Chapter 7

Reduction of cardiac and lung complication probabilities after breast irradiation using conformal radiotherapy with or without intensity modulation

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Abstract

Purpose. The main purpose of this work is to reduce the cardiac and lung dose by applying conformal tangential beam irradiation of the intact left breast with and without intensity modulation, instead of rectangular tangential treatment fields. The extension of the applicability of the maximum heart distance to conformal tangential fields as a simple patient selection criterion, identifying patients for which rectangular and conformal tangential fields without intensity modulation will result in unacceptable NTCP values for late cardiac mortality (e.g., > 2%), was also investigated.

Materials and methods. 3D treatment planning was performed for 17 left-sided breast cancer patients. Three different tangential beam techniques were compared: 1) optimised wedges without blocks, 2) optimised wedges with conformal blocks and 3) intensity modulation. Plans were evaluated using dose-volume histograms (DVHs) for the planning target volume (PTV), the heart and the lungs. Normal tissue complication probabilities (NTCPs) for radiation pneumonitis and late cardiac mortality were calculated using the DVH data. The maximum heart distance (MHD) was measured for all rectangular (MHD_{rectangular}) and conformal (MHD_{conformal}) treatment plans.

Results. For all patients, on average part of the PTV receiving a dose between 95% and 107% of the prescribed dose of 50 Gy in 25 fractions of 2 Gy was 90.8% (SD: 5.0%), 92.8% (SD: 3.5%) and 92.8% (SD: 3.6%) for the IMRT, conformal and rectangular field treatment technique, respectively. The NTCP for radiation pneumonitis was 0.3% (SD: 0.1%), 0.4% (SD: 0.4%) and 0.5% (SD: 0.6%) for the IMRT, conformal and rectangular field technique, respectively. The NTCP for late cardiac mortality was 5.9% (SD: 2.2%) for the rectangular field technique. This value was reduced to 4.0% (SD: 2.3%) with the conformal technique. A further reduction to 2.0% (SD: 1.1%) could be accomplished with the IMRT technique.

The NTCP for late cardiac mortality could be described as a second order polynomial function of the MHD. This function could be described with a high accuracy and was independent of the technique for which the MHD was determined ($r^2 = 0.88$). In order to achieve a NTCP value for late cardiac mortality below 1%, 2% or 3%, the MHD should be equal to or smaller than 11 mm, 17 mm or 23 mm, respectively. If such a maximum complication probability cannot be accomplished, a treatment using the IMRT technique should be considered.

Conclusions: The use of conformal tangential fields decreases the NTCP for late cardiac toxicity on average by 30% compared to using rectangular fields, while the tangential IMRT technique can further reduce this value by an additional 50%. The MHD can be used to estimate the NTCP for late cardiac mortality if rectangular or conformal tangential treatment fields are used.
**Introduction**

Radiation therapy after breast conserving surgery of patients with breast cancer is effective in reducing the risk of a local recurrence. Postoperative radiotherapy of the breast is typically delivered with rectangular tangential fields. With this technique appreciable dose inhomogeneity within the irradiated volume can be present [2,4], and the dose delivered to the lung, and heart can be high [12,15,27].

Intensity modulation radiation therapy (IMRT) techniques have been developed in order to reduce these dose variations and spare the organs at risk. Some of these techniques use tangential fields with a non-divergent dorsal field edge [3,6,7]. Others have developed conformal tangential IMRT techniques in which the beam intensity profile is conformed to the chest wall or delineated target volume [13,24,25,29,30]. The shape of the IMRT profile can be optimised based on geometrical parameters such as the shape of the breast and thoracic wall or on dosimetric parameters using inverse planning. Most of these studies had as a main purpose to make the dose distribution in the breast more homogeneous, using geometrical parameters. Consequently, it was not always possible to establish a satisfactory compromise between the dose delivered to the target volume and the dose delivered to the organs at risk. Inverse planning does provide a method for minimizing the dose in the organs at risk while maintaining adequate target coverage.

