Inflammatory advanced breast cancer: The role of different radiation techniques

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I have no conflicts of interest
A few facts:
Locally advanced *inflammatory* breast cancer represents 10-15% of all LABC cases

International guidelines recommend:

Neoadjuvant chemotherapy → surgery → radiation therapy

surgery not possible → radiation therapy → surgery

Gain from radiation therapy: limited data, retrospective, no RCT

Most national and international guidelines recommend comprehensive PMRT irrespective of response to neoadjuvant systemic therapy

So what are the technical challenges to perform an optimal loco-regional RT?
Step 1: teamwork
Multidisciplinary setting extremely important

Ensure optimal imaging and diagnostic work up
Pre-chemotherapy this is:
Standard loco-regional imaging with mammography and US,
MR mammography,
clinical photos,
CT of neck-thorax-abdomen (preferably in radiation treatment position with iv contrast)
Consider PET-CT if available
Step 2
Neoadj chemotherapy → Operable → Mastectomy + ALND → PMRT

Planning CT scan:
Use a designated breast board, tattoos and a strict positioning protocol

Seromen? If symptomatic evacuate and ideally wait a few days before scan

Bolus according to a protocol. Bolus is recommended after IBC either along the mastectomy scar (if good response to chemotherapy) or on involved skin

If there were nodal metastases before chemotherapy not removed at surgery then use iv contrast in planning CT scan to help delineation and decision on a boost

Use respiratory gated technique in every patient treated with loco-regional RT
Dose comparison – free breathing/inspiration

<table>
<thead>
<tr>
<th>Target</th>
<th>Mean Heart dose</th>
<th>Mean Lung dose</th>
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</thead>
<tbody>
<tr>
<td>Breast + nodes + IMN</td>
<td>- 5 Gy</td>
<td>- 3 Gy</td>
</tr>
</tbody>
</table>

Courtesy C Taylor & M Aznar
Use all pre-chemotherapy imaging information. Ensure optimal target volume delineation where the tumour was located. Surgical report and ideally clips are very useful.

Offersen et al, R&O 2015 & 2016
Target delineation
Use ESTRO consensus guideline and include chest wall, level I-IV + interpectoral nodes. Some guidelines accept omitting the dissected axilla from the target volume depending on the extent of nodal disease and number of removed nodes.

Include IMN in all cases and preferably to IC4
But is this wise??
DBCG-IMN: A Population-Based Cohort Study on the Effect of Internal Mammary Node Irradiation in Early Node-Positive Breast Cancer


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**Table:**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>IMNI Patients</th>
<th>IMNI Events</th>
<th>No IMNI Patients</th>
<th>No IMNI Events</th>
<th>8-year survival rate (%)</th>
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</thead>
<tbody>
<tr>
<td>Lateral 1–3 nodes</td>
<td>511</td>
<td>91</td>
<td>564</td>
<td>91</td>
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<tr>
<td>Medial/central 1–3 nodes</td>
<td>353</td>
<td>67</td>
<td>382</td>
<td>88</td>
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<tr>
<td>Lateral ≥ 4 nodes</td>
<td>392</td>
<td>137</td>
<td>384</td>
<td>170</td>
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<tr>
<td>Medial/central ≥ 4 nodes</td>
<td>224</td>
<td>86</td>
<td>259</td>
<td>131</td>
<td></td>
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<tr>
<td>All patients</td>
<td>1,480</td>
<td>381</td>
<td>1,589</td>
<td>480</td>
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</table>

**Figure 4:** Overall survival rates and corresponding hazard ratios (HR) with versus without internal mammary node irradiation (IMNI) within subgroups defined by tumor location and the number of axillary nodes involved.

**Note:** Absolute OS gain 8-10%
Figure 1. Rate of Major Coronary Events According to Mean Radiation Dose to the Heart, as Compared with the Estimated Rate with No Radiation Exposure to the Heart.

