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Combination Treatment: High Dose Rate Brachytherapy Boost

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Conflict of Interest Statement

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- Institutional research funding from Cancer Research UK, NIHR, MRC and Yorkshire Cancer Research
- Member of ESTRO Uro-GEC group
- Member of EAU Prostate Cancer Guidelines Group
- Deputy Editor Clinical Oncology

Overview

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- Updates on clinical trials utilizing HDR boost
- Population data from NPCA
- Update on on-going PIVOTALboost RCT

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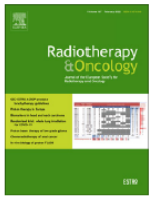
journal homepage: www.thegreenjournal.com



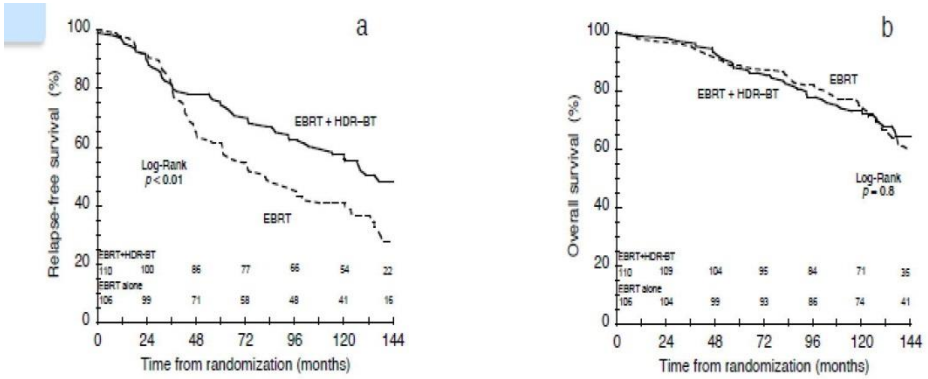
Guidelines

GEC-ESTRO ACROP prostate brachytherapy guidelines

Ann Henry [a], Bradley R. Pieters [b], Frank André Siebert [c], Peter Hoskin [d,e,*],
on behalf of the UROGEC group of GEC ESTRO with endorsement by the European Association of Urology [1]

[a] St James University Hospital, Leeds, UK; [b] Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, The Netherlands; [c] University of Kiel/University Hospital Schleswig-Holstein Campus Kiel, Germany; [d] Mount Vernon Cancer Centre, Northwood; and [e] University of Manchester, Manchester, UK

Update on MV HDR boost RCT



Randomised trial of external-beam radiotherapy alone or with high-dose-rate brachytherapy for prostate cancer: mature 12-year results. Peter J. Hoskin et al
Published:October 01,2020
DOI:https://doi.org/10.1016/j.radonc.2020.09.047

- Significant improvement in long term relapse
- No difference in OS
- No increase in late G3+ GU/GI toxicity

Criticisms – single centre with non-standard 55Gy in 20# comparator; variable use of ADT

Challenge - demonstrate impact on distant progression and prostate cancer specific survival

