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New research in prostate brachytherapy

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PIVOTAL boost opening 2017

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ICR The Institute of Cancer Research

Boost Randomisation

Eligible patient group: Patients with node-negative localised prostate cancer and:

- NCCN high risk or locally advanced disease (T3-T4, dominant Gleason 4-5, PSA>20nk/ml) , **OR**
- NCCN intermediate risk (T2a-c, Gleason 7, PSA 10-20 ng/ml) with adverse features (MTL>5mm or ≥50% biopsy cores positive)

At randomisation specify:

- Risk group, hormone duration, boost volume on MRI (none, <50% or >50%)

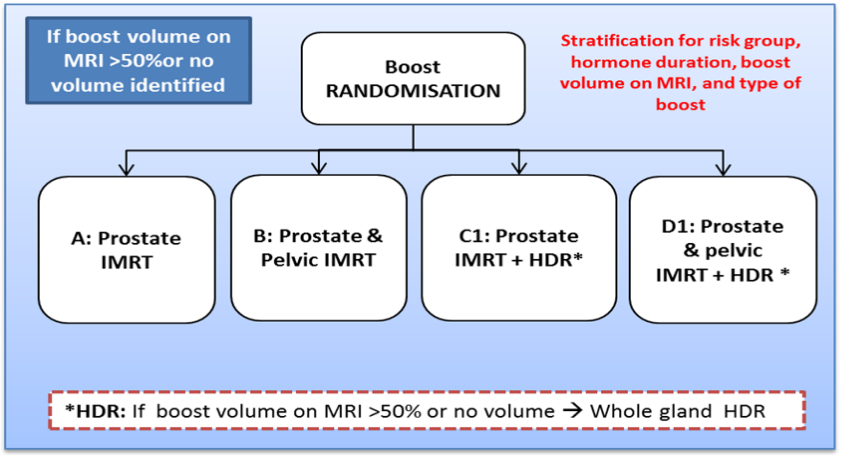
If there is, on staging MRI

- No boost volume identified or boost volume >50% of prostate volume

And

- Patient suitable for HDR brachytherapy and available

➡ **Boost Randomisation**



To evaluate

- The benefits of pelvic lymph node radiotherapy
- HDR brachytherapy in patients with no boost volumes or a boost volume >50% of the prostate
- Focal boost IMRT or focal HDR boost in patients with a boost volume on staging MRI

Functional MRI imaging to define radiotherapy randomisation.

mp MRI identifies GTV

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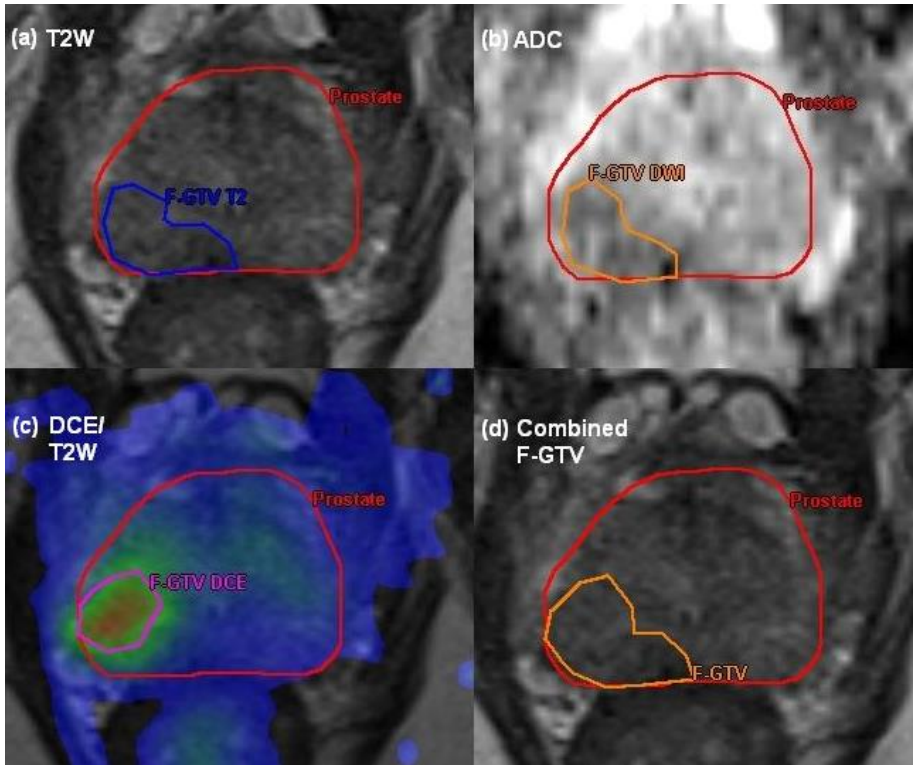

