Improving radiotherapy treatment for left-sided breast cancer

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Citation for published version (APA):
Chapter 3

INTENSITY MODULATED VERSUS NON-INTENSITY MODULATED RADIOTHERAPY IN THE TREATMENT OF THE LEFT BREAST AND UPPER INTERNAL MAMMARY LYMPH NODE CHAIN: A COMPARATIVE PLANNING STUDY

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Radioth Oncol. 2002 Feb;62(2):127-36
3.1 ABSTRACT

Purpose. To compare and evaluate intensity modulated (IMRT) and non-intensity modulated radiotherapy techniques in the treatment of the left breast and upper internal mammary lymph node chain.

Materials and Methods. The breast, upper internal mammary chain (IMC), heart and lungs were delineated on a CT-scan for 12 patients. Three different treatment plans were created: 1) tangential photon fields with oblique IMC electron-photon fields with manually optimized beam weights and wedges, 2) wide split tangential photon fields with a heart block and computer optimized wedge angles, and 3) IMRT tangential photon fields. For the IMRT technique, an inverse planning program (KonRad) generated the intensity profiles and a clinical 3-D treatment planning system (U-MPlan) optimized the segment weights. U-MPlan calculated the dose distribution for all three techniques. The normal tissue complication probabilities (NTCPs) for the organs at risk (ORs) were calculated for comparison.

Results: The average standard deviation of the differential dose-volume histogram of the breast PTV was 4.6, 3.9 and 3.5% and the average mean dose to the IMC was 97.2, 108.0 and 99.6% for the oblique electron, wide split tangent and IMRT techniques, respectively. The average NTCP for the ORs (i.e. heart and lungs) were comparable between the oblique electron and IMRT techniques (<0.7%). The wide split tangent technique resulted in higher NTCP values (≥2%) for the ORs.

Conclusions: The lowest NTCP values were found with the oblique electron and the IMRT techniques. The IMRT technique had the best breast and IMC target coverage.

3.2 INTRODUCTION

Intensity modulated radiotherapy (IMRT) is a relatively new development that has already been applied to several sites. These include prostate [10,36,41], lung [6,12,13], head and neck [5,7,11,14,60] and breast [15,28,35] primaries. For the treatment of head and neck tumours, IMRT and conformal blocking have been shown to provide better sparing of the parotid gland [14,27,33,60]. Similarly, in prostate cancer, IMRT can reduce the risk of rectal complications and thereby permit the escalation of dose. There is mounting evidence a higher total dose decreases the risk of biochemical failure in prostate cancer [26,45]. Although superior survival rates with IMRT compared to non-IMRT techniques remains an open question, the general radiobiological and oncological principles underpinning the use of IMRT are sound [32,39,43,48] and its application continues to be an area of active investigation.

Post-operative radiotherapy reduces the risk of local recurrence in early breast cancer patients treated with breast conserving surgery to a level comparable to mastectomy [1,8,16,56,57]. Although several studies [2,9,17,29] have suggested an increase in overall survival, the majority do not demonstrate a clear benefit. However, two clinical trials [44,49] have demonstrated improved survival in high risk node positive premenopausal patients when both the chest wall and regional lymph nodes, including the internal mammary chain (IMC), are irradiated following mastectomy. These conclusions remain controversial and several authors [18,21,42] have criticized these studies. How much the
IMC irradiation contributes to the overall survival is, therefore, still unknown. A European Organization for Research and Treatment of Cancer (EORTC) clinical trial [4] is currently underway to confirm or refute this survival advantage.

A large meta-analysis published by the Early Breast Cancer Trialists' Collaborative Group [1] did not show a clear overall survival advantage at 10 years with local irradiation. Their analysis suggests, however, a small improvement in survival may have been offset by an increase risk in death from other causes. Suboptimal radiotherapy techniques may account for this finding. This could, in part, be due to older radiotherapy techniques using lower energy photons resulting in greater dose inhomogeneity. Also, irradiation of the heart from radiotherapy has been linked with an increased risk of cardiovascular mortality [23-25,51,52]. Another meta-analysis, published by Whelan et al., found that locoregional radiation after surgery in patients treated with systemic therapy reduced mortality [58]. This suggests that to maximize any potential survival advantage from radiotherapy, the technique must be carefully considered to ensure adequate coverage of the target volume and to minimize the risk of cardiovascular mortality.