10 year outcomes RADAR RCT

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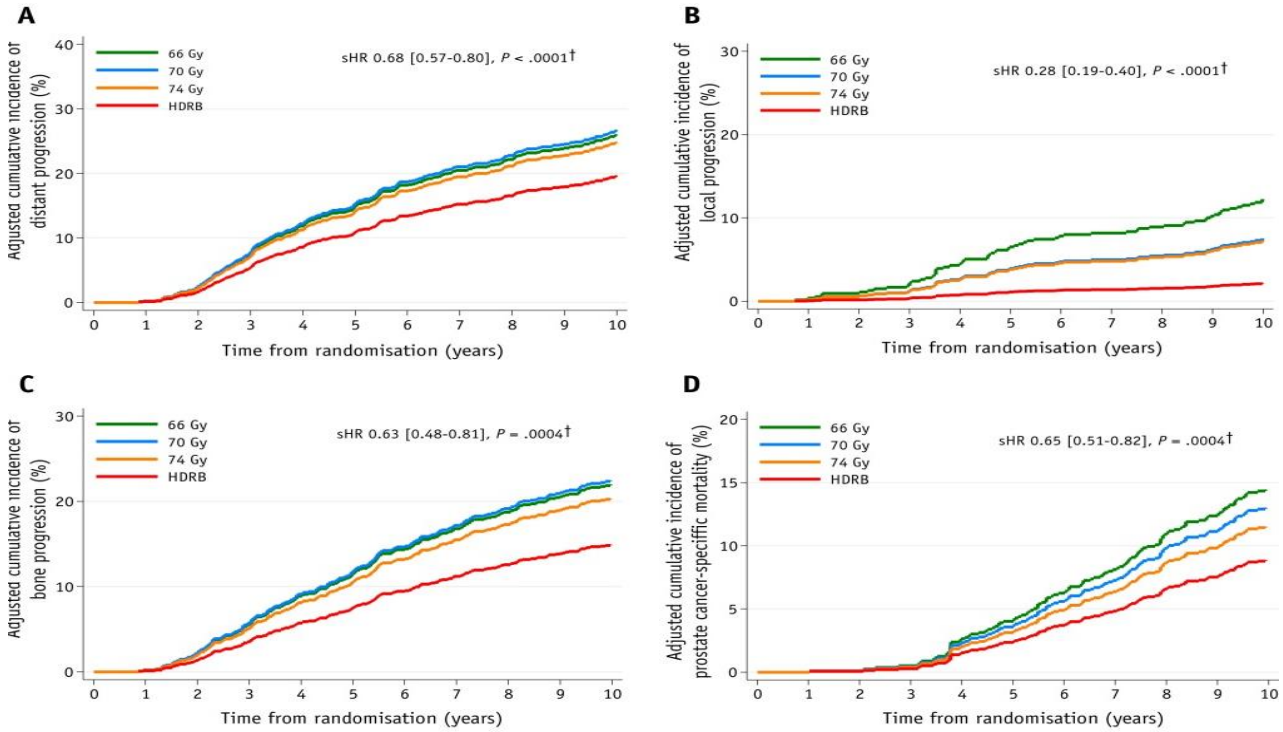

Reduced local, bone and distant progression BUT as only 4 of 23 centres had HDRBT not randomised

International Journal of Radiation Oncology, Biology, Physics 2020 106693-702DOI: (10.1016/j.ijrobp.2019.11.415)

