Journal of Medical Radiation Sciences

Open Access

ORIGINAL ARTICLE

Tangential intensity modulated radiation therapy (IMRT) to the intact breast

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Keywords
Breast cancer, intensity modulated radiotherapy, radiotherapy, radiotherapy planning

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Funding Information
No funding information is provided.

Received: 14 October 2015; Revised: 6 April 2016; Accepted: 11 April 2016

J Med Radiat Sci **63** (2016) 217–223

doi: 10.1002/jmrs.185

Abstract

Introduction: Inverse-planned intensity modulated radiation therapy (IP-IMRT) has potential benefits over other techniques for tangential intact breast radiotherapy. Possible benefits include increased homogeneity, faster planning time, less inter-planner variability and lower doses to organs at risk (OAR). We therefore conducted a pilot study of previously treated intact breast patients to compare the current forward-planned 'field-in-field' technique (FP-IMRT) with an IP-IMRT alternative. **Methods:** The IP-IMRT plans of 20 patients were generated from a template created for the planning system. All patients were prescribed adjuvant whole breast radiotherapy using a hypofractionated regimen of 40.05 Gy in 15 fractions over 3 weeks. Plans were assessed based on visual inspection of coverage as well as statistical analysis and compared to the clinically acceptable FP-IMRT plans. Patients were planned retrospectively in Monaco 3.2® using a laterality-specific, tangential planning template. Minor adjustments were made as necessary to meet the planning criteria in the protocol. Dose coverage, maximums, homogeneity indices and doses to OAR were recorded. **Results:** The IP-IMRT plans provided more consistent coverage (38.18 Gy vs. 36.08 Gy of D95; $P = 0.005$), a comparable though higher average maximum (D2 = 42.52 Gy vs. 42.08 Gy; $P = 0.0001$), more homogeneous plans (homogeneity index = 0.908 vs. 0.861; $P = 0.01$) and somewhat lower V20 heart and lung doses (0.11% vs. 0.89% for heart; 5.4% vs. 7.52% for lung) than FP-IMRT ($P > 0.05$). **Conclusion:** Clinically acceptable plans have been generated using the IP-IMRT templates in Monaco. Improvements in consistency and quality were seen when compared to the FP-IMRT plans. The template-based process is an efficient method to inversely plan IMRT for breast patients.

Introduction

Intensity modulated radiation therapy (IMRT) has become a standard technique for improving conformality while minimising radiation doses to adjacent normal structures in numerous tumour sites, including breast cancer.[1–3] Inverse-planned tangential IMRT (IP-IMRT) can produce clinically suitable plans similar to forward-planned 'field-in-field' IMRT (FP-IMRT) breast techniques.[4] van Asselen et al.[4–8] reported that inverse planning increased dose homogeneity, lowered doses to critical structures and reduced planning times due to less variation between planners, when compared with forward-planned techniques. These studies, however, included multi-directional IMRT and volumetric modulated arc therapy techniques, rather than limiting the fields to the traditional breast radiotherapy technique of directly opposed tangential photon fields.

In the current quality improvement study, we aimed to develop a planning template for the generation of inverse-planned IMRT breast radiotherapy, maintaining the traditional opposed tangential beams with a non-divergent posterior edge, to ascertain whether we could replicate the plans achieved using our current technique. Our focus is on the clinical applicability of the generated plans. We will then use the resultant plans to assess the robustness of the template.

Materials and Methods

The data sets of 20 consecutive patients who had previously received tangential radiotherapy to the intact breast using our standard FP-IMRT technique were selected from our patient database. These cases were re-planned retrospectively in February of 2013 by two radiation therapists using an inverse planning algorithm in Elekta Monaco 3.2 (Elekta-CMS Software, Riverport Drive, Maryland Heights, MO 63043).

Ten patients of each laterality were included in the analysis; all patients were Stage 1 (N0M0). As this was a planning study centred on whole breast irradiation techniques, dose contribution from the tumour bed boost was not included in the analysis.

Patients were simulated on the Civco MT-350™(Civco Medical Solutions, Kiotoweg 407, 3047BG Rotterdam, the Netherlands) breast board with a suitable incline, and borders were marked clinically by the attending radiation oncologist (RO). For most patients, borders were marked as per the eviQ adjuvant short-course breast protocol[9]: a medial edge at mid-line, lateral edge marked at the mid-axillary line or 1.5 cm posterior to palpable breast tissue, inferior border marked 1.5 cm inferior to palpable breast tissue and a superior border at the level of the inferior head of the clavicle (sternal notch level).

