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Personalized automated treatment planning for breast plus locoregional lymph nodes using Hybrid RapidArc

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Running title: Automated planning for breast plus nodes

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Conflict of Interest Notification

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Abstract

Purpose

Breast cancer patients who require locoregional lymph node (LLN) irradiation can be treated using a hybrid RapidArc technique combining two tangential and three RapidArc fields. Since the creation of hybrid RapidArc plans is complex and labor-intensive, we developed an automated treatment planning workflow using the scripting application programming interface of the Eclipse treatment planning system.

Methods and Materials

15 patients (5 right and 10 left-sided) previously treated with breast+LLN radiotherapy were replanned using the script. The automated workflow included: i) optimal placement of the tangential fields based on the planning target volume (PTV) and organ-at-risk (OAR) contours, followed by optimization of field weights and beam energy, ii) positioning of the RapidArc fields, iii) subsequent RapidArc optimization using the RapidPlan knowledge-based planning solution.

Results

Average total planning times were 163±97 and 33±5 minutes for the manual and automated plans, respectively, with approximately 130 and 5 minutes of user interaction. Dosimetrically, both sets of plans were very similar, with comparable PTV dose homogeneity values and OAR mean dose differences of ≤1.9Gy. In 14/15 patients, the physician judged that the automated plan was either preferred (n=4) or equal (n=10) to the manual plan.

Conclusions

The complex hybrid RapidArc planning process for patients requiring breast+LLN irradiation was automated by optimizing the tangential field setup and integrating RapidPlan. The quality of the
automated and manual plans was comparable while automated planning times were substantially shorter. The principles described here could be used to automate other planning workflows.

Introduction

Breast cancer accounts for a significant proportion of patients treated with radiotherapy. In patients requiring treatment of the locoregional lymph nodes (LLN) in addition to the breast, treatment planning is more complex and labor-intensive, and more prone to variation between planners. As shown previously, automated planning solutions may increase planning efficiency and reduce variability, leading to improved plan quality and consistency, while reducing planning times. For breast cancer, Purdie et al. automated treatment planning for breast-only radiotherapy, based on tangential fields (TFs) for which the gantry angle was determined by lead wires placed on the body surface to indicate the target volume. This technique has been made commercially available (RayAutoBreast, RaySearch laboratories, Stockholm, Sweden). However, we are unaware of automated treatment planning solutions for breast plus LLN irradiation taking into account multiple organs-at-risk (OARs) surrounding the planning target volume (PTV), or that combine different planning techniques into a single treatment plan.

Until 2014, our institute used a straightforward technique combining half-beam blocked TFs for the breast and half-beam blocked anterior-posterior and posterior-anterior (AP-PA) fields for the LLN. This technique, however, was considered sub-optimal after the clinical introduction of deep-inspiration breath-hold (DIBH) for breast cancer, due to its susceptibility to inter-breath-hold breast position variations with risks of under- or overdosing the PTVs. Additionally, it delivered non-conformal dose distributions to the LLN with maximum doses up to 115% and provided limited potential for sparing of healthy tissues. We therefore developed and clinically implemented a hybrid RapidArc® (Varian Medical Systems, Palo Alto, USA; hybrid-RapidArc) technique in 2014. This consists of two TFs with unequal cranial field edges above the breast, plus three RapidArc volumetric-
modulated arc therapy (VMAT) fields which homogenize the breast doses and deliver the full dose to the cranial lymph nodes. However, this combination of techniques makes the planning process labor-intensive since the field setup and beam energies are often optimized through trial-and-error, and additional help-structures to support the optimization are needed.

Our aim was to automate this treatment planning process while still providing patient-specific treatment plans using the scripting application programming interface (API) of the Eclipse™ treatment planning system (Varian) and automatically incorporating RapidPlan™ knowledge-based planning (Varian) to determine the optimal placement of optimization objectives. For each patient, this requires optimal tangential field positioning based on the shape of the PTV contour, followed by positioning of RapidArc fields and optimization using RapidPlan predictions to generate the optimization objectives. The present work provides a technical overview of the automated solution and the results of an initial planning comparison for 15 patients comparing the automated plans against their respective manual plans.