If the planning target volume (PTV) includes only the breast, then the technique typically consists of two tangential fields placed medially and laterally to the breast. This field arrangement attempts to minimize the amount of underlying normal tissue irradiated. However, if the PTV also includes the IMC lymph node then simple tangential fields usually does not offer the best solution.

Treating the breast and IMC lymph nodes is problematic. The inclusion of IMC creates an irregular concave volume difficult to irradiate adequately without delivering significant dose to the heart, particularly in left-sided breast cancer patients. Several techniques have been investigated to treat the IMC [3,30,59]. To minimize the dose to the heart, some advocate the use of an abutting oblique electron field over the parasternal area to treat the IMC [30,59]. But the resulting reduction in cardiac dose can only be obtained at the expense of increased dose inhomogeneity, particularly along the matchline between the medial tangential photon and the abutting electron fields. Planning studies reveal a high dose region of the order of 10-20% and a dose variability of up to 40% [30,59]. The main disadvantage of this technique is the significantly increased complexity of treatment planning and delivery.

Anatomically, the majority of the IMC lymph nodes lie superioiy, between the first and third intercostal spaces [40,55]. Instead of treating the entire IMC, Marks et al [37] suggest the use of partly wide tangents (or wide split tangents) to cover the breast and superior IMC with a block placed to shield part of the heart. This technique improves dose homogeneity by avoiding field matching between the tangential and IMC fields while reducing the dose to the heart.
3.3 PURPOSE

The purpose of this planning study is to evaluate and compare intensity modulated (IMRT tangents) and non-intensity modulated radiotherapy (oblique electrons and wide split tangents) techniques in the treatment of the left breast and upper internal mammary lymph node chain.

3.4 MATERIALS AND METHODS

3.4.1 Patient Selection

Treatment planning was performed retrospectively on twelve left-sided breast cancer patients previously treated at the Netherlands Cancer Institute. All patients underwent CT-scanning following their breast conserving surgery. The images were obtained with the patients lying supine with the ipsilateral arm abducted above their heads. The scans extended approximately from the mid-clavicle to the upper abdomen to include the entire lung in 5 or 10 mm thick CT slices.

3.4.2 Volumes of Interest

The breast PTV included all visible breast parenchyma as seen on the CT slices, excluding 5 mm from the superficial skin surface. The internal mammary vessels, visible on the CT scans, were assumed to mark the centre of the IMC PTV. The IMC PTV was defined by an ellipsoid, with a major (lateral) and minor (anterior-posterior) axes of 30 and 20 mm respectively, centred on the IMC vessels. This extended between the inferior aspect of the ipsilateral clavicular head and the 4th intercostal space to ensure only the first three intercostal spaces were included.

The heart was defined as all the visible myocardium, excluding the pericardium, from the apex to the right auricle, atrium and infundibulum of the ventricle. The pulmonary trunk, the root of the ascending aorta and the superior vena cava were excluded. In order to estimate the overall dose to the body and the dose to the contralateral breast, a partial body volume consisting of the volume enclosed by the external contour minus the left breast, IMC, heart and lungs was defined. An experienced radiation oncologist delineated all volumes of interest except for the external surface, lung and partial body contours which were generated automatically by the treatment planning system. The CT slices were reviewed to ensure adequate coverage of the IMC.

