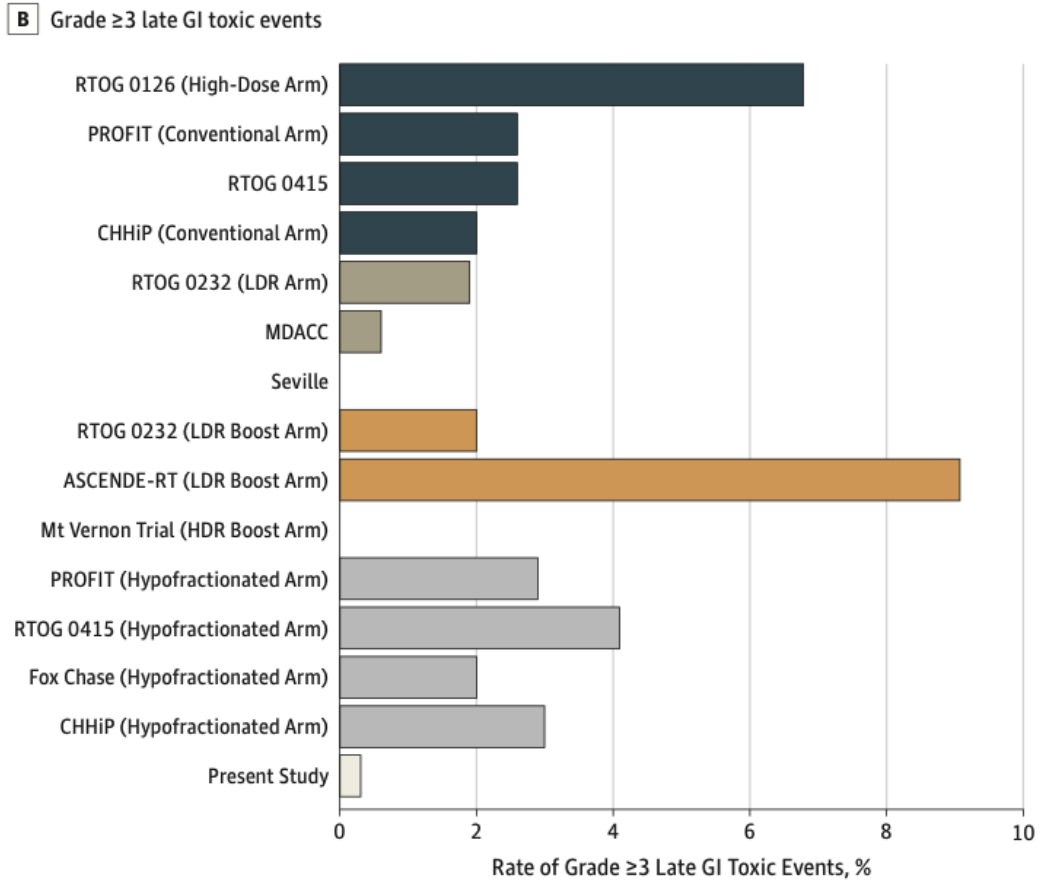
Abstract

Key Points

Kishan et al, JAMA Open 2019

Comparative rates of Grade 3 or higher side effects across various radiotherapy modalities



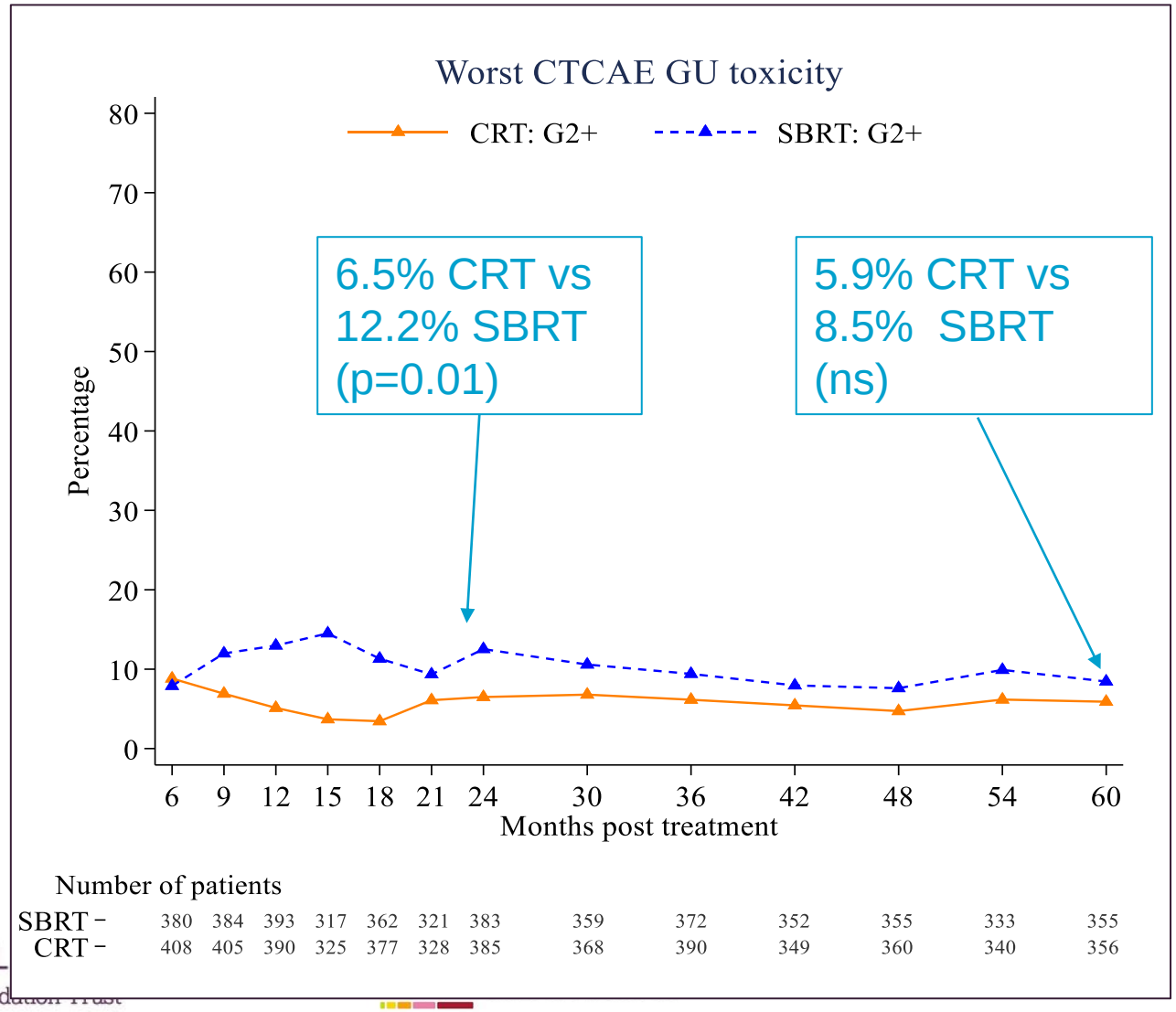


The ROYAL MARSDEN NHS Foundation Trust

ICR The Institute of Cancer Research

CTCAE GU G2+ toxicity – what about after 2 years?