Methods and Materials

Hybrid RapidArc technique

The hybrid-RapidArc technique consists of two half-beam TFs plus three partial RapidArc arcs. The cranial field edges of the TFs differ by 2 cm to create a slip-zone that results in a gradual decrease of the delivered dose in order to minimize hot/cold spots in case there is variation between the breath holds of a fraction. The standard total prescribed dose ($D_{p}$) is 42.72Gy in 16 daily fractions of 2.67Gy, with the prescribed dose for the TFs ($D_{p,TF}$) being 2.30Gy/fraction. The aim is to deliver 85% of the TF dose (1.96Gy) to 99% of the breast PTV below the slip-zone ($PTV_{BREAST}$) and 95% (2.19Gy) to 85% of $PTV_{BREAST}$. The RapidArc fields are used to homogenize the breast and slip-zone doses, and to deliver the full dose to the remaining target volume, e.g. the supraclavicular lymph nodes. This technique therefore combines the advantages of tangential beams to the breast and conformity of RapidArc.
Compared to full VMAT and fixed-beam intensity-modulated radiotherapy (IMRT) techniques, hybrid-RapidArc minimizes low-dose spread to the lungs, heart, and contralateral breast\(^{12}\). In addition, the TFs are wide-open at the ventral side of the breast ensuring adequate PTV coverage during breathing and if breast deformation/swelling occurs, see Figure 1, in contrast to a full RapidArc plan optimized on a standard PTV. Compared to full three-dimensional conformal techniques, intensity modulation in the cranial part of the hybrid-RapidArc treatment volume makes it easier to conform the dose to the LLN and spare OARs such as the esophagus, spinal cord and thyroid gland (Figure 2).

**Automated Hybrid RapidArc treatment planning workflow**

Using the scripting API (Eclipse v13.7), a script was developed in CSharp (C#) using Microsoft Visual Studio 2015 (Community Edition) to automate the planning of right- and left-sided breast plus LLN radiotherapy. As input, the script requires a planning CT-scan with delineated breast and LLN clinical target volumes (CTV), and contours of the ipsilateral and contralateral-lung, contralateral-breast, heart, liver, thyroid, esophagus and spinal cord. These structures are used to generate various PTVs, optimization help structures, and to automate field setup. In our clinic, the breast and LLN CTVs are delineated by the treating physician using the ESTRO consensus guideline on target volume definition for elective radiation therapy of early stage breast cancer\(^{13}\), and surgical clips mark the lumpectomy cavity. Figure 3 shows a flowchart of the automated process. PTV\(_{\text{BREAST}}\) and LLN PTV (PTV\(_{\text{LLN}}\)) are created from CTVs using expansions of 5mm and 8mm (5mm medially). The isocenter is positioned at the center-of-mass of the total PTV (PTV\(_{\text{TOTAL}}\)), which is the combined volume of PTV\(_{\text{BREAST}}\) and PTV\(_{\text{LLN}}\). For optimization and dose reporting, a virtual dose build-up region is created above the lowest cranial field edge of the tangential fields where PTV\(_{\text{TOTAL}}\) extends outside the body contour ventrally\(^{14}\). Finally, a ring structure is created by first combining PTV\(_{\text{TOTAL}}\) with the 80% isodose level after TF dose calculation, and performing an isotropic expansion of 50mm. We then subtracted the
total PTV from this structure, and only saved the region that fell within the body. By assigning maximum dose objectives, this ring structure is used to control high dose areas surrounding the PTV. To automate TF positioning, we first determine the optimal gantry angles and field settings of the mediolateral (ML) field by iterating over 90 different gantry angles (0°-90° or 360°-270° for right- or left-sided patients, respectively). At each gantry angle, the projection of the target (PTV\textsubscript{BREAST}) in the beams-eye-view (BEV) is modeled by the developed software, around which the jaws and individual multileaf collimator (MLC) leaves are fitted using a ~3mm margin (Figure 1). The leaves are opened ventrally to ensure coverage of the breast in case of swelling. The optimal gantry angle is selected based on the minimized weighted sum of the projection percentage of the contralateral-breast, heart, ipsilateral-lung and liver/abdomen (right/left-sided treatment) within the BEV. The opposing lateromedial (LM) field is created such that the beam divergence is matched with the ML-field.