Breast planning target volumes were generated to calculate the IP-IMRT plans as the planning system required a volume for optimisation; these volumes were then applied to the FP-IMRT plans purely for statistical analysis. These planning volumes were generated from a standard set of landmarks as follows: a tangent box was created with a posterior edge matching the clinically marked posterior and medial edges from simulation and extending outside the patient contour to ensure that the whole breast was covered. Using this volume and the 3D auto-margin tool in the planning system, a *PTVeval* was created; excluding the superior, inferior and posterior borders by 1 cm, excluding the chest wall (by up to 1 cm from lung at RO discretion) and clipping inside the patient contour by 0.5 cm. A visual check was completed to ensure that breast tissue was covered by this volume and edited as required by the RO. This volume will be referred to as the *PTVeval* as it is not a true planning target volume (PTV), but a clinically relevant volume encompassing the breast tissue with no expansion, and clipped 0.5 cm within the patient contour. This method of voluming was defined to provide a tuning structure for the optimiser in the planning system as well as a volume for statistical analysis. For left-sided patients an additional constraint was applied to this structure to crop the lateral extents of the *PTVeval* to prevent the volume wrapping around the chest wall adjacent to the cardiac contour. As published literature has demonstrated a correlation with inhomogeneity and breast volume as well as field separation, these values were recorded for analysis.[4,10]

In our department, the standard protocol is a forward-planned field-in-field technique, planned in XiO 4.62®, to deliver a hypofractionated regimen of 40.05 Gy in 15 fractions over 3 weeks.

The FP-IMRT plans were produced by one of a number of radiation therapists, according to the departmental protocol (aligned with eviQ short-course breast protocol[9]) and subjected to peer review, prior to that plan being used clinically. The FP-IMRT planning process is an iterative process, and involved calculation of open 6 MV fields normalised to an appropriate weight point (ICRU 50).[11] Where appropriate, a proportion of 15 MV fields may be introduced to improve coverage on the chest wall and decrease peripheral hotspots; this was introduced sparingly to ensure superficial dose was not compromised. Additional fields were then added and segmented to shield out hotspots. The same 20 patients were then parallel planned with IP-IMRT by two radiation therapists starting with a basic template and making adjustments to create a plan that satisfied the criteria defined in the departmental protocol.

The same prescription (40.05 Gy in 15 fractions) was applied to the inverse optimisation in Monaco® as part of a template. At the time this study was conducted it was not possible to use mixed energies for IMRT in the planning system, thus limiting us to the use of 6 MV beams. The template included a pair of tangential beams, directly opposing (180° apart) with an asymmetric, non-divergent posterior edge on both beams. A laterality-specific template was used for left- and right-sided patients. Once the template was applied, the beam angles were manually optimised for each patient to match the posterior field borders used in the FP-IMRT plans. The Monaco prescription only included the Breast *PTVeval* and patient contour for optimisation. Initially the heart was included in the optimisation prescription, however using opposed tangential fields limited the optimiser, decreasing the options to modulate dose around the heart, resulting in 'dose dumping' on each side. We established that by modifying the *PTVeval* so that the

optimiser did not need to 'work' around the heart, we could achieve more homogeneous dose within the *PTVeval*. We achieved this by adding another structure parallel to the posterior edge of the tangent box (the green structure as seen in Fig. 2), matched with the anterior border of the cardiac contour. Using the auto-margin tool in the planning system this volume was also excluded by up to 1 cm at RO discretion to stop the *PTVeval* conforming to the chest wall laterally. The pre- and post-modification structures are illustrated in Figures 1 and 2. This modification produced a similar result to the inclusion of cardiac and lung shielding used for the FP-IMRT plans.

Lung was also excluded from the prescription as it resulted in similar dose dumping to when the heart was included. Doses to heart and lung were managed by a combination of the above modifications to the *PTVeval* and dose constraint cost functions.

Thus, the optimisation prescription included the breast *PTVeval* and external patient contour, but not the heart or lungs. The breast *PTVeval* utilised a cost function to drive coverage to 95% of the volume with 95% of the prescribed dose (TD) (i.e. 38 Gy) and another cost function to control the maximum dose allowed in the volume (a dose to 2% of the volume less than 107% of TD, i.e. 42.85 Gy). A cost function was then applied to the patient (all of the area outside the breast *PTVeval*, but still within the external patient contour) to restrict the 95% isodose line to just covering the *PTVeval*. Another cost function was added to the patient contour and optimised over all voxels to control the absolute maximum over the whole plan.