Most IMRT studies show a potential clinical benefit compared to rectangular tangential fields without conformal blocks, either in sparing organs at risk or in improved dose homogeneity over the target volume. However, implementation in clinical practice of such IMRT techniques will require additional resources compared to conventional breast treatment because IMRT delivery and verification will be more time consuming and complex. Therefore, it would be useful to distinguish between patients for whom IMRT is needed, and patients, who can be treated satisfactorily without IMRT.

Hong et al. showed a benefit of IMRT plans when compared to standard treatment planning techniques using optimised beam weights and wedges and superior and inferior corner blocks in the tangential fields if needed [13]. However, they did not compare these treatment plans with standard rectangular tangential fields that are widely used in clinical practice. The dose distribution can already be more conformed to the target volume if 3D data are available and conformal treatment fields are used compared to using rectangular tangential fields, consequently reducing the dose to the organs at risk. Intensity modulation can be considered as an additional step and allows for greater freedom in improving the dose distribution than a combination of open and wedged beams. This may result in a further
improvement of the dose distribution in both the target volume and the organs at risk. The relative improvement attributable to the intensity modulated irradiated fields versus conformed fields is not yet known for breast irradiation.

The aim of this study is to quantify the possible reduction in radiation toxicity of the organs at risk using conformal radiotherapy with and without the use of intensity modulation, compared to simple rectangular tangential field irradiation. It was also investigated if it is possible to extent the applicability of the maximum heart distance to conformal tangential fields as a simple patient selection criterion, identifying patients for which rectangular and conformal tangential fields without intensity modulation will result in unacceptable NTCP values for late cardiac mortality [15].

Methods and Materials

Patient data

The CT data of 17 randomly selected left-sided breast cancer patients were used for this retrospective treatment planning study. CT slices of the thorax were acquired every 5 mm with the patient lying in supine position. Ten patients were positioned with both arms resting in an arm-rest placed above the head equivalent to the treatment position, while the other 7 had their arms placed besides but not touching their body. This position has been shown to enable treatment planning of tangential fields without the arms extending into the treatment fields, without changing the breast shape significantly [11,18]. The CT scan included the complete left and right lung, both breasts and the heart. The average separation between the most medial and most lateral aspect of the breast was 21.1 cm (range: 18.0-26.5 cm).

Definition of planning target volume and organs at risk

The clinical target volume (CTV) was delineated by a radiation oncologist using a standard window level (0 HU) and width (500 HU), which is in our institution considered optimal for visibility of the glandular breast tissue. The CTV was assumed to start 5 mm below the skin and to be smooth.

A planning target volume (PTV) was generated by expanding the CTV 7 mm isotropically, except in the direction of the skin surface, to account for the uncertainty in the patient set-up and CTV delineation. The average PTV
was 796 cm$^3$ (range: 180-1883 cm$^3$).

The cranial extent of the heart included the infundibulum of the right ventricle, the right atrium, and the right atrium auricle but excluded the pulmonary trunk, the ascending aorta and the superior vena cava. The lowest external contour of the heart was the caudal border of the myocardium. The pericardium was excluded from the heart volume. The contours of the lungs and skin were automatically outlined.

**Rectangular and conformal plans**

The gantry and collimator angles of the tangential 6 MV photon fields were chosen using the beam's-eye view option of our 3D treatment planning system U-Mplan (version 339) [8]. A margin of 6 mm was taken between the field edge and the breast PTV to account for the beam penumbra. The dorsal field edges of the tangential fields were made non-divergent to reduce the irradiated lung volume. The rectangular plans did not include any blocks in the treatment fields. In the conformal plans, an automatically generated conformal block around the PTV with a margin of 6 mm was added to these fields. The treatment planning was performed using the 3-D treatment planning system. An octree/edge model [9] is used for photon beam dose calculations in combination with an equivalent path length algorithm to account for tissue inhomogeneities [19]. The optimum wedge angle and beam weights were calculated using the optimisation module (version 1.0) of U-Mplan. The goal of the optimisation is to obtain a homogeneous dose, between 95% and 107% of the prescribed dose of 50 Gy in the PTV, while maintaining a low dose in the lungs and heart. The quadratic objective function, the mean square deviation between calculated and prescribed dose values in the PTV and dose constraints for the organs at risk, was optimised. The parameters of the physical objective function are listed in Table 1.