CTCAE G3 GU
1/381 (0.3%) conventional vs
1/380 (0.3%) SBRT at 2 years



van As et al, ASTRO 2023

What about outcomes post TURP?

Safety of Prostate Stereotactic Body Radiation Therapy after Transurethral Resection of Prostate (TURP): A Propensity Score Matched Pair Analysis

Vedang Murthy, MD • Shwetabh Sinha, MD • Sadhana Kannan, MSc • ... Ganesh Bakshi, MS • Gagan Prakash, MS • Rahul Krishnatry, MD • Show all authors

50 prostate cancer patients who had undergone a single TURP, good baseline urinary function were chosen and propensity score matched to a similar non-TURP cohort

Median follow up of 26 months

Median duration between TURP and start of SBRT = 10 months

No significant difference between non-TURP and TURP cohort RTOG acute and late GU toxicity, stricture rates and incontinence rates.

Clinical Oncology 34 (2022) e392–e399

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

Surgical Treatments of Benign Prostatic Hyperplasia and Prostate Cancer Stereotactic Radiotherapy: Impact on Long-Term Genitourinary Toxicity

C. Huck *, V. Achard *†, T. Zilli *†

150 prostate cancer patients treated with SBRT

24 (16%) history of surgical treatment of BPH – 19 – TURP; among them 3 with repeated TURP – and 5 with adenomectomy

Median follow up of 45 months

Baseline and treatment characteristics of patients with acute or late grade 3 genitourinary toxicity

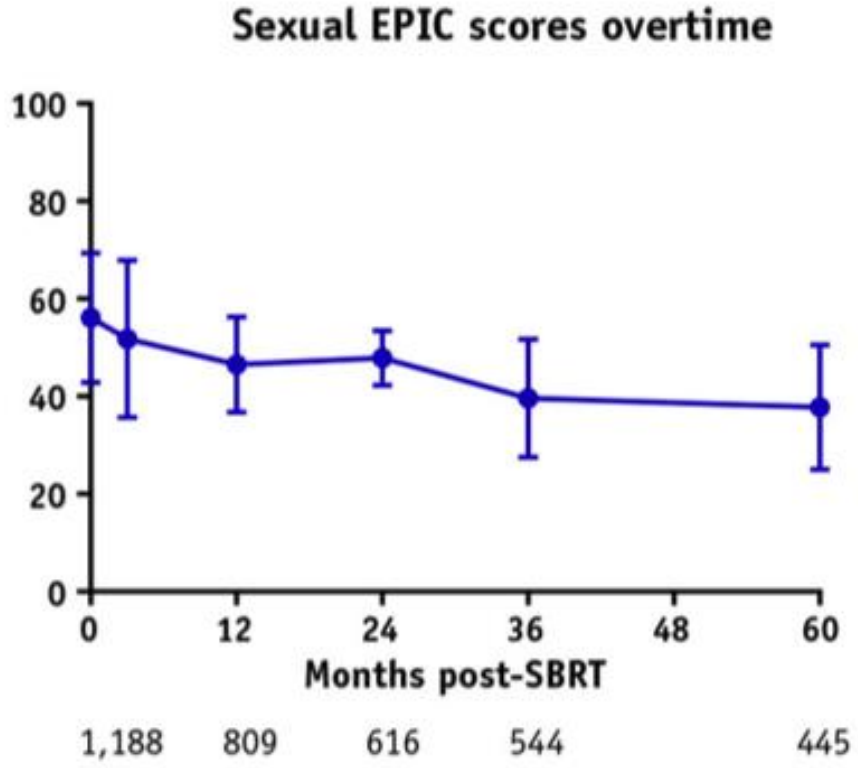
	Age (years)	Interval time between surgery and radiotherapy (months)	Adenomectomy or TURP (no. TURP)	Prostate size on MRI (cm^3)	Postsurgical cavity volume (cm^3)	Radiotherapy dose (Gy)	Genitourinary status at baseline (CTCAE v.4.0)	Genitourinary toxicity after adiotherapy (CTCAE v.4.0)	Time to onset grade 3 genitourinary toxicity after completion of treatment (months)
Patient #1	75	60	TURP ($n = 2$)	58	3.7	36.25	Grade 1 retention	Late grade 3 cystitis	16
Patient #2	67	2	TURP ($n = 3$)	53	15.4	36.25	Grade 1 frequency	Acute grade 3 cystitis	6
Patient #3	74	20	Adenomectomy	50	5.7	40	Grade 0	Late grade 3 cystitis	9
Patient #4	77	204	Adenomectomy	81	4.2	36.25	Grade 0	Late grade 3 cystitis	22
Patient #5	72	84	TURP ($n = 1$)	141	2.6	36.25	Grade 0	Late grade 3 cystitis	9

CTCAE, Common Terminology Criteria for Adverse Events; MRI, magnetic resonance imaging; TURP, transurethral resection of the prostate.

The ROYAL MARSDEN NHS Foundation Trust

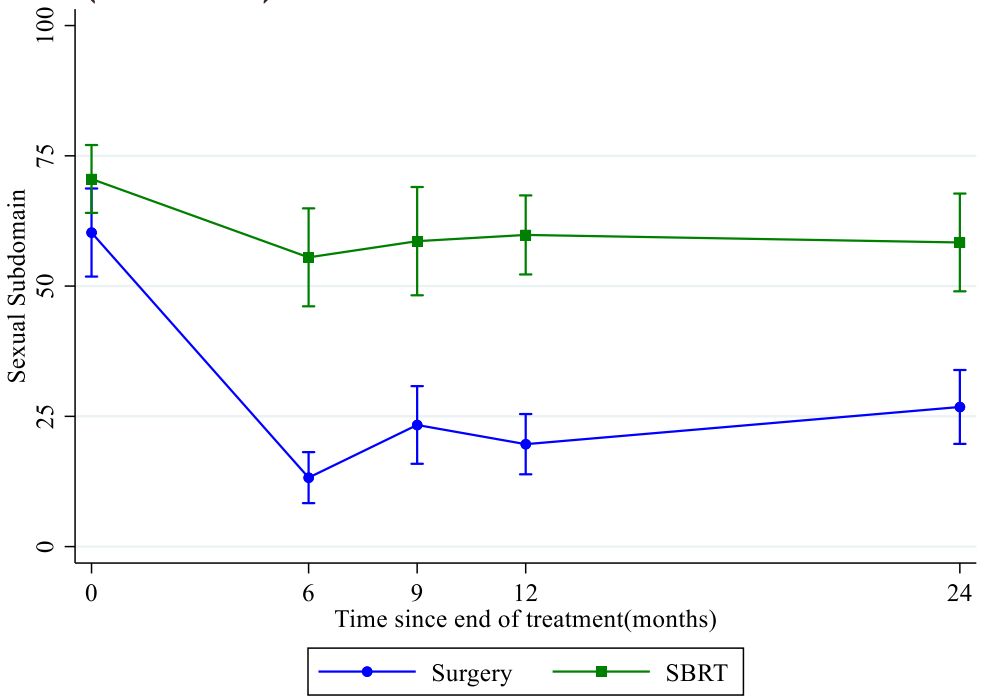
ICR The Institute of Cancer Research

What about sexual function?



