Chapter 5

Limited benefit of inversely optimised intensity modulation in breast conserving radiotherapy with simultaneously integrated boost

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Abstract

Purpose: To examine whether in breast conserving radiotherapy (RT) with simultaneously integrated boost (SIB), application of inversely planned intensity modulated radiotherapy (IMRT-SIB) instead of three-dimensional RT (3D-CRT-SIB) has benefits that justify the additional costs, and to evaluate whether a potential benefit of IMRT-SIB depends on specific patient characteristics.

Materials and Methods: 3D-CRT-SIB and various IMRT-SIB treatment plans were constructed and optimised for 30 patients with early stage left-sided breast cancer. Coverage of planning target volumes (PTV) and dose delivered to organs at risk (OAR) were determined for each plan. Overlap between heart and breast PTV (OHB), size of breast and boost PTVs and boost location were examined in their ability to identify patients that might benefit from IMRT-SIB.

Results: All plans had adequate PTV coverage. IMRT-SIB generally reduced dose levels delivered to heart, lungs, and normal breast tissue relative to 3D-CRT-SIB. However, IMRT-SIB benefit differed per patient. For many patients, comparable results were obtained with 3D-CRT-SIB, while patients with OHB >1.4 cm and a relatively large boost PTV volume (>125 cm³) gained most from the use of IMRT-SIB.

Conclusion: In breast conserving RT, comparable results are obtained with 3D-CRT-SIB and IMRT-SIB. Patient characteristics could be used to identify patients that are most likely to benefit from IMRT-SIB.
Introduction

Breast-conserving therapy with the adjuvant use of radiotherapy (RT) has been acknowledged as standard treatment for early stage breast cancer since survival rates proved to be similar to those obtained with radical surgery [1,2]. Moreover, recent data confirmed that local control can be improved by an additional boost of 16 Gy to the lumpectomy cavity after administration of 50 Gy to the whole breast [3]. Traditionally, delivery of this boost dose has been performed sequentially, i.e., after completion of whole-breast RT [4]. However, with the clinical introduction of intensity-modulated RT (IMRT) in breast cancer, the so-called simultaneously integrated boost (SIB) has also been introduced for breast-conserving RT [5]. With the SIB method, the initial planning target volume (PTV) includes breast PTV and boost PTV, integrated in a single treatment plan that is applied during each fraction throughout the course of treatment. In general, a higher dose per fraction is delivered to the boost PTV allowing for a reduction of the number of treatment fractions.

Recently, we reported on the use of a more advanced three-dimensional conformal technique using SIB (3D-CRT-SIB) [6]. This 3D-CRT-SIB technique allowed for a significantly improved dose-to-boost-target conformity as compared to the classical sequential 3D-CRT technique. Direct comparisons between whole breast IMRT and classical 3D-CRT techniques showed favourable results for IMRT regarding the dose delivered to normal tissues [7,8]. As the results obtained with our 3D-CRT-SIB technique with regard to the amount of normal breast tissue that received excess boost dose outside the boost PTV appeared to be similar to those described with IMRT-SIB [9], the question arises as to whether the dose distributions obtained with 3D-CRT-SIB are comparable to those obtained with IMRT-SIB.

While breast IMRT may generally reduce dose to organs at risk (OAR) below the levels obtained with conventional 3D-CRT, the actual reductions that can be obtained with manually optimised SIB are not yet clear. In addition, when a potential benefit of IMRT-SIB exists, it may be observed in specific subgroups of
patients only. This could be of particular interest for institutes that do not (yet) have the capability to prescribe IMRT to all of their patients, i.e., implementation of 3D-CRT-SIB instead of the conventional sequential 3D-CRT boost technique could be a very cost effective solution in countries where treatment with IMRT requires substantial investments and may increase the costs of radiotherapy [10,11].

Therefore, a planning comparative study was performed to examine different strategies for breast IMRT-SIB and to determine whether the dose delivered to OAR can be reduced compared to 3D-CRT-SIB. In addition, we examined specific patient characteristics in relation to potential reductions of dose delivered to OARs with IMRT-SIB.

