Simultaneous optimization of photons and electrons for mixed beam radiotherapy

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Abstract

The aim of this work is to develop and investigate an inverse treatment planning process (TPP) for mixed beam radiotherapy (MBRT) capable of performing simultaneous optimization of photon and electron apertures.

A simulated annealing based direct aperture optimization (DAO) is implemented to perform simultaneous optimization of photon and electron apertures, both shaped with the photon multileaf collimator (pMLC). Validated beam models are used as input for Monte Carlo dose calculations. Consideration of photon pMLC transmission during DAO and a weight re-optimization of the apertures after deliverable dose calculation are utilized to efficiently reduce the differences between optimized and deliverable dose distributions. The TPP for MBRT is evaluated for an academic situation with a superficial and an enlarged PTV in the depth, a left chest wall case including the internal mammary chain and a squamous cell carcinoma case. Deliverable dose distributions of MBRT plans are compared to those of modulated electron radiotherapy (MERT), photon IMRT and if available to those of clinical VMAT plans.

The generated MBRT plans dosimetrically outperform the MERT, photon IMRT and VMAT plans for all investigated situations. For the clinical cases of the left chest wall and the squamous cell carcinoma, the MBRT plans cover the PTV similarly or more homogeneously than the VMAT plans, while OARs are spared considerably better with average reductions of the mean dose to parallel OARs and $D_{2\%}$ to serial OARs by 54\% and 26\%, respectively. Moreover, the low dose bath expressed as $V_{10\%}$ to normal tissue is substantially reduced by up to 45\% compared to the VMAT plans.
A TPP for MBRT including simultaneous optimization is successfully implemented and the dosimetric superiority of MBRT plans over MERT, photon IMRT and VMAT plans is demonstrated for academic and clinical situations including superficial targets with and without deep-seated part.

Keywords: mixed beam radiotherapy, simultaneous optimization, direct aperture optimization, Monte Carlo

(Some figures may appear in colour only in the online journal)

1. Introduction

Electron beams are well suited to treat superficial targets, while sparing organs at risk (OARs) due to their sharp distal dose fall-off in tissue. Nowadays, electron radiotherapy is still based on cumbersome and inefficient delivery methods, where patient-individually molded cut-outs are needed in order to shape the dose to the target. To overcome this limitation and to exploit intensity and energy modulation for improved plan quality, some research groups investigated several approaches for modulated electron radiotherapy (MERT) using different motorized multileaf collimators. The collimation devices applied were a few leaf electron collimator (FLEC) (Al-Yahya et al. 2005, 2007, Alexander et al. 2010, 2012), an electron multileaf collimator (eMLC) (Gauer et al. 2008, Vatanen et al. 2009, Jin et al. 2014) or a photon multileaf collimator (pMLC) (du Plessis et al. 2006, Jin et al. 2008, Klein et al. 2009, Salguero et al. 2009, 2010, Surucu et al. 2010, Henzen et al. 2014a, 2014b). However, there are some dosimetric limitations of applying MERT: Firstly, due to the broad penumbra of electron beams, OARs located nearby to the target in lateral direction with respect to beam direction cannot be spared adequately. Secondly, the dose cannot be delivered homogeneously to targets with a part located deeper than 5 cm from the surface (called deep-seated part), because the range delivering 95% of the maximal dose of the beam with highest energy supported by conventional treatment units (typically 22 MeV) is insufficient, especially for smaller field sizes.

Photon beams have a completely different characteristics than electron beams with their steep penumbra and exponential dose fall-off. With the most advanced techniques like photon intensity modulated radiation therapy (IMRT) (Bortfeld 2006) and volumetric modulated arc therapy (VMAT) (Otto 2008), photon beams can be delivered conformal to the target and thus nearby OARs are spared efficiently. However, in contrast to electron beams, low doses are delivered over a large volume of normal tissue, also known as the low dose bath.

Given the different characteristics of photons and electrons, mixed beam radiotherapy (MBRT) promises high potential by combining the advantageous properties of both particle types for treating superficial tumor sites possibly with a deep-seated part. Finding the optimal contribution of photon and electron dose distributions during the treatment planning process (TPP) and delivering both types of beams in a convenient manner for the same treatment are two of the major challenges for MBRT. Optimizing photon and electron apertures simultaneously is desirable compared to sequentially, because then the freedom of exploiting intensity and energy modulation and the choice between different beam directions and particle types is given within one single process.

simultaneous optimization. For whole breast treatments including boost, Xiong et al. (2004) compared five different MBRT techniques. In the most sophisticated technique, two intensity modulated photon beams were combined with an intensity modulated electron beam. The eMLC shaped electron beam is set up with the intention to deliver the dose to the boost volume. A fluence map optimization (FMO) was used to simultaneously optimize the intensity maps of the photon and electron beams using a gradient search method. Subsequently, a leaf sequencing algorithm was used to translate the intensity maps into deliverable segments. With the comparison of five different techniques for MBRT, it was underlined that simultaneously optimized MBRT plans achieved improved plan quality compared to sequentially optimized MBRT plans. Alexander et al. (2012) developed a TPP for MERT using a FLEC for collimation. A direct aperture optimization (DAO) (Shepard et al. 2002) was used to obtain a MERT plan for a squamous case with a superficial target. Subsequently, a gradient optimization algorithm further simultaneously optimized the weights of the electron FLEC apertures of the MERT plan with the weights of $1 \times 1$ cm$^2$ photon beamlets to obtain an MBRT plan. The MBRT plan was superior to a photon IMRT plan in terms of dose homogeneity in the PTV and sparing of OARs. However, a post processing fluence map segmentation was not performed for the MBRT plan in their study and the electron FLEC apertures were fixed in their shape during FMO. For three cases of partial breast irradiations, Palma et al. (2012) simultaneously optimized photon and electron beamlets with an FMO. The fluence maps were subsequently sequenced to deliverable pMLC segments for the use on a Siemens Primus. The MBRT plans showed similar dose homogeneity and improved sparing of OARs compared to photon IMRT plans.

