RT CHARM: Phase III Randomized Trial of Hypofractionated Post Mastectomy Radiation with Breast Reconstruction

Eligibility Criteria (see Section 3.2)
Histologically confirmed invasive carcinoma of the breast. (See §3.2.1)
Pathologic stage T0N1-2a, T1N1-2a, T2N1-2a, T3N0-2a, all M0 status. (See §3.2.2)
No prior radiation therapy to the chest, neck or axilla.
No prior history of ipsilateral breast cancer (invasive disease or DCIS). (See Section 3.2.4)
No history of prior or concurrent contralateral invasive breast cancer. (See §3.2.5)
No active collagen vascular diseases, such as: systemic lupus erythematosus, scleroderma, or dermatomyositis.
Negative inked histologic margins from mastectomy pathology. (See §3.2.7)
No significant post mastectomy complications requiring an unplanned re-operation, or admission for IV antibiotics. (See 3.2.8)
Intent to meet dose constraints. (See §3.2.9)
Radiation oncologist is planning to treat regional lymph nodes including internal mammary nodes.
Radiation oncologist is NOT planning to utilize a chest wall/scar boost.
Patient has undergone breast reconstruction or is planning to undergo reconstruction.
If using tissue expander, no air expander, only fluid filled expanders (See §3.2.13)
For patients with diabetes, hemoglobin A1C test must have been performed ≤ 90 days prior to registration.
No co-existing medical conditions with life expectancy < 5 years.
No other malignancy within 5 years of registration with exception of basal cell or squamous cell carcinoma of the skin. (See §3.2.16)
Negative serum or urine β-HCG in women of child-bearing potential ≤ 7 days prior to registration (See §3.2.17)
Women of child-bearing potential must agree to utilize a form of birth control or agree to undergo sexual abstinence during radiation therapy.
ECOG (Zubrod) Performance Status 0-1
Patient ≥ 18 years of age

Schema

Mastectomy with nodal evaluation/dissection +/- adjuvant chemotherapy with planned breast reconstruction

Conventional PMRT: 50Gy/2Gy Chest wall and/or reconstructed breast with 50Gy/2Gy to regional nodes* over 5-6 weeks.

Hypofractionated PMRT: 42.56Gy/2.66Gy to Chest wall and/or reconstructed breast with 42.56Gy/2.66Gy to regional nodes* over 3-4 weeks.

* Regional Nodes will include axilla (Levels I, II, III), supraclavicular fossa and internal mammary nodes. If an axillary dissection has been performed, RT will only be directed to the un-dissected axilla.

** Patients will be stratified before randomization for immediate versus delayed and autologous versus implant only reconstruction. All reconstruction must be completed before radiation to be classified as immediate and autologous reconstruction is autologous tissue +/- implant.

All patients will undergo reconstruction of the breast; either before or after radiation, but it must be completed within 18 months after finishing radiation therapy, unless medically contraindicated.
Patients will be followed until 15 years after completion of radiation therapy or until death, whichever comes first.

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.

There is no surgical credentialing required for participation on this study.
Radiation therapy requires credentialing and submission of patient plans for review. See Sections 7.5 and 14.0 for more detail.

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3.0 PATIENT SELECTION

For questions regarding eligibility criteria, see the Study Resources page. Please note that the Study Chair cannot grant waivers to eligibility requirements.

3.1 On-Study Guidelines

This clinical trial can fulfill its objectives only if patients appropriate for this trial are enrolled. All relevant medical and other considerations should be taken into account when deciding whether this protocol is appropriate for a particular patient. Physicians should consider the risks and benefits of any therapy, and therefore only enroll patients for whom this treatment is appropriate.

Physicians should consider whether any of the following may render the patient inappropriate for this protocol:

- Psychiatric illness which would prevent the patient from giving informed consent.
- Medical condition such as uncontrolled infection (including HIV), uncontrolled diabetes mellitus or cardiac disease which, in the opinion of the treating physician, would make this protocol unreasonably hazardous for the patient.
- Women of reproductive potential should agree to use an appropriate method of birth control throughout their participation in this study due to the teratogenic potential of the therapy utilized in this trial. Appropriate methods of birth control include abstinence, oral contraceptives, implantable hormonal contraceptives or double barrier method (diaphragm plus condom).

3.2 Eligibility Criteria

Use the spaces provided to confirm a patient’s eligibility by indicating Yes or No as appropriate. It is not required to complete or submit the following page(s).

When calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test were done on a Monday, the Monday one week later would be considered Day 7.

3.2.1 Histologically confirmed invasive carcinoma of the breast of any of the following histologies (ductal, lobular, mammary, medullary, or tubular). In-situ disease alone is not allowed.

3.2.2 Patients will be staged according to the TNM staging system. Pathologic stage T0N1-2a, T1N1-2a, T2N1-2a, T3N0-2a, all M0 status. Pathological stage for all patients not receiving neoadjuvant chemotherapy. Higher of the clinical or pathological T and N stage, if receiving neoadjuvant chemotherapy. Patients with pathological N0 at the time of mastectomy are only eligible if biopsy-proven clinically N1 or N2 disease is documented prior to induction chemotherapy.

Note: All patients with clinical, radiographic or pathological T4, N3 or involved internal mammary disease (N1b, N1c, and N2b) will not be eligible to enroll.

3.2.3 No prior radiation therapy to the chest, neck or axilla.

3.2.4 No prior history of ipsilateral breast cancer (invasive disease or DCIS). LCIS and benign breast disease is allowed.

3.2.5 No history of prior or concurrent contralateral invasive breast cancer. Benign breast disease, LCIS or DCIS of contralateral breast is allowed.

3.2.6 No active collagen vascular diseases, such as: systemic lupus erythematosus, scleroderma, or dermatomyositis.
3.2.7 Negative inked histologic margins from mastectomy pathology (no invasive cells at margin).

3.2.8 No significant post mastectomy complications in the ipsilateral breast requiring an unplanned re-operation or admission for IV antibiotics. Re-operation for margins evaluation, nodal completion and routine reconstruction is acceptable.

3.2.9 Radiation oncologist intends to treat all target volumes described in section 7.4 and respect all normal tissues identified in section 7.4.3 in accordance with the dosimetric constraints described (simulation before registration recommended).

3.2.10 Radiation oncologist is planning to treat regional lymph nodes including internal mammary nodes and meet acceptable protocol dosimetric requirements.

3.2.11 Radiation oncologist is NOT planning to utilize a chest wall/scar boost.

3.2.12 Patient must have undergone immediate reconstruction at the time of mastectomy or be planning to undergo reconstruction within 18 months after radiation.

3.2.13 If a tissue expander is utilized it needs to be a fluid filled expander, NO air expander (unless completely deflated) during radiation therapy.

3.2.14 For patients with diabetes, hemoglobin A1C test must have been performed \( \leq 90 \) days prior to registration.

3.2.15 No co-existing medical conditions with life expectancy < 5 years.

3.2.16 No other malignancy within 5 years of registration with the exception of basal cell or squamous cell carcinoma of the skin treated with local resection only or carcinoma in situ of the cervix.

3.2.17 Negative serum or urine \( \beta \)-HCG in women of child-bearing potential \( \leq 7 \) days prior to registration.

A female of childbearing potential is a sexually mature female who has not undergone a hysterectomy or bilateral oophorectomy and has not been naturally postmenopausal for at least 12 consecutive months.

3.2.18 Women of child-bearing potential must agree to utilize a form of birth control or agree to undergo sexual abstinence during radiation therapy.

3.2.19 ECOG (Zubrod) Performance Status 0-1

3.2.20 Patient \( \geq 18 \) years of age