**Materials and Methods**

**Patients**

Thirty patients with early stage left-sided breast cancer who had previously undergone RT after breast-conserving surgery were selected for this study. Patients were selected in such a way that an equal distribution of breast shapes, breast sizes, boost locations and cardiac anatomy was obtained. Of each patient, a planning computed tomography (CT) scan was available, acquired in treatment position with a slice thickness and index of 3 mm. All patients had provided informed consent before starting RT, and the ethics committee at the University Medical Center Groningen approved the procedures followed.

**Regions of interest and 3D-CRT-SIB treatment planning**

Definition of regions of interest and the 3D-CRT-SIB technique have been described previously in more detail [6]. Briefly, breast and boost clinical target volumes (CTVs) were delineated and expanded with a margin of 5 mm to generate the breast and boost PTVs. The breast and boost PTVs were restricted to 6 mm within the skin surface. Radiotherapy treatment planning was performed with the Pinnacle³ treatment planning system (TPS), using 6 MV photons, and the adaptive convolve algorithm for all dose calculations. Dose distributions were calculated
taking into account a SIB schedule of 28 fractions, with a daily dose of 1.81 Gy delivered to the breast PTV and 2.30 Gy delivered to the boost PTV.

The 3D-CRT-SIB treatment plans were constructed by using tangential breast beams with multileaf collimator (MLC) shielding conformal to the breast PTV. Gantry angles for the breast beams were chosen such that maximum avoidance of the heart, ipsilateral lung, and contralateral breast was achieved. Three boost beams were added with MLC shielding conformal to the boost PTV. Boost beam gantry angles were selected on the basis of patient anatomy and boost location. In general, one or more boost beams had non-tangential beam directions, avoiding the heart as much as possible and excluding the contralateral breast at all times. Manually shaped MLC segments (up to a maximum number of 3 for each plan) were added to enable dose plan optimisation. All beams had the same isocenter and the same dose-normalization point, that were both placed centrally in the boost PTV. Manual optimisation of the SIB dose plan was performed by adjusting beam weights, wedge fractions and MLC settings for all beams in such a way that the 95%-isodose closely encompassed the PTVs in three dimensions, and volumes receiving ≥107% of the dose prescribed to the PTVs were minimised (Table 1).

100%IMRT-SIB and 25%IMRT-SIB treatment planning

Four direct aperture optimisation (DAO)-based IMRT treatment plans were constructed for each patient: two fully segmented plans (100%IMRT-SIB) and two plans combining conformal beams with skin flash and IMRT segments (25%IMRT-SIB). In the 25%IMRT-SIB plans, 65% of the prescribed total dose was delivered with beams conformal to the breast PTV, 10% with beams conformal to the boost PTV and 25% with IMRT segments. In each patient, beam directions used in the IMRT-SIB plans were always similar to those used in the 3D-CRT-SIB plan. Conformal beams included a skin flash of 3 cm whenever appropriate. DAO-settings were the same for each IMRT-SIB plan: a minimal segment size of 4 cm², at least 4 monitor units per segment, and a maximum of 10 segments for each beam direction. The IMRT-SIB optimisation process was performed on the basis of a series of structures that were created in addition to the OARs and PTVs (Fig. 1).
Objectives and objective values were entered for each structure and adjusted during treatment plan optimisation to comply best with the criteria for dose plan acceptance (Table 1).