10 year outcomes RADAR RCT

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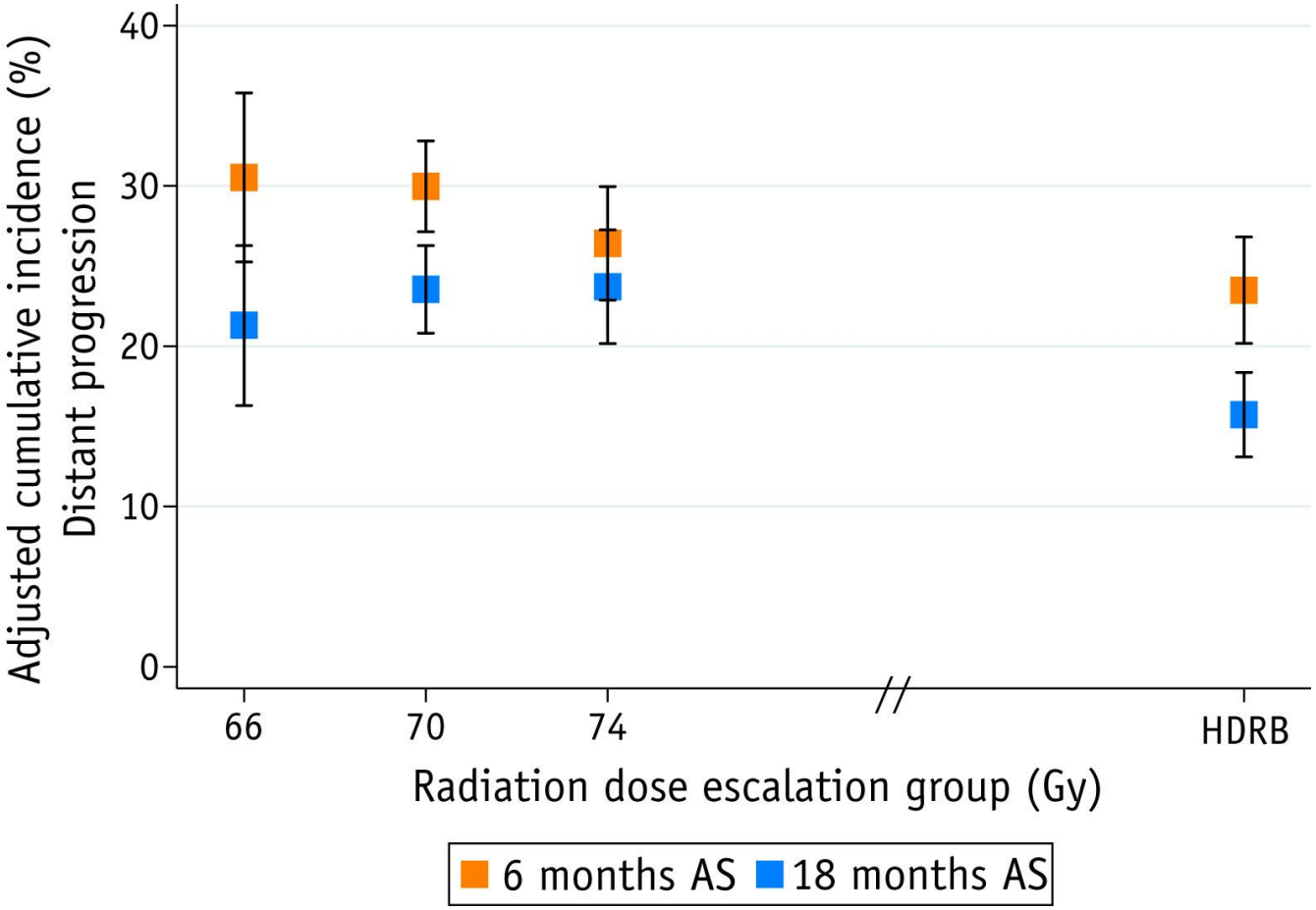

HDRB group ass with significantly less distant progression

International Journal of Radiation Oncology, Biology, Physics 2020 106693-702DOI: (10.1016/j.ijrobp.2019.11.415)

Population outcomes from NPCA

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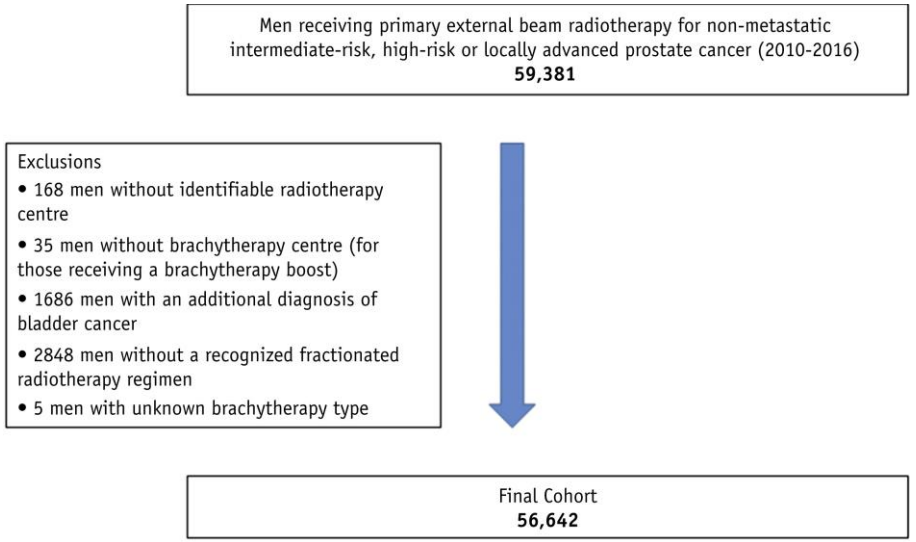
- Provides real world evidence
- Mandatory reported RT dataset combined with HES and patient survey (single time 18 months post RT)
- Median FU 4.4-4.6 years
- 2765 HDR-BT boost (5.1%)
- 330 LDR-BT boost (0.6%)
- All men treated 2010-16