Jackson WC et al. IJROBP 2019: 104(4):778-789

EPIC sexual subdomain scores up to 2 years (PACE A)

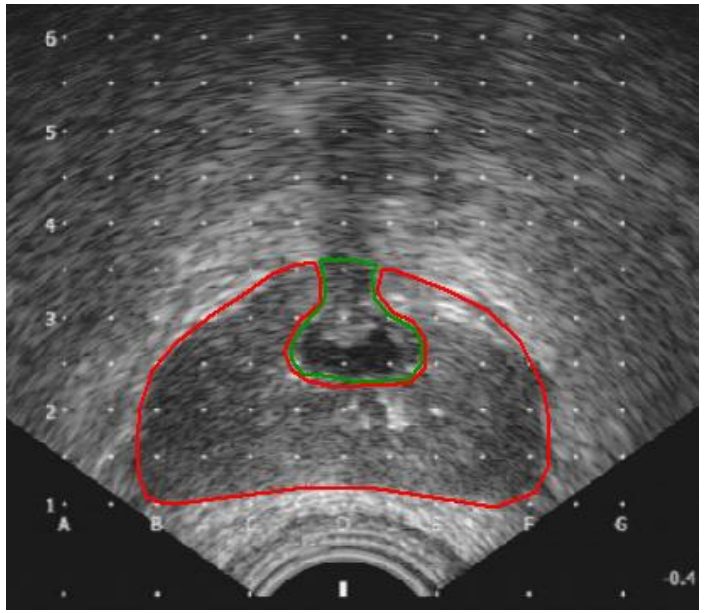


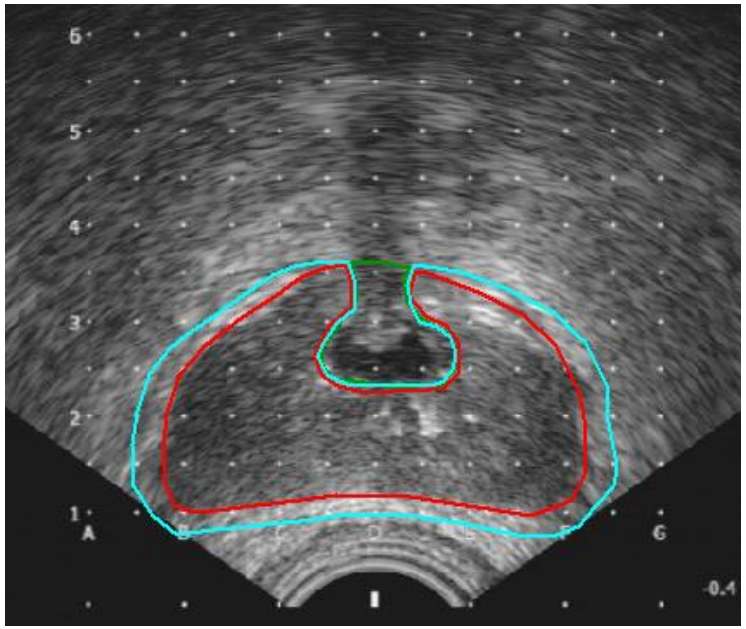
Graph courtesy of Nick van As, ASTRO 2023

Defender for Brachytherapy

Prof. Ann Henry

Guidelines for BT post-TURP planning

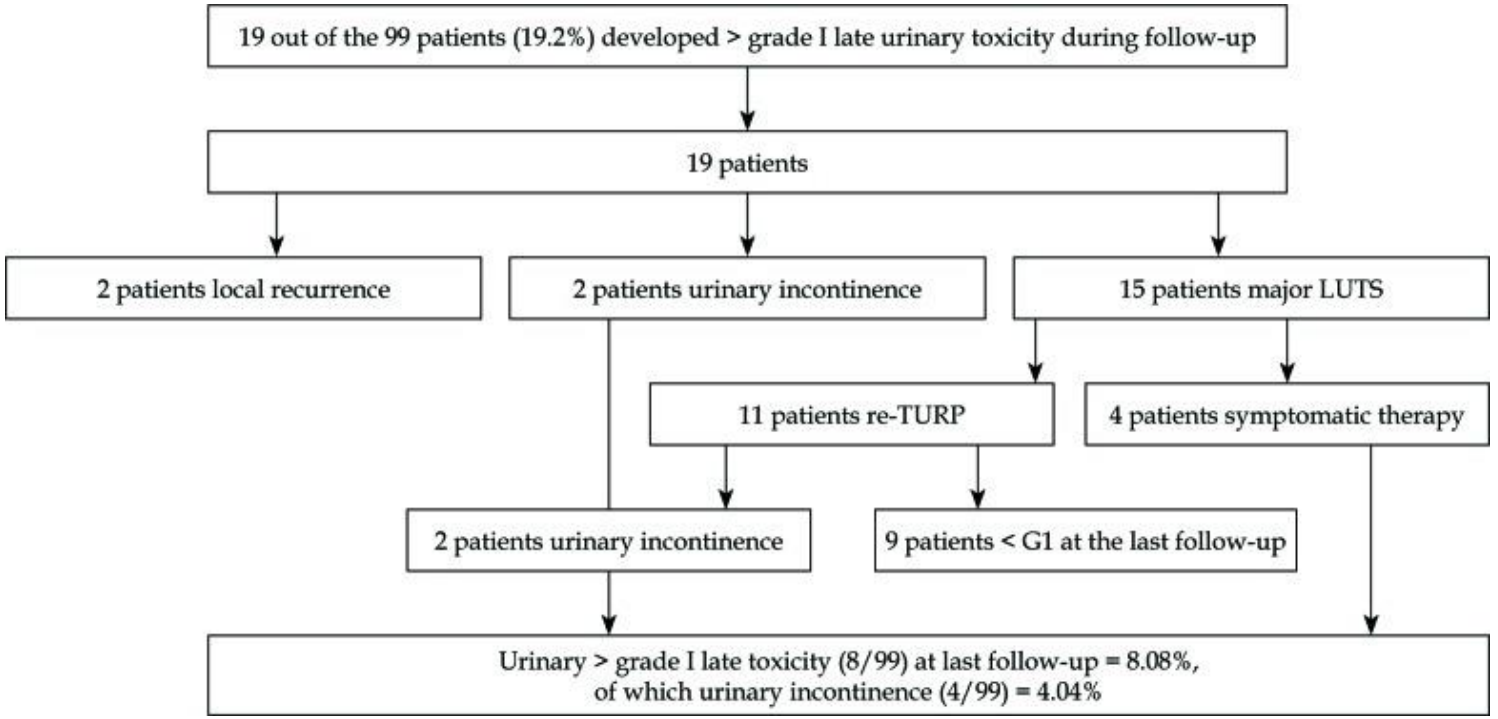




Prospective multi-center dosimetry study of low-dose Iodine-125 prostate brachytherapy performed after transurethral resection
Carl Salembier et al
J Contemp Brachytherapy 2013; 5, 2: 63-69
DOI: https://doi.org/10.5114/jcb.2013.36174