Table 1. Criteria of acceptance for 3D-CRT-SIB and IMRT-SIB dose plans

<table>
<thead>
<tr>
<th>Objects</th>
<th>3D-CRT-SIB</th>
<th>Class solution IMRT-SIB</th>
<th>Optimised solution IMRT-SIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Planning target volumes</td>
<td>≥98% of volume, ≥95% of dose</td>
<td>≥98% of volume, ≥95% of dose</td>
<td>≥98% of volume, ≥95% of dose</td>
</tr>
<tr>
<td>Volume ≥108% boost dose</td>
<td>≤2 cm³</td>
<td>≤2 cm³</td>
<td>≤2 cm³</td>
</tr>
<tr>
<td>Volume ≥95% breast dose</td>
<td>minimized&lt;sup&gt;a&lt;/sup&gt;</td>
<td>≤3D-CRT-SIB</td>
<td>≤3D-CRT-SIB / minimized priority 3</td>
</tr>
<tr>
<td>Volume ≥107% breast dose</td>
<td>minimized&lt;sup&gt;a&lt;/sup&gt;</td>
<td>≤3D-CRT-SIB</td>
<td>≤3D-CRT-SIB / minimized priority 3</td>
</tr>
<tr>
<td>Volume ≥95% boost dose</td>
<td>minimized&lt;sup&gt;a&lt;/sup&gt;</td>
<td>≤3D-CRT-SIB</td>
<td>≤3D-CRT-SIB / minimized priority 3</td>
</tr>
<tr>
<td>Heart V30 / mean heart dose</td>
<td>minimized&lt;sup&gt;a&lt;/sup&gt;</td>
<td>≤3D-CRT-SIB</td>
<td>≤3D-CRT-SIB / minimized priority 1</td>
</tr>
<tr>
<td>Lungs V20 / mean lung dose</td>
<td>minimized&lt;sup&gt;a&lt;/sup&gt;</td>
<td>≤3D-CRT-SIB</td>
<td>≤3D-CRT-SIB / minimized priority 2</td>
</tr>
<tr>
<td>Contralateral breast</td>
<td>avoided&lt;sup&gt;b&lt;/sup&gt;</td>
<td>avoided&lt;sup&gt;b&lt;/sup&gt;</td>
<td>avoided&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Abbreviations: 3D-CRT-SIB = three-dimensional conformal radiotherapy including simultaneously integrated boost; IMRT-SIB = intensity modulated radiotherapy including simultaneously integrated boost; Vx = proportion of organ at risk receiving 2x Gy.

<sup>a</sup> Optimisation was performed manually by using a maximum total of 3 forward planned sub-beams and effective use of multileaf collimator shielding.

<sup>b</sup> Beam directions were chosen on the basis of patient anatomy to exclude the right breast, on condition that adequate coverage of the breast planning target volume was maintained.

<sup>priority 1-3</sup> Optimisation was performed without harming other objectives and objectives with higher priority.

**IMRT-SIB objectives**

For each patient, two optimisation methods were used for both the 25%IMRT-SIB and the 100%IMRT-SIB plans: 1) an ‘optimised solution’ (OS), and; 2) a ‘class solution’ (CS) optimisation method. First, OS plans were created for all patients. The aim was to create plans with (in order of priority) minimised heart dose, minimised lung dose and a minimised volume receiving ≥107% of the prescribed breast dose, without allowing deterioration of the dose distribution as obtained with 3D-CRT-SIB (Table 1). Objective values and weights were entered for the various structures and adjusted each sequence while optimising OS plans for all
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patients until a result was reached that optimally complied with the OS plan objectives. After completing all OS plans for all patients, the final objective values and weights entered for all OS plans were evaluated and compiled into a standard set of inverse planning parameters (class solution) meant to serve as a starting point for the CS optimisation process. The aim of the CS optimisation process was to produce plans that complied at least with the criteria for 3D-CRT-SIB while requiring a minimum number of optimisation sequences, so they could be planned in a time span similar to that needed to plan 3D-CRT-SIB (Table 1). The CS optimisation procedure ended as soon as an acceptable, not necessarily optimal, solution was reached.

Figure 1. Structures created in addition to organs at risk and planning target volumes
Additional structures were created to enable direct aperture optimisation-based intensity modulated radiotherapy including simultaneously integrated boost: structure A) extending 4 mm inside boost planning target volume (PTV); structure B) surrounding the boost PTV with a margin of 10 mm; structure C) including the breast PTV, yet excluding the boost PTV with surrounding structure; structure D) extending 4 mm inside structure C, and; structure E) extending from the breast PTV in the medio-dorsal direction with a margin of 3 cm.
Target coverage, irradiated volumes and OAR dose