The pMLC is already part of conventional accelerator treatment heads, while FLEC and eMLC devices have to be mounted and unmouted from the applicator. Hence, the approach used by Palma et al. (2012) is the most convenient regarding delivery and treatment workflow, because both beam types are collimated with the pMLC without applicator. However, their work focuses only on MBRT plans determined for partial breast irradiations in comparison to photon IMRT plans. Thus, the potential of MBRT with simultaneous optimization of pMLC shaped apertures determined for other treatment sites, especially to targets with a deep-seated part remains unknown. Moreover, using a FMO and subsequent leaf sequencing leads to a degradation of the optimized fluence map dose distributions. The alternative DAO directly optimizes the apertures and their weights under consideration of mechanical pMLC constraints and possibly pMLC transmission (Shepard et al. 2002, Bergman et al. 2006). Furthermore, DAO leads to fewer pMLC segments and less monitor units (MUs) and thus to shorter treatment times.

The aim of this work is to develop an MC beamlet based inverse TPP for MBRT performing simultaneous optimization of photon and electron apertures with a simulated annealing based DAO. The apertures are determined to be delivered in a segmented manner and collimated with the pMLC for both photon and electron beams. We demonstrate the dosimetric superiority of MBRT plans compared to MERT, photon IMRT and VMAT plans for academic and clinical situations including superficial targets with and without deep-seated part.

2. Materials and methods

An MC beamlet based inverse TPP for MERT previously developed by Henzen et al. (2014a) is extended to generate treatment plans for MBRT. The extension is accompanied by the idea to handle the photon beams analogously to the electron beams in all aspects of the TPP. In the
following subchapters, the TPP for MBRT, the MC simulations, the simultaneous optimization and the performed evaluations with an academic and two clinical situations are presented.

2.1. Treatment planning process for MBRT

The TPP for MBRT starts with the import of the CT images into a research version of the Eclipse treatment planning system (TPS) (Varian Medical Systems, Palo Alto, CA) and the contouring of the planning target volume (PTV) and the OARs. Next, the photon and electron fields are manually defined by the beam energy and direction and isocenter position. Preferentially, the isocenter of the photon fields is located in the PTV while for the electron fields the isocenter is positioned such that the source to surface distance (SSD) is reduced leading to a smaller penumbra (du Plessis et al 2006, Klein et al 2009). The settings of the secondary collimator jaws for the photon fields correspond to the respective PTV projection in the beams eye view with a margin of 0.6 cm. For the electron fields, the positions of the secondary collimator jaws are fixed to $15 \times 35 \text{ cm}^2$. Beamlet dose distributions are then calculated in the Eclipse TPS interfaced framework of the Swiss Monte Carlo Plan (SMCP) (Fix et al 2007) for every field based on pre patient phase spaces. To create these pre patient phase spaces, a beamlet grid is positioned on the mid-plane of the pMLC. Particles are transported through the treatment head and stored in the corresponding beamlet pre patient phase space. Once all beamlet dose distributions are calculated the following input needs to be defined to perform a simultaneous optimization of photon and electron apertures: the number of apertures per field and dose-volume objectives prioritized with factors. The output of the optimization are the optimized dose distribution, the aperture shapes and their absolute weights in MUs. Because the previous beamlet based optimization did not consider the pMLC impact like tongue-and-groove effects and pMLC particle scattering except pMLC transmission of photon beams, a dose prediction error (DPE) is present (Jeraj 2002). Hence, an MC deliverable dose calculation is then performed for every aperture in the SMCP framework considering the impact of the pMLC. The weights of the apertures are then re-optimized based on their deliverable dose distributions to reduce the DPE caused optimization convergence error (OCE) (Jeraj 2002, Dogan et al 2006, Mihaylov and Siebers 2008). Finally, the deliverable weight re-optimized dose distribution of the total plan is loaded back into the Eclipse TPS for plan evaluation.

2.2. Monte Carlo simulations

In this work, all MC dose calculations are performed for a TrueBeam (Varian Medical Systems, Palo Alto, CA) equipped with a Millennium 120 pMLC (Varian Medical Systems, Palo Alto, CA) using the VMC++ (Kawrakow and Fippel 2000) and the MMC (Neuenschwander and Born 1992, Neuenschwander et al 1995, Fix et al 2013) algorithms for photon and electron beams, respectively. For the inner leaf pairs of the pMLC, a beamlet grid resolution of $0.3 \times 0.5 \text{ cm}^2$ and $0.5 \times 0.5 \text{ cm}^2$ is used for the photon and electron fields, respectively. For the outer leaf pairs, the beamlet size perpendicular to leaf travel direction is 1 cm for both photon and electron fields corresponding to the doubled leaf width compared to the inner leaf pairs.