Initially, 6MV energies are selected for both beams, and the anisotropic analytical algorithm (AAA) is used because of its fast dose calculation. The field weight of the ML-field is iteratively varied and, after normalizing PTV\textsubscript{BREAST} such that 95% of D\textsubscript{P,TF} is received by 85% of PTV\textsubscript{BREAST} (V95%=85%), the combination of field weights resulting in a minimum D\textsubscript{MAX} is selected, and final dose is calculated using the Acuros® algorithm. The treatment plan is considered acceptable when the criteria for the dose maximum (D\textsubscript{P,TF} D\textsubscript{MAX}<123%), the PTV\textsubscript{BREAST} mean dose (D\textsubscript{P,TF} D\textsubscript{MEAN}<102%) and coverage (>99% of D\textsubscript{P,TF} volume receives 85%) are met. If the plan fails one of these dose criteria, the energy of the beam with the largest distance from the original tumor location, defined by position of the high density surgical clips, is increased to 10MV/15MV, and the aforementioned process is repeated until the criteria are reached. If no surgical clips are present in the patient, the energy of the ML beam is chosen to be increased by default. Where necessary, the script will increase the energy of both beams to 10MV/15MV. Finally, the slip-zone is created and the dose is recalculated.
The RapidArc plan comprised three 80° arcs allowing different collimator angles and field settings such that each arc optimally covers PTV\textsubscript{TOTAL} while minimizing the field size. The script sets gantry start/stop angles and collimator angles according to standard clinical practice. Since RapidArc is used to deliver the full dose to the cranial lymph node regions, these should ideally be covered from all gantry angles. For optimization and dose reporting purposes, the script crops all the PTVs to 5mm below the body structure, which includes the virtual bolus. In line with our clinical practice, however, the maximum lateral field size is limited to 19cm in order to facilitate beam modulation. The script automatically closes the jaw that overlap least with PTV\textsubscript{LNN}. Subsequently, a knowledge-based planning solution (RapidPlan) was used to determine patient-specific positioning of the optimization objectives. RapidPlan requires the creation of a model based on a library of treatment plans for a certain clinical indication/treatment technique. For each included OAR, the model correlates the geometric features (e.g. relative OAR/PTV volumes and distances) to the dose received by that OAR. As a result, the RapidPlan model can be used to predict achievable OAR doses for new patients (i.e. not included in the model) allowing for optimal placement of the optimization objectives. For this study, we created a RapidPlan model based on a library of 54 patients (25/29 right/left-sided) which was used to generate optimization objectives for the heart, ipsilateral/contralateral-lung, contralateral-breast, esophagus, trachea and thyroid. Targets are assigned fixed lower/upper objectives along with upper objectives for ring and spinal cord. In the script, RapidPlan is called and model structures are assigned to the treatment plan structures, after which the optimization objectives are generated. The RapidArc optimization uses the dose distribution of the TFs as a starting point (“base-dose plan”). After completion of the optimization and Acuros dose calculation, a “continue previous optimization” (CPO) plan is created where the optimization priorities of all PTV objectives were increased to ensure adequate PTV dose coverage\cite{15}. Finally, the hybrid-RapidArc treatment plan is created by combining all TF and RapidArc fields into one hybrid plan.
By including RapidPlan in the workflow, a fully automated planning process was realized without necessitating manual interactivity during the optimization process. However, since our version of the scripting API does not allow inclusion of a base-dose plan, the TF plan with slip-zone has to be assigned manually before starting RapidArc optimization. In addition, dose calculation of the hybrid-RapidArc plan needs to be initiated manually as the current API does not allow for dose calculation using preset monitor units (MU).

**Study endpoints**

To evaluate the automated treatment planning solution, 15 (left n=5, right n=10, not included in the RapidPlan model) breast breast+LLN patients were arbitrarily selected from all patients treated at our department since commencing treatment using the hybrid-RapidArc technique in 2014, and re-planned using the script. More left-sided patients were selected since these present a higher challenge for the algorithm, since limiting heart dose is a higher concern. These patients were not part of the 54 patient RapidPlan model. As per clinical practice, all left-sided breast cancer patients were treated using a deep-inspiration breath-hold (DIBH) technique, while this was not used for the right-sided patients.