Target coverage was determined for all plans by evaluating proportions of the breast and boost PTVs receiving ≥95% of the prescribed dose. In addition, irradiated volumes were determined receiving ≥95% and ≥107% of the prescribed breast dose and ≥95% of the prescribed boost dose. For each plan, the proportion of heart receiving ≥30 Gy (V30), mean heart dose, proportion of both lungs combined receiving ≥20 Gy (V20), mean dose of both lungs combined, proportion of contralateral breast receiving ≥1 Gy (V1), ≥5 Gy (V5) and contralateral breast mean dose were obtained from the dose–volume histograms (DVH). In order to get insight into what extend differences in lung dose distributions translate into different NTCP-values, NTCP calculations were performed using parameter values derived by Seppenwoolde et al. [12], and Semenenko et al. [13].

Predictive patient characteristics

Patient characteristics were collected that might relate to a potential benefit of IMRT-SIB: the overlap between heart and breast PTV (OHB), measured as the maximum distance of the heart contour projected within the breast PTV on a beam’s-eye-view of the tangential beams (Fig. 2), the absolute volume of the breast and boost PTVs, and the location of the boost volume. The boost volume location was sub-divided in the cranio-caudal direction (cranial, central and caudal), and in the medio-lateral direction (medial, central and lateral).

Statistical analyses

Correlation statistics were performed for the aforementioned patient characteristics in relation to relevant effect variables, i.e., reductions with IMRT-SIB when compared with 3D-CRT-SIB with respect to the total volume receiving ≥107% of the prescribed breast dose (V54.23), heart V30, mean heart dose, lung V20 and mean lung dose. Receiver operating characteristics (ROC) were used to evaluate the predictive value of the individual patient characteristics and to determine optimum threshold values (cut-off values). On the basis of these threshold values and for each of the patient characteristics, patients were divided
into two groups, patients with a lower value and patients with a higher value. Mean OAR dose reductions with IMRT-SIB were determined for each group and two-sided non-parametric rank tests were used to determine if values in patient groups were statistically different ($p \leq 0.05$).

Figure 2. Overlap between heart and breast planning target volume
The overlap between heart and breast planning target volume (PTV) was measured as the maximum distance of the heart contour projected within the breast PTV on a tangential beam’s-eye-view.

Results

Treatment planning
Treatment planning time was similar for CS IMRT-SIB plans that were generally completed after 1 – 3 optimisation sequences, and 3D-CRT-SIB. Optimising OS IMRT-SIB plans could take an additional 4 hours and included multiple optimisation sequences.
PTV coverage and irradiated volumes

At least 98% of the volume of the breast and boost PTVs received at least 95% of the prescribed dose in all plans and all patients. However, the absolute irradiated volumes receiving ≥95% and ≥107% of the prescribed breast dose were smaller with the various IMRT-SIB strategies when compared to 3D-CRT-SIB (Table 2). IMRT-SIB resulted in volumes receiving excess boost dose outside the boost PTV (≥95% boost dose) that were comparable to those with 3D-CRT-SIB (Table 2).

Table 2. Irradiated volumes and dose delivered to organs at risk with 3D-CRT-SIB and IMRT-SIB