The beam model used as input for the MC simulation of a 6 MV photon beam is a phase space located above the secondary collimator jaws (Magaddino et al 2011). For validating the photon beam model for a TrueBeam accelerator, depth dose curves and dose profiles are measured with a microDiamond (PTW, Freiburg, Germany) detector in a MP3 water tank (PTW, Freiburg, Germany) in units of cGy/MU for several pMLC collimated field sizes of $1 \times 1 \text{ cm}^2$. 

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and larger applied with an SSD of 100 cm. Corresponding dose calculations agree within 2% of the maximal dose value or 1 mm distance to agreement.

The input used for MC simulations of 6, 9, 12, 15, 18 and 22 MeV electron beams as available on the TrueBeam is a multiple source model consisting of foil and jaw sources for every beam energy (Henzen et al. 2014c). The electron beam model is commissioned with microDiamond measurements for a TrueBeam accelerator. Calculated and measured depth dose curves and dose profiles in units of cGy/MU of several pMLC collimated field sizes of $2 \times 2 \text{cm}^2$ and larger collected with an SSD of 70 and 80 cm agree within 3% of the maximal dose value or 2 mm distance to agreement for all available beam energies. Supporting an SSD of up to 80 cm is highly appreciated to overcome field setups leading to patient or couch collisions with an SSD of 70 cm.

2.3. MBRT optimization

The optimization of photon and electron apertures is performed by a simulated annealing based DAO (Shepard et al. 2002). Our object oriented C++ implementation of the DAO optimizes plans for MBRT, MERT and photon IMRT without any adjustment of the algorithm. The focus of the implementation is to guarantee smooth extendibility for future investigations like supporting other types of objectives, to support optimizations performed in parallel differing in the number of apertures per field and objective definitions and not primarily on minimal computation time.

pMLC transmission is considered during DAO for photon beams based on the work of Bergman et al. (2006) but further extended with transmission factors increasing gradationally towards the leaf tip in direction of leaf travel. Transmission factors of 25.5%, 4.7% and 1.6% are used for the range of 0–0.3 cm, 0.3–0.9 cm and > 0.9 cm from the leaf tip (measured in the isocenter plane). The dose distributions of photon beamlets blocked by leaves are weighted according to these factors. These transmission factors are determined by comparing beamlet and deliverable dose distributions of a set of rectangular pMLC segments.

The DAO minimizes the value of an objective function iteratively by changing the shape or weights of the apertures according to a cooling schedule. The objective function used is a sum of squared differences between achieved and desired dose voxel deposits (Wu and Mohan 2000) given by

$$f = \sum_{k=1}^{M} p_k \sum_{i=1}^{N_k} \left( \theta(a_k(D_i - D_k)) \cdot \theta(a_k(D(V_k) - D_i)) \cdot (D_i - D_k)^2 \right)$$

where $D_i$ is the dose value in the $i$th voxel of the structure considered (PTV or an OAR), $\theta$ is the Heaviside function, $p_k$ is the priority factor, $D_k$ is the desired dose, $D(V_k)$ is the dose received by at least the tolerated volume $V_k$ and $N_k$ is the number of voxels to be considered for the $k$th of in total $M$ dose-volume objectives. $a_k$ equals 1 for objectives penalizing dose values higher than $D_k$, otherwise $-1$.

The number of apertures per field are user defined and can be determined by running several DAOs using different number of apertures per field until no more substantial improvements are achieved anymore. The initial shape of an aperture corresponds to the PTV projection in the beams eye view in the resolution of the beamlet grid of the corresponding field. The initial weight of an aperture, given in MUs, is set in two steps. First, each aperture weight is initialized with the inverse of the average of its ten largest dose voxel values in the PTV. This initial value guarantees equal initial conditions for apertures of different beam types and distances from the patient surface to the PTV and is less sensitive to statistical noise of the MC.
calculated dose distribution as compared to using the maximal dose. Afterwards all aperture weights of the plan are normalized such that 50% of the PTV receives a dose value of at least the prescribed dose.

In every DAO iteration of in total \( N \) iterations, an aperture gets selected randomly and with a probability of \( P_S \) its shape is changed, otherwise its weight. A change is always accepted if the objective function value decreases. If the objective function increases, the change is accepted with a probability of

\[
P = 2 \cdot P_0 \cdot \frac{1}{1 + \frac{t_N(P + P_0)}{P}}
\]

(2)

where \( n_S \) and \( n_W \) are the previous total accepted shape and weight change iterations, respectively, \( N_A \) is the number of apertures and \( T_P \) and \( P_0 \) are the cooling rate and the initial value of \( P \), respectively. In case of a shape change, a leaf is randomly selected and its position is randomly changed according to a normal distribution around the current leaf position and a width of

\[
\sigma_S = 1 + (\sigma_{S_0} - 1) \cdot e^{-\frac{ln(n_S + 1)}{T_S}}
\]

(3)

where \( N_L \) is the total number of leaf pairs of all apertures and \( T_S \) and \( \sigma_{S_0} \) are the cooling rate and the initial width of the normal distribution, respectively. Both \( \sigma_S \) and \( \sigma_{S_0} \) are given in discretized units of number of beamlets. Similar for a weight change, the weight is changed according to a normal distribution around the current aperture weight \( w \) and a width of

\[
\sigma_W = 0.01 + (\sigma_{W_0} - 0.01) \cdot e^{-\frac{ln(n_W + 1)}{T_W}}
\]

(4)

where \( T_W \) and \( \sigma_{W_0} \) are the cooling rate and the initial width of the normal distribution, respectively. Both \( \sigma_W \) and \( \sigma_{W_0} \) are given in relative units of \( w \). Adjusting the cooling formulas of Shepard \textit{et al.} (2002) to be dependent on \( N_A \) and \( N_L \) allows a more flexible usage for arbitrary number of apertures. In this work, the following parameter set is used: \( N = 1000000 \), \( P_S = 90\% \), \( T_P = 3 \), \( P_0 = 3.5\% \), \( T_S = 2 \), \( \sigma_{S_0} = 40 \), \( T_W = 3 \), \( \sigma_{W_0} = 50\% \). To only perform a weight re-optimization, \( P_S \) is set to 0.

