

NSABP B-39/RTOG 0413: A Randomized Phase III Study of Conventional Whole Breast Irradiation (WBI) Versus Partial Breast Irradiation (PBI) for Women with Stage 0, I, or II Breast Cancer

FAST FACTS

ELIGIBILITY CRITERIA

1. Patients must have stage 0, I, or II Breast Cancer. If stage II, tumor size must be 3 cm or less. See section 19.1 for information regarding accrual closure to low-risk patient populations.
2. Patients must be ≥ 18 years old.
3. Patient should have a life expectancy of at least ten years, excluding her diagnosis of breast cancer.
4. Surgical treatment of the breast must have been a lumpectomy and **must have been performed prior to study entry**. The margins of the resected specimen must be histologically free of tumor (DCIS and invasive)
5. Women with **invasive** breast cancer are required to have axillary staging which can include sentinel biopsy alone (If sentinel node is negative), sentinel node
6. Biopsy followed by axillary dissection or sampling with a minimum total of 6 axillary nodes (if sentinel node is positive), or axillary dissection alone (with a minimum of 6 axillary nodes). For a woman to be eligible, she can have no more than 3 axillary nodes that are histologically positive. Axillary staging is not required for patients with DCIS.
7. Target lumpectomy cavity must be clearly delineated and the target lumpectomy cavity/whole breast reference volume must be $\leq 30\%$ based on the postoperative/pre-randomization CT scan.
8. Women must be registered to the study within 42 days following the last surgery for breast cancer (lumpectomy, re-excision of margins, or axillary staging procedure).
9. Patients must have an estrogen receptor (ER) analysis performed on the primary tumor prior to randomization. If ER analysis is negative, then progesterone receptor (PgR) analysis must be performed. If ER analysis is positive, PgR analysis is desired but not mandatory. (Marginal or borderline results [i.e., those not definitively negative] will be considered positive regardless of the methodology used) See section 19.1 for information regarding accrual closure to low-risk patient populations.
10. Patients are eligible if, based on the postoperative/pre-randomization CT scan, PBI is judged to be technically deliverable by a technique for which the radiation oncology facility has been credentialed.
11. At time of randomization, patients must have had an H&P within 4 months and a bilateral mammogram within 6 months.
12. Patients with a history of *non-breast* malignancies are eligible if they have been disease-free for 5 or more years prior to randomization and are deemed by their physician to be at low risk for recurrence. Patients with the following cancers are eligible if diagnosed and treated within the past 5 years: carcinoma in situ of the cervix, carcinoma in situ of the colon, melanoma in situ, and basal cell and squamous cell carcinoma of the skin

INELIGIBILITY CRITERIA

1. Men are not eligible for this study.
2. T₂ (> 3.0 cm), T₃, Stage III, or Stage IV Breast Cancer (See appendix A for TNM nomenclature and staging).
3. More than 3 histologically positive axillary nodes
4. Axillary nodes with definite evidence of microscopic or macroscopic extracapsular extension.
5. One of more positive **non-axillary** sentinel node(s). (Intramammary nodes are staged as axillary nodes).
6. Palpable or radiographically suspicious ipsilateral or contralateral axillary, supraclavicular, infraclavicular, or internal mammary nodes, unless there is histologic confirmation that these nodes are negative for tumor.
7. **Suspicious** microcalcifications, densities, or palpable abnormalities (in the ipsilateral or contralateral breast) unless biopsied and found to be benign.
8. Non-epithelial breast malignancies such as sarcoma or lymphoma.