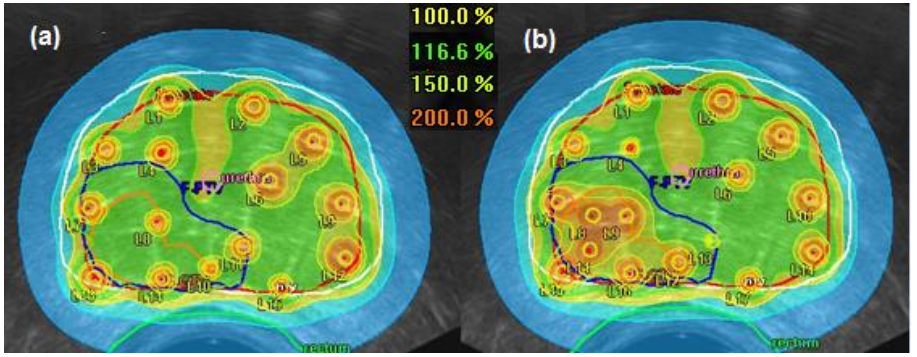

Can you give additional dose to the Focal-GTV with the aim of improving local control?

Overall Trial Schema

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PIVOTAL BOOST: A phase III trial of Prostate and pelvIs Versus prOsTate ALone with or without prostate BOOST for intermediate and high risk localised prostate cancer

Eligible patient group: Patients with node-negative localised prostate cancer and:

- NCCN high risk (T3-T4, dominant Gleason 4-5, PSA>20 ng/ml) or
- NCCN intermediate risk (T2a-c, Gleason 7, PSA 10-20 ng/ml) with adverse features (MTL>5mm or ≥50% biopsy cores positive)

Determined pre-randomisation:

- Boost volume on fMRI: none, <50% or >50%
- Intended method of dose escalated RT to prostate (HDR brachytherapy, focal boost with IMRT or HDR)

RANDOMISATION
Minimisation balancing for risk group, boost volume on MRI and type of boost

Arms depend on:

- **Availability of technique at centre**
- **Boost volume seen on fMRI**
- **Patient suitability for HDR**

A: Prostate Alone IMRT

B: Prostate & pelvic IMRT

C: Prostate boost RT

D: Prostate boost RT & pelvic IMRT

RT treatment (3-5 weeks):
Acute toxicity (RTOG) weekly during RT and week 12
Follow up:
Late toxicity and patient reported outcomes
6 monthly until year 2 and then annually for 10 years.

Primary endpoint: Biochemical (PSA) Progression Free Survival
Secondary endpoints: Local progression, metastatic relapse and overall survival, Freedom from hormone therapy, acute and late toxicity, Patient Reported Outcomes, health economic endpoints

Focal Boost Randomisation

Eligible patient group: Patients with node-negative localised prostate cancer and:

- NCCN high risk or locally advanced disease (T3-T4, dominant Gleason 4-5, PSA>20ng/ml) , **OR**
- NCCN intermediate risk (T2a-c, Gleason 7, PSA 10-20 ng/ml) with adverse features (MTL>5mm or ≥50% biopsy cores positive)