<table>
<thead>
<tr>
<th>Age at irradiation (years)</th>
<th>Mean heart dose (Gy)</th>
<th>Cumulative risk (%) by attained age</th>
<th>Absolute risk (%) of radiation-related IHD death by age 80 years</th>
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<tr>
<td></td>
<td>0</td>
<td>0.09 0.5 1.9</td>
<td>0.0</td>
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<tr>
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<td>0.09 0.5 2.0</td>
<td>0.1</td>
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<td>3</td>
<td>0.11 0.6 2.4</td>
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<td>9</td>
<td>0.14 0.8 3.2</td>
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<tr>
<td></td>
<td>10</td>
<td>0.15 0.8 3.4</td>
<td>1.5</td>
</tr>
</tbody>
</table>

1.3%
Dose and fractionation

Most prevalent: 50 Gy / 25 fr
UK and NL use moderate hypofractionation as standard

4 randomized trials open, the 2 largest are the DBCG Skagen trial and the HYPOG-01

Patient being candidate for loco-regional RT

50 Gy / 25 fractions

40 Gy / 15 fractions
Common field arrangements

Isocentric half beam technique
“full” IMRT / VMAT / rotational therapy = many angles, not only tangents

Institut Curie, F: Tomotherapy 3% 2012 – 10% 2017
Tilburg, NL: 3% VMAT, 20% hybrid (all locoregional RT)
Danish RT departments: <5% IMRT/hybrid VMAT

Personal communication Youlia Kirova (F) & Sandra Hol (NL)
What to do if the patient is NOT operable after neoadj chemotherapy?
Poor response to neoadjuvant chemotherapy
Still inoperable, no distant mets on new imaging, go for loco-regional RT

Use the same strategy as already described with few additions

DBCG strategy: 50 Gy / 25 fr to breast and regional nodes, sequential boost to breast. Use a boost to nodes not planned for removal at later surgery (usually 16 Gy / 8 fr.)
Concommittant Cyclophosphamide 850 mg / m² before start and week 4 and 8
Bolus on tumour / breast

Timing of surgery after RT: 6 weeks (no evidence)
A case demonstrating the potential of radiation therapy in non-operable inflammatory breast cancer

- 35 yr woman, 5 mth baby, breast-feeding: fast growing lump rigth breast
- Mammography + needle biopsy → central tumour + edema + pathologic nodes level I-III
- MR mammography: edema, skin involved, swelling of breast, tumour 70x60x50 mm and large mets in level I-III
- T4dN3M0
- Core needle biopsy: carcinoma, ER neg, HER2 neg, Ki-67 90%, nodes with similar findings
- Accelerated genetic counseling: no BRCA mutations
Initial MR mammography: 70 x 60 x 50 mm

DBCG guideline: EC/Taxan 8 cycles

May 2016, start chemotherapy

June 2016, at 3rd EC

MR 64 x 54 x 43 mm, nodes a little smaller

July 2016, after 4xEC

MR NC; breast nodes a little smaller

Sept 2016, after 6th EC-Paclitaxel

MDT conference: new biopsy and consider referral to phase I unit. 73 tumour specific mutations detected, but she was not a candidate for immunotherapy trial
October 2016

- Continues to 8 x EC-TAX
- MR mammography: NC in tumour/nodes
- CT thorax, abdomen, pelvis: no distant metastasis
- Pt is inoperable
- Now what?

4 cycles 5-FU+vinorelbine
RT 54 Gy to breast, 46 Gy to nodal areas
All 2 Gy/fr, Surgery 6 weeks after RT

Chargari C et al, Radiother Oncol 2008
Oct-Nov 2016 loco-reg RT
50 Gy / 25 fx to all loco-regional volumes (a.m. ESTRO) with bolus on breast
4 Gy / 2 fx to breast with bolus
Deep inspiration breath hold, iv contrast, daily IGRT
Concommittant Cyclophosphamide 850 mg/m2 every 4 weeks, 3 cycles
95% isodose
Bolus used during RT

Notice very medial CTVp_breast guided by imaging and clinical photos
6 weeks after RT: mastectomy with immediate autologous reconstruction and ALND with removal of nodes level I - II – III

3 mm inv duct carc, ER-, HER2-, 1micro / 17 LN
Conclusion: MDT conference and repeated optimal imaging
Use state of the art radiation treatment planning and delivery
Be aggressive on the cancer and try avoid high dose to OAR

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