Comparison of normal tissue dose with three-dimensional conformal techniques for breast cancer irradiation including the internal mammary nodes

Hans Paul van der Laan, Wil V. Dolsma, Aart A. van ‘t Veld, Henk P. Bijl, Johannes A. Langendijk

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Abstract

**Purpose:** To compare the Para Mixed technique for irradiation of the internal mammary nodes (IMN) with three commonly used strategies, by analyzing the dose to the heart and other organs at risk.

**Materials and Methods:** Four different three-dimensional conformal dose plans were created for 30 breast cancer patients. The IMN were enclosed with the Para Mixed technique by a widened medio-lateral tangential photon beam and an anterior electron beam, with the Patched technique by an anterior electron beam, with the Standard technique by an anterior photon and electron beam, and with the PWT technique by partially wide tangential beams. All techniques were optimised for conformity and produced equally adequate target coverage.

**Results:** Heart dose was lowest with the Para Mixed and Patched technique for all patients and with the PWT technique for right-sided treatment only. Lung dose was highest with the PWT, lowest with the Patched, and intermediate with the Para Mixed and Standard techniques. Skin dose was highest with the Patched, lowest with the PWT, and intermediate with the Para Mixed and the Standard techniques. The Para Mixed technique resulted in a 13-Gy lower dose in an overlap area, and the PWT technique was the only technique that incorporated considerable volumes of the contralateral breast.

**Conclusion:** The Para Mixed technique yielded the overall best results. No other technique resulted in a lower heart dose. Lung and skin were equally spared instead of one of them being compromised, and the contralateral breast was avoided.
Introduction

There is no general consensus with regard to the indications for elective irradiation of the internal mammary nodes (IMN) in the treatment of breast cancer [1]. The higher probability of radiation-induced toxicity is of concern, and it remains unclear whether such treatment will provide better loco-regional control and prevent further dissemination. The IMN were routinely incorporated into the target volume in a number of breast cancer trials that proved the benefits of radiotherapy with respect to survival. However, no difference in outcome has been observed yet in randomized studies that specifically focused on the possible benefit of IMN irradiation [2,3]. Only a few studies showed a decreased incidence of loco-regional recurrence in small subgroups of patients [4,5]. A number of studies pointed out that patients who received partial irradiation of the heart had an increased risk of dying from cardiac disease [6-9]. This thin line between advantages and side effects has caused actual practise to be culture driven rather than evidence-based [10,11]. Nevertheless, it should be realised that in many studies and trials that proved the benefits and harms of IMN irradiation, outdated treatment techniques were used, and in many cases relatively large volumes of the heart were irradiated. Currently, a number of tools and techniques are available that enable us to reduce the dose to organs at risk, such as the heart and lungs.

While treatment planning moved toward the era of three-dimensional conformal radiotherapy (3D-CRT), Marks et al. [12] proposed a possible solution to reduce normal tissue dose with the so-called partially wide tangents (PWT) technique. With this technique, the heart and lungs could be spared more adequately than with conventional two-dimensional techniques. In 1998, Jansson et al. [13] drew attention to the drawbacks of the PWT technique, which included the relatively high lung dose, the high heart dose in left-sided treatment, and the irradiation of the contralateral breast with the PWT technique. The Patched technique was proposed. With this technique, the medial chest wall and the IMN were treated with electrons. Although the dose to the heart, lungs, and contralateral breast was further reduced compared with the PWT technique, this Patched
technique had the drawback of a high skin dose and matchline problems. In 2000, Hurkmans et al. [14,15] described two techniques to treat the IMN with a mix of photons and electrons. With these techniques, both skin dose and lung dose were reduced. On the basis of these and other techniques, a number of investigators performed comparative planning studies. Although the PWT technique was advocated in three of these studies [16-18], questions could be raised regarding the way treatment planning was performed. Non-conformal photon–electron techniques were compared with PWT techniques that were constructed to effectively shield normal tissue. In recent studies, similar normal tissue complication probabilities (NTCPs) for heart and lung were predicted for intensity-modulated radiotherapy (IMRT) and photon–electron techniques [19,20]. In these studies, similar target volumes and margins were used with all techniques. However, the photon–electron plans were not yet created with the optimal use of 3D-CRT. At the University Medical Center Groningen, we developed a new technique to irradiate the parasternal region with a mix of photons and electrons, the Para Mixed technique [21]. This technique is a further improvement of the techniques proposed by Hurkmans and others because all beams are constructed, shaped, and weighted according to individual patient characteristics. The beam configuration used enables a further reduction of normal tissue dose while adequate target coverage is maintained. In this study, we compared the Para Mixed technique with three other commonly used strategies that were all optimised with the use of 3D-CRT. Our purpose was to test the hypothesis that the Para Mixed technique is the most optimal technique in case of IMN irradiation in terms of heart dose, lung dose, skin dose, and dose in the contralateral breast.