- 1 cm rim of prostate tissue around the post-TURP urethral defect at the postero-lateral sides of the prostate + at least a 3-month interval between TURP and BT
- TURP defect (GREEN) excluded from CTV (RED) and zero expansion to PTV (BLUE)
- Higher V150 (the percentage of the CTV that receives 150% of the prescription dose) allowed, should be equal to or less than 70%

Risk of urinary incontinence <5%

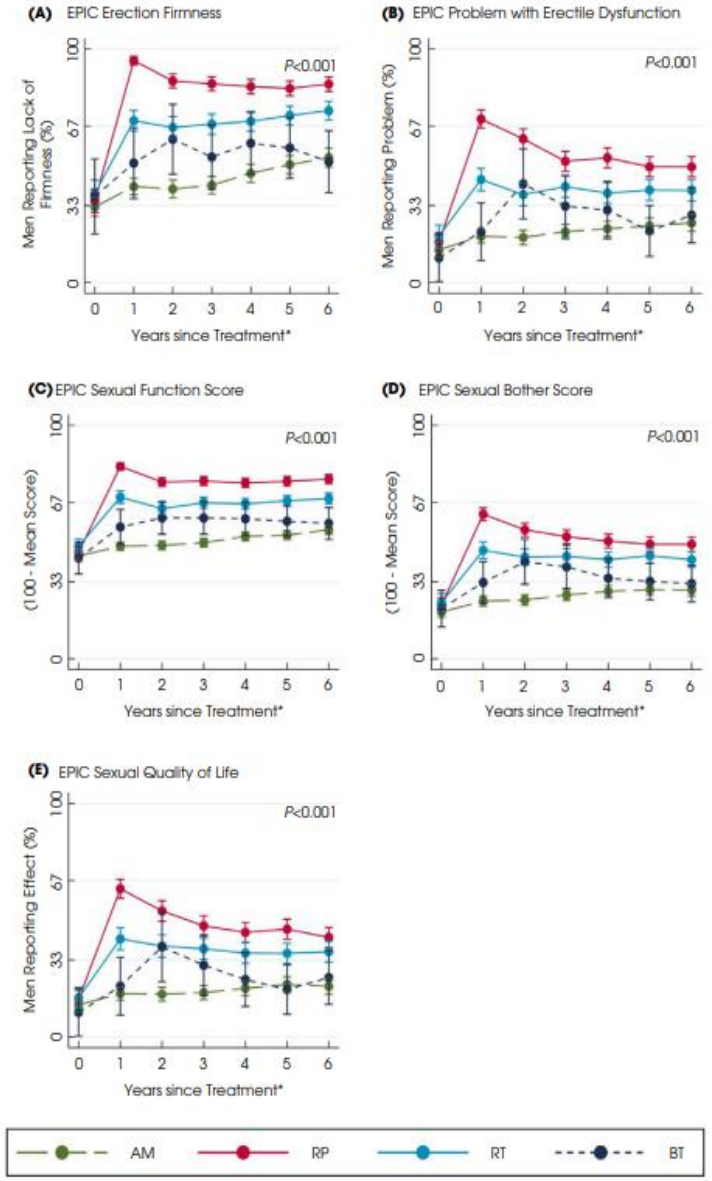


A history of transurethral resection of the prostate should not be a contra-indication for low-dose-rate (125)I prostate brachytherapy: results of a prospective
Uro-GEC phase-II trial.
Carl Salembier et al
J Contemp Brachytherapy, 2020. 12: 1.
https://pubmed.ncbi.nlm.nih.gov/32190063

BT ‘probably’ best for sexual function

- ‘Treatment received’ analysis of ProtecT trial
- 77 patients opted for BT
- Reliable results - based on a large and well characterised population-based cohort with 6 years annual follow-up, and low attrition
- PROMs up to 6 years show BT sexual function outcomes similar to AM and better than EBRT cohort
- BJU Int 2022; 130: 370–380 doi:10.1111/bju.15739

Fig. 2 Patient-reported sexual symptoms and QoL after primary treatments for localised prostate cancer over 6 years. *Questionnaires completed e.g., year 2 as between 1 and 2 years after treatment. Higher scores or percentages indicate worse symptoms. Points are estimated means from models with error bars representing 95% CIs. *P* value based on likelihood-ratio test for overall comparison of treatments.