All automatically generated treatment plans were made for the TrueBeam linac with the Millennium 120 MLC. The manual hybrid RapidArc plans (manual) used to benchmark the automatically generated treatment plans were created by an experienced dosimetrist. All treatment plans were reviewed by a breast cancer radiation oncologist (P.M.) and medical physicist (W.V.). For all patients, a comparison between manual and automated hybrid-RapidArc plans was made, taking into account the required (interactive) planning time, MU, gantry angles and beam energy, as well as dose metrics such as PTV coverage (homogeneity index [HI, calculated as HI=100%*(D2%-D98%)/D50%], V95% and V107%), $D_{MEAN}$ of contralateral-breast, heart, lungs, esophagus, trachea and thyroid, and spinal cord $D_{MAX}$. V5Gy is reported for heart and contralateral/ipsilateral-lung, along with V20Gy for ipsilateral-
A Wilcoxon signed rank test was used to investigate whether differences were significant (p<0.05).

Results

An automated hybrid-RapidArc plan could be generated for all patients. In 4/15 (27%) cases the quality of the automated plan was judged superior to the manual plan by the physician based on a lower $D_{\text{MAX}}$ or lower dose to ipsilateral-lung. In one case the manual plan was preferred because of a lower contralateral-breast dose. For the remaining cases, manual and automated plans were considered comparable by the physician.

Average total treatment planning times were $33\pm5$ (range: 24-42) and $163\pm97$ (range: 120-480) minutes for the automated and manual plans, respectively. The average interaction time during the automatic process was 5min, whereas almost continuous interaction was required for the manual plans (average ~130min). Averaged over all cases, the automated process therefore resulted in an effective time gain of about 2 hours per treatment plan, which for individual cases could be as high as 7 hours. An example of the user interface for the automated workflow is shown in Figure 4. The patient and structure set have to be selected before starting the automated planning process. After optimizing TF positioning the OAR percentage within the ML-field is displayed as a function of gantry angle.

Table 1 summarizes field parameters for the manual/automated plans. For 6 patients, the automated plan resulted in a lower energy combination (6/10MV instead of 6/15MV), while a higher energy was selected in 1 patient. Dosimetric results of the manual and automated plans are summarized in Table 2. The automated plan OAR doses were typically comparable to or better than in the manual plans, with more homogeneous target doses. No differences results between the left- and right-sided patients could be noted.
Patient 8 showed the largest differences in treatment planning time (40min for automated vs. 480min for manual), beam energies and plan dosimetry. Although the PTV volume of 2340cm$^3$ was substantially more than the average (1261cm$^3$), an automated plan was still successfully generated. The manual plan used a combination of 6MV/15MV for the TFs with 4 partial-arcs of 10MV, whereas the automated plan achieved a comparable dose distribution using 6MV/10MV for the TFs and 3 standard, partial 6MV arcs (Figure 5). The automated plan resulted in more homogeneous PTV$_{TOTAL}$ doses and improved sparing for several OARs, including the lungs, trachea and esophagus.

The manual plan was preferred for one patient because of higher contralateral-breast doses in the automated plan. Figure 4 shows the ML-field gantry angles in both plans. The manual plan has a higher volume of heart within the TFs whereas the TF gantry angle of the automated plan results in slightly more contralateral-breast within the TFs. As a result, the automated plan increased contralateral-breast V2Gy/D$_{MEAN}$ (3.9%/0.5Gy), while decreasing heart V5Gy/D$_{MEAN}$ (1.2%/0.5Gy).