<table>
<thead>
<tr>
<th>Volume; priority</th>
<th>Minimum dose (Gy)</th>
<th>Maximum dose (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart; 1</td>
<td>49.5 (75)</td>
<td>24 (5)</td>
</tr>
<tr>
<td>PTV; 2</td>
<td></td>
<td>50 (50)</td>
</tr>
<tr>
<td>Left lung; 3</td>
<td>15 (2.5)</td>
<td></td>
</tr>
<tr>
<td>Right lung; 4</td>
<td>15 (2.5)</td>
<td></td>
</tr>
<tr>
<td>Total body volume; 5</td>
<td>15 (1)</td>
<td></td>
</tr>
</tbody>
</table>

*Table 1.* Objective function used in the inverse planning process. The penalties are given in brackets. The priority determines to which volume voxels will be assigned in KonRad in case different volumes overlap.
IMRT plans

Using the same gantry angles as applied in the rectangular field plans, tangential 6 MV photon beam intensity profiles were calculated using the inverse planning program KonRad version 1.2 beta 10 (MRC Systems GmbH, Heidelberg, Germany) [26]. The same physical objective function used in the optimisation of the rectangular and conformal treatment plans was used to calculate the optimal intensity profiles.

The resolution of the intensity matrices was set to 10 mm (leaf width) by

\[
\text{Beam's eye view of tangential field}
\]

**Figure 1.** The maximum heart distance (MHD) is defined as the maximum distance of the heart contour, as seen in a beam's-eye view of the medial tangential field, to the medial field edge, determined perpendicular to the dorsal field border. The MHD of the rectangular field \((MHD_{\text{rectangular}})\) is measured to the medial field border determined by the collimator jaw, while the MHD of the conformal field \((MHD_{\text{conformal}})\) is measured to the medial field border determined by the conformal block.

5 mm (direction of leaf travel). A separate sequencer developed at the Radiotherapy Department of the Utrecht Medical Centre, The Netherlands, combined with in-house developed software was used to convert the KonRad fluence profiles to suitable step-and-shoot segments, which allows delivery on an Elekta treatment unit. To minimize the number of segments, a 1-D median filter (bixelwidth: 5) along the direction of leaf travel was applied to the continuous fluence profiles. These were then stratified into 10 equally spaced intensity levels. It was estimated that this number of levels would yield no more than 30 segments per fraction. This was considered the maximum acceptable number of segments for clinical implementation in our institute at the time this study took place due to the time needed to deliver

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30 segments and the amount of console input needed after every segment at an Elekta linear accelerator without Elekta RTD step-and-shoot software.

After sequencing, the segment weights were refined with the optimisation module of U-Mplan, using the same objective score function. This additional optimisation accounted for the differences in the segment normalization between U-Mplan and KonRad. The final dose distribution was calculated using U-Mplan. Thus, the same dose calculation algorithm was used for all rectangular, conformal and step-and-shoot IMRT plans.

### Table 2. Mean PTV coverage and heart and lung complication probabilities for the IMRT, conformal and rectangular irradiation techniques.