<table>
<thead>
<tr>
<th>Irradiated volumes</th>
<th>3D-CRT-SIB</th>
<th>Class solution IMRT-SIB</th>
<th>Optimised solution IMRT-SIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>25%IMRT</td>
<td>1076 (325-1861)</td>
<td>1022 (310-1845)</td>
<td>988 (298-1790)</td>
</tr>
<tr>
<td>100%IMRT</td>
<td>988 (305-1798)</td>
<td>1037 (311-1781)</td>
<td>989 (305-1798)</td>
</tr>
<tr>
<td>≥95% breast dose (cm³)</td>
<td>405 (179-866)</td>
<td>350 (154-720)</td>
<td>345 (151-731)</td>
</tr>
<tr>
<td>≥107% breast dose (cm³)</td>
<td>166 (51-470)</td>
<td>170 (55-455)</td>
<td>170 (58-451)</td>
</tr>
<tr>
<td>≥95% boost dose (cm³)</td>
<td>167 (51-467)</td>
<td>167 (51-467)</td>
<td>167 (51-467)</td>
</tr>
<tr>
<td>Heart</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V30 (%)</td>
<td>2.1 (0.0-8.0)</td>
<td>1.6 (0.0-6.5)</td>
<td>1.1 (0.0-4.7)</td>
</tr>
<tr>
<td>Mean dose (Gy)</td>
<td>4.1 (1.9-8.2)</td>
<td>3.5 (1.8-7.1)</td>
<td>3.0 (1.6-5.3)</td>
</tr>
<tr>
<td>Lungs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V20 (%)</td>
<td>5.0 (1.0-12.2)</td>
<td>4.4 (0.9-11.0)</td>
<td>3.8 (0.8-9.7)</td>
</tr>
<tr>
<td>Mean dose (Gy)</td>
<td>3.7 (1.5-7.5)</td>
<td>3.4 (2.2-6.7)</td>
<td>3.2 (2.0-6.3)</td>
</tr>
<tr>
<td>Contralateral breast</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V1 (%)</td>
<td>15.0 (0.1-38.0)</td>
<td>16.8 (0.7-34.6)</td>
<td>17.5 (0.3-39.9)</td>
</tr>
<tr>
<td>V5 (%)</td>
<td>0.2 (0.0-1.6)</td>
<td>0.1 (0.0-1.9)</td>
<td>0.2 (0.0-3.3)</td>
</tr>
<tr>
<td>Mean dose (Gy)</td>
<td>0.5 (0.2-1.2)</td>
<td>0.6 (0.2-1.6)</td>
<td>0.6 (0.2-1.1)</td>
</tr>
</tbody>
</table>

Abbreviations: 3D-CRT-SIB = three-dimensional conformal radiotherapy including simultaneously integrated boost; 25%IMRT = 75% conformal beams with skin flash and 25% IMRT segments; 100%IMRT = fully segmented IMRT; IMRT-SIB = intensity modulated radiotherapy including simultaneously integrated boost; Vx = proportion of organ at risk receiving ≥x Gy.

Data presented as mean values, with ranges in parenthesis.

Dose to OARs

With the results of all studied patients combined, the mean parameter values for heart and lung dose with 3D-CRT-SIB were somewhat lower with IMRT-SIB (Table 2). The average reduction of heart V30 with the IMRT-SIB strategies ranged from 0.5% - 1.0% relative to 3D-CRT-SIB and the average reduction of mean heart dose ranged from 0.6 Gy to 1.1 Gy. The average reduction of lung V20 with the various IMRT-SIB strategies ranged from 0.6% - 1.2% relative to 3D-CRT-SIB and
the average reduction of mean lung dose ranged from 0.3 Gy to 0.7 Gy. Only marginal differences were found between the different IMRT-SIB strategies, with a slight benefit for the 100%IMRT-SIB methods. NTCP values for radiation pneumonitis Grade 2 or higher were zero for both IMRT-SIB and IMRT-SIB when using the model parameters derived by Seppenwoolde et al., whereas it ranged from 1.5% with IMRT-SIB to 1.7% with 3D-CRT-SIB when using the model parameters derived by Semenenko et al.. Similar dose was delivered to the contralateral breast with 3D-CRT-SIB and the various IMRT-SIB strategies, except for a slight increase in the low dose values with IMRT-SIB.

**Predictive patient characteristics**

In the second part of the analysis, we investigated whether OAR dose reductions with IMRT-SIB, observed in the group of patients as a whole, would also apply to particular subgroups of patients. It appeared that significant correlations were present between the OHB and reductions in heart V30 with IMRT-SIB ($r = 0.38$, $p <0.001$), the size of the boost PTV and reductions in $V_{54.23}$ ($r = 0.54$, $p <0.001$), the size of the breast PTV and reductions in $V_{54.23}$ ($r = 0.24$, $p = 0.01$), the boost location in cranio-caudal direction and reductions in lung V20 ($r = 0.51$, $p <0.001$), the boost location in cranio-caudal direction and reductions in mean lung dose ($r = 0.60$, $p <0.001$), the boost location in medio-lateral direction and reductions in lung V20 ($r = 0.24$, $p = 0.01$) and the boost location in medio-lateral direction and reductions in mean lung dose ($r = 0.24$, $p = 0.01$).