3.4.3 Treatment Techniques

3.4.3.1 Non-intensity Modulated Techniques

3.4.3.1.1 Oblique Electron

All 12 patients were previously planned using this technique in another study [30]. The supraclavicular (SC) fossa was irradiated and a table rotation was applied to minimize
the beam divergence between the tangential and SC fields. For the purposes of this planning study, the SC region was not treated but the table rotations were retained for the sake of simplicity. Each plan consisted of 4 fields (2 tangential photon, 1 parasternal photon and 1 parasternal electron). To minimize beam divergence, a mono-isocentric technique was used. The isocentre was placed at the junction between the breast and the supraclavicular field, 40 mm ipsilateral from the sternum midline at the inferior aspect of the clavicular head. The dorsal border of the tangential photons was aligned with the isocentre, 40 mm ipsilateral from the sternum midline. Using beam’s-eye-view (BEV) and gantry rotation, the tangential fields were designed to ensure the breast was adequately covered with a margin (7 mm) in the cranial, caudal and lateral extent of the PTV to account for beam penumbra. The matching IMC fields treated the medial aspect of the breast PTV. A 7 mm margin around the IMC’s PTV was used to create the IMC photon field. To avoid overdosing the skin, a mixed electron-photon field (weighted approximately 2:1) was used to treat the IMC. The photon IMC field was matched on skin with no overlap 40 mm ipsilateral from the midline and the gantry was rotated such that it matched the tangential fields without any divergence. The IMC electron field was placed 45 mm from midline to allow for a 5 mm overlap with the tangential fields. Due to a wider beam penumbra, a margin of 16 mm was used for the parasternal electron field with the same gantry angle as the parasternal photon field plus a 7° rotation which was found in a previous study [30] to minimize over- and underdosage at the junction. The electron energy was chosen to ensure the 85% isodose covered the deepest node plus 5 mm. If required, blocks were employed to shape the field around the IMC. An experienced clinical physicist optimized the beam weights.

Figure 3-1. Setup of oblique electron technique. (A=isocentre, AB=non-divergent dorsal field edge of tangential photon beam, ABCD=non-divergent oblique IMC photon field (electrons not shown), E=IMC, S=source).
3.4.3.1.2 Wide Split Tangents

The gantry and collimator were rotated to minimize the amount of irradiated lung and heart. The field and block edges were placed 7 mm from the PTV edge of both the breast and the IMC to account for beam penumbra. Using the BEV, blocks were used to shield as much heart as possible without compromising coverage of the PTV (Figure 3-1). The isocentre was placed in the mid-separation of the PTV on the central slice, approximately at the lower third of the perpendicular distance of the breast between the pectoral muscle and the skin surface. Wedge angles and beam weights were optimized using the U-MPlan’s optimization module.

![Figure 3-2. Beam’s-eye-view of the medial tangential field of wide split tangent technique. Block (BK) placed in the lower left corner to spare as much heart (H) as possible without compromising coverage of the breast (B) and IMC.](image)

3.4.3.2 Intensity Modulated Technique

3.4.3.2.1 Intensity Modulated Tangents

The same isocentre and gantry directions used in the wide split tangents were used for the IMRT tangent plans. KonRad generated the beam intensity profile and this profile was sequenced into 10 uniform quantized levels. The resulting beam segment weights were optimized using U-MPlan’s optimization module. No table rotation was applied.
3.4.3.3 Optimization

The patients were planned using a 3-D treatment planning system (U-MPlan version 3.39) [19]. The photon beam dose was calculated using an octree/edge model [20] with an equivalent path length algorithm [31] to account for tissue inhomogeneities. Electron beam dose was modeled using a modified 3-D pencil beam algorithm [38].

All beam and segment weights were optimized using the Optimization Module of U-MPlan (version 1.0) except for the oblique electron plan. Optimization was performed by a simulated annealing search algorithm. Segments with a relative beam weight less than 0.5% were discarded. The total number of beam segments per plan was limited to 99.

KonRad version 1.2 beta 10 (MRC Systems GmbH, Heidelberg, Germany) [46], an inverse planning system, was used to generate the beam intensity profiles. The photon beam dose was calculated using a simplified ray-tracing model with a tissue-phantom ratio algorithm which ignored lateral scatter. The entire CT scanned volume was used in the dose calculation. The bixel (beamlet element) dimensions were 10 mm (leaf width) by 5 mm (direction of leaf travel). A back-projection algorithm generated the beam intensity profiles. Optimization was performed by means of a steepest-descent gradient search. Beam segments were generated by sequencing the fluence profile into 10 uniformly quantized intensity levels. IMRT was delivered using a "step-and-shoot" technique. Because the dose algorithms used in U-MPlan and KonRad are different, all IMRT plans were recalculated using our clinical treatment planning system, U-MPlan, after undergoing beam weight optimization in U-MPlan’s optimization module. A similar quadratic cost function was used for both U-MPlan’s optimization and for KonRad’s beam intensity profile (Table 3-1).
Table 3.1. Cost function parameters used in treatment planning and optimization. (EXT=external contour, IMC=internal mammary chain, VOI=volume of interest).