Materials and Methods

Patients

Thirty patients scheduled for radiotherapy after mastectomy or breast-conserving surgery were included in this study. All patients were planned to receive irradiation of the IMN and supraclavicular nodes as part of the treatment. Thirteen
patients were treated for right-sided breast cancer (breast = 6, chest wall = 7), and 17 patients were treated for left-sided breast cancer (breast = 8, chest wall = 9). A planning CT scan was made for each patient. Of the 35 patients who were initially included in this study, 5 with IMN exceeding a depth of 5 cm were excluded because the adequate use of electrons would be precluded in these patients.

Patient positioning and acquisition of CT data
Patients were positioned on a breast board with the sternum parallel to the table, and the ipsilateral arm was abducted above the head. Before the CT scan, skin marks were placed to enable patient repositioning during treatment. Radiopaque catheters and markers were placed to locate the palpable breast, scar, and skin marks on the CT images. Patients were scanned from the level of the larynx to the level of the upper abdomen, including both lungs, with a scan thickness and index of 5 mm. CT data for all patients were transferred to the Helax-TMS 3D treatment-planning system (Nucletron, Veenendaal, The Netherlands), version 6.1B.

Target volumes and organs at risk
After breast-conserving surgery, the clinical target volume (CTV) consisted of the ipsilateral breast, the IMN, and the supraclavicular nodes. The breast CTV was defined as the breast parenchyma visible on the CT images, which was generally consonant with the palpable breast marked by the radiopaque catheter. After mastectomy, the CTV consisted of the residual tissue of the chest wall, the IMN, and the supraclavicular nodes. The chest wall CTV extended within the confines of the markers placed on the skin surface before the CT scan. The most posterior aspect of the chest wall CTV was the anterior rib surface. The supraclavicular nodes CTV was defined from the level of the cricoid cartilage to the supraclavicular fossa. The IMN CTV was defined by an elliptical cylinder with lateral and anterior–posterior diameters of 15 mm and 10 mm, respectively, placed adjacent to the edge of the sternum medially and to the pleura posteriorly. The IMN CTV extended from the inferior aspect of the ipsilateral clavicular head through the fourth intercostal
space. The planning target volume (PTV) was obtained for each CTV by applying a margin of 5 mm in three dimensions. The heart was contoured to the level of the pulmonary trunk superiorly, excluding the major vessels. Both lungs were contoured with the automatic contouring tool of the Helax-TMS planning system, edited, and then verified. The contralateral breast was contoured as the breast parenchyma visible on the CT images.

**General conditions for treatment planning**

An identical matchline was used with all techniques. Superior to the matchline, the supraclavicular nodes PTV was treated. Seventy-five percent of the prescribed dose was delivered to the supraclavicular nodes with an anterior photon beam, and 25% with a posterior photon beam. The central axes and inferior borders of these beams were aligned with the matchline. All techniques produced the same dose distribution superior to the matchline. The relative volume of breast or chest wall PTV receiving at least 95% of the prescribed dose was never more than 2% different between the techniques. At least 98% of the IMN PTV received 85% of the prescribed dose with all techniques, which is consistent with the requirements of European Organization for Research and Treatment of Cancer (EORTC) protocol 22922-10925 [2]. This protocol states that the target area of the IMN should be covered by at least the 85% isodose.