2.4. Academic situation

To systematically evaluate the TPP for MBRT in a simplified setup, an academic situation is defined with the following purposes:

1. To demonstrate that MBRT is not like MERT limited to deliver the dose homogenously to targets with a deep-seated part.
2. To evaluate whether the benefit of MBRT over photon IMRT decreases for a target with a deep-seated part compared to a target without.
3. To analyze the photon and electron contributions of MBRT plans.
4. To evaluate the reduction of the DPE after deliverable dose calculation and the reduction of the OCE after performing the weight re-optimization due to considering photon pMLC transmission.
5. To evaluate whether the drawback of photon IMRT compared to MBRT could be fully compensated by utilizing more photon apertures.
The academic situation consists of a cylindrical, homogenous water phantom with a radius of 10 cm and a length of 40 cm and includes contours of two PTVs (PTV-Superficial and PTV-Enlarged), two OARs (OAR-Distal and OAR-Lateral) and two Avoidance structures (figure 1 on the left). All mentioned structures have an extension of 7.4 cm in the direction perpendicular to the transversal plane. The PTV-Enlarged is an enlargement of the PTV-Superficial from a maximal depth from the surface of 5 cm to 7.5 cm. The Avoidance structures are 0.5 cm thick shells with a margin of 0.5 cm around the PTV-Superficial and PTV-Enlarged, respectively. Their purpose is to avoid hot spots close to the corresponding PTV.

For the first three purposes, plans for MBRT, MERT and photon IMRT, each with 40 apertures are generated using the presented TPP for both PTV contours. The photon and electron fields and the number of apertures per field of the created plans for MBRT, MERT and photon IMRT are listed in table 1 and visualized in figure 1 (left). The plans are compared by means of isodose lines, DVHs and the objective function value. For purpose four, the DVH differences between optimized, deliverable and deliverable weight re-optimized dose distributions of the MBRT plan are examined and compared to another MBRT plan with the same number of apertures per field but optimized without consideration of photon pMLC transmission.

**Figure 1.** Photon (top) and electron (bottom) fields with their beam direction (dashed line), position of the isocenter (circle) and secondary collimator jaws (field width) displayed on transversal views for the academic situation (left), the chest wall case (center) and the squamous cell carcinoma case (right). The contours of the following structures are visible: PTV-Superficial (red), PTV-Enlarged (red and orange), OAR-Distal (blue), OAR-Lateral (magenta) and body (light green) for the academic situation, PTV (red), ipsilateral lung (blue), contralateral lung (green), contralateral breast (yellow), heart (magenta), body (light green) and bolus (white) for the chest wall case and PTV (red), brain (blue), brain stem (magenta), body (light green) and bolus (white) for the squamous cell carcinoma case. For each PTV, the deepest part with respect to all electron field directions is indicated with a white arrow.
fractional DPE and OCE reductions achieved by considering the photon pMLC transmission during optimization are quantified by

\[
r_{DPE} = 1 - DPE^c/DPE^n = 1 - \frac{f_d^c - f_d^n}{f_d^o - f_d^n}\]

and

\[
r_{OCE} = 1 - OCE^c/OCE^n = 1 - \frac{f_w^c - f_w^n}{f_w^o - f_w^n}\]

where the superscripts \(c\) and \(n\) refer to as transmission considered and not considered during optimization, respectively and the subscripts \(o\), \(d\) and \(w\) refer to as optimized, deliverable and deliverable weight re-optimized dose distributions, respectively. \(f\) is given by equation (1). Note that both \(r_{DPE}\) and \(r_{OCE}\) are only estimates assuming that a deliverable MC dose calculation is an accurate estimate for the actual dose delivered to the patient and that the objective function value of the truly optimal dose distribution optimized based on the most accurate dose calculation can be estimated with \(f_{c,c}^o\). For purpose five, several MBRT and photon IMRT plans targeting the PTV-Enlarged are created with a number of apertures in the range of 15–75. In case of the MBRT plans, the number of electron apertures is thereby

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### Table 1. Photon and electron fields and the number of apertures per field used to create the coplanar MBRT, MERT and photon IMRT plans for the academic situation. The number of apertures per field is the same independent whether the plan is targeting the PTV-Superficial or the PTV-Enlarged.