<table>
<thead>
<tr>
<th>Volume of interest</th>
<th>Parameter</th>
<th>IMRT</th>
<th>Conformal</th>
<th>Rectangular</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (SD)</td>
<td>% (SD)</td>
<td>% (SD)</td>
<td></td>
</tr>
<tr>
<td>PTV</td>
<td>Mean dose</td>
<td>100 (0.0)</td>
<td>100 (0.0)</td>
<td>100 (0.0)</td>
</tr>
<tr>
<td></td>
<td>Mean SD of the dose to the PTV</td>
<td>4.3 (1.3)</td>
<td>4.0 (0.9)</td>
<td>4.0 (0.9)</td>
</tr>
<tr>
<td></td>
<td>( V_{D95%} - V_{D107%} )</td>
<td>90.8 (5.0)</td>
<td>92.8 (3.5)</td>
<td>92.8 (3.6)</td>
</tr>
<tr>
<td></td>
<td>( V_{D95%} ; V_{D107%} )</td>
<td>93.0 ; 2.2</td>
<td>95.2 ; 2.5</td>
<td>95.5 ; 2.8</td>
</tr>
<tr>
<td>Heart</td>
<td>NTCP</td>
<td>2.0 (1.1)</td>
<td>4.0 (2.3)</td>
<td>5.9 (2.2)</td>
</tr>
<tr>
<td></td>
<td>( V(D95%) )</td>
<td>1.0 (1.0)</td>
<td>4.0 (4.1)</td>
<td>4.9 (3.6)</td>
</tr>
<tr>
<td>Both lungs</td>
<td>NTCP</td>
<td>0.3 (0.1)</td>
<td>0.4 (0.4)</td>
<td>0.5 (0.6)</td>
</tr>
<tr>
<td></td>
<td>Mean dose</td>
<td>9.8 (2.5)</td>
<td>9.2 (6.3)</td>
<td>11.3 (7.1)</td>
</tr>
</tbody>
</table>

\( ^1 \text{SD : standard deviation} \)

\( ^2 V_{D95\%} - V_{D107\%} : \) The part of the PTV that receives a dose higher than 95% and less than 107% of the prescribed dose.

### Data analysis

The prescribed dose was 2 Gy per fraction, with a total treatment dose of 50 Gy delivered over 5 weeks. In order to compare the dose distribution in the PTV objectively between the different techniques, each plan was normalized to the mean dose and the dose variation was characterized by its standard deviation. It is assumed that similar differential DVHs, as defined by their mean and standard deviation, would yield identical treatment results, i.e., local control, for the breast for all techniques. The more commonly used homogeneity parameter \( V_{95\%-107\%} \), the part of the PTV receiving at least 95% but less than 107% of the reference dose, was also calculated for the breast PTV [20]. The breast separation, defined as the distance between the medial and lateral field borders at the cranio-caudal position of the nipple, was measured to be able to determine the dependence of the dose homogeneity in the breast on this parameter.
To quantify lung and heart toxicity, the physical dose distribution was first converted into a normalized total dose (NTD) distribution [23], using the linear quadratic model with an $\alpha/\beta$ ratio of 3 Gy. For the heart, the Normal Tissue Complication Probability (NTCP) for excess cardiac mortality after 10-15 years caused by myocardial infarcts or ischaemic heart diseases was calculated using a fractionation schedule of 2 Gy per fraction and by applying the relative seriality model [21] with parameter values $s=1$, $D_{50}=52.3$ Gy and $\gamma=1.28$ as derived by Gagliardi et al. [10].

In order to find a simple selection criterion for patients who cannot be treated adequately without IMRT, the maximum heart distance (MHD) was determined for the rectangular (MHD$_{\text{rectangular}}$) and conformal (MHD$_{\text{conformal}}$) technique [15]. This quantity is defined as the maximum distance of the heart contour to the medial field edge of a rectangular or blocked field, measured parallel to the caudal field edge, as can be seen on a beam’s-eye view of the medio-lateral tangential field (Figure 1).

In the calculations of lung toxicity, the left and right lungs are treated as a single organ. After the NTD calculation, the mean normalized total dose (NTD$_{\text{mean}}$) is calculated and used to compute the NTCP for radiation pneumonitis. The clinical results of a large multi-centre study of the relation between the incidence of radiation pneumonitis and DVH parameters [22]
were used. Paired two-sided Student t-tests were used to test if the differences in PTV homogeneity and NTCP values between the three irradiation techniques were statistically significant.

**Results**

The dose variation in the PTV (SD) is not significantly different between the three techniques (p-values > 0.3), resulting in similar treatment results for the breast for all techniques (Table 2). The average number of segments per fraction for the IMRT technique is 15 (range: 7-25), which meets our planned constraint that the total number of segments per fraction should not exceed 30. An example of the difference between the IMRT and conformal dose distribution in the plane perpendicular to the beam axis at the position where the largest part of the heart is inside the conformal fields is shown in Figure 2.