When electron beams were used, they were shaped and directed in such a way that the IMN PTV received the required dose. Multileaf collimator shielding was used with all photon beams. A heavy metal mould was used to collimate the electron beams. All shielding was conformal to the PTV, with a margin of 5 mm outside the PTV to account for penumbra. Wedges were used in the tangential beams with all patients. In addition to this, a maximum of three small sub-beams was used to obtain a homogeneous dose distribution. The wedge fraction and the relative weights of any sub-beams were weighted manually (i.e., by forward planning). The treatment plans were normalized at the International Commission on Radiation Units and Measurements (ICRU) reference point of the breast or chest wall PTV [22]. The point was chosen to conform to the General
Recommendations for Reporting Doses [22] at the center of the PTV, at or close to the isocenter, and always in a region where there is no steep dose gradient. The ICRU reference dose was 2 Gy per fraction, with a total treatment dose of 50 Gy. The dose delivered to the IMN region was prescribed to an IMN dose calculation point. The photon energy was 6 MV in all cases. The electron energy ranged from 8 to 14 MeV. The pencil beam algorithm of the Helax-TMS treatment-planning system was used to calculate full 3D dose distributions, and lung density corrections were used for all techniques.

**Para Mixed technique treatment planning**

Inferior to the matchline, three tangential photon beams and one anterior electron beam were matched. For the tangential beams, tabletop rotations and collimator rotations were used to create a divergence-free match to the inferior borders of the supraclavicular beams. Two standard tangential beams and one additional widened medio-lateral tangential beam were used to treat the breast or chest wall PTV. The rotation point of these beams was placed centrally in the breast or chest wall PTV. The widened medio-lateral tangential beam enclosed the IMN PTV and the medial part of breast or chest wall PTV that was excluded with the standard tangential beams. The dose delivered to these regions was then supplemented with an anterior electron beam (gantry angle 0°, source-to-surface distance 100 cm).

There was an overlap area between the electron beam and the two standard tangential beams. The ipsilateral border of the electron field was defined slice by slice to include the PTV region that was excluded with the standard tangential beams. The location of the overlap area was anticipated when the gantry angles of the standard tangential beams were defined. For chest wall irradiation, a more lateral ipsilateral location was chosen for the overlap area to reduce the dose to the heart and the ipsilateral lung. As a result of this, not only the IMN region, but also the medio-caudal part of the chest wall was irradiated with a mix of photons and electrons.
The electron energy was determined by the depth of the IMN. The IMN dose-calculation point was placed centrally in the electron beam at the depth of the dose maximum. An average of 62% of the prescribed dose was delivered to the IMN dose-calculation point with the electron beam. The widened medio-lateral photon beam was weighted to deliver the remaining percentage of the prescribed dose to the IMN dose-calculation point. In this way, the volume of lung receiving $\geq 20$ Gy was limited, and skin dose in the parasternal region was limited to a dose of 36 Gy. The 36-Gy skin dose (defined at a depth of 1 mm) resulted from the photon–electron mix of 38%/62% when 10-MeV or 12-MeV electrons were used. When 14-MeV electrons were used, in case of deeper IMN, electrons became less efficient, and skin dose increased. For this reason, a lower percentage of electrons (58%) was used in a mix containing 14-MeV electrons and a higher percentage of electrons (66%) was used in a mix containing 8-MeV electrons.

The combined weight of the two medio-lateral tangential beams was identical to that of the single latero-medial tangential beam. The gantry angle for the widened medio-lateral tangential beam was chosen to minimise lung dose and heart dose, without including the contralateral breast. Shielding of the heart was further optimised by changing the multileaf collimator settings of the standard tangential beams, as long as the ipsilateral border of the electron beam could be shaped accordingly without compromising adequate target coverage.

**Patched, Standard, and PWT technique treatment planning**

The Para Mixed technique was compared with the Patched, the Standard, and the PWT techniques (Fig. 1). With the Patched technique, a conformal anterior electron beam was used to treat the IMN. The beam configuration was identical to that with the Para Mixed technique, except that the widened medio-lateral tangential beam was excluded. The two remaining tangential beams were of the same weight, and the weight of the electron beam was adjusted to deliver 100% of the prescribed dose to the IMN.
Figure 1. Overview of the techniques compared in this study

The Para Mixed technique (A); The Patched technique (B); The Standard technique (C); and The Partially Wide Tangents technique (D). The dose distribution is represented by the 20%, 50% (dark blue), 85% (blue), 95% (green), 125% (orange), and 140% (red) isodose lines.
With the Standard technique, a mix of anterior photon and electron beams was used to deliver the prescribed dose to the IMN. The beam configuration with the Standard technique was identical to that with the Patched technique, except that a 6-MV photon beam was added with a field shape identical to that of the electron beam. Heavy metal shielding blocks were used, and the superior border was matched divergence-free to the matchline. The contribution of the electron beam was similar to that with the Para Mixed technique.