**Discussion**

This paper presents an automated solution for creating patient-specific breast and locoregional lymph node hybrid-RapidArc radiotherapy plans, combining the benefits of open tangential fields and RapidArc. The tangential fields minimize low-dose spread to lungs, contralateral-breast and heart, and, since they are opened in the anterior direction, are relatively insensitive for breathing/breath-hold variation and deformation / swelling of the breast, while RapidArc facilitates the creation of a conformal dose distribution around the lymph nodes, resulting in sparing of the esophagus, thyroid, trachea and spinal cord. Although previous work demonstrated automated tangential field positioning, the clinical scenario, incorporating a slip-zone junction and integrating knowledge-based planning (RapidPlan) in the automated workflow are novel features of the current study. Because of limitations in our version of the scripting API (v13.7), the addition of a base-dose plan to the optimizer and dose calculation of the hybrid plan still needed to be performed manually, however it should be technically feasible to automate these steps in the future. Using the Millennium 120 MLC,
and TrueBeam platform, an automated treatment plan could successfully be created for all cases (n=15) included in this study, while use of the automated script reduced average interactive treatment planning times by about 95% (2 hours) per treatment plan. On average, the automated plans resulted in more homogenous PTV doses and lower OAR doses with comparable MUs. In 10/15 and 4/15 cases respectively, the automated plan was considered to be comparable to, or better than the manual plan by the physician. Factors important in realizing an acceptable automated solution include, 1) improved positioning of the tangential fields through the gantry angle optimization process, 2) optimization of the field weights leads to a better starting point for the optimization of the subsequently added RapidArc fields, and 3) the incorporation of knowledge-based planning which drives the optimizer to reach patient-specific levels of achievable OAR sparing.

In this study, the automated and manual plans were compared using plans that did not compromise PTV dose coverage in favor of OAR sparing. However, in routine clinical practice, for selected patients the sparing of certain OARs, such as the heart, may take priority. In this case, the selection of the gantry angle can be adapted by changing the priorities of individual structures and the remaining volume of heart within the beam’s eye view can be blocked by MLCs. With respect to PTV coverage, the script iterates over all possible field weight combinations to select the combination resulting in the lowest $D_{\text{max}}$. In general, this leads to the selection of lower energies compared to manual plans, which is favorable for PTV dose coverage near the skin.

The biggest gain in automating this treatment planning process was time. Manual generation of the additional structures together with the trial-and-error process to select optimal field weights and beam energies for the TFs can be time consuming, especially when the breast volume is large. This means that some patients require a full working day (8 hours), for most of which the planner is interactively engaged, to create a treatment plan meeting the planning criteria (adequate PTV coverage and acceptable OAR sparing), while the automated process takes under an hour (with 5 minutes of user interaction). It is worth noting that all manual plans used in this study were created
by an experienced dosimetrist (E.B.). The gains in planning time and dosimetry may therefore be greater when benchmarked against inexperienced planners. The script is designed to generate high quality plans independent of the user, and is programmed such that multiple patients could be batched. This way, all treatment plans could be created sequentially at any time of the day.

Previous studies presented different approaches to automate treatment planning of a two-field tangential IMRT technique for breast only treatments. Penninkhof et al. proposed a method for individualized selection of isocenter and beam angles, based on a database of IMRT plans\textsuperscript{16}. Zao et al. demonstrated the feasibility of using a support vector machine based algorithm to determine optimal beam placement for prone- and supine treated patients, reducing the OAR doses without compromising PTV dose homogeneity and coverage\textsuperscript{17}. Purdie et al. presented an automatic workflow used routinely in the clinic, involving segmentation of different OARs together with gantry and collimator angle selection using heuristic optimization\textsuperscript{9,18}. In this study, however, selection of higher beam energies was not possible and most OARs were combined into a single structure, except for the ipsilateral/contralateral-lungs and heart. In addition, the breast anatomy was indicated by external land marks instead of a delineated target. In our clinical experience, fields positioned based on external land marks are frequently adapted to increase breast coverage or to minimize OAR doses. Although the present paper described automation of a complex planning technique, the process starts with the creation of the two TFs. The script could therefore be adapted to create breast only treatment plans. Similarly, it is currently not possible to deliver a boost dose to the breast with the script, although this too would be straightforward to implement, as would the use of flattening filter free treatment beams\textsuperscript{19}. Although the automated hybrid-RapidArc technique may not be in widespread use, it is worth noting that a large number of functions of the software are also applicable to more conventional treatment planning techniques, such as the automated and optimized positioning of the tangential fields. In addition, the software could be easily adapted to create, for example, 4-field plans for breast+LLN irradiation which is more commonly used.
A number of limitations deserve mention. Firstly, all automated plans were generated using a single research computer (with 32Gb of RAM and a 2.00GHz Intel Xeon dual core processor). It would therefore be possible to decrease computation times using various techniques, including distributed calculation over multiple computers. This was indeed used when creating the manual treatment plans in our clinical treatment planning system, substantially shortening the dose calculation times. Secondly, standard collimator angles are used for all fields, along with standard gantry start and stop angles for each arc. Further dosimetric improvements could be anticipated if these parameters were optimized for individual patients. In addition, the isocenter is currently placed in the center-of-mass of the combined PTV, but further sparing of the lungs may be possible by positioning the isocenter in the lung, thereby reducing the beam divergence. Furthermore, selection of the ML field gantry angles could be adapted by changing the weights of the different OAR overlap volumes, as mentioned previously. The TF positioning in the automated plans is also dependent on the delineation, as contouring inconsistencies may influence the selected gantry angles and therefore the dosimetry. Thirdly, we acknowledge that the plan review process was not performed in a blinded fashion. However, we believe that in this case the possibility of bias was minimized because the physician did not have to choose one plan over another, he was allowed to indicate that the plans were clinically comparable. As a result of this, in 10/15 patients the manual and automated plans were considered comparable. Furthermore, in all 4 cases where the automated plan was preferred and the single case where the manual plan was preferred, this was supported by objective dosimetric differences. Finally, the current version of the Eclipse scripting API has a number of limitations, such as the need to manually select a base-dose plan and calculate with pre-set MU values. These shortcomings have been communicated to Varian Medical Systems.