**Table 3.** Mean PTV coverage and heart and lung complication probabilities for the IMRT, conformal and rectangular irradiation techniques.

<table>
<thead>
<tr>
<th>Volume of interest</th>
<th>Parameter</th>
<th>IMRT % (SD)</th>
<th>Conformal % (SD)</th>
<th>Rectangular % (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>Mean dose</td>
<td>100 (0.0)</td>
<td>100 (0.0)</td>
<td>100 (0.0)</td>
</tr>
<tr>
<td></td>
<td>Mean SD of the dose to the PTV</td>
<td>4.3 (1.3)</td>
<td>4.0 (0.9)</td>
<td>4.0 (0.9)</td>
</tr>
<tr>
<td></td>
<td>V95% - V107%</td>
<td>90.8 (5.0)</td>
<td>92.8 (3.5)</td>
<td>92.8 (3.6)</td>
</tr>
<tr>
<td></td>
<td>V95% ; V107%</td>
<td>93.0 ; 2.2</td>
<td>95.2 ; 2.5</td>
<td>95.5 ; 2.8</td>
</tr>
<tr>
<td>Heart</td>
<td>NTCP</td>
<td>2.0 (1.1)</td>
<td>4.0 (2.3)</td>
<td>5.9 (2.2)</td>
</tr>
<tr>
<td></td>
<td>V(D95%)</td>
<td>1.0 (1.0)</td>
<td>4.0 (4.1)</td>
<td>4.9 (3.8)</td>
</tr>
<tr>
<td>Both lungs</td>
<td>NTCP</td>
<td>0.3 (0.1)</td>
<td>0.4 (0.4)</td>
<td>0.5 (0.6)</td>
</tr>
<tr>
<td></td>
<td>Mean dose</td>
<td>9.8 (2.5)</td>
<td>9.2 (6.3)</td>
<td>11.3 (7.1)</td>
</tr>
</tbody>
</table>

1SD : standard deviation  
2V95% - V107% : The part of the PTV that receives a dose higher than 95% and less than 107% of the prescribed dose.

Compared to the conformal dose distribution, The IMRT dose is reduced with approximately 20% near the dorsal border of the PTV, thus reducing the dose in the lungs and heart. The IMRT dose is increased with approximately 5% in the middle of the PTV to achieve a more homogeneous dose distribution in that part. Overall, the standard deviation of the dose distribution in the breast is not significantly different between the two techniques, but the position of the low and high dose regions is reallocated. The average dose homogeneity, expressed as V95%-107%, is 90.8% for the IMRT technique compared to 92.7% and 92.8% for the two other
techniques. The differences in $V_{95\%-107\%}$ between the IMRT and conformal technique and conformal and rectangular field technique are not statistically significant with p-values of 0.13 and 0.48, respectively. The use of 6 MV beams results in an acceptable homogeneous dose for our clinically used rectangular field technique in almost all patients. Using this technique, only for 2 patients, with a breast separation greater than 24 cm, is the $V_{95\%-107\%}$ less than 90%. The dose variation over the PTVs was almost uncorrelated with the breast separation ($r^2 < 0.2$) and the variation was only weakly correlated with breast volume ($r^2 < 0.4$).

The average NTCP value for late cardiac mortality is 5.9% for the rectangular field technique. This value is reduced to 4.0% and 2.0% using the conformal or IMRT technique, respectively. These reductions are both highly significant with p-values <0.001. The NTCP values calculated for the three techniques for each patient are shown in Figure 3. For patient #13, a slightly higher NTCP value was found for the conformal technique than for the rectangular field technique. This was caused by an altered dose distribution in the PTV. The high dose region in the PTV shifted slightly to the inferior side of the breast. This resulted in a lower mean dose to the PTV relative to the dose to the heart than for the rectangular plan. After renormalization of the plan to the mean PTV dose, the dose to the heart in the conformal plan was slightly higher than the dose to the heart in the rectangular plan.