<table>
<thead>
<tr>
<th>VOI</th>
<th>PRIORITY</th>
<th>MIN DOSE (%)</th>
<th>PENALTY</th>
<th>MAX DOSE (%)</th>
<th>PENALTY</th>
</tr>
</thead>
<tbody>
<tr>
<td>BREAST</td>
<td>2</td>
<td>99</td>
<td>75</td>
<td>100</td>
<td>50</td>
</tr>
<tr>
<td>IMC</td>
<td>3</td>
<td>99</td>
<td>75</td>
<td>100</td>
<td>50</td>
</tr>
<tr>
<td>HEART</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>48</td>
<td>5</td>
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<td>LUNGS</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>30</td>
<td>2.5</td>
</tr>
<tr>
<td>EXT</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>30</td>
<td>1</td>
</tr>
</tbody>
</table>

3.4.4 Cost Function

A quadratic cost function with different penalty weights for over- and underdosage was used. The parameters applied in the optimization are described in Table 3-1. The cost functions differ slightly in implementation between KonRad and U-MPlan. In KonRad, a weighted quadratic penalty was applied to the calculated maximum (or minimum) dose above (or below) the prescribed maximum (or minimum) dose. Therefore, only a single point on the DVH curve was used in each costlet function. In U-MPlan, a weighted quadratic penalty was applied, in effect, to each voxel above the prescribed maximum dose. Its costlet function depended on the area under the DVH curve above the dose threshold. To account for this difference, the weighting penalty for each costlets was normalized to the total number of voxels to find the cost of the average voxel.

3.4.5 Dose Prescription

All patients were planned to receive a total dose of 50 Gy in 25 daily equal fractions over 5 weeks (2 Gy/d), prescribed to the PTV mean dose of the whole breast. The dose to the IMC fields was calculated at the middle of the IMC’s PTV.

3.4.6 Evaluation and Analysis

We evaluated the dose-volume histograms (DVHs) for all volumes of interest (VOI), including the partial body volume. We used the mean dose and the standard deviation (SD) of the differential DVH (dDVH) of the target volumes (i.e. breast and IMC) to evaluate their dose distribution. We assumed this would result in clinically similar DVHs of the breast with similar local control to allow valid intra- and interpatient comparisons.

We used the V_{D95\%} (volume which receives 95% of the dose or more) and V_{D107\%} (volume which receives 107% of the dose or more) to estimate the dose homogeneity within the PTV. However, they can be misleading if a small volume of very high or very low dose is present. The SD dDVH is a stricter measure of dose homogeneity since it depends on the shape of the entire dose distribution and is independent of the mean dose. A large SD dDVH is likely to be less clinically significant than a large difference in the mean dose (from 100% dose) since the mean dose represents a systematic 72
under- or overdosage. The \( V_{D95,107\%} \) (volume enclosed between the 95% and the 107% isodose surfaces) was used to measure the overall coverage of the target volume and this metric does depend on mean dose and SD dDVH.

To calculate the normal tissue complication probability (NTCP), the absolute dose values were converted into normalized total dose (NTD) with an \( \alpha/\beta \) ratio of 3 Gy for both heart and lungs. We calculated the NTCP for excess late cardiac mortality using the relative seriality model with parameters derived by Gagliardi et al [22]. The mean NTD to the lungs was used to estimate the NTCP for radiation pneumonitis [34]. Both lungs were considered as one organ. All pair-wise comparisons were performed using a two-tailed Student t-test with a significance level of 0.05.