Parry et al.

International Journal of Radiation Oncology, Biology, Physics

Volume 109 Issue 5 Pages 1219-1229 (April 2021)



Included fractionated regimes:

EBRT only cohort RT regimen (Gy/Fractions)	BB cohort RT regimen (Gy/Fractions)	BB cohort BT regimen (Gy)
72-79/35-49	36-39/15	< 30 (HDR)
72/32	43-47/22-25	≥ 100 (LDL)
70/35	50/28	
69/37		
50-60/16,19-20 (hypofractionated)		

Outcomes from NPCA

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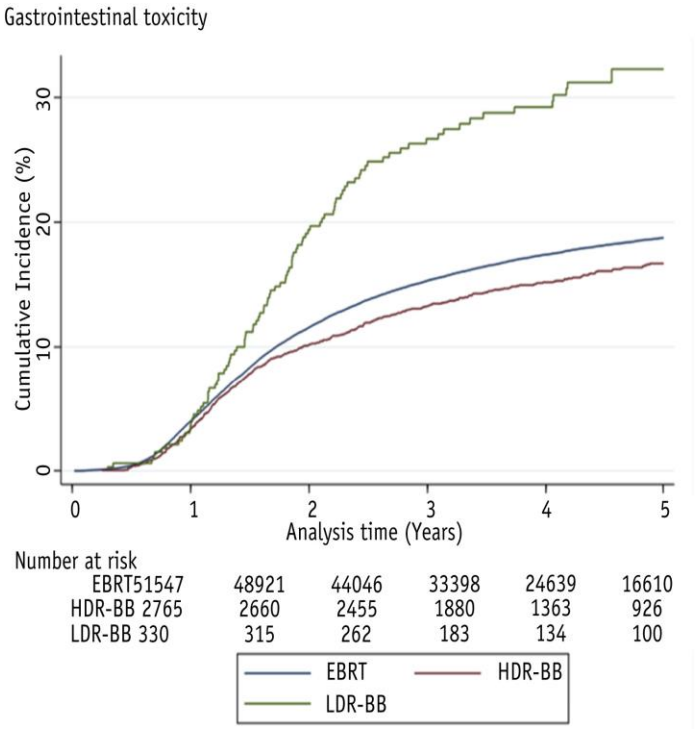