At randomisation specify:

- Risk group, hormone duration, boost volume on MRI (none, <50% or >50%)

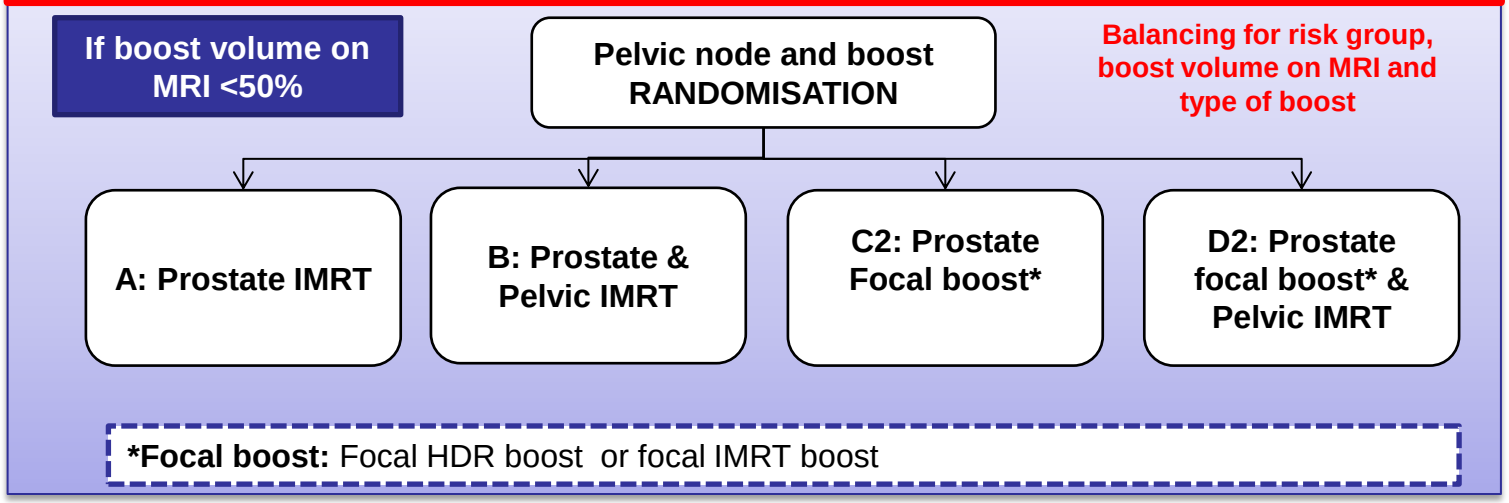
If there is, on staging MRI

- Boost volume <50% of prostate volume

And

- Focal boost IMRT or HDR available at site - *if both techniques are available at site, choose according to patient's suitability and preference*