### 3.5 RESULTS

#### 3.5.1 Target Dose Coverage

The average mean dose to the breast was 100% (SD=0%), by definition (Table 3-2). With respect to the breast, the IMRT technique had the lowest SD dDVH (3.5%) while the oblique electron technique had the highest (4.6%). This difference was significant \( (p=0.01) \). In contrast, the \( V_{D95\%} \) and \( V_{D107\%} \) were the highest for the oblique electron technique (97.4% and 7.8%) and lowest for the IMRT technique (93.7% and 2.0%) which was also found to be significantly different \( (p=0.0008 \text{ and } p=0.0001 \text{, respectively}) \). The \( V_{D95,107\%} \) was not significantly different between any of the plans and the average dDVH curves almost overlap with each other (Figure 3-4A-B).

**Table 3-2.** Summary statistics for the volumes of interest. Numbers in the table are sample averages (%), with standard deviations (±). The \( p \)-values for the pair-wise comparisons are given in the last three columns. \( \text{BODY} = \) partial body, \( \text{dDVH} = \) differential DVH, \( \text{IMC} = \) internal mammary chain, \( \text{NA} = \) not applicable, \( \text{NTCP} = \) normal tissue complication probability, \( \text{V} = \) versus, \( \text{OBL} = \) oblique electron technique, \( \text{IMRT} = \) IMRT tangent technique, \( \text{WIDE} = \) wide split tangent technique, \( \text{SD} = \) standard deviation, \( \text{V}_{Dx\%} = \) DVH volume point at \( x\% \) dose, \( \text{V}_{D95,107\%} = V_{D95\%} \text{ minus } V_{D107\%} \), \( \text{VOI} = \) volume of interest.

<table>
<thead>
<tr>
<th>VOI</th>
<th>%</th>
<th>OBL</th>
<th>WIDE</th>
<th>IMRT</th>
<th>OBL V</th>
<th>OBL V</th>
<th>OBL V</th>
<th>WIDE</th>
<th>WIDE</th>
<th>WIDE</th>
</tr>
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<tr>
<td>BREAST</td>
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<td>100.0±0.0</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD dDVH</td>
<td>4.6±0.8</td>
<td>3.9±1.1</td>
<td>3.5±1.0</td>
<td>0.05</td>
<td>0.009</td>
<td>0.5</td>
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<td></td>
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</tr>
<tr>
<td>( V_{D95%} )</td>
<td>97.4±1.8</td>
<td>94.1±5.1</td>
<td>93.7±3.3</td>
<td>0.08</td>
<td>0.0008</td>
<td>0.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( V_{D107%} )</td>
<td>7.8±1.9</td>
<td>5.0±4.9</td>
<td>2.0±2.6</td>
<td>0.1</td>
<td>0.0001</td>
<td>0.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( V_{D95,107%} )</td>
<td>89.6±3.1</td>
<td>89.0±9.4</td>
<td>91.7±5.6</td>
<td>0.9</td>
<td>0.2</td>
<td>0.5</td>
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<tr>
<td>IMC</td>
<td>mean</td>
<td>97.2±2.5</td>
<td>108.0±7.5</td>
<td>99.6±0.7</td>
<td>0.0002</td>
<td>0.005</td>
<td>0.002</td>
<td></td>
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<tr>
<td>SD dDVH</td>
<td>2.8±1.0</td>
<td>3.8±1.1</td>
<td>4.6±1.1</td>
<td>0.04</td>
<td>0.0007</td>
<td>0.05</td>
<td></td>
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</tr>
<tr>
<td>( V_{D95%} )</td>
<td>80.0±18.8</td>
<td>97.5±3.5</td>
<td>89.3±3.9</td>
<td>0.01</td>
<td>0.1</td>
<td>0.0001</td>
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<tr>
<td>( V_{D107%} )</td>
<td>0.1±0.2</td>
<td>41.3±37.3</td>
<td>2.5±3.9</td>
<td>0.003</td>
<td>0.06</td>
<td>0.004</td>
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</tr>
<tr>
<td>( V_{D95,107%} )</td>
<td>79.9±18.7</td>
<td>56.2±35.9</td>
<td>86.8±6.4</td>
<td>0.09</td>
<td>0.2</td>
<td>0.02</td>
<td></td>
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<tr>
<td>HEART</td>
<td>( V_{D95%} )</td>
<td>0.1±0.2</td>
<td>1.9±2.7</td>
<td>0.1±0.2</td>
<td>0.03</td>
<td>0.4</td>
<td>0.04</td>
<td></td>
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</tr>
<tr>
<td>( V_{D107%} )</td>
<td>0.6±0.6</td>
<td>2.1±2.3</td>
<td>0.6±0.5</td>
<td>0.02</td>
<td>0.8</td>
<td>0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( V_{D95,107%} )</td>
<td>13.9±3.3</td>
<td>20.5±8.2</td>
<td>15.3±3.2</td>
<td>0.005</td>
<td>0.1</td>
<td>0.02</td>
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<tr>
<td>LUNGS</td>
<td>mean</td>
<td>8.6±0.3</td>
<td>2.2±3.2</td>
<td>0.7±0.3</td>
<td>0.08</td>
<td>0.2</td>
<td>0.1</td>
<td></td>
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</tr>
<tr>
<td>BODY</td>
<td>mean</td>
<td>8.8±3.8</td>
<td>14.8±6.1</td>
<td>7.2±2.5</td>
<td>0.002</td>
<td>0.007</td>
<td>0.0003</td>
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</tbody>
</table>
Figure 3-4A-B. Average dose-volume histograms for the breast. (imrt=IMRT tangent technique, obl=oblique electron technique, wide=wide split tangent technique).
Figure 3-4C-D. Average dose-volume histograms for the internal mammary lymph node chain. (imrt=IMRT tangent technique, obl=oblique electron technique, wide=wide split tangent technique).
Figure 3-4E-F. Average dose-volume histograms for the organs at risk: heart and lungs. (imrt=IMRT tangent technique, obl=oblique electron technique, wide=wide split tangent technique).
SECTION 3.5 RESULTS