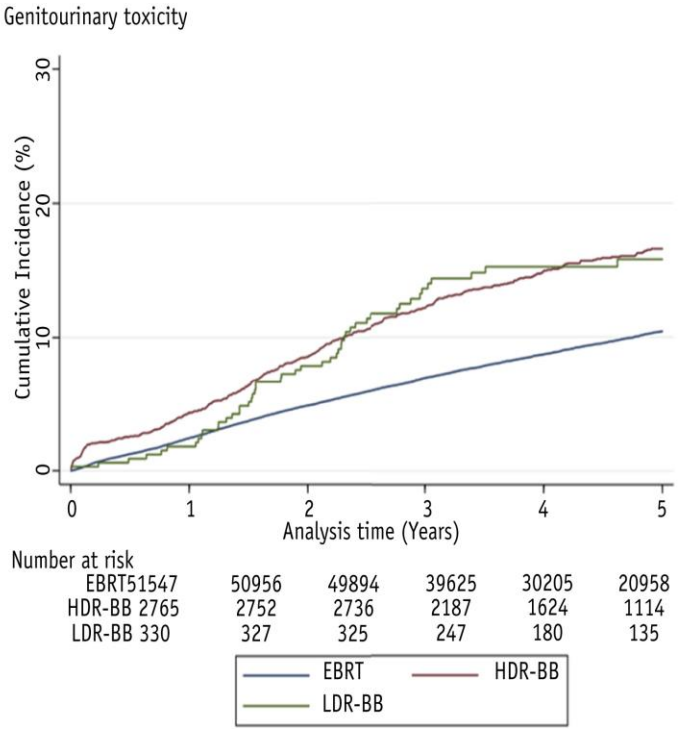

IJROBP109;5:1219-1229 (April 2021)

Outcomes from NPCA

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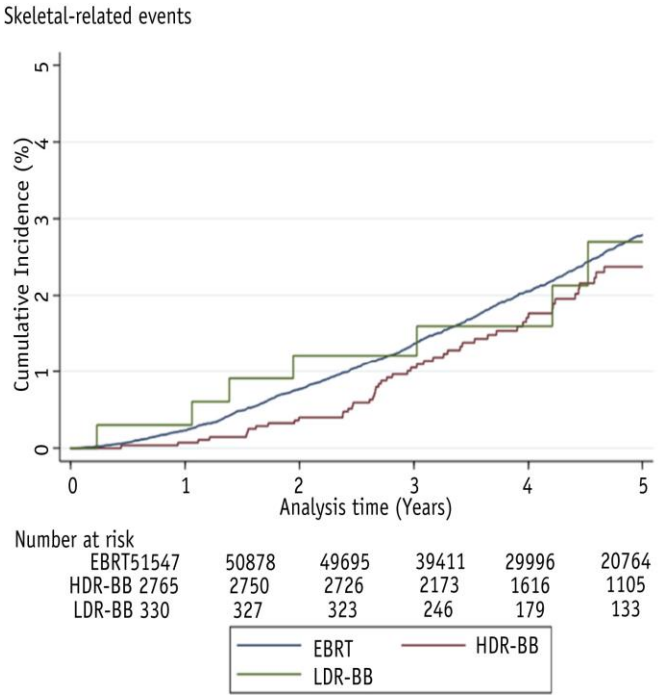