Pelvic Node and Boost Randomisation



Sector boosting vs. F-GTV definition

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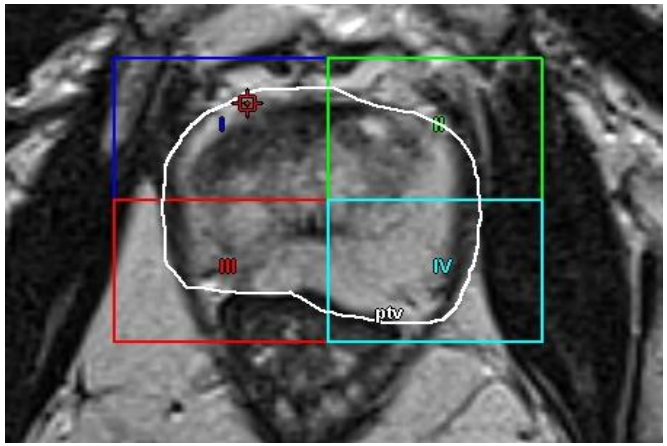
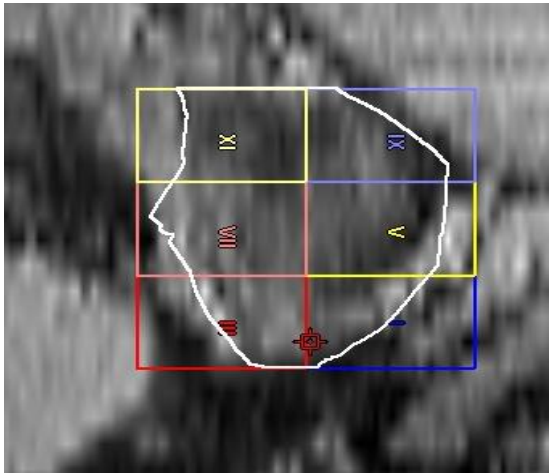
- **Problems**: Observer variability in contouring, hormone effects, needles distorting gland
- **12 prostate sectors were defined:**
  - three base, mid-gland and apex segments
  - then dividing each of these into four sectors: right anterior, left anterior, right posterior and left posterior
- Comparison of median F-GTV D90
  - in F-PTV boosted plans was 162%
  - in the sector boosted plans was 149%
  - **An acceptable compromise**





Comparison of focal boost high dose rate prostate brachytherapy optimisation methods. Mason et al. 2015 RO:117(3):521-4

Timelines

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- Ethics and HRA approvals underway
- RTTQA packs sent
- Boost contouring ideally by 26th May
- Boost contouring workshop Monday 12th June, London
  - Parallel sessions for clinicians and radiographers/physicists
  - Contact pivotalboost-icrctsu@icr.ac.uk

POWER: Hemi vs. whole gland BT

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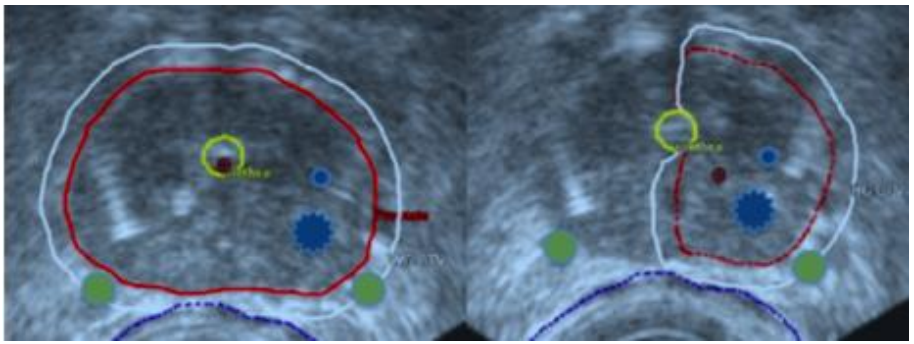
- Will partial prostate brachytherapy lead to less erectile dysfunction than whole gland BT?
- PI Bradley Pieters, Amsterdam
- UK PI Peter Hoskin
- Randomisation between hemi vs. whole gland
- Funded by Dutch Cancer Society + industry



Aims to recruit 254 patients to demonstrate a 20% improvement in cumulative 5 year sexual function with an event defined as 5 point drop in IIEF or need to use 5PDE or other meds

Entry criteria

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- Histologically adenocarcinoma on template prostate biopsies (> 20 cores)
- Unilateral tumour confirmed by both histology and mpMRI.
- Clinical stage T1c-T2b
- Gleason score 3 + 3 or Gleason score 3 + 4
- PSA ≤15 ng/ml and Gleason 7 or PSA ≤20 ng/mL and Gleason 6
- Baseline IIEF-5 score ≥12
- Sexually active by having intercourse

Treatment delivery

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- Either 144Gy I-125 or 19Gy HDR monotherapy
- GTV contoured from the midline excluding the urethra. A 3mm margin is generated for the CTV except at the anterior midline and rectum
- Non-involved hemigland should be contoured and V100 restricted to ≤ 15%