**Figure 3-4G.** Average dose-volume histogram for partial body. (imrt=IMRT tangent technique, obl=oblique electron technique, wide=wide split tangent technique).

**Figure 3-5.** Normal tissue complication probability for excess late cardiac mortality by patient and technique. Patients sorted by the wide split tangent technique’s NTCP values. (wide= wide split tangent, obl= oblique electrons, imrt= IMRT tangent)
Figure 3-6. Normal tissue complication probability for radiation pneumonitis by patient and technique. Patients sorted by the wide split tangent technique's NTCP values. Patient numbers correspond to the previous figure. (wide=wide split tangent, obl=oblique electrons, imrt=IMRT tangent)

With respect to the IMC, the average mean doses were 97.2, 108.0 and 99.6% for the oblique electron, wide split tangent and IMRT plans, respectively (Figure 3-4C-D). The means were all significantly different ($p<0.005$). The average SD dDVH was highest for the IMRT (4.6%) and lowest for the oblique electron plan (2.8%). The $V_{D95\%}$ and $V_{D107\%}$ was the lowest for the oblique electron and highest for the wide split tangent plan. The $V_{D95-107\%}$ was 79.9, 56.2 and 86.8% for the oblique electron, wide split tangent and IMRT tangent techniques, respectively.

The $V_{D95\%}$, $V_{D107\%}$ and $V_{D95-107\%}$ of the oblique electron plan were not significantly different from the IMRT plan ($p=0.06$, $0.1$ and $0.2$, respectively).

### 3.5.2 Normal Tissue Complication Probability

The average NTCP for excess late cardiac mortality was 0.6, 2.1 and 0.6% for the oblique electron, wide split tangent and IMRT techniques, respectively. The differences between the IMRT and wide split tangent plans and between the oblique electron and wide split tangent plans were significantly different ($p=0.03$ and $p=0.02$, respectively). The individual NTCP values for the heart showed a consistent, systematic decrease of approximately 70% when going from the wide split to the other two techniques (Figure 3-5).

The average NTCP for radiation pneumonitis was 0.6, 2.2 and 0.7% for the oblique electron, wide split tangent and IMRT techniques, respectively. Although the reduction in the individual lung NTCP values between the wide split and the other two techniques
was suggestive, the differences were not significantly different (Figure 3-6). No obvious correlation between the heart and lung NTCPs were found.