<table>
<thead>
<tr>
<th>Gantry angle (°)</th>
<th>Beam</th>
<th>SSD (cm)</th>
<th>MERT</th>
<th>Photon IMRT</th>
<th>MBRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6 MV</td>
<td>96.5</td>
<td>—</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>60</td>
<td>6 MV</td>
<td>95.0</td>
<td>—</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>95</td>
<td>6 MV</td>
<td>91.7</td>
<td>—</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>245</td>
<td>6 MV</td>
<td>89.3</td>
<td>—</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>285</td>
<td>6 MV</td>
<td>94.0</td>
<td>—</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>0</td>
<td>6, 9, 15, 18, 22 MeV</td>
<td>70.0</td>
<td>8, 8, 8, 8, 8</td>
<td>—</td>
<td>2, 2, 2, 2, 2</td>
</tr>
</tbody>
</table>

---

### Table 2. The dose-volume objectives used for generating the MBRT, MERT and photon IMRT plans for the academic situation. The first two objectives listed are either applied to the PTV-Superficial or the PTV-Enlarged.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Objective type</th>
<th>Priority factor</th>
<th>Dose (%)</th>
<th>Volume (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV-Superficial &amp; PTV-Enlarged</td>
<td>Lower</td>
<td>35</td>
<td>98</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Upper</td>
<td>39</td>
<td>102</td>
<td>0</td>
</tr>
<tr>
<td>OAR-Distal</td>
<td>Upper</td>
<td>2</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>Upper</td>
<td>6</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>OAR-Lateral</td>
<td>Upper</td>
<td>2</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Upper</td>
<td>4</td>
<td>35</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>Upper</td>
<td>4</td>
<td>55</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Upper</td>
<td>4</td>
<td>75</td>
<td>0</td>
</tr>
<tr>
<td>Avoidance</td>
<td>Upper</td>
<td>4</td>
<td>90</td>
<td>0</td>
</tr>
</tbody>
</table>
kept constant at 10. For all five purposes, every optimization of plans for MBRT, MERT and photon IMRT is performed using the same objectives listed in table 2. Thus, the objective function value is a useful quantity to compare the quality of plans for MBRT, MERT and photon IMRT.

### 2.5. Chest wall case

To evaluate the presented TPP for MBRT for a clinical case with a superficial target, an MBRT plan with 50 apertures is created for a left chest wall case including the internal mammary chain with a prescribed dose of 50 Gy determined to be delivered in 25 fractions. The MBRT plan is compared to plans for MERT and photon IMRT generated with the same TPP and the same number of apertures and its photon and electron contributions are analyzed. The photon and electron fields and the number of apertures per field of the created plans for MBRT, MERT and photon IMRT are listed in table 3 and visualized in figure 1 (center). A clinical coplanar two-arc VMAT plan is also used for comparisons. The dose distribution of the VMAT plan is recalculated using VMC++ for comparison with the MC based MBRT, MERT and photon IMRT plans. Plan comparisons are performed by means of isodose lines, DVHs, the dose homogeneity in the PTV expressed as $HI = V_{95\%} - V_{107\%}$, $D_{mean}$ to the OARs and the extent of the low dose bath expressed as $V_{10\%}$ of the normal tissue.

To evaluate whether MBRT can also be applied without using a bolus while keeping the treatment plan quality, another MBRT plan is created (MBRT-WOB) for the chest wall case. The resulting DVHs are compared to the MBRT plan created with bolus. Due to the change in the geometrical situation in the case without using a bolus, different number of apertures per field are used for the MBRT-WOB plan, however the total number of apertures is maintained (table 3).

### 2.6. Squamous cell carcinoma case

An MBRT plan with 60 apertures is created for a squamous cell carcinoma case with a prescribed dose of 66 Gy determined to be delivered in 33 fractions to evaluate the presented TPP for MBRT for a clinical case with a superficial target including a deep-seated part. The MBRT plan is compared to plans for MERT and photon IMRT generated with the same TPP.

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**Table 3.** Photon and electron fields and the number of apertures per field used to create the coplanar MBRT, MERT and photon IMRT plans for the chest wall case.

<table>
<thead>
<tr>
<th>Gantry angle (°)</th>
<th>Beam</th>
<th>SSD (cm)</th>
<th>Number of apertures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>MERT</td>
<td>Photon IMRT</td>
</tr>
<tr>
<td>110</td>
<td>6 MV</td>
<td>93.7</td>
<td>—</td>
</tr>
<tr>
<td>135</td>
<td>6 MV</td>
<td>88</td>
<td>—</td>
</tr>
<tr>
<td>145</td>
<td>6 MV</td>
<td>86.1</td>
<td>—</td>
</tr>
<tr>
<td>30.75</td>
<td>6 MV</td>
<td>93.4</td>
<td>—</td>
</tr>
<tr>
<td>320</td>
<td>6 MV</td>
<td>94.7</td>
<td>—</td>
</tr>
<tr>
<td>350</td>
<td>6 MV</td>
<td>96.2</td>
<td>—</td>
</tr>
<tr>
<td>355</td>
<td>12, 15 MeV</td>
<td>73.4</td>
<td>—</td>
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<td>4</td>
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<td>73.3</td>
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<td>22</td>
<td>6, 9, 12 MeV</td>
<td>75.1</td>
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<tr>
<td>31</td>
<td>6, 9, 12 MeV</td>
<td>76.6</td>
<td>0, 5, 4</td>
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and the same number of apertures and its photon and electron contributions are analyzed. The photon and electron fields and the number of apertures per field used to create the coplanar MBRT, MERT and photon IMRT plans for the squamous cell carcinoma case are listed in table 4 and visualized in figure 1 (right). A clinical non-coplanar five-arc VMAT plan is also used for comparisons. The dose distribution of the VMAT plan is recalculated using VMC++. The plan comparisons are performed by means of isodose lines, DVHs, HI in the PTV, $D_{\text{mean}}$ and $D_{2\%}$ to parallel and serial OARs, respectively and $V_{10\%}$ of the normal tissue. $D_{2\%}$ is reported instead of the maximum dose as $D_{2\%}$ is clinically more relevant and less dependent on the statistical uncertainty of MC dose calculations (Gregoire and Mackie 2011).