With the PWT technique, wide tangential photon beams were matched divergence-free inferior to the matchline. With the use of beam’s-eye-view projections, optimal gantry angles were determined to achieve maximum avoidance of the heart and the ipsilateral lung, without including more than 25% of the contralateral breast.

**Analyses of normal tissue dose**

In studies focusing on patients receiving radiotherapy for breast cancer and Hodgkin’s disease, 30 Gy has been suggested as a threshold dose for ischemic heart disease [9,23-25]. Therefore, the relative volume of the heart receiving \( \geq 30 \) Gy \( (V_{30}) \) and the mean heart dose were obtained from the dose–volume histograms (DVHs) of the different techniques. The mean lung dose and the relative volume of lung receiving \( \geq 20 \) Gy \( (V_{20}) \) are regarded to be predictors of radiation pneumonitis [26,27]. Therefore, the mean lung dose and the lung \( V_{20} \) (considering both lungs as one organ) were obtained from the DVHs.

Irradiation of the contralateral breast gives reason for concern. It is demonstrated that the risk of breast cancer is closely associated with breast tissue dose [28]. A linear dose relationship is maintained at lower radiation doses, and there exists no low-dose threshold below which there is no excess risk. The contralateral breast mean dose and its relative volume receiving \( \geq 3 \) Gy \( (V_{3}) \) and \( \geq 10 \) Gy \( (V_{10}) \) were used to quantify the volume of contralateral breast irradiated with the different techniques.

Bad cosmetic results and up to a 72% chance for late radiation-induced telangiectasia have been reported in patients receiving full electron irradiation for
breast cancer [29,30]. Therefore, the dose delivered to the skin in the IMN region was evaluated for all techniques. Owing to limitations of the treatment-planning system, it was not possible to obtain accurate DVHs of the skin. The skin dose was therefore estimated according to data on beam characteristics of photons and electrons measured at our institution. When beams overlap below the surface of the skin, high doses can accumulate, and subcutaneous fibrosis is often seen as a late side effect. For all techniques in which an overlap was present, the maximum dose was calculated by the treatment-planning system. The average maximum equivalent dose in 2-Gy fractions was calculated with an $\alpha/\beta$ of 1.7 Gy, as defined for subcutaneous fibrosis by Bentzen and Overgaard [31].

**Statistical analysis**

To compare DVH parameters of the different techniques, the mean values were analyzed with the Wilcoxon signed ranks test or the paired-samples t-test whenever appropriate. All tests were two-tailed, and differences were considered statistically significant when the p value was 0.05 or less.

**Table 1. Mean dose in Gy and percent volume of heart, lung, and contralateral breast irradiated**

<table>
<thead>
<tr>
<th>Technique</th>
<th>Heart Mean dose</th>
<th>Heart V30</th>
<th>Lung Mean dose</th>
<th>Lung V30</th>
<th>Lung V20</th>
<th>Lung V3</th>
<th>Lung V10</th>
<th>Contralateral breast Mean dose</th>
<th>Contralateral breast V3</th>
<th>Contralateral breast V10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Para Mixed</td>
<td>3.8 (1.3)</td>
<td>1.2 (1.8)</td>
<td>8.7 (3.5)</td>
<td>7.4 (5.8)</td>
<td>9.3 (1.8)</td>
<td>18.0 (4.3)</td>
<td>1.0 (0.3)</td>
<td>2.4 (2.1)</td>
<td>0.5 (0.9)</td>
<td></td>
</tr>
<tr>
<td>Patched</td>
<td>4.3 (1.6)*</td>
<td>1.9 (2.2)*</td>
<td>7.5 (2.6)*</td>
<td>7.1 (5.3)*</td>
<td>7.9 (1.5)*</td>
<td>14.4 (3.3)*</td>
<td>0.6 (0.2)*</td>
<td>0.3 (0.8)*</td>
<td>0.1 (0.3)*</td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td>7.2 (1.7)*</td>
<td>3.8 (2.9)*</td>
<td>12.9 (3.8)*</td>
<td>9.6 (5.7)*</td>
<td>9.5 (2.0)</td>
<td>16.5 (4.2)*</td>
<td>0.7 (0.2)*</td>
<td>0.5 (0.9)*</td>
<td>0.1 (0.3)*</td>
<td></td>
</tr>
<tr>
<td>PWT</td>
<td>3.4 (1.0)</td>
<td>1.9 (3.4)</td>
<td>11.1 (4.4)*</td>
<td>16.0 (4.2)*</td>
<td>12.2 (2.5)*</td>
<td>26.3 (5.3)*</td>
<td>2.8 (1.6)*</td>
<td>15.7 (7.8)*</td>
<td>5.2 (4.3)*</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: PWT = partially wide tangents.

