Study Protocol

Cover Page

Official Title: Stereotactic Body Radiotherapy Boost Versus Simultaneous Integrated Boost to Pelvic Nodes Among Patients Receiving Radical Chemoradiation in Carcinoma Cervix

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ClinicalTrials.gov Identifier (NCT Number): *not yet assigned*

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Protocol Summary

This is a prospective, open-label, non-randomized comparative interventional study in patients with stage IIIC carcinoma of the cervix receiving radical chemoradiation. The study compares two nodal boost approaches: stereotactic body radiotherapy (SBRT) boost versus simultaneous integrated boost (SIB) to involved pelvic lymph nodes, with the primary objective of comparing acute grade 3 or higher gastrointestinal and genitourinary toxicity within 30 days of treatment completion.

Background and Rationale

Stage IIIC carcinoma cervix with radiologically involved pelvic lymph nodes is commonly treated with radical chemoradiation, but dose escalation to nodal disease can increase toxicity to nearby organs such as bowel, bladder, rectum, and sigmoid colon. The protocol evaluates whether an SBRT nodal boost can provide a safer alternative to conventional SIB while maintaining nodal treatment intensification.

Objectives

Primary Objective

To compare the safety profile of SBRT boost versus SIB to involved pelvic nodes by assessing the incidence of grade 3 or higher acute gastrointestinal and genitourinary toxicity, measured within 30 days of completion of treatment using CTCAE version 5.0.

Secondary Objectives

To compare the safety profile of SBRT boost versus SIB to involved pelvic nodes by assessing the incidence of grade 3 or higher acute gastrointestinal and genitourinary toxicity, measured at 6 months of completion of treatment using CTCAE version 5.0.

Study Design

This is a single-center, prospective, open-label, non-randomized comparative study conducted at the National Cancer Institute, AIIMS, New Delhi. Patients with stage IIIC cervical cancer meeting eligibility criteria will be assigned to one of two treatment groups according to the study plan and institutional workflow rather than random allocation.

The study includes two active treatment groups:

- **Group 1:** SBRT boost to involved pelvic lymph node(s) in addition to standard pelvic chemoradiation.

- **Group 2:** Conventional SIB to involved pelvic lymph node(s) during standard pelvic chemoradiation. Planned enrollment is 150 participants, with 75 patients in each group.

- **Eligibility Criteria**

Inclusion Criteria

- Female patients aged 18 to 65 years with stage IIIC carcinoma cervix.
- Pathologically confirmed squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the cervix.
- No prior pelvic radiotherapy or definitive pelvic surgery.
- ECOG performance status 0 to 2.
- Pelvic nodal burden less than 3 cm or less than 30 cc, with up to 4 lymph nodes, and eligible for radical chemoradiation.
- Adequate hepatic, renal, and cardiac function, and written informed consent.

Exclusion Criteria

- Stage I, stage II, or stage IV disease.
- Prior malignancy, active autoimmune disease, or uncontrolled medical comorbidity.
- Melanoma, small cell carcinoma, or basal cell carcinoma histology.
- Previous pelvic radiotherapy, hysterectomy, other prior oncologic treatment, or contraindication to contrast-enhanced MRI or brachytherapy.

Interventions

Group 1: SBRT Boost Arm

Participants will receive pelvic external beam radiotherapy to 45 Gy in 25 fractions with concurrent weekly cisplatin, followed by an SBRT boost of 14 Gy in 2 fractions to involved pelvic lymph node(s), typically delivered during the first and second weeks of treatment. Brachytherapy will then be delivered as per institutional protocol.

Group 2: SIB Arm

Participants will receive pelvic external beam radiotherapy to 45 Gy in 25 fractions with a simultaneous integrated boost to involved pelvic lymph node(s) to a total dose of 55 Gy or 57.5 Gy in 25 fractions, along with concurrent weekly cisplatin, followed by brachytherapy as per institutional protocol.

Treatment Procedures

Radiotherapy planning includes immobilization in the supine position with an abdominopelvic thermoplastic shell, contrast-enhanced planning CT, and fusion with pelvic MRI and PET-CT where available. Contouring follows EMBRACE II principles, and organ-at-risk constraints are predefined for bowel bag, sigmoid, bladder, rectum, spinal cord, femoral heads, kidneys, duodenum, and active bone marrow.

Concurrent chemotherapy consists of weekly cisplatin 40 mg/m² for up to 5 cycles, subject to adequate renal function and treatment tolerance. Brachytherapy will be delivered using intracavitary or interstitial technique, with 7 Gy per fraction for 4 fractions and target/OAR constraints according to the institutional curative protocol.

Outcome Measure

- **Primary outcome:** Grade 3 or higher acute GI/GU toxicity within 30 days of treatment completion.
- **Secondary outcome:** Grade 3 or higher late GI/GU toxicity at 6 months.
- **Secondary outcome:** Dosimetric comparison of organs at risk during treatment planning.
- **"Secondary outcome**: Local control or radiologic response at 3 months or 6 months.

Statistical Analysis

The incidence of grade 3 or higher treatment-related adverse events will be summarized as percentages with 95% confidence intervals and compared between groups using chi-square testing. Dosimetric variables will be compared using t-test or Wilcoxon rank-sum testing, and local control analyses will use Kaplan-Meier methods, log-rank testing, and Cox regression adjusting for covariates.

Ethics and Oversight

The study has Institute Ethics Committee approval, with approval number AIIMSA1645/09.07.2024, RP-17/20. The board is the Institute Ethics Committee, All India Institute of Medical Sciences, and the current registration record lists the study as active, not recruiting.