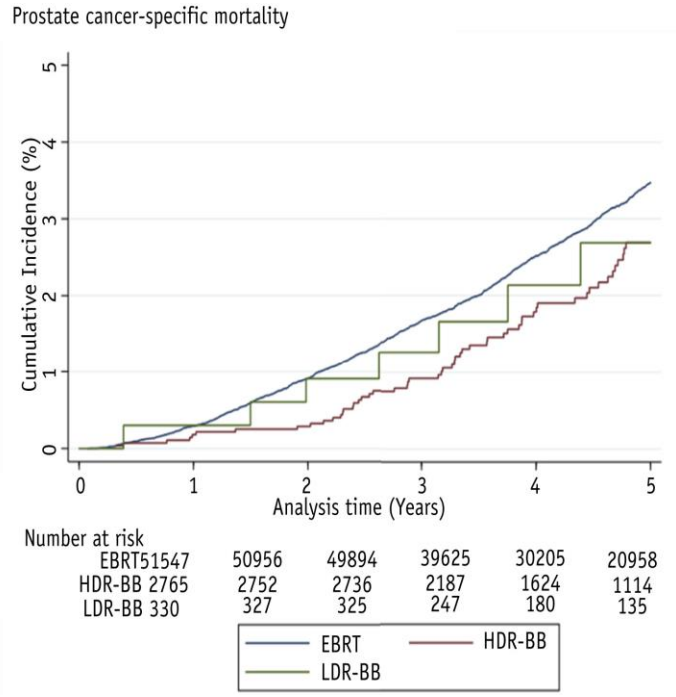

Focal boosting

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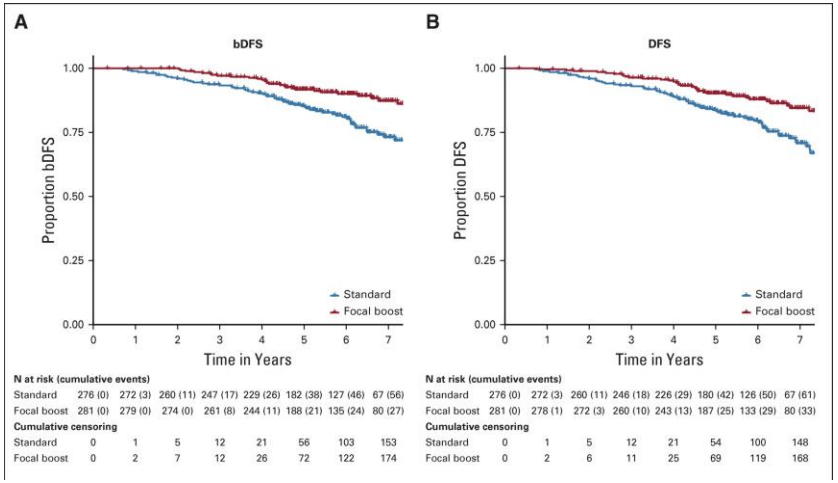
- Global dose escalation can increase toxicity
- Recurrence after RT usually at DiL
- Smarter boosting uses MR to identify and focally boost
- FLAME Ph3 RCT
  - 15% EAU intermediate risk
  - 84% EAU high risk
  - No increase in toxicity



Kaplan-Meier curves up to 7 years for (A) biochemical disease-free survival (bDFS) (P < .001), (B) disease-free survival (DFS) (P < .001), comparing the standard treatment of 77 Gy in 35 fractions to the whole prostate with an additional focal boost to the macroscopic visible tumor up to 95 Gy.

Kerkmeijer; *Journal of Clinical Oncology* 2021 39787-796.
DOI: 10.1200/JCO.20.02873

PIVOTALboost- Aim of the Study

Patients with localised prostate cancer with high risk features

- Benefit from pelvic node RT and/or
- Benefit from dose escalation (using HDR/focal boost) – **not designed to compare boosting techniques**

Primary endpoint

Failure-free survival (FFS) **Biochemical failure.**

- Recommencement of ADT.
- Local recurrence.
- Lymph node/pelvic recurrence.
- Distant metastases or death due to prostate cancer.

Secondary endpoints

- Adherence to dose constraints.
- Acute bladder and bowel toxicity at 3 months.
- Late toxicity.
- Quality of life.
- Health economic endpoints.