In conclusion, using the Eclipse scripting API and incorporating a knowledge-based planning solution, we developed an automated solution for personalized treatment planning of breast plus locoregional lymph nodes using a hybrid RapidArc technique. Resulting plan quality was generally comparable to or better than the respective manual plans, while substantial gains in treatment planning times were
obtained. Automated solutions like this may help to manage departmental workloads and facilitate the spread and adoption of new treatment techniques.

Figure Legends

Figure 1. A beams-eye-view projection of the two (mediolateral [ML] and lateromedial [LM]) tangential fields used in the hybrid RapidArc technique, before creation of the slip-zone region. Dorsally, the multileaf collimator (MLC) is used to block out the heart and lungs, while the jaws are fully opened ventrally to ensure that adequate dose coverage is obtained when breast swelling or deformation occurs.

Figure 2. Typical field setup and resulting dose distributions for the conventional (left) and hybrid RapidArc (hybrid-RapidArc, right) techniques for a single left-sided patient. The tangential fields are shown in (a), along with contours of the PTV$_{TOTAL}$, contralateral-breast, lungs and heart. (b) Shows the slip-zone region, denoted by the arrow, and delineated PTV$_{TOTAL}$ and ipsilateral lung. (c) And (d) show the locoregional lymph node regions with the PTV$_{TOTAL}$, ipsilateral-lung, trachea and spinal cord delineated. Finally, (e) shows the total resulting dose distributions for both techniques, illustrating that hybrid-RapidArc can deliver homogeneous PTV doses while minimizing the low-dose spread to the OARs.

Figure 3. Detailed flowchart of the automated planning process. The general overview (a) shows the required input to the script, the creation of tangential fields and RapidArc plans. The dotted lines indicate the manual steps in the process. More detailed information illustrates the steps needed to optimize the mediolateral (ML) field setup (b), the beam energies and field weights (c) and the RapidArc field setup (d).

Figure 4. Example of the user interface of the automated planning solution. The graphs display the relationship between the gantry angles of the tangential fields and the resulting overlap with the organs-at-risk (OARs). The gantry angle that was considered optimal is indicated by the vertical line
for the manual (solid) and automated (dashed) treatment plans, respectively 310 and 305 degrees for this patient. It should be noted that the graphs are magnified to only show the relevant gantry angles, the actual gantry angle optimization was performed considering all angles between 270 and 360 degrees.

Figure 5. Dose-volume histogram (DVH) comparison for a left sided manual (solid) and automated (dashed) plan of the same patient. DVH-lines for the $\text{PTV}_{\text{TOTAL}}$, ipsilateral/contralateral-lungs, contralateral-breast and heart are shown in (a), with (b) showing the spinal cord, thyroid, trachea and esophagus.

