Locally advanced breast cancer
Radiation therapy

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## Locally advanced breast cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
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<tbody>
<tr>
<td>IIB</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIIA</td>
<td>T1</td>
<td>N2</td>
<td>M0</td>
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<td>T2</td>
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</tr>
<tr>
<td></td>
<td>Any</td>
<td>N3</td>
<td>M0</td>
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</table>
Effects of adjuvant radiation therapy

• 70% proportional decrease in local recurrence at 5 years
• 50% proportional decrease in any first recurrence at 10 years
• 17% proportional decrease in breast cancer mortality at 15 years

Management of LABC

- LABC potentially curable

- Multidisciplinary approach: medical oncology, surgical oncology, radiation oncology, reconstructive surgery, diagnostics, cancer genetics, cancer nursing, allied health

- Optimal sequencing of treatment modalities requires investigation

- Neoadjuvant systemic therapy (NAST) standard of care
  - High risk of systemic recurrence
  - To enable breast conservation without compromising survival
Management of LABC: local-regional therapy

• Significance of local-regional therapy: failure to eradicate persistent local-regional disease after effective NAST increases risk of distant relapse

• Surgery indicated post NAST
  – Breast conserving surgery (BCS) or mastectomy: disease stage at presentation, treatment response, patient characteristics and preferences

• RT indicated post NAST
  – Sequencing with surgery: treatment response, reconstructive considerations
Management of LABC: local-regional therapy

• Primary surgery an option for resectable disease in selected patients
  – Adjuvant systemic therapy indicated
  – Adjuvant RT indicated

• Progressive disease on NAST
  – Post-operative or primary RT indicated
Indications for RT in LABC

- Post NAST
- Post primary surgery
- Primary RT for unresectable disease or inoperable patients
RT post NAST: impact of pCR

- pCR after NAST associated with decreased recurrence risk

- Controversy: incorporating response to NAST in RT decision
  - Few data on local-regional recurrence risk after NAST
  - Risk factors for local-regional recurrence may differ after NAST vs primary surgery

- Following pCR to NAST in selected patients with LABC (cT3 N0-1): insufficient evidence to recommend for or against
  - Regional nodal RT in addition to breast RT after BCS
  - Local-regional RT after mastectomy
RT post NAST for stage I-II disease: B18 & 27
RT post NAST: meta-analysis of Gepar-trials

- 3481 patients with operable and non-operable disease

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<thead>
<tr>
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<th>5-year LRFS</th>
<th>5-year DFS</th>
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<tbody>
<tr>
<td></td>
<td>RT</td>
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</tr>
<tr>
<td>pCR</td>
<td>96%</td>
<td>87%</td>
</tr>
<tr>
<td>No pCR</td>
<td>89%</td>
<td>81%</td>
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JCO 2015;33:1008
RT after NAST: NRG 9353

Clinical T1–T3 N1 M0 breast cancer

Axillary nodal involvement (FNA or core-needle biopsy)

NACT (plus anti-HER2 therapy for HER2+ patients)

Definitive surgery with histological documentation of negative axillary nodes (either by axillary dissection or by SLNB ± axillary dissection)

Stratification
By type of surgery (mastectomy vs lumpectomy), ER status (+ vs –), HER2 status (+ vs –), pCR in breast (yes vs no)

Randomization

No regional nodal XRT
Breast XRT if breast-conserving surgery, but no chest-wall XRT if mastectomy

Regional nodal XRT
With breast XRT if breast-conserving surgery, or chest-wall XRT if mastectomy

- Patients with clinical high-risk, T4 or N2-3 disease excluded
RT for LABC: radiation target volume

- Recommended target volume: breast/chest wall, supraclavicular (including apical axillary) and internal mammary (IM) lymph nodes

- Levels I-II axillary RT generally not recommended after axillary dissection
  - Recurrence in dissected axilla uncommon
  - Radiation toxicity including lymphoedema
  - May be considered for extensive axillary disease after dissection or if dissection not undertaken

ASTRO/ASCO/SSO consensus guidelines JCO 2016;34
Radiation target volume for LABC

- Controversy on inclusion of IM nodes
  - EBCTCG: IM nodes irradiated in 20/22 trials of post-mastectomy RT showing benefits of RT
  - Insufficient evidence to identify subgroups for omission of IM nodal RT

ASTRO/ASCO/SSO consensus guidelines JCO 2016;34
# Internal mammary nodal RT

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<thead>
<tr>
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<th>Danish</th>
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<tbody>
<tr>
<td><strong>N</strong></td>
<td>1332</td>
<td>3089</td>
</tr>
<tr>
<td><strong>FU years</strong></td>
<td>8.6</td>
<td>8.9</td>
</tr>
<tr>
<td><strong>RT</strong></td>
<td>CW+SC</td>
<td>CW+SC+IM</td>
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<tr>
<td><strong>DFS %</strong></td>
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<td>53</td>
</tr>
<tr>
<td><strong>Distant DFS</strong></td>
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<tr>
<td><strong>BC mortality</strong></td>
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<tr>
<td><strong>Overall survival</strong></td>
<td>59</td>
<td>63</td>
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Conclusions

- RT integral to multidisciplinary care of patients with LABC

- Omission of RT following pCR to NAST in selected patients with LABC may be considered only in context of clinical trial

- Advances in risk-adaptive strategy for personalising RT in LABC may be driven by integrating disease burden with tumour biology and increasing efficacy of systemic therapy