Boosting DiL – EBRT or HDR-BT

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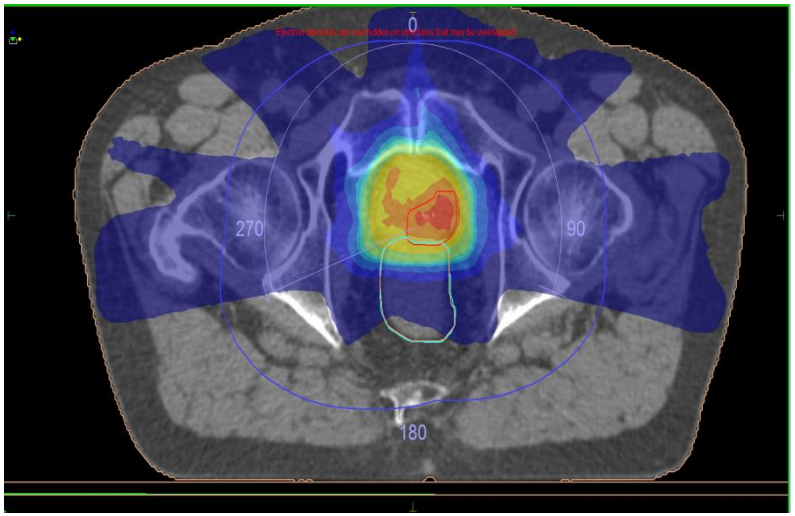
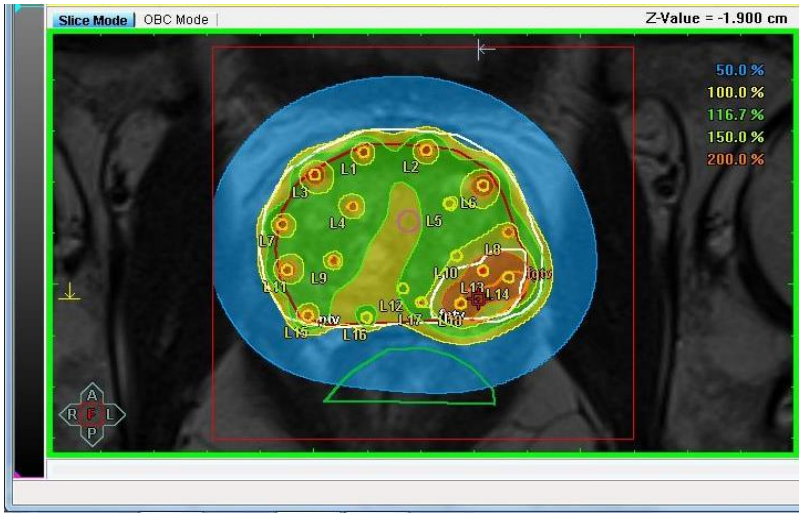




Change in the trial design

- 2-way AvB randomisation closed (recruitment target for Arm-B met)
- 4-way randomisation AvBvCvD changed to 3-way randomisation AvCvD (Arm B closed).
- Allocation ratio switch from 2:2:3:3 to 1:1:1.
- Overall recruitment target changed to 2195. The sample size has been amended as fewer arm B patients were randomised via the 4 arm option than originally expected.
- Recruitment period extended to 2024.
- PIVOTALboost participants can now also take part in the SPRUCE study within a trial for quality of life data collection.