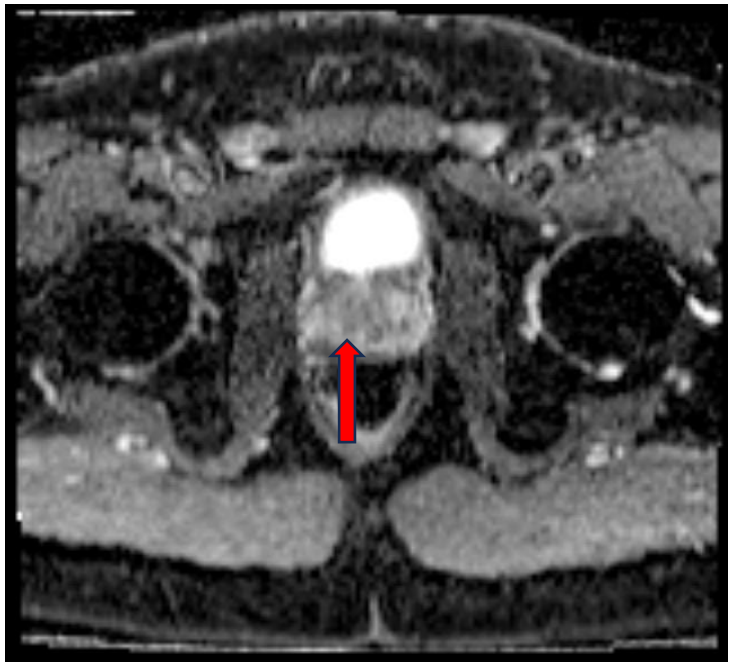


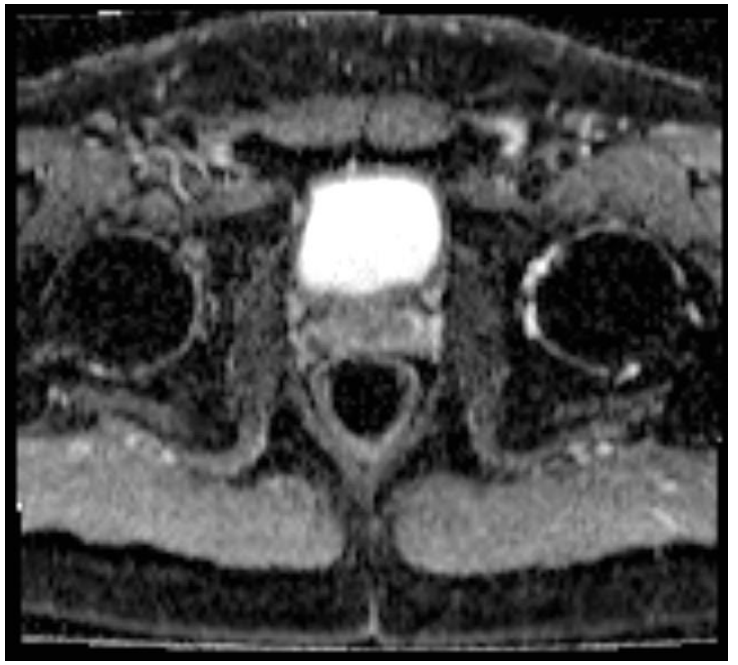
Audience Vote Again Case-1

Case-2

Focal Lesion at Base

- 48 yrs old, BMI 37, PS=0
- Q Max=24
- T2c
- PSA=3.3
- GG2 in 3/6 cores right posterior (10% pattern 4 and 11m max core length involvement)
- MRI:13mm right mid gland to base lesion abutting capsule





Brachy or SABR

Initial Audience Vote: Case-2

Proponent of SABR

Dr Julia Murray

Patient factors:

Age:

Fertility

Second malignancy

Radiotherapy and Oncology 161 (2021) 241–250

Contents lists available at ScienceDirect

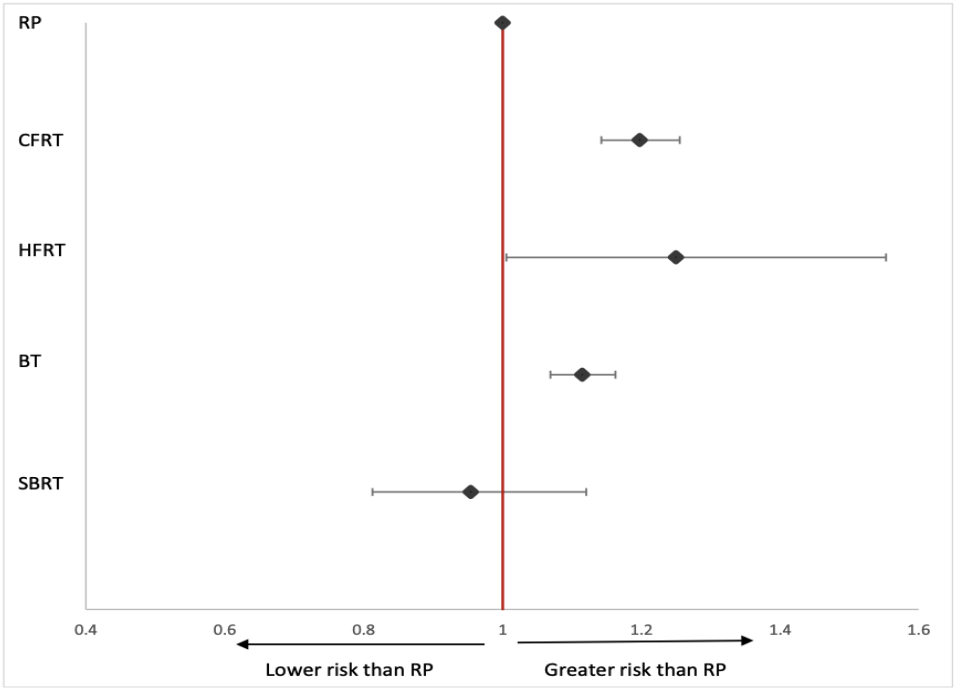
Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Second malignancy probabilities in prostate cancer patients treated with SBRT and other contemporary radiation techniques

Edward Christopher Dee [a,1], Vinayak Muralidhar [b], Martin T. King [b], Neil E. Martin [b], Anthony V. D'Amico [b], Kent W. Mouw [b], Peter F. Orio [b], Paul L. Nguyen [b], Jonathan E. Leeman [b,*]



Raised BMI:

MR linac - abdominal girth limit

Challenging fiducial marker placement

Discussion about lifestyle/exercise

International Journal of Radiation Oncology*Biology*Physics

Volume 114, Issue 3, Supplement, 1 November 2022, Page e217

2486

Correlation between Obesity and Treatment Failure Following Stereotactic Body Radiation Therapy (SBRT) for Clinically Localized Prostate Cancer

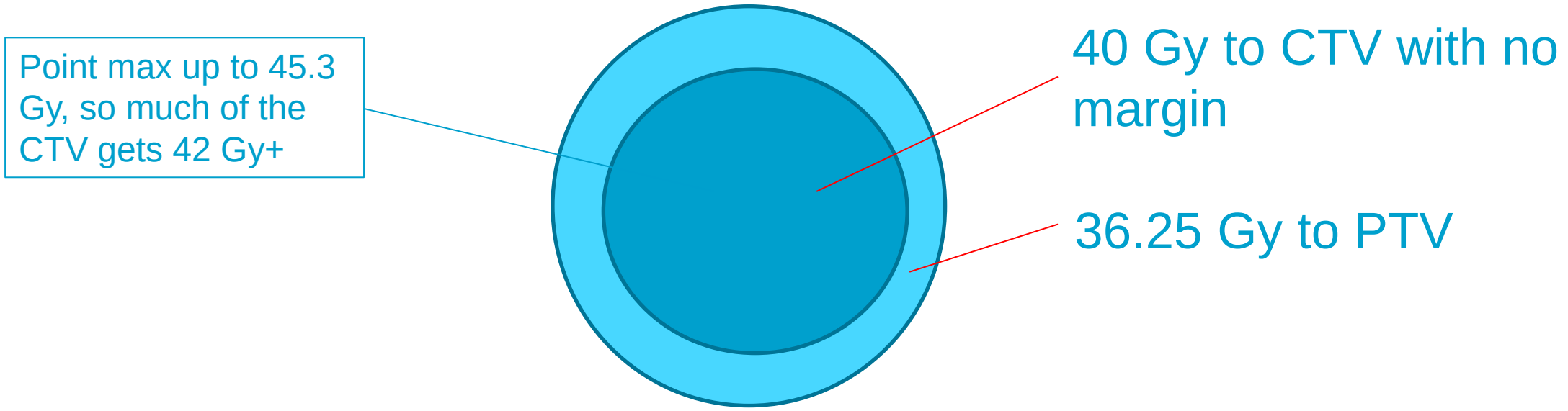
D. Conroy [1], T. Sholklapper [2], M.K. Lawlor [2], J.M. Cantalino [3], A. Zwart [4], M.J. Ayoob [4], M. Danner [1], T. Yung [4], B.T. Collins [1], S. Lei [4], A. Rashid [4], D. Kumar [5], S. Suy [1], N. Aghdam [6], S.P. Collins [1]