The average partial body mean dose was 8.8, 14.8 and 7.2% for the oblique electron, wide split tangent and IMRT tangent techniques (Figure 3-4G). These were all significantly different ($p<0.007$).

3.6 DISCUSSION

3.6.1 Target Dose Coverage

3.6.1.1 Breast

With respect to the breast, the smallest SD dDVH was found with the IMRT tangent technique, implying better dose homogeneity compared to the other techniques. The IMRT plan also had the lowest $V_{D95\%}$ suggesting the greater dose inhomogeneity seen in other techniques was caused by overdosage (as demonstrated by $V_{D107\%}$) as opposed to underdosage. The coverage of the breast target volume was similar between the IMRT tangent and the wide split tangent technique as demonstrated by the SD dDVH, $V_{D95\%}$ and $V_{D107\%}$. The SD dDVH between the oblique electrons and IMRT tangent technique were significantly different.

However, when we examine the breast target coverage, as measured by the $V_{D95-107\%}$, no significant differences were found between any of the techniques studied. Comparable target coverage should be achieved before evaluating the other dosimetric data.

3.6.1.2 Internal Mammary Chain

The IMC’s mean dose differed significantly between all plans ($p<0.007$). This is clearly seen in Figure 3-4D. The lowest mean dose was found with the oblique electron technique (97.2%) and the highest, with the wide split tangent technique (108.0%).

If the intent of treatment is to adequately treat the IMC then a low mean dose is particularly undesirable. Our findings are consistent with others who have reported a relative underdosage in the IMC with the oblique electron technique [3,30]. The underdosage is even more prominent in the other studies as they were treating the entire IMC, making the target coverage more difficult. The wide split tangent technique had a notable amount of overdosage in the IMC. This may be due to the practical limitations of this technique. The use of wedges created unavoidable regions of higher dose. Given that wedges correct dose only along one dimension and that the breast is curved along two dimensions, it is not surprising significant overdosage is present. Furthermore, it is not possible to optimally treat both the breast and IMC simultaneously using simple wedges. One advantage present in the IMRT tangent technique is the ability to compensate dose along two dimensions which, by itself, will improve the dose homogeneity.
As a first order approximation to estimate the gain attributable to the addition of intensity modulation, one can compare the IMRT tangent and the wide split tangent techniques. The SD dDVH is the largest for the IMRT tangent technique suggesting greater dose inhomogeneity. However, when we examine the dDHVs (Figure 3-4D), the wide split tangent technique clearly appears to have the largest SD dDVH. This counter-intuitive observation appears to contradict the results stated in Table 3-2. To explain this, a distinction needs to be made between the average used for the mean dose and the average used for the SD dDVH. For the wide split technique, the average mean dose for the entire sample is associated with a large amount of variability (SD=7.5%). When the dDVH for all wide split tangent patients are averaged together, the resulting curve is quite wide, reflecting the large standard deviation. However, the dose homogeneity, as measured by the SD dDVH, depends only on the width of the dDVH curve and is independent of the mean dose. The smaller SD dDVH associated with the wide split tangent technique suggests better dose homogeneity but does not necessarily imply better target coverage. To illustrate, one could have a SD dDVH of 0.1% but a mean dose 50%. Although one has excellent dose homogeneity, the target coverage is clearly suboptimal due to the inadequate mean dose.

To take the SD dDVH and mean dose into account when measuring target coverage, we use the $V_{D95-107\%}$. When we compare the $V_{D95-107\%}$ between the different plans, the IMRT tangent technique has the best IMC coverage (86.8%), followed by the oblique electrons (79.9%) and then the wide split tangents (56.2%). The IMRT technique has significantly better target coverage compared to the wide split tangent technique ($p=0.02$).

### 3.6.2 Normal Tissue Complication Probability

#### 3.6.2.1 Heart

The lowest NTCP for excess late cardiac mortality was found with the oblique electron (0.6%) and IMRT tangent techniques (0.6%). Both these techniques were significantly different from the wide split tangent technique. Although these values were small, the NTCP model parameters used to estimate them have relatively large uncertainties so the absolute values should be interpreted with caution. As better prospective dosimetric and outcome data become available, the accuracy of these models should improve. However, the relative differences between the different techniques are unlikely to change, even with more accurate data, in light of the consistent, systematic decrease in the heart NTCP from the wide split tangent technique to the other two techniques (Figure 3-5).