Dose data presented in Gy and volume data in %, with the standard deviation in parenthesis.

* Significantly different from Para Mixed technique, p ≤0.05.
Results

Heart

With left-sided treatment, the heart received the least dose with the Patched and Para Mixed technique, considering both the mean heart dose and the heart V30 (Table 1). With right-sided treatment, the heart received the least dose with the Para Mixed and the PWT technique. The heart dose was significantly higher with the Standard technique for both left- and right-sided treatment together with the PWT technique for left-sided treatment. The only significantly better result compared with the Para Mixed technique was the mean heart dose with the Patched technique for left-sided treatment (7.5 Gy vs. 8.7 Gy).

Lungs

The mean lung dose and lung V20 with the Para Mixed technique were lower than with the PWT technique but higher than with the Patched technique (Table 1). The lung dose with the Para Mixed technique was comparable to that with the Standard technique. The PWT technique resulted in a relative volume of lung receiving ≥35 Gy that was almost two times greater than with the other techniques (Fig. 2). All techniques resulted in a significantly greater lung V20 and mean lung dose for the chest wall cases, whereas the absolute differences between the techniques were generally the same for the breast and chest wall cases.

Contralateral breast

The contralateral breast was excluded in most cases with the Para Mixed technique. Because the contralateral breast was often close to the widened tangential photon beam, a higher dose was delivered to the contralateral breast with the Para Mixed technique than with the Patched and Standard techniques (Table 1). The greatest volume of contralateral breast was irradiated with the PWT technique. The relative volume receiving ≥10 Gy with the PWT technique was 10 times greater than with the Para Mixed technique.
Figure 2. Cumulative average dose–volume histograms
Dose volume histograms represent the heart in left-sided treatment (n = 17), the heart in right-sided treatment (n = 13), and the lungs (n = 30). Abbreviation: PWT = partially wide tangents.
Chapter 6

Table 2. Skin dose IMN region and maximum dose overlap area

<table>
<thead>
<tr>
<th>Skin</th>
<th>Estimated dose (Gy)</th>
<th>Overlap area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average maximum dose (Gy)</td>
<td>Average maximum equivalent dose in 2 Gy fractions (Gy)</td>
</tr>
<tr>
<td>Para Mixed</td>
<td>36</td>
<td>77</td>
</tr>
<tr>
<td>Patched</td>
<td>44</td>
<td>90</td>
</tr>
<tr>
<td>Standard</td>
<td>36</td>
<td>90</td>
</tr>
<tr>
<td>PWT</td>
<td>25</td>
<td>-</td>
</tr>
</tbody>
</table>

**Abbreviations:** IMN = internal mammary nodes; PWT = partially wide tangents.

*The average maximum equivalent dose in 2-Gy fractions was calculated with an α/β of 1.7 Gy, as defined for subcutaneous fibrosis by Bentzen and Overgaard [31].

**Skin and overlap**

The estimated skin dose in the area covered by the electron beam was highest with the Patched technique (Table 2). Skin dose with the Para Mixed and Standard techniques was estimated to be 7 Gy lower than with the Patched technique. The PWT technique resulted in the lowest skin dose because no electron beams were used. The Para Mixed technique resulted in an average maximum dose in the overlap area that was 13 Gy lower compared with the Patched and Standard techniques. No overlap was present in the PWT technique.

**Discussion**

In the present study, the Para Mixed technique was compared with three commonly applied radiotherapy strategies. 3D-CRT treatment planning was performed for all techniques, and all techniques produced equally adequate target coverage of the PTV. The Para Mixed technique performed well compared with the other techniques. The Patched technique resulted in a lower lung dose but delivered the highest dose to the skin and the overlap area. The Standard technique resulted in a higher heart dose and a higher dose in the overlap area. The PWT technique was easier to construct because no electron beams were used. Although high doses to the skin and overlap area were avoided, the PWT resulted in the highest lung dose, a higher heart dose in left-sided treatment, and a considerable
volume of the contralateral breast was irradiated. Unlike with the other techniques, partial irradiation of the contralateral breast could not be avoided with the PWT technique because this would have resulted in a significant increase of the dose delivered to the heart and lungs.