Figure 3. Calculated NTCP values for late cardiac mortality for the rectangular field technique (grey bars), the conformal technique (open bars) and the IMRT technique (black bars).
There is a strong correlation between $\text{MHD}_{\text{rectangular}}$ and the NTCP for late cardiac mortality for the rectangular field technique, and a corresponding correlation between $\text{MHD}_{\text{conformal}}$ and the NTCP for the conformal technique. The NTCP data of the rectangular and conformal technique are fitted to a single second-degree polynomial function of the MHD, with a high correlation ($r^2 = 0.88$), independent of the technique used. This simple patient selection curve can easily be used clinically to select patients for IMRT treatment. The data and polynomial fit with 95% confidence interval of the fit are shown in Figure 4.

![Figure 4](image)

**Figure 4.** NTCP for late cardiac mortality versus maximum heart distance for the rectangular (■) and conformal (○) technique. The data of a previous study (x) using the rectangular field technique [14] has also been included. The straight line represents the best fit through all data points using a second order polynomial, while the dotted lines show the 95% confidence interval of the fitted curve ($r^2 = 0.88$).

The average NTCP for radiation pneumonitis was already low for the rectangular field technique (0.5%). This value was further reduced to 0.4% and 0.3% using the conformal and IMRT technique, respectively. However, the difference between the conformal and IMRT technique is not significant ($p=0.28$). The differences between the IMRT technique and rectangular field technique and between the conformal and rectangular field technique are, however, significant ($p=0.05$ and $p=0.003$, respectively). Cumulative dose-volume histograms for the lung and heart for one patient (patient #8) are given as an example in figure 5.
Figure 5. Cumulative dose-volume histograms for the lung (A) and heart (B) for one patient (patient #8).

Discussion

The IMRT treatment planning procedure is more time consuming than the rectangular or conformal field treatment planning procedure. The extra steps in the planning process involve: 1) Transportation of the CT scans and
contours to the inverse treatment planning system. 2) Defining the gantry and collimator angles of the beams and optimising the beam fluence profiles using the objective function. 3) Sequencing of the beams to produce step-and-shoot segments that can be delivered on an Elekta accelerator and 4) Transportation of these beam segments back to our clinical treatment planning system. These extra steps in the planning procedure take approximately 20 minutes. This extra time only applies for the specific combination of the KonRad and U-Mplan treatment planning systems used in our institution and will be different if other treatment planning systems are used.

3D treatment planning is not always needed to prevent high lung or heart doses. To minimize the treatment preparation workload on a CT scanner and in the treatment-planning department, we suggest one can start with standard simulation of tangential fields on a conventional simulator. Only when the maximum heart distance [15] or central lung distance [1] exceeds certain limits, full 3D treatment planning is needed. For instance, if one wants a maximum estimated NTCP for late cardiac mortality of 1%, 2% or 3%, the MHD should be equal to or smaller than 11 mm, 17 mm or 23 mm, respectively (see Figure 4). If the MHD is, for example, 22 mm using rectangular fields, but can be reduced to 15 mm or less by conforming the fields to the PTV by applying the simulator images, than full 3-D planning can still be avoided if an estimated NTCP of 2% or less is acceptable. However, if the MHD still exceeds 17 mm, a full 3-D IMRT treatment plan should be considered to reduce the NTCP for late cardiac mortality below 2%.

By conformation of the treatment fields to the target volume, part of the heart is blocked which results in the observed reduction in NTCP values for cardiac mortality compared to the rectangular field technique. The observed dose reduction to the heart when going from the conformal technique to the IMRT technique is mainly attributed to the reduction in dose in the area between the PTV edge and the block edge, i.e., the 7 mm margin around the PTV (Figure 2). This isotropic margin to account for the beam fringe, i.e., the distance between the 95% and 50% isodose surface, required in the conformal plan is not needed in the IMRT plan. The size of the IMRT beam only depends on the dose based objective function and the position of the PTV with respect to the organs at risk, and not on predefined minimum margins between the beam edge and the PTV. A similar result might also be reached by placement of a block to shield the heart completely. However, such a procedure will result in a decrease in dose in the PTV.