References


4. XXXX

5. XXXX


11. XXXX

12. XXXX


15. XXXX


Table 1. Summarized field parameters. The gantry angles are averaged over all patients, separated between patients with left and right sided breast cancer. The Table also shows the transitions in selected beam energies between the manual and automated plans (MPs and APs, respectively). In the majority of cases, lower beam energies were used in the APs, compared to the MPs. If a boost PTV was present, the field located furthest from this structure was chosen to use the higher beam energy. Otherwise the ML field was selected.

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<th>Gantry angles of the tangential fields (°)</th>
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<th>Automated Plans (APS)</th>
<th>Number of plans</th>
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<td>Lateromedial field</td>
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<tr>
<td>Left</td>
<td>137 ± 5</td>
<td>135 ± 5</td>
<td>10</td>
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<tr>
<td>Right</td>
<td>224 ± 4</td>
<td>229 ± 1</td>
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Comparison of beam energies

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RapidArc fields

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Table 2. Dosimetric metrics averaged over all 15 patients and shown for both the manual and the automated hybrid treatment plans. Mean dose for heart is separated for right-sided (R) and left-sided (L) patients. Total number of monitor units (MU) is for both the tangential fields (TF) and the RA arcs.

<table>
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<tr>
<th>Structure</th>
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<tbody>
<tr>
<td>PTV&lt;sub&gt;TOTAL&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HI (%)</td>
<td>10.8 ± 1.8</td>
<td>8.7 ± 0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>V107% (d) (%)</td>
<td>1.2 ± 0.8</td>
<td>0.4 ± 0.3</td>
<td>0.002</td>
</tr>
<tr>
<td>V95% (d) (%)</td>
<td>98.3 ± 1.1</td>
<td>98.6 ± 0.4</td>
<td>0.28</td>
</tr>
<tr>
<td>PTV&lt;sub&gt;LLN&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HI (%)</td>
<td>11.3 ± 1.7</td>
<td>9.8 ± 1.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>V107% (d) (%)</td>
<td>2.1 ± 1.4</td>
<td>0.6 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>V95% (d) (%)</td>
<td>98.2 ± 1.3</td>
<td>97.9 ± 0.8</td>
<td>0.41</td>
</tr>
<tr>
<td>PTV&lt;sub&gt;BREAST&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HI (%)</td>
<td>9.4 ± 2.4</td>
<td>6.9 ± 1.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>V107% (d) (%)</td>
<td>0.6 ± 0.9</td>
<td>0.1 ± 0.1</td>
<td>0.06</td>
</tr>
<tr>
<td>V95% (d) (%)</td>
<td>98.6 ± 1.1</td>
<td>99.3 ± 0.6</td>
<td>0.02</td>
</tr>
<tr>
<td>Contralateral breast</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V2Gy (d) (%)</td>
<td>7.2 ± 5.8</td>
<td>7.8 ± 5.8</td>
<td>0.33</td>
</tr>
<tr>
<td>D&lt;sub&gt;MEAN&lt;/sub&gt; (Gy)</td>
<td>0.8 ± 0.2</td>
<td>0.8 ± 0.3</td>
<td>0.29</td>
</tr>
<tr>
<td>Heart R (N=5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V5Gy (d) (%)</td>
<td>0.0 ± 0.1</td>
<td>0.1 ± 0.1</td>
<td>0.11</td>
</tr>
<tr>
<td>D&lt;sub&gt;MEAN&lt;/sub&gt; (Gy)</td>
<td>1.2 ± 0.1</td>
<td>1.2 ± 0.1</td>
<td>0.89</td>
</tr>
<tr>
<td>Heart L (N=10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V5Gy (d) (%)</td>
<td>6.1 ± 5.5</td>
<td>5.4 ± 5.1</td>
<td>0.14</td>
</tr>
<tr>
<td>D&lt;sub&gt;MEAN&lt;/sub&gt; (Gy)</td>
<td>2.7 ± 1.2</td>
<td>2.6 ± 1.2</td>
<td>0.54</td>
</tr>
<tr>
<td>Ipsilateral lung</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V5Gy (d) (%)</td>
<td>11.8 ± 1.7</td>
<td>11.1 ± 1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>D&lt;sub&gt;MEAN&lt;/sub&gt; (Gy)</td>
<td>50.0 ± 5.2</td>
<td>47.9 ± 5.8</td>
<td>0.03</td>
</tr>
<tr>
<td>V20Gy (d) (%)</td>
<td>24.0 ± 4.7</td>
<td>22.5 ± 4.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Contralateral lung</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V5Gy (d) (%)</td>
<td>1.0 ± 0.1</td>
<td>0.8 ± 0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>D&lt;sub&gt;MEAN&lt;/sub&gt; (Gy)</td>
<td>2.0 ± 1.4</td>
<td>0.3 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D&lt;sub&gt;MEAN&lt;/sub&gt; (Gy)</td>
<td>8.2 ± 4.5</td>
<td>7.5 ± 4.1</td>
<td>0.06</td>
</tr>
<tr>
<td>Esophagus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D&lt;sub&gt;MEAN&lt;/sub&gt; (Gy)</td>
<td>6.6 ± 1.9</td>
<td>4.7 ± 1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Spinal cord</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D&lt;sub&gt;MAX&lt;/sub&gt; (Gy)</td>
<td>12.7 ± 1.9</td>
<td>12.2 ± 1.6</td>
<td>0.16</td>
</tr>
<tr>
<td>Body-PTV&lt;sub&gt;TOTAL&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V5Gy (d) (%)</td>
<td>17.5 ± 2.3</td>
<td>16.7 ± 2.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>V40Gy (d) (%)</td>
<td>2.4 ± 0.6</td>
<td>2.0 ± 0.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Monitor units</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tangential fields</td>
<td>132 ± 18</td>
<td>129 ± 19</td>
<td>0.14</td>
</tr>
<tr>
<td>RapidArc</td>
<td>126 ± 9</td>
<td>130 ± 25</td>
<td>0.32</td>
</tr>
</tbody>
</table>

