In the last 5-10 years, there has been a significant shift in the radiation of women with intact breast cancer to shorter, more cost effective and convenient treatment courses. As the outcomes with traditional post mastectomy are already considered safe and effective, this trial is designed as a non-inferiority trial to ensure that a shorter time course of radiation is as safe as the current standard of care. There are two pressing and currently outstanding questions related to hypofractionation that require resolution in a phase III setting:

1. What is the rate of radiation related complications in reconstructed chest walls treated with shortened course radiotherapy? and
2. Is hypofractionation safe when treating regional nodal volumes (where the brachial plexus is located)?

These two questions have been contentious and their uncertainty will directly affect patient care for years to come, unless a well-designed study can define the unknowns. In this study, both of these questions will be tested and resolved as primary and secondary endpoints. This trial design also will collect much needed prospective data regarding the true complication rates for post mastectomy radiation therapy (PMRT) with breast reconstruction, given the multitude of options for breast reconstruction timing and techniques. This trial design also collects much needed prospective data regarding the true complication rates for PMRT with breast reconstruction, given the multitude of options for breast reconstruction timing and techniques.
Objective

Primary
- Non-inferior reconstruction complication rate at 24 months post radiation with hypofractionation.
- Complications will include any re-operation or hospitalization considered as non-routine, as well as any Baker 3 or 4 contracture.

Secondary
- Acute and late radiation complications, based on CTCAE 4.0 toxicity.
- Local and local regional recurrence rate.
- Photographic cosmesis 24 months after radiation.
- Lymphedema at 24 months after radiation.
- Patient satisfaction and well-being at 24 months after radiation (Breast Q).
- Compare reconstruction complication rates based on reconstruction method and timing of reconstruction.
- Cost and healthcare utilization based on hypofractionation and reconstruction technique.
Alliance A221505: RT CHARM: Phase III Randomized Trial of Hypofractionated Post Mastectomy Radiation with Breast Reconstruction

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Study Schema

Rationale
Objective
Study Schema
Treatment Plan
Eligibility Criteria
Follow Up

Please use the headings above to navigate through the different sections of the poster

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

Randomize

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

Hypofractionated PMRT
42.5Gy/2.66Gy Chest wall and/or reconstructed breast with 42.5Gy/2.66Gy to regional nodes over 3-4 weeks.

Regional Nodes will include axilla (Level 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.
<table>
<thead>
<tr>
<th><strong>Surgery</strong></th>
<th><strong>Reconstruction</strong></th>
<th><strong>Radiation Therapy</strong></th>
<th><strong>Chemotherapy</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Total, simple, skin sparing, nipple sparing or modified radical mastectomy.</td>
<td>• Reconstruction of the breast may occur before or after radiation.</td>
<td>• Similar volume based planning to A11202 and NSABP B51.</td>
<td>• Per standard of care</td>
</tr>
<tr>
<td>• Margins should be negative, defined as no tumor on ink.</td>
<td>• Tissue expander may be placed before or after radiation and maybe inflated or deflated for radiation.</td>
<td>• RT must start within 84 days of mastectomy or adjuvant chemo (whichever is later)</td>
<td>• Neoadjuvant or adjuvant allowed</td>
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<tr>
<td>• Focally positive deep margin will be acceptable if the deep margin is the pectoralis fascia and the pectoralis fascia was noted as removed in the operative description or pathology report.</td>
<td>• Plastic surgeon may use any combination of allograft, implant or tissue flap for reconstruction.</td>
<td>• 2.66Gy x 16 daily to reconstructed CW and regional nodes (IM coverage required). No boost allowed.</td>
<td>• May be delivered before or after PMRT</td>
</tr>
<tr>
<td>• Lymph nodes must be evaluated by sentinel node biopsy or axillary dissection.</td>
<td>• Reconstruction intent must be stated at the time of registration (timing and implant vs. autologous)</td>
<td>• RT QA through IROC Rhode Island</td>
<td>• No concurrent chemotherapy with RT other than anti-Her2 or other biological therapy</td>
</tr>
<tr>
<td>• If contralateral breast surgery, no invasive disease in contra-lateral breast (DCIS okay)</td>
<td>• Intent to complete reconstruction within 8 months of radiation (approximately 1 year from mastectomy)</td>
<td>• Data submission within 3 days of starting RT</td>
<td>• Minimum 21 days between chemotherapy and RT</td>
</tr>
<tr>
<td></td>
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<td>• IMRT QA grand-fathered if completed for A11202/B51</td>
<td>• Adjuvant hormonal therapy per treating physician</td>
</tr>
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<td>• If Neoadjuvant chemotherapy, surgery must occur within 56 days of finishing chemotherapy</td>
</tr>
</tbody>
</table>
Eligibility Criteria

- Women ≥ 18 years of age.
- ECOG performance status of 0 or 1.
- AJCC Stage IIa–IIla. T4, N3 and involved internal mammary disease (N1b, N1c, and N2b) will not be allowed.
- Clinical N1 or N2 disease prior to induction chemotherapy are allowed if pathologically N0-N2 at the time of mastectomy.
- Treating physician must plan to deliver regional nodal radiation.
- Negative inked histologic margins of mastectomy.
- Chemo allowed neoadjuvant or adjuvant (before or after RT).
- Planned chest wall reconstruction is required with intent declared for autologous vs. implant and immediate vs. delayed reconstruction before randomization.
- Reconstruction can take place before or after post mastectomy radiation.
Alliance A221505: RT CHARM: Phase III Randomized Trial of Hypofractionated Post Mastectomy Radiation with Breast Reconstruction

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