

MRI-Guided Focal Boost in Prostate Cancer Radiotherapy

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Background & Rationale

Prostate cancer is a major cause of morbidity and mortality. Radiotherapy is central to treatment, and while dose escalation improves control, it is limited by toxicity to nearby organs. mpMRI identifies dominant intraprostatic lesions (DILs), the main sites of recurrence, but conventional radiotherapy treats the prostate uniformly, risking underdosing of aggressive areas.

MRI-guided focal boost enables targeted dose escalation to DILs while sparing normal tissue, improving biochemical control without added toxicity (as shown in the FLAME trial). It is emerging as a standard approach, though prospective real-world data on outcomes and feasibility are still needed.

Aim

To evaluate toxicity, disease control, and patient-reported outcomes of MRI-guided focal boost radiotherapy.

Objective

To determine

1. FFBE of MRI-based focal boost in high-risk and node-positive prostate cancer
2. Acute and late genito-urinary and gastrointestinal toxicities
3. Acute and long-term patient-reported outcomes
4. Interobserver variability of focal boost segmentation
5. Concordance of PSMA-PET based boost with MRI based boost

To make a planned comparison FFBE, toxicity and patient reported outcomes of MRI-based focal boost with a historical cohort of moderate and ultra-hypofractionated radiotherapy.

Study Design: Single-arm, prospective observational study

Population:

Inclusion criteria:

1. Age: above 18 years.
2. Participants must be histologically proven adenocarcinoma prostate
3. High-risk localized prostate cancer as per NCCN risk criteria (cT3/T4 or Gleason 8-10 or PSA > 20 ng/ml) or Prostate cancer with metastases confined to pelvic lymph nodes (cN1) on mpMRI and PSMA PET-CT scan

4. No contraindications for long-term hormone therapy/ orchidectomy
5. Karnofsky Performance Score >70 (Appendix 1)

Exclusion criteria:

1. Patients in whom a pelvic MRI is contraindicated.
2. Prior history of radiotherapy to the pelvis or prostatectomy.
3. Severe urinary symptoms or a high IPSS score > 15 which in the opinion of the physician, precludes RT
4. Patients with known obstructive symptoms with stricture.
5. Any contraindication to radiotherapy, such as severe inflammatory bowel disease.
6. Unable to report for regular follow up

Radiotherapy Techniques

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Moderate hypofractionated RT,

Will receive a total dose of 62 Gy in 20# to the entire prostate and seminal vesicles over 4 weeks, with treatment being delivered daily. Elective nodal regions will receive a dose of 44 Gy in 20# to the pelvic nodes. **A focal boost of up to 77Gy in 20 fractions** as a simultaneous integrated boost (SIB) will be delivered. Boost to gross nodal disease will be considered based on the response to hormonal therapy to a dose of 54-60 Gy/20Fr# as SIB.

Extreme hypofractionation with SBRT,

Will receive a total dose of 36.25Gy in 5# to the entire prostate and seminal vesicles over 5 weeks, with treatment being delivered once a week. Elective nodal regions will receive a dose of 25 Gy in 5# to the pelvic nodes. **A focal boost of up to 42 Gy in 5 fractions** as a simultaneous integrated boost (SIB) will be delivered. Boost to gross nodal disease will be considered based on the response to hormonal therapy to a dose of 32-35Gy/5Fr# as SIB.

Target recruitment: A Bayesian analysis will be performed. The minimum required sample size under the primary scenario is 95 evaluable patients, corresponding to 105 recruited after 10% attrition. The study will target recruitment of N = 122 patients over three years, with a ceiling of N = 130.

Primary endpoint: To assess the 5 year Freedom from Biochemical Failure (FFBF)

Secondary endpoint:

1. To evaluate acute and late toxicity with both treatments.
2. To find Prostate cancer specific survival and overall survival of patients receiving focal boost to the DIL
3. To assess quality of life
4. To compare outcomes, toxicities and patient-reported outcomes of this cohort with a historical prospective randomized cohort of patients treated with moderate and ultra-hypofractionated radiotherapy without focal boost in the PRIME trial

5. To determine inter-observer variability in delineation of boost volume in urethra

Tertiary endpoint: To determine the accuracy of an autosegmentation model for MRI based intraprostatic lesion segmentation.

Follow-up:

- All patients will follow up 3-6 weeks from end of radiotherapy, followed by 3-6 monthly for the first two years depending on the clinical need and 6 monthly thereafter. At baseline and every follow-up data will be collected and recorded in CRF
- Physician assessment of toxicity with RTOG toxicity criteria and CTCAE ver 6.0 criteria for proctitis, rectal pain, rectal bleeding and urinary complaints at baseline and follow up.
- Physician assessment during and end of RT with scoring of toxicity and IPSS scoring
- Physician assessment with clinical examination and serum PSA.
- QOL will be assessed at baseline and 6 monthly using the QLQC30 and PR25 EORTC Questionnaire.