We examined the various patient characteristics in their ability to predict whether IMRT-SIB would result in a more than average reduction of the correlated dose parameters. We found that the OHB factor was a good predictor for a more than average reduction in heart V30 (>0.7%). The ROC area under the curve (AUC)-value was 0.75 (95% CI: 0.66 – 0.84), and the optimal cut-off value was 1.4 cm (Fig. 3). Patients with an OHB >1.4 cm had a significantly larger mean reduction in heart V30 with IMRT-SIB (a mean reduction of 1.3%) than patients with OHB ≤1.4 cm (a mean reduction of 0.5%, $p <0.001$). Similarly, we found that the size of the boost PTV was a good predictor for a more than average reduction in
V54.23 (>50 cm³). The ROC AUC-value was 0.77 (95% CI: 0.68 – 0.85), and the best cut-off value was a boost PTV of 125 cm³. Patients with a larger boost PTV also had a significantly larger mean reduction in V54.23 (a mean reduction of 83 cm³) than patients with a smaller boost PTV (a mean reduction of 21 cm³, p < 0.001). The size of the breast PTV appeared not to be a good predictor for a reduction in V54.23. The ROC AUC-value was 0.60 (95% CI: 0.49 – 0.71) and no cut-off value could discriminate two groups that had significantly different reductions in V54.23 with IMRT-SIB.

![Figure 3. Receiver operating characteristic curves](image)

The receiver operating characteristic (ROC) curves and the associated areas under the curve for A: the overlap between heart and breast planning target volume (OHB) (Fig. 2) as a predictor of a more than average reduction in the proportion of the heart receiving 30 Gy or more (V30) with intensity modulated radiotherapy including simultaneously integrated boost (IMRT-SIB) when compared to three-dimensional conformal radiotherapy (3D-CRT)-SIB, and B: the size of the boost planning target volume (PTV) as a predictor of a more than average reduction in the volume receiving ≥107% of the prescribed dose to the breast (V54.23) with IMRT-SIB when compared to 3D-CRT-SIB.

Significantly different reductions in lung dose with IMRT-SIB were found for the various boost locations. In the case of cranial boost locations, IMRT-SIB showed larger mean reductions in lung dose (V20: 1.3%; mean lung dose: 0.9 Gy) than in the case of caudal boost locations (V20: 0.6%; mean lung dose: 0.1 Gy, both p < 0.001). Similarly, in the case of medial boost locations, IMRT-SIB showed larger mean reductions in lung dose (V20: 1.0%; mean lung dose: 0.7 Gy) than in
the case of lateral boost locations (V20: 0.7%, p = 0.02; mean lung dose: 0.4 Gy, p = 0.03). However, with regard to lung dose, NTCP values were almost similar with each of the various techniques. Therefore the relevance of using the boost location as a predictor for a benefit of IMRT-SIB is unclear. When the OHB factor and the size of the boost PTV would both be used to identify patients that might benefit from IMRT-SIB, 18 of the 30 patients examined in this study would be identified, 8 on the basis of the OHB factor alone and 14 on the basis of the size of the boost PTV alone.