The difference in the average $V_{95\%-107\%}$ between the techniques is not statistically significant. This can be expected, as the standard deviation of $V_{95\%-107\%}$ within each technique is much larger than the difference of the average $V_{95\%-107\%}$ between the techniques. The dose in the medial part of
the PTV is slightly reduced for some patients using the IMRT technique, which is not evident from the DVH data. This was reviewed by one of our clinicians, who judged these small reductions clinically not significant, also keeping in mind the large inter-observer variations in the delineation of the target volume [16].

The NTCP model parameters to model excess cardiac mortality resulting from radiotherapy were determined by Gagliardi et al. These parameters were considered most clinically applicable since they were derived from the data of two large randomised trials concerning breast cancer irradiation i.e., the Stockholm and Oslo breast cancer trials [14,28]. However, the uncertainty in the scoring of excess cardiac deaths was still large and the 95% confidence interval ranged from 0 to 15%. This attributed to a considerable uncertainty in the determination of the parameter values. However, a large meta-analysis of eight clinical breast cancer trials for patients that received a radical or modified mastectomy and radiotherapy, including the Oslo and Stockholm trials, confirmed the existence of excess cardiac mortality [5]. No significant differences in excess cardiac mortality between the trials were found, which suggest the values predicted by the NTCP model are in the same range as the generally observed values. Still, one has to be careful to rely on the absolute NTCP values only and one should take dose-volume or other treatment parameters into account as well.

In this study, the margin between the PTV and CTV was 7 millimetres. This margin is considered adequate to take set-up and CTV delineation uncertainty into account. The size of the set-up errors has been determined in a number of institutions [17]. The effect of set-up errors on the dose homogeneity in the PTV and on the NTCP values will be the subject of future work. These effects may be important for the delivery of both the conformal and IMRT technique. The dose to the contralateral breast will probably not differ much between the standard and conformal techniques studied, if the conformal field shape is generated using multileaf collimation. The difference in contralateral breast dose between these two techniques and the IMRT technique will depend on the practical clinical implementation, e.g. MLC generated versus use of compensators or physical wedges, of the IMRT technique [3]. Treatment verification of the dose distribution and dose delivery in clinical practice using a liquid ionisation chamber EPID is currently investigated in our institution. The appropriate margin that should be applied in order to also incorporate CTV delineation uncertainty depends on the variation in CTV delineation. Data about these variations are scarce and more data are needed to properly account for delineation uncertainties.

A single global objective function for all patients was used which resulted in an overall decrease in heart and lung NTCP while still maintaining adequate dose homogeneity in the PTV. Thus, the planning of the IMRT
技术可以被用于临床实践而不会消耗大量的时间。

比较剂量分布的标准偏差，将PTV的剂量分布正常化到平均PTV剂量，可以潜在地允许我们比较来自不同机构的不同技术。另一个参数，D95% - D5%，其中D95%和D5%分别表示PTV内至少95%和5%的最高剂量，由van Asselen等人[30]用于比较DVHs。这个参数的优点是它的归一化程序的独立性。然而，不同的归一化程序会影响PTV内和风险器官的绝对剂量水平。因此，具有相似D95% - D5%值的IMRT技术可能不会暗示相似的PTV治疗结果。因此，在仅比较剂量到器官时，必须小心地评估具有相似D95% - D5%值的不同治疗技术。

PTV的剂量变化与乳腺分离和乳腺体积几乎无关。尤其是对于IMRT技术，我们可能期望PTV剂量的均匀性主要是归因于对峙束的剂量特性，这取决于乳腺的大小和分离。该研究的主要目的是避免心脏的损害，而不影响PTV剂量的均匀性。因此，一个剂量分布从扩散到PTV和乳房大小或分离的IMRT治疗计划的正相关是偶然的。

结论

在本研究中，定义了三种切线乳腺治疗技术并进行了评估。使用单个全局评分函数用于逆向治疗计划优化。MHID被测量了矩形和规范治疗技术，并可用于估算NTCP延迟心脏死亡。使用规范的切线场，可以显著降低NTCP延迟心脏毒性平均约30%，而强度调节甚至可以进一步降低50%的风险。
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References