<sup>a</sup> Overall p-value for dose differences between the manual and automated plans.

<sup>b</sup> Planning target volume (PTV) for the combined volumes of locoregional lymph nodes PTV (PTV<sub>LLN</sub>) and breast PTV (PTV<sub>BREAST</sub>).

<sup>c</sup> Homogeneity index (HI) for the PTVs.

<sup>d</sup> Vx %/Gy: Volume receiving x% of total dose / xGy.

<sup>e</sup> Results for heart are separated for right-sided (R) and left-sided (L) treated breast.
Figure 1
Figure 3

(a) RapidArc (RA)
- Create RapidArc plan
- Create three RA fields (standardized settings)
- Optimize field setup
- Add base dose plan
- RapidPlan optimization (PO v13.7) and subsequent dose calculation (Acuros)
- CPO and subsequent dose calculation (Acuros)

(b) Optimization ML field setup
- Set gantry angle
- Fit jaws and MLC
- Record field-structure overlap for contralateral breast, ipsilateral lung, heart and liver
- Iterate gantry angle over 90 degrees
  - Right sided: 0 – 90 degrees
  - Left sided: 270 – 359 degrees
- Select gantry angle with minimum field-structure overlap

(c) Optimization beam energies and field weights
- Set initial beam energies (6MV / 6MV)
- Set initial field weights (1.0 / 1.0) and Dose calculation (AAA)
- Normalize plan (D85% PTV = 95%) and record Dmax
- Select field weights with minimum Dmax
- Dose Calculation (Acuros) and Normalize plan
- Dmax < 123%
  - D99% > 85%
  - Dmean < 103%
  - Yes
- Set optimal beam energies and field weights
- Iteratively change field weights:
  - ML field: 0.1 – 2.0 (0.1 steps)
  - LM field: 1.0
  - Change beam energy of one field*
  - (10MV / 15MV)

* High energy side chosen based on position of surgical clips with respect to center breast PTV

(d) Optimization RA field setup
- Fit lateral field size around locoregional lymph nodes PTV, lower field caudally to cover breast PTV
- Lateral field size 19 cm?
  - ≤ 19cm
  - Enlarge field size to increase volume of breast PTV in field
    - Reduce field size at lateral side locoregional lymph nodes PTV
  - > 19 cm
  - Set lateral field size
Figure 4

Automated Breast Planning

Patient ID: [Patient 7]  Go
Structure Set: SS 1

Create Tangential Fields  Create RapidArc Fields  Optimize

Ipsilateral Lung

Heart

Contralateral Breast

Liver / Abdomen

Overlap (%) vs. Gantry Angle (degrees)
Figure 5