### 3. Results

The dose distributions of the MBRT, MERT and photon IMRT plans presented in this section are deliverable weight re-optimized if not stated otherwise. All treatment plans are normalized such that 50% of the PTV receives a dose value of at least the prescribed dose. A voxel size of $2.5 \times 2.5 \times 2.5 \, \text{mm}^3$ is used for the dose calculations and dose values are reported to medium. All dose calculations in this work are performed in parallel on a Linux high-performance-computing cluster using 100 cores of Intel Xeon CPUs of type E5-2650 v2—2.60 GHz or similar. The computation time to generate the beamlet dose distributions of the field setups for the presented MBRT plans takes 2–6 h depending on the number of fields. The statistical uncertainty (expressed as one standard deviation) of a single beamlet dose distribution is thereby about 2%. A history by history method considering only dose values above 50% of the maximal dose value is used to determine the statistical uncertainty (Walters et al 2002). Deliverable dose calculation of the presented MBRT plans with a statistical uncertainty of about 1.5% needs $<1$ h depending on the number of apertures. The optimizations are performed with a computation time of $<1$ h depending on the number of voxels to be considered.

<table>
<thead>
<tr>
<th>Gantry angle (°)</th>
<th>Beam</th>
<th>SSD (cm)</th>
<th>Number of apertures</th>
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<tr>
<td></td>
<td>Beam</td>
<td>MERT</td>
<td>Photon IMRT</td>
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<tr>
<td>35</td>
<td>6 MV</td>
<td>95.9</td>
<td>—</td>
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<tr>
<td>111</td>
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<td>96.5</td>
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<td>—</td>
</tr>
<tr>
<td>246</td>
<td>6 MV</td>
<td>84.7</td>
<td>—</td>
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<td>88.5</td>
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<td>6 MV</td>
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</tr>
<tr>
<td>38.5</td>
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<tr>
<td>57</td>
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</tr>
<tr>
<td>90</td>
<td>6, 9, 12, 15, 18, 22 MeV</td>
<td>80.1</td>
<td>5, 5, 1, 5, 5, 6</td>
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</table>

Table 4. Photon and electron fields and the number of apertures per field used to create the coplanar MBRT, MERT and photon IMRT plans for the squamous cell carcinoma case.
Isodose lines and DVHs of treatment plans for MBRT, MERT and photon IMRT targeting the PTV-Superficial and the PTV-Enlarged are compared in figures 2 and 3, respectively. The MBRT plans outperform the MERT and the photon IMRT plans in terms of objective function value (233.7 compared to 826.8 and 402.8 for the PTV-Superficial and 268.6 compared to 4526.2 and 701.2 for the PTV-Enlarged). The improved dose homogeneity in the PTV and the better sparing of the OARs are visible in the DVHs and isodose lines. Only the sparing of the OAR-Lateral is slightly better for dose values above 32% for the photon IMRT plan targeting the PTV-Superficial and the sparing of both OARs for dose values below 20% is partially better for both MERT plans compared to the MBRT plans. The low dose bath is slightly reduced for the MBRT plans compared to the photon IMRT plans, but increased with respect to the

3.1. Academic situation

Isodose lines and DVHs of treatment plans for MBRT, MERT and photon IMRT targeting the PTV-Superficial and the PTV-Enlarged are compared in figures 2 and 3, respectively. The MBRT plans outperform the MERT and the photon IMRT plans in terms of objective function value (233.7 compared to 826.8 and 402.8 for the PTV-Superficial and 268.6 compared to 4526.2 and 701.2 for the PTV-Enlarged). The improved dose homogeneity in the PTV and the better sparing of the OARs are visible in the DVHs and isodose lines. Only the sparing of the OAR-Lateral is slightly better for dose values above 32% for the photon IMRT plan targeting the PTV-Superficial and the sparing of both OARs for dose values below 20% is partially better for both MERT plans compared to the MBRT plans. The low dose bath is slightly reduced for the MBRT plans compared to the photon IMRT plans, but increased with respect to the
The MERT plan targeting the PTV-Enlarged would fail to cover the PTV-Enlarged homogeneously due to the enlarged depth.

The dose distributions and dose profiles of the photon and electron contributions of the MBRT plans targeting the PTV-Superficial and the PTV-Enlarged are presented in figure 4. Note that for both plans the electron beams dominantly cover the region between the surface and the OAR-Distal, while the photon beams cover the main part of the deepest part of the PTV. Neither in the electron nor in the photon contribution steep dose gradients are present.

**Figure 4.** Dose distributions (left) and dose profiles (right) indicated with (A), (B), (C) and (D) of the photon and electron contributions of the MBRT plans targeting the PTV-Superficial (top) and the PTV-Enlarged (bottom).

The dose distributions and dose profiles of the photon and electron contributions of the MBRT plans targeting the PTV-Enlarged either optimized with or without consideration of photon pMLC transmission. For better visibility, the DVHs of the optimized and deliverable dose distributions without weight re-optimization are not displayed in case of the plan optimized without consideration of photon pMLC transmission.

