New research in prostate brachytherapy

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PIVOTAL boost opening 2017

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
- No boost volume identified or boost volume >50% of prostate volume
And
- Patient suitable for HDR brachytherapy and available

Boost Randomisation

If boost volume on MRI >50% or no volume identified

A: Prostate IMRT
B: Prostate & Pelvic IMRT
C1: Prostate IMRT + HDR
D1: Prostate & pelvic IMRT + HDR

Stratification for risk group, hormone duration, boost volume on MRI, and type of boost

*HDR: If boost volume on MRI >50% or no volume → Whole gland HDR

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.
Can you give additional dose to the Focal-GTV with the aim of improving local control?
PIVOTAL BOOST: A phase III trial of Prostate and pelvic Versus prostate ALone with or without prostate BOOST for intermediate and high risk localised prostate cancer

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- 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

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:
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- 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
- 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

If boost volume on MRI <50%
- A: Prostate IMRT
- B: Prostate & Pelvic IMRT
- C2: Prostate Focal boost*
- D2: Prostate focal boost* & Pelvic IMRT

*Focal boost: Focal HDR boost or focal IMRT boost
Sector boosting vs. F-GTV definition

- **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

- 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

- 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

- 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

- 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%