Change to the Randomisation options

1. Check eligibility
2. Look at the staging MRI (suitable boost yes or no)

- **No boost volume:**

  Patient eligible to enter the A C1 D1 HDR whole brachytherapy

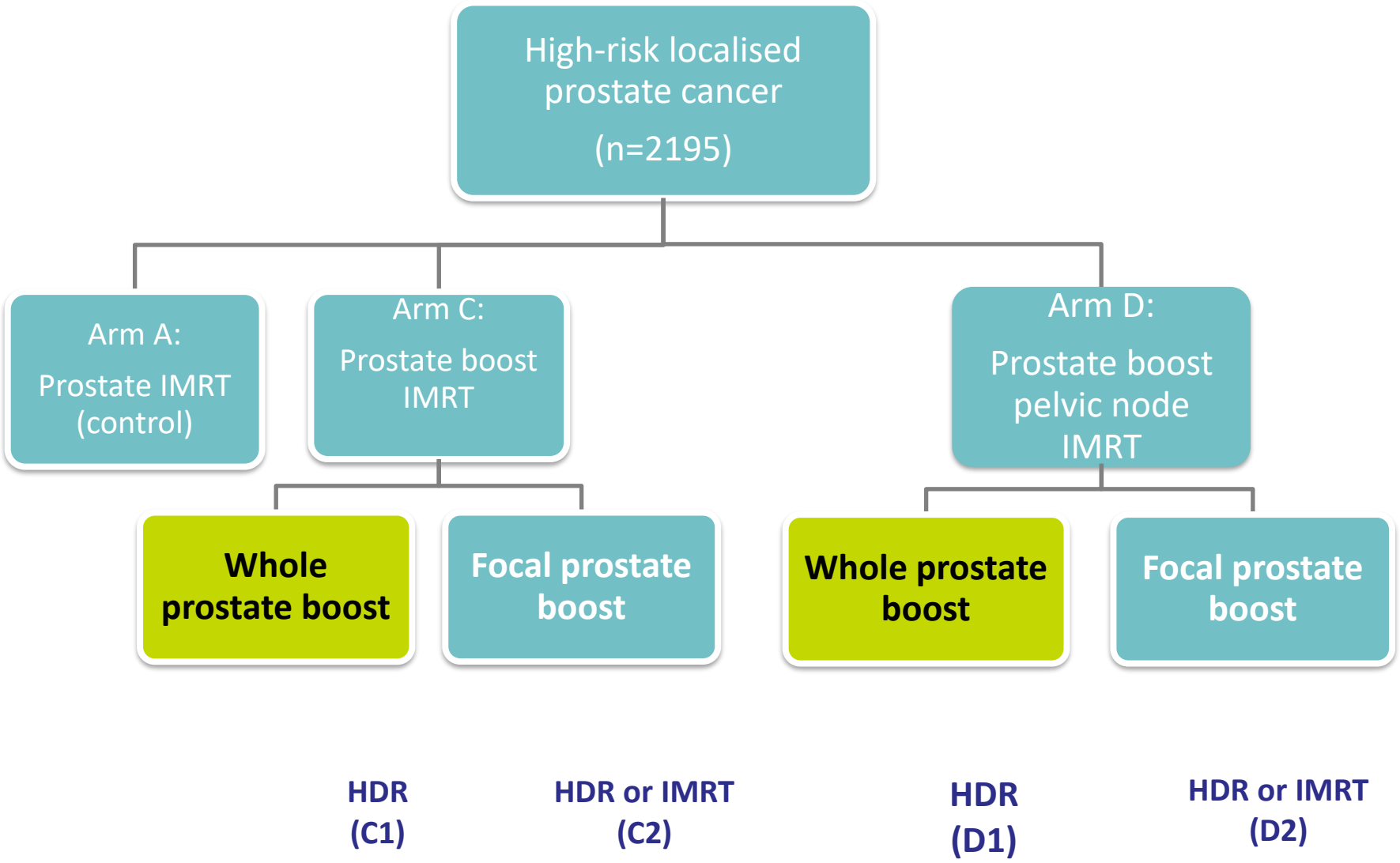
  3-arm, A vs C1 vs D1

- **Suitable Boost volume:**

  Randomisation Option : Pelvic node and focal boost (HDR or IMRT)

  3-arm, A vs C2 vs D2

New Trial Design



Selection for focal boosts

	n = 1458	
High risk group	1313	90%
A B	749	51%
Boost not available	**413**	**55%**
Boost not suitable	**336**	**45%**
A B C D		
External beam DiL boost	236	84%
HDR DiL boost	46	16%

Boost randomisations

Not available (55%)	
Planning	Benchmark cases, IGRT capacity
Planning MRI	It is possible to use the diagnostic MRI
Skill and expertise	Investigator training and support
HDR capacity	
Not suitable (45%)	
Large local tumour	HDR capacity and availability
	Since COVID more patients present with large tumours
Skill and expertise	Investigator training and support
	FLAME trial results

Impact of HDR-BT boost

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- Level 1 evidence supports improved relapse free survival > 10 years with HDR-BT boost
- Level 2 evidence supports reduced local, bone and distal progression > 10 years
- NPCA suggest in real world higher cumultative GU toxicity with improved prostate cancer mortality
- PIVOTALboost RCT exploring benefit of DiL boosting using HDR-BT – recruitment continues

Thank you – Any Questions?