**Discussion**

The application of SIB in breast conserving RT has proven feasible with both 3D-CRT and IMRT [6,9]. While reports on whole breast IMRT have demonstrated that dose delivered to OARs can be reduced as compared to whole breast 3D-CRT [7,8], the results of the present study demonstrated, that in the case of SIB, relevant reductions with IMRT are present in subgroups of patients only. The benefits of IMRT-SIB compared to 3D-CRT-SIB appeared to be a reduced V54.23 and a slightly lower heart V30 in subgroups of patients. In fact, when these reductions in dose were analyzed in relation to the size of the boost PTV and the OHB value, it appeared that the added value of using IMRT-SIB instead of 3D-CRT-SIB was minimal in patients with a boost PTV volume ≤125 cm³ and an OHB ≤1.4 cm. Although we also found that with IMRT-SIB, reductions in lung dose can be obtained, this reduction did not translate into a reduced NTCP-value of radiation pneumonitis, i.e., the probability of this complication was similar, regardless of the SIB technique used. With regard to physical dose reductions in heart and breast tissue, it remains unclear if these might result in reduced NTCP-values of cardiac morbidity and breast fibrosis, as reliable and validated NTCP-models for these endpoints are still lacking. Future research should therefore be focused on the validation of existing NTCP models [14,15], and the collection of data providing insight in the clinical relevance of different dose distributions in various OARs.
Although specific subgroups of patients could benefit more from IMRT-SIB because of the lower heart V30 in some patients, it should be noted that the use of breath-hold techniques may also reduce heart dose values [16]. As breath-hold techniques can also be used in combination with 3D-CRT-SIB, this could further diminish the additional benefit of IMRT-SIB relative to 3D-CRT-SIB with respect to potential heart dose reduction.

Some may argue that as many patients as possible should be treated with IMRT, regardless the magnitude of its potential benefit. However, it should be noted that this can only be the realised in institutes that have a long experience with IMRT, have access to multiple accelerators that are IMRT compatible, have invested in treatment planning software up to twice the cost of conventional software, have educated all personnel to ensure quality of each step in the IMRT process, have the disposal of additional physicists to perform the necessary quality assurance tests and can still treat all patients in the case IMRT would result in increased treatment delivery time per patient. In addition, the total annual radiotherapy costs would largely increase when all breast cancer patients are to receive IMRT instead of 3D-CRT. In a comprehensive report evaluating the cost effectiveness of IMRT, the Belgium government has calculated in 2007 that implementation of IMRT instead of 3D-CRT for each Belgium breast cancer patient would imply a total increase of the total annual radiotherapy costs of 18.7% [11]. Therefore, the authors feel that in the absence of clinical trials proving that IMRT-SIB results in improved local control or decreased side effects, alternative treatments that are easier to implement but have similar dose distributions, should be considered. Moreover, it is of particular interest to know whether particular patients may benefit from the use of IMRT-SIB or, conversely, that similar results can also be obtained with 3D-CRT-SIB.

It was already demonstrated by Hurkmans and colleagues for whole breast IMRT that the maximum heart distance, defined as the maximum distance of the heart contour to the medial field edge as seen in a beam’s-eye-view of the medial tangential field, correlated with dose levels delivered to the heart [7]. However, when applying (fully segmented) IMRT-SIB, no conformal beams are available for
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appropriate measurement of the maximum heart distance. Therefore we propose the use of the OHB factor as a criterion when identifying patients for IMRT-SIB.

In the present study, we examined two IMRT-SIB strategy variables: 1) the method of IMRT optimisation, and 2) the method of IMRT segmentation. With regard to the optimisation method, we found that dosimetric results with CS plans, generated on the basis of a standard set of structures and objectives, were similar to that with OS plans thoroughly optimised to minimise dose to OARs. With regard to the segmentation method it appeared that with 100%IMRT-SIB, dose delivered to the heart could be slightly lower than with 25%IMRT-SIB. This might indicate the CS 100%IMRT-SIB as the preferred strategy when IMRT-SIB is implemented.

In our previous study on 3D-CRT-SIB [6], target coverage was considered adequate when ≥95% of the prescribed dose was delivered to at least 99% of the PTV, while in the current study we accepted a coverage of 98%. This allowed for better sparing of the heart with both 3D-CRT-SIB and IMRT-SIB. As a result, OAR dose values with 3D-CRT-SIB in the current study are somewhat lower than those in our previous study.

Conclusions

In breast conserving RT, similar results can be obtained with forward planned 3D-CRT-SIB and inversely planned IMRT-SIB for a large proportion of patients. Although IMRT-SIB is generally capable to reduce absolute dose values to OARs, the actual benefit of IMRT-SIB was different for specific patient subgroups. Patient characteristics, such as the OHB factor and the size of the boost PTV, can be used to identify patients that are most likely to benefit from IMRT-SIB.
References