The findings of the present study are not consistent with reports from three other studies that proposed the PWT technique to be the most favourable technique. In a study conducted by Severin et al. [16], the PWT technique was compared with a technique in which a mix of photons and electrons was used to treat the IMN region. Patients with deep IMN (>6 cm) were not excluded, resulting in high-energy photons and electrons with the photon–electron technique, although an adequate coverage of the IMN could not be achieved. This is why patients with deep IMN were excluded in the present study and another study [14]. In the studies conducted by Severin et al. [16] and Arthur et al. [17], custom-shaped blocks were used with the PWT technique. The heart and ipsilateral lung were effectively shielded, allowing only limited volumes to be irradiated. The PWT technique was compared with a photon–electron technique in which standard beams without shielding of the heart and the ipsilateral lung were used. In a study conducted by Pierce et al. [18], the PWT technique was modified to completely shield the heart and then treat the shielded area with electrons. Although the method used in constructing these electron beams was not specified, it seems that heart and lung dose were minimised because no margins for penumbra or position uncertainties were used to define the field edges around the IMN with the PWT technique, and relatively low-energy electrons were used (6–9 MeV). The PWT technique was compared with two photon–electron techniques, in which standard IMN beams were used without effective shielding for the heart and the ipsilateral lung. Severin et al. [16] reported that 24.5% of the contralateral breast received ≥2.5 Gy with the PTW technique.

Comparative planning studies in which similar margins and shielding were applied for all techniques consistently show similar or better results with photon–electron techniques than with techniques in which wide tangential photon beams are used [13,19,20,32]. Two photon–electron techniques were compared by...
Hurkmans et al. [14,15]: the Standard technique and the Improved technique. With both techniques, beam configurations with a fixed position and width for the IMN beams were defined, and a standard overlap size was used. In the present study, the Standard technique was modified and optimised to be compared with the Para Mixed technique. Although the Para Mixed technique was based on the ideas proposed by Hurkmans et al., some technical improvements were introduced. A new beam configuration was used to enable more effective shielding and optimisation. Moreover, the Para Mixed technique is a real 3D-CRT technique with an integrated electron beam, which is individually weighted and shaped for each patient to obtain adequate target coverage and limit the radiation dose to normal tissue. In the studies conducted by Hurkmans et al., the Improved technique was proposed to be the most favourable technique. It was later referred to as the Oblique electron technique in a study by Cho et al. [20]. They compared it with a PWT technique and an IMRT technique. Higher NTCPs for heart and lungs were found with the PWT technique compared with the Oblique electron technique and the IMRT technique. The heart and lung NTCPs were similar for the Oblique electron technique and the IMRT technique. In a study conducted by Johansson et al. [19], similar NTCPs were found for IMRT and the Patched technique. However, the photon–electron plans discussed were not yet created with the optimal use of 3D-CRT, and they can be further improved.

3D-CRT solutions like the Para Mixed technique require more resources than conventional two-dimensional plans. However, the level of complexity involved with the construction and delivery of the Para Mixed technique is similar to that of other advanced multi-beam 3D-CRT techniques. Whereas treatment-planning is performed by a select group of dosimetrists, the delivery is performed by all radiation technologists. During this study, IMN irradiation was restricted to patients who had an internal mammary sentinel node that was identified by lymphoscintigraphy (either unexamined or proved positive by histopathologic evaluation). This resulted in a group of more than 30 patients who were treated with the Para Mixed technique.
Study outcomes are influenced by the way target volumes and margins are defined. For many years, tangential radiation fields were defined during simulation, according to X-ray imaging and exterior patient anatomy. Even at present, when CT data are available, many studies use standard field borders for clinical target definition. There seems to be a certain reluctance to use density information and margins when these might result in larger fields including larger volumes of normal tissue within the treated volume. The same inconsistency is observed regarding the definition of the IMN CTV. Although the internal mammary vessels were used as a reference in many studies, varying volumes were delineated to include the IMN. In this study, the IMN CTV extended through the fourth intercostal space, in accordance with EORTC protocol 22922-10925 [2]. This protocol states that the IMN target volume should include at least the IMN chain in the first three intercostal spaces but, depending on tumour location, can be extended through the fifth intercostal space. We chose an intermediate range as a constant factor with all patients. The ipsilateral edge of the sternum and the pleura were regarded as the outer boundaries enclosing the IMN in lateral and dorsal directions, respectively. It is clear that questions regarding this issue remain and that study results are affected by the way the target volumes are defined. Recently published material might help provide solutions [33,34]. It also remains unclear which margins should be used around the CTV to take into account position uncertainties and penumbra. We believe that the margins used in this study were sufficient for breast cancer radiotherapy. Most importantly, the margins were kept the same for all techniques to make a reliable assessment of the normal tissue dose with the different techniques.