**Figure 5.** Objective function value (left) and DVH (right) comparisons of optimized, deliverable and deliverable weight re-optimized dose distributions of two MBRT plans targeting the PTV-Enlarged either optimized with or without consideration of photon pMLC transmission. For better visibility, the DVHs of the optimized and deliverable dose distributions without weight re-optimization are not displayed in case of the plan optimized without consideration of photon pMLC transmission.

MERT plans as expected. The MERT plan targeting the PTV-Enlarged would fail to cover the PTV-Enlarged homogeneously due to the enlarged depth. The dose distributions and dose profiles of the photon and electron contributions of the MBRT plans targeting the PTV-Superficial and the PTV-Enlarged are presented in figure 4.
The fraction of the integral dose in the PTV (PTV dose contribution) of the photon apertures is 44.3% and 53.3% for the MBRT plans targeting the PTV-Superficial and PTV-Enlarged, respectively. The difference is explained with the enlarged part of the PTV-Enlarged only sufficiently coverable with photon beams.

Figure 5 compares the optimized, deliverable and deliverable weight re-optimized dose distributions of two MBRT plans targeting the PTV-Enlarged (either optimized with or without consideration of photon pMLC transmission) in terms of the objective function value and the DVHs. The rDPE is 28% and the rOCE is 49%. Hence, a DPE caused by not considering photon pMLC transmission could not be compensated by applying the weight re-optimization. Comparing the deliverable weight re-optimized dose distributions shows that not considering photon pMLC transmission leads to increased dose values to both OARs. There is still a remaining OCE even if photon pMLC transmission is considered during optimization. However, the DVHs of the deliverable weight re-optimized dose distribution are similar to those of the optimized dose distribution, which is used as the estimate for the truly optimal objective function value in this work (both optimized considering photon pMLC transmission). Only the dose homogeneity in the PTV and the dose values delivered to the OAR-Lateral below 30% are marginally reduced and increased, respectively.

Figure 6 illustrates the dependency of MBRT and photon IMRT plans targeting the PTV-Enlarged on the number of apertures utilized. An MBRT plan consisting of only 5 photon and 10 electron apertures has a 3% lower objective function value than a photon IMRT plan with 75 photon apertures.

3.2. Chest wall case
The treatment plans for MBRT, MERT, photon IMRT and VMAT determined for the chest wall case are compared in figure 7 and table 5. The HI in the PTV for the MBRT plan is similar than for the VMAT plan and 5% higher than for the MERT and photon IMRT plans. The
MBRT plan outperforms the VMAT plan in terms of OAR sparing and the volume of the low dose bath (visible in the isodose line comparison). The mean dose delivered to the ipsilateral lung, heart, contralateral lung and breast and the $V_{10\%}$ of normal tissue are lower by 11%, 31%, 83%, 77% and 45%. For the MERT plan, the low dose bath is even more reduced and the sparing of the OARs is similar to the MBRT plan except for the ipsilateral lung, while for the photon IMRT plan only the sparing of the contralateral lung is similar to the MBRT plan.

Figure 8 compares the dose distributions of the photon and electron contributions of the MBRT plan. The electron beams dominantly cover the region of the internal mammary chain and the shallower part of the chest wall, while the photon beams cover the major part of the deeper located part of the chest wall adjacent to the ipsilateral lung. For this case, the PTV dose contribution of the photon apertures is with 38.7% considerably smaller than of the electron apertures.
Figure 8. Dose distributions (top) and dose profiles (bottom) indicated with (A) and (B) of the photon and electron contributions of the MBRT plan determined for the chest wall case.

Figure 9. DVHs (bottom) of the MBRT and the MBRT-WOB plans determined for the chest wall case.

Figure 9 compares the DVHs of the MBRT and MBRT-WOB plans. While the dose homogeneity in the PTV and the sparing of the heart for dose values above 10 Gy are marginally worsened, the sparing of the ipsilateral lung, the heart and normal tissue for dose values below 10 Gy is marginally improved for the MBRT-WOB plan compared to the MBRT plan.
3.3. Squamous cell carcinoma case

The treatment plans for MBRT, MERT, photon IMRT and VMAT determined for the squamous cell carcinoma case are compared in figure 10 and table 6. The HI in the PTV for the MBRT plan is 2.2% higher than for the VMAT plan and 8.2% higher than for the MERT plan. Only the photon IMRT plan has a similar HI in the PTV. The MBRT plan outperforms the VMAT plan in terms of OAR sparing and extent of the low dose bath except for the high dose...
values in the brain ($D_{2\%}$ is 5% higher for the MBRT plan). $D_{\text{mean}}$ or $D_{2\%}$ to all other OARs are 5%–62% lower and the $V_{10\%}$ of normal tissue is 28% lower for the MBRT plan compared to the VMAT plan. The mentioned quantities for the contralateral eye, lens and parotid glands and the normal tissue are even more reduced by the MERT plan. However, all other OARs, especially the brain, ipsilateral cochlea and the spinal cord are spared considerably less. In case of the photon IMRT plan, all OARs are spared less or similar to the MBRT plan. In contrast to the VMAT plan, the photon IMRT plan has an increased $D_{2\%}$ value in the brain compared to the MBRT plan.