The calculated heart NTCP values using the oblique electron technique were smaller than those reported by Hurkmans et al [30]. Instead of treating the entire IMC chain, as they did, we limited our irradiation to only the upper portion (1st-3rd intercostal
3.6 DISCUSSION

spaces) of the IMC. Consequently, the heart received less dose resulting in lower NTCP values.

3.6.2.2 Lungs

All three techniques had relatively low lung NTCP values (range: 0.6-2.2%). No significant differences were found between any of the techniques. No obvious correlation between the heart and lung NTCPs were found (Figure 3-6). If such a correlation existed, the patient order in Figure 3-6 would be similar to Figure 3-5.

3.6.2.3 Partial Body

The scatter dose to the contralateral breast was not specifically investigated. However, DVHs for the partial body dose were studied (Figure 3-4G) which could be used to approximate the scatter dose. The IMRT technique had significantly less mean dose compared to the other techniques.

3.6.3 Other Considerations

With the oblique electron technique, the use of electrons minimizes the dose to deeper structures, particularly heart and lungs. However, it is resource-intensive due to more complicated treatment planning and delivery. Junctioning between the photon and electron match-line as well as the use of the anterior oblique parasternal fields to irradiate the IMC all contribute to increased dose inhomogeneity. Also, the IMC depth determines the electron energy used and this may limit its effectiveness in treating very deep IMCs.

The wide split tangent technique, conversely, had better coverage of the breast but significantly overdosed the IMC. This technique generally resulted in the highest NTCP values for both excess late cardiac mortality and radiation pneumonitis. Although it is the simplest to plan and implement, the higher risk of complications suggests, at the very least, caution in its use.

The IMRT technique offered the best compromise between the two competing interests of the PTV (breast and IMC) and organs at risk (ORs). It was able to maintain low NTCP values for both heart and lungs, comparable to the oblique electron technique, and to offer the best target coverage of the breast and IMC. The use of IMRT, however, requires significant resources and can be time-consuming to plan, verify and deliver compared to the wide split tangent technique. Whether the IMRT technique is more resource-intensive than the oblique electron technique requires further study. However, if they both require comparable resources and time, then a strong argument could be made on dosimetric grounds to justify the use of the IMRT technique.

In the “oligobeam” approach (<5 beams), beam direction becomes an important factor [47,50,53,54]. Parallel opposed beam directions are known to be suboptimal when using
IMRT. Despite the suboptimal tangential beam directions used in this planning study, the IMRT tangent technique was still able to significantly reduce dose to the ORs in most patients. Orthogonal beams directions should theoretically improve dose conformity, particularly when concave target volumes are involved. We expect the results of IMRT using more optimal beam directions to be even better than what was achieved in this study.

Another potential area of improvement involves beam segmentation. The average number of segments required for each beam was 19.4 (range: 10-30). This number is probably the upper limit for two reasons. Firstly, several beam segments had relative beams weights of less than 3%. If these segments were excluded, it is unlikely the overall dose distribution would be significantly affected. Secondly, we know the use of uniformly quantized intensity levels is not the ideal solution. Non-uniform quantized intensity levels could be a method of minimizing the number of beam segments without significantly compromising the beam intensity profile. This would have several practical advantages in treatment planning and delivery. The magnitude of this benefit, however, still remains to be quantified.

The effect of non-standard IMRT beam directions in treating the breast and IMC as well as optimal sequencing are currently being investigated and will be reported in the near future.

3.7 Conclusions

In conclusion, the lowest lung and heart NTCP values are found with the oblique electron and IMRT tangent techniques. However, the IMRT tangent technique gave the best target coverage of the breast and IMC.

3.8 Acknowledgements

The authors would like to gratefully acknowledge the help of Drs. Harry Bartelink, Joos Lebesque and the MRC Systems GmbH (Heidelberg, Germany).

3.9 References