In the case of loco-regional irradiation, the target volume often has a curved shape, with internal concave regions. One can use PWT to avoid the problems of a photon–electron match, but this will include all normal tissue within the concavity of the target volume. Conversely, one can use an electron beam to treat the medial part of the target volume to reduce the size of the concavity that is included within the tangential photon beams. This will involve problems of a photon–electron match and sometimes hot spots. With the Para Mixed technique, a compromise is
reached with respect to both the problems of the photon-electron match and the dose delivered to the normal tissues internally.

In many other planning studies, oblique electron beams were used. In the present study anterior electron beams were used, and an overlap with the tangential photon beams, resulting in a local hot spot, was accepted. To quantify the dimensions of the hot spot with the Para Mixed technique, the local volumes receiving ≥107%, ≥130%, and ≥140% of the prescribed dose were determined for 6 typical patients (breast = 3, chest wall = 3). The volumes were 43 cm$^3$, 15 cm$^3$, and 8 cm$^3$ for the breast cases and 46 cm$^3$, 8 cm$^3$, and 3 cm$^3$ for the chest wall cases, respectively. The average length of the overlap area was 12.0 cm for the breast cases and 15.3 cm for the chest wall cases. This illustrates that the maximum dose delivered to the overlap area (Table 2) is confined to a relatively small volume. Although side effects have not been specifically scored, a few cases of acute erythema, but no severe detrimental effects, have yet been observed in the group of patients treated with the Para Mixed technique in our institution since 2002.

We investigated the behaviour of anterior and oblique electron beams at our institution. It seemed that with an anterior electron beam, the deepest points within the IMN PTV could be reached with the use of lower electron energies. This resulted in a lower heart dose, lung dose, and skin dose. The target coverage within the IMN PTV was more adequate with the anterior electron beam. Even in rather slim patients, oblique electron beams failed to yield adequate target coverage. This is consistent with reports from others [15,20,35]. When oblique electron beams are used, there is a greater risk of under-dosage to the breast or chest wall PTV at the place where the photon and electron beams are matched, due to position uncertainties and patient motion during treatment. To maintain adequate target coverage with all techniques and for all patients, we used anterior electron beams. With the Para Mixed technique, the electron beam is integrated in the treatment plan. In this way apertures conformal to the PTV can be created in beam’s-eye-view. Photons and electrons can be mixed to achieve an optimal sparing of normal tissue while adequate target coverage is maintained. The electron beam model implemented in our treatment-planning system, in conjunction with the pencil
beam algorithm used, has been compared with measurements in water at our institution and with dose distributions in patient CT, calculated by a state-of-the-art algorithm [36]. It proved to be accurate with respect to the parameters reported in this study, beam output, depth of 90% electron isodose, and depth of dose profiles, as well as the maximum overall dose in the treatment plan. Its poor penumbra modelling had no influence on these parameters. Although electrons have valuable dose-limiting characteristics, their role is still limited in 3D-CRT. In this study, we demonstrated that the integration of electrons in 3D-CRT can further improve existing techniques and should therefore be the subject of future research. Application of better electron dose calculation algorithms provides a valuable improvement for this purpose [36].

Conclusions

Normal tissue dose and especially heart dose can outweigh the benefits of IMN irradiation. The Para Mixed technique is an improved 3D-CRT technique in which the IMN are treated by a mix of photons and electrons. In this study, we compared the dose to the heart and other organs at risk with the Para Mixed technique with that with three other commonly applied radiotherapy strategies. All techniques were optimised and produced equally adequate target coverage. The Para Mixed technique yielded the overall best results. No other technique resulted in a lower heart dose. Lung and skin were equally spared instead of one of them being compromised, and the contralateral breast was avoided.
References