9. Proven multicentric carcinoma (invasive cancer of DCIS) is more than one quadrant or separated by 4 or more centimeters.
10. Paget's disease of the nipple
11. Synchronous bilateral invasive or non-invasive breast cancer
12. History of invasive breast cancer or DCIS. (Patients with a histo of LCIS treated by surgery alone are eligible)
13. Surgical margins that cannot be microscopically assessed or are positive at pathologic evaluation. (If surgical margins are rendered free of disease by re-excision, the patient is eligible).
14. Clear delineation of the extent of the target lumpectomy cavity not possible.
15. Treatment plan that includes regional node irradiation.
16. Any treatment with radiation therapy, chemotherapy, biotherapy, and/or hormonal therapy administered for the currently diagnosed breast cancer prior to randomization. The only exception is hormonal therapy, which may have been given for no more than a total of 28 days anytime after diagnosis and before randomization. For patients who will be receiving chemotherapy, hormonal therapy must stop at or before randomization and resume following completion of chemotherapy. For patients who will not be receiving chemotherapy, hormonal therapy may continue.
17. Current therapy with any hormonal agents such as Raloxifene (Evista[®]), Tamoxifen, or other selective estrogen receptor modulators (SERMS), either for osteoporosis of breast cancer prevention. (Patients are eligible only if these medications are discontinued prior to randomization)
18. Breast implants (Patients who have had implants removed are eligible).
19. Prior breast or thoracic RT for any condition.
20. Collagen vascular disease, specifically dermatomyositis with a CPK level above normal or with an active skin rash, systemic lupus erythematosus, or scleroderma.
21. Pregnancy or lactation at the time of proposed randomization. Women of reproductive potential must agree to use an effective non-hormonal method of contraception during therapy.
22. Psychiatric or addictive disorders or other conditions that, in the opinion of the investigator, would preclude the patient from meeting the study requirements.

PRE-STUDY PARAMETERS

1. History & physical – Within 4 months prior to randomization
2. Wt; Breast assessment/exam; Bra cup size - postop
3. Menopausal status – See appendix B
4. CBC/Platelets; Alkaline phosphatase; AST or ALT– May be preoperative or postoperative
5. Pregnancy Test – Within 2 weeks prior to randomization for women of childbearing potential
6. Chest CT or x-ray; Abdominal CT (in the presences of hepatomegaly or alkaline phosphatase, AST/ALT, or bilirubin > ULN for the lab); bone scan (if alkaline phosphatase is elevated and/or patient c/o pain or other symptoms suggestive of skeletal metastasis)
7. Serum Collection – For patients who have agreed to serum banking, *after randomization but before therapy begins*; and at time of first breast cancer recurrence
8. Tissue blocks/slides – For patients who have agreed to tissue submission, blocks and slides are required; submit within 3 months following randomization
9. Evaluation by Radiation Oncologist
10. Ipsilateral breast CT (postoperative assessment; CT should be performed within 14 days following surgery; however, any time following surgery and before entry is acceptable)
11. Bilateral Mammogram (within 6 months prior to randomization)
12. QOL Questionnaire
13. MD-Reported Cosmesis (A radiation oncologist should complete these reports. If this is not possible, the patient's surgeon may complete the reports. Every effort should be made to have these assessments performed y the same physician all three time pointes)
14. Digital Images (Breast Photos) – Photographs may also be taken after randomization but before any adjuvant treatment begins.

Treatment Plan on Following Page

TREATMENT PLAN

| | Radiation Therapy Group 1 – Whole Breast Irradiation WBI | Radiation Therapy Group 2 – Partial Breast Irradiation PBI*** |
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| Radiation Therapy | Whole Breast Irradiation* | PBI Techniques 34 Gy in 3.4 Gy fractions using multi-catheter brachytherapy or 34 Gy in 3.4 Gy fractions using MammoSite® balloon catheter or 38.5 Gy in 3.85 Gy fractions using 3D conformal external beam radiation For all PBI techniques: RT given to tissue surrounding lumpectomy cavity only, BID 9 with a fraction separation of at least 6 hours), for a total of 10 treatments given on 5 days over a period of 5 to 10 days |
| Dose | 50 Gy (2.0 Gy/fraction) or 50.4 Gy (1.8 Gy/fraction) to whole breast, followed by optional boost** to 60.0 Gy-66.6 Gy | |
| Start Date | Within 3 weeks of study entry | Within 9 weeks following lumpectomy or re-excision of margins and within 3 weeks of study entry |
| Duration | 5 days per week for 5 to 7 weeks | 10 treatments given on 5 days over a period of 5 to 10 days |
| Timing with Chemotherapy (if given) | WBI will follow chemotherapy | Chemotherapy will follow PBI |

* See Protocol Section 15.0 for instructions regarding chemotherapy and hormonal therapy. Chemotherapy, if given, will be administered before WBI and following PBI.

** Brachytherapy boost is not allowed . See Section 11.1.4

*** The PBI technique utilized will be at the physician's discretion and will be based on technical considerations, radiation oncology facility credentialing (See section 5.0) as well as patient preference.