Figure 11 compares the dose distributions of the photon and electron contributions of the MBRT plan. The superior transversal view shows that the electron contribution covers the whole PTV dominantly on this slice. Only the part of the PTV adjacent to the left eye has a photon contribution higher than 30%. On the inferior slice, the electron apertures cover only the shallow part dominantly, while the central region and especially the deep-seated part adjacent to the brain, brain stem and ipsilateral cochlea (located superiorly to the slice shown) is covered dominantly by the photon apertures. Also for this clinical case, the PTV dose contribution of the photon apertures is with 46.9% smaller than of the electron apertures.

### 4. Discussion

A simulated annealing based DAO is implemented to create MBRT plans with pMLC shaped photon and electron apertures. It is demonstrated for the MBRT plan targeting the PTV-Enlarged in the academic situation that the differences between optimized and deliverable weight re-optimized dose distributions are efficiently minimized. Consideration of photon pMLC transmission factors during DAO and performing a weight re-optimization of the deliverable dose distributions are utilized for this purpose. Compared to DAO, a fluence-based
approach could not account for transmission until leaf-sequencing. A downside of the simulated annealing based DAO is the requirement to predefine the number of apertures per field. Thus, several optimizations with different number of apertures per field have to be executed until the desired plan is found. The presented TPP for MBRT partially circumvents this issue as it allows executing optimizations differing in the number of apertures per field and the objectives in parallel. An alternative solution would be to use a column generation based DAO, because of the included pricing mechanism used to add apertures to the plan (Romeijn et al 2005). However, the algorithm is confronted with other limitations, e.g. the fixed shape of added apertures.

The evaluations of the TPP with the academic situation show for both PTVs that the objective function is clearly further minimized for optimizations of MBRT plans than of MERT and photon IMRT plans. In case of targeting the PTV-Enlarged, the benefit of using MBRT is even more pronounced. This is not expected with respect to photon IMRT, as the electron beams cover even a smaller fraction of the PTV-Enlarged. Moreover, this underlines that MBRT is not like MERT limited to deliver the dose homogenously to targets with a deep-seated part. For photon IMRT plans targeting the PTV-Enlarged, even a higher number of photon apertures cannot reach the benefit of electron apertures.

The plan comparisons for the clinical situations indicate that MBRT plans are well suited to treat chest wall and squamous cell carcinoma cases. The comparisons of the photon and electron contributions demonstrate that the DAO efficiently exploits the dosimetric characteristics of photon and electron beams. However further investigations for these treatment sites

Figure 11. Dose distributions (left) and dose profiles (right) indicated with (A) and (B) of the photon and electron contributions of the MBRT plan determined for the squamous cell carcinoma case.
are required to make treatment site specific conclusions. Basically every target with at least a superficial part can be considered to be investigated for MBRT, because it is shown for the squamous cell carcinoma case and the academic situation that MBRT is ideally suited to treat superficial targets with a deep-seated part. The results of the MBRT-WOB plan for the chest wall case further indicate that MBRT can be applied to targets closely located to the patient surface without using the bolus but still with a similar treatment plan quality. The clinical workflow is improved without bolus as the risk to accidentally miss to place the bolus before delivery is not present.

Regarding applicability of the presented MBRT plans for the clinical cases: they can already be delivered in the developer mode of a TrueBeam with XML files. Moreover, all dose distributions presented are based on deliverable weight re-optimized dose distributions, calculated with validated beam models and MC dose calculation algorithms. The SSD of the electron fields is chosen between 70 and 80 cm with a margin of at least 5 cm to the patient and the couch such that no collision is expected under consideration of the CT data set. Building a complete 3 D model of the patient and the couch could be implemented to certainly prevent collisions. For both clinical cases, the isocenter positions of the electron fields differ from the isocenter position of the photon beams. For the chest wall case, the electron fields share the same isocenter position, while for the squamous cell carcinoma case, the isocenter position of the electron fields differ in vertical direction. Thus, couch movements are required every time another isocenter position is needed and, as in stereotactic treatments, appropriate image guidance techniques combined with six degree of freedom couches will play an important role (Schmidhalter et al 2014). For performing a patient specific QA of an MBRT plan, it is suggested to compare 2D calculated dose distributions in a water phantom to measurements with the TrueBeam built-in electronic portal imaging device (EPID) positioned at SSD = 100 cm. The EPID is well established for dosimetric verification of photon IMRT plans and on the other side Chatelain et al (2013) showed the feasibility to use a standalone EPID positioned with an SSD = 70 cm as an efficient verification tool for MERT plans. Moreover, using the built-in EPID at SSD = 100 cm for dose verification of electron beams is already explored (Henzen et al 2014d).

5. Conclusions

An MC beamlet based inverse TPP for MBRT including a simulated annealing based DAO capable of performing simultaneous optimization of pMLC shaped photon and electron beams is successfully implemented and tested for an academic situation with two PTV definitions and two clinical cases. MBRT plans dosimetrically outperformed MERT, photon IMRT and VMAT plans for all investigated academic and clinical situations. MBRT is a possible solution to known limitations and downsides of treatments using only photons or only electron beams: Compared to photon only plans, the low dose bath delivered to distal OARs and normal tissue is considerably reduced. Compared to electron only plans, MBRT is not limited due to the depth of the target and the sparing of OARs located nearby to the target is substantially improved. The results indicate that MBRT has the potential to become an alternative modality for treating superficial targets with and without deep-seated part.

Acknowledgments

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