1306 pts, retrospective chart review

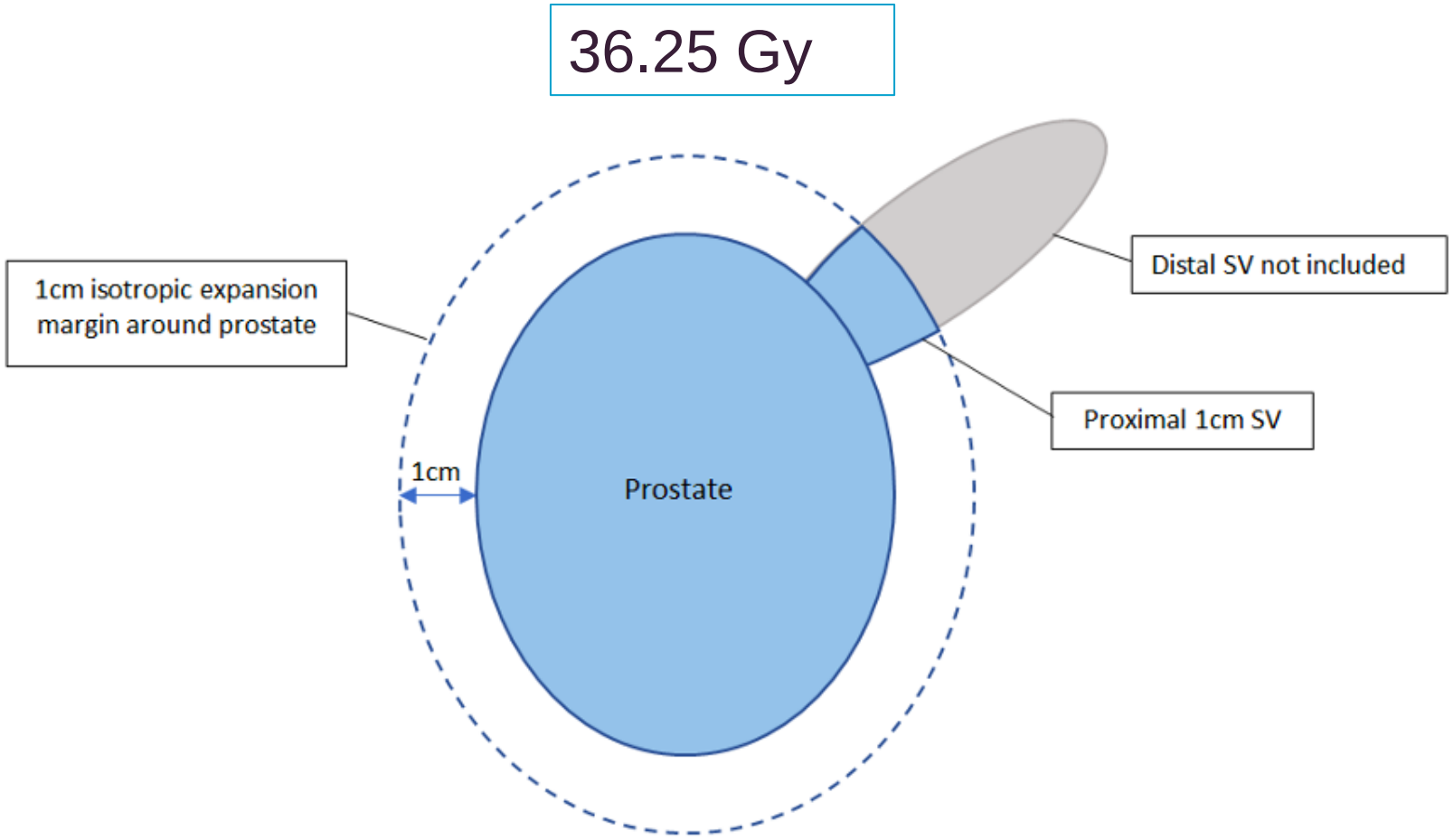
No statistically sig difference in biochemical disease-free survival, dMFS or disease specific survival between BMI subgroups

How do we do SBRT in PACE?

Most international experience with 36.25 Gy in 5 fractions (with or without 40 Gy to CTV)



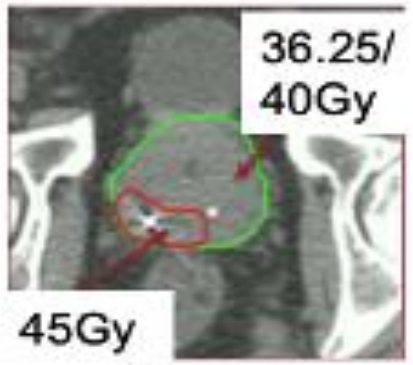
How to contour the CTV – PACE B



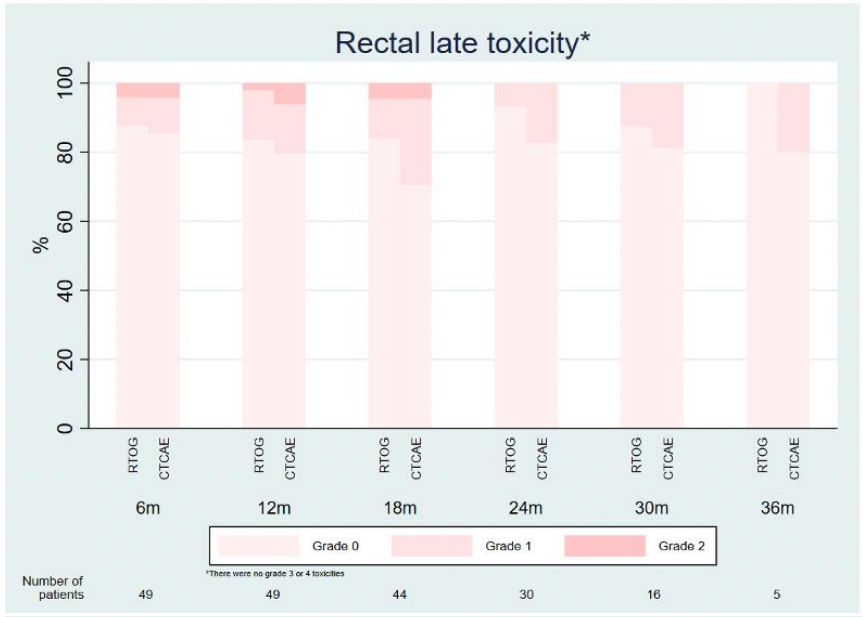
Dose escalation to the dominant nodule

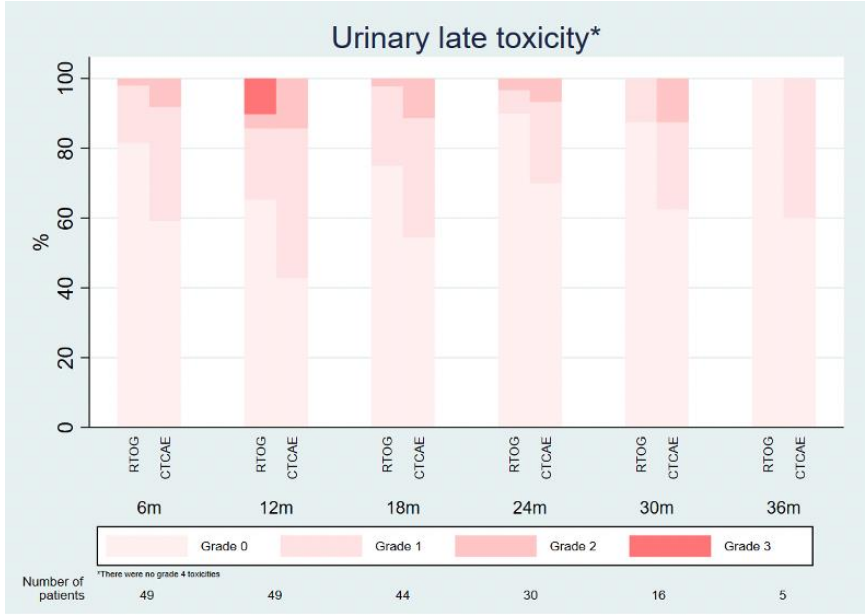
DELINEATE

Cohort E:



over 2 weeks





At any point over 2 years post radiotherapy 11.1% have some bowel effect (Grade 2 RTOG)

(Equivalent for PACE B 7.8% RTOG G2+)

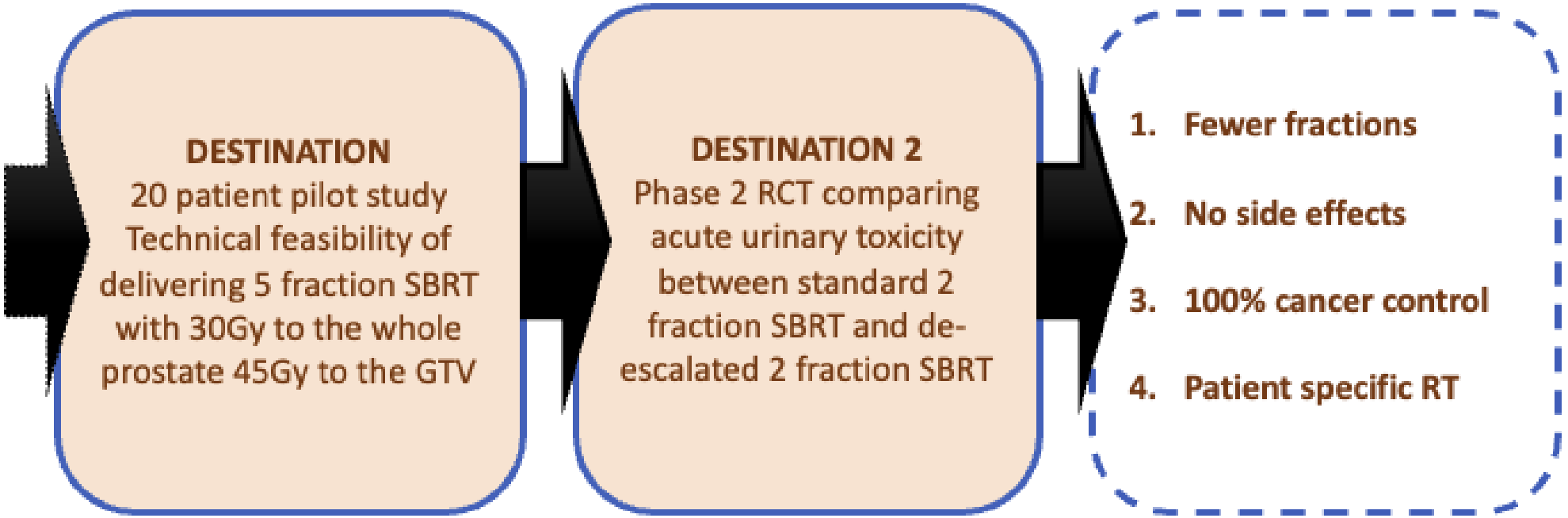
At any point over 2 years post radiotherapy 17.1% have some bladder effect (Grade 2)

(Equivalent for PACE B 18.3%)

ESTRO 2022

The ROYAL MARSDEN
NHS Foundation Trust

DESTINATION – dose de-escalation



Dose DESTINATION

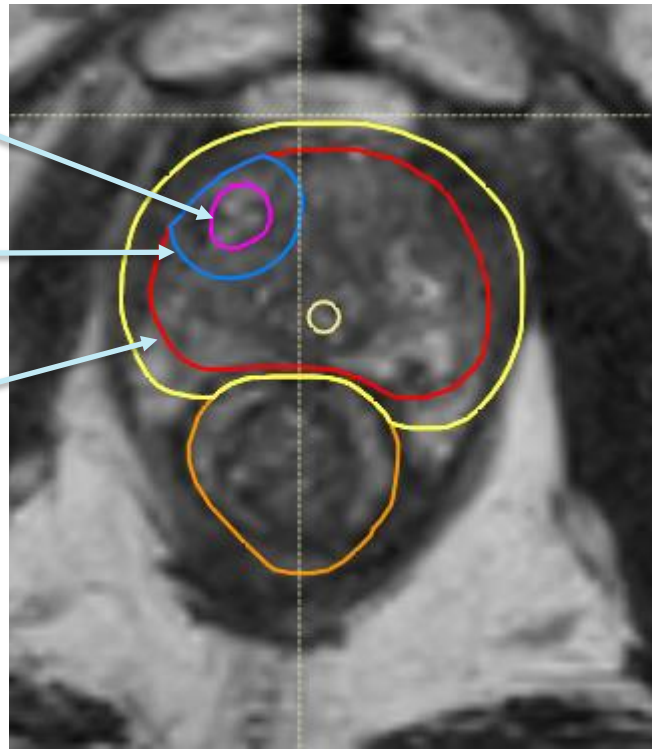
Group 1.
Standard 2 fraction SBRT

26Gy in 2 fractions over 8 days with a GTV boost to 27Gy

GTV

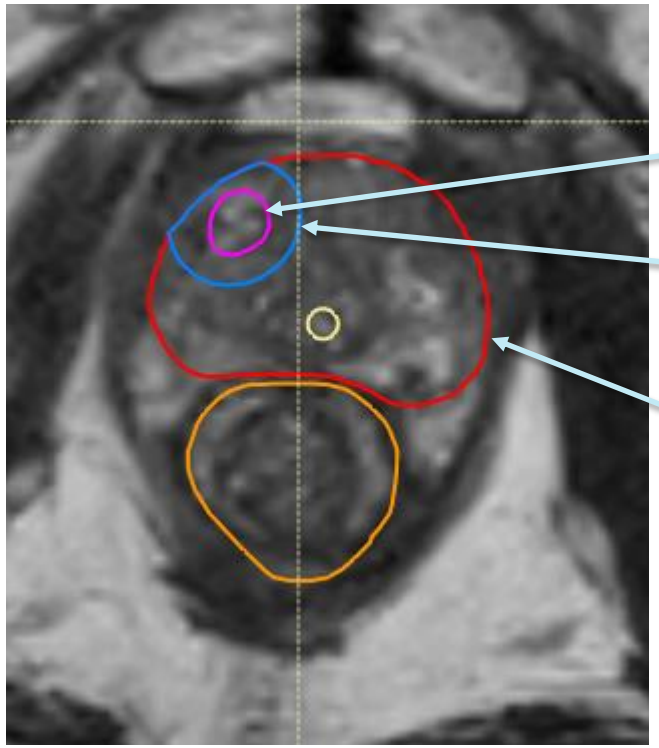
30Gy to GTV+4mm

26Gy to CTV+3mm=PTV



Group 2.
De-escalated 2 fraction SBRT

20Gy in 2 fractions over 8 days with a GTV boost to 27Gy



GTV

30Gy to GTV+4mm

20Gy to CTV=PTV

Defender for Brachytherapy

Prof. Ann Henry

Young and high BMI

- Potential for reduced second cancer risk from brachytherapy
  - Weak evidence from modelling and population studies
- Outcomes for men aged < 60 years excellent
  - BPFS expected to be 90%
- Avoids EBRT planning issues of image quality and set-up in high BMI
- BUT lesion at base and close to capsule?

Patterns of Prostate Cancer Recurrence After Brachytherapy Determined by Prostate-Specific Membrane Antigen–Positron Emission Tomography and Computed Tomography Imaging

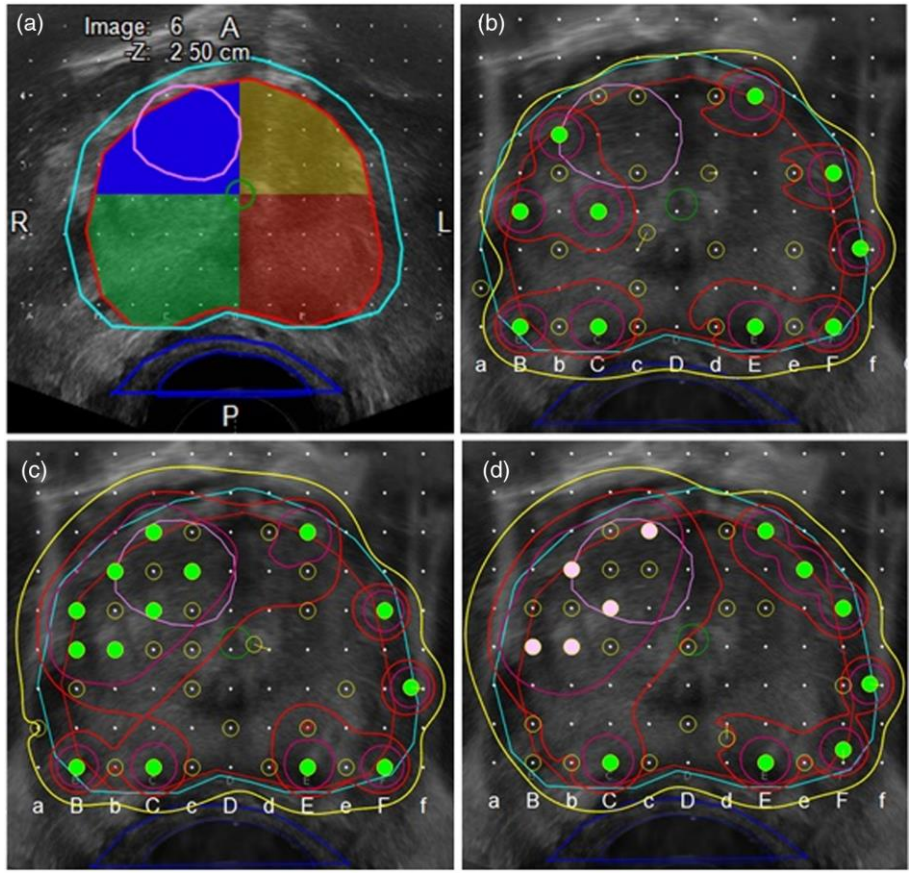
- 86 patients (median prescan PSA 6.0) with a positive PSMA
- Most common location of relapse was local;
- Isolated local recurrence was seen in 54.3% of monotherapy patients versus only in 12.5% of boost patients **(dose not in right place?)**
- Metastatic failure was seen in 28.6% of monotherapy patients versus 68.8% of the boost patients.
- Local recurrences (69.0%) were found within the same prostate biopsy sextant involved with the tumor at diagnosis, and **76.0% of patients with seminal vesicle recurrences had prostate-base involvement at diagnosis.**

Int J Radiation Oncol Biol Phys, Vol. 112, No. 5, pp. 1126−1134, 2022
https://doi.org/10.1016/j.ijrobp.2021.12.164

OPTiMAL: Optimizing the Management of High-risk and Unfavorable Intermediate-risk Disease: the Use of Advanced Imaging, Trans-perineal Mapping Biopsies, and Dual-strength Brachytherapy Sources to Minimize Radiation Dose to Normal Tissues

- Ph2 single arm multi-centre study
- Recruiting 105 participants from BCCC
- 2 year GU toxicity endpoint
- DiL boost using LDR
- Dual-strength sources

Should we be delivering smarter BT with DiL boosting?



Audience Vote Again: Case-2

Mr Philip Conford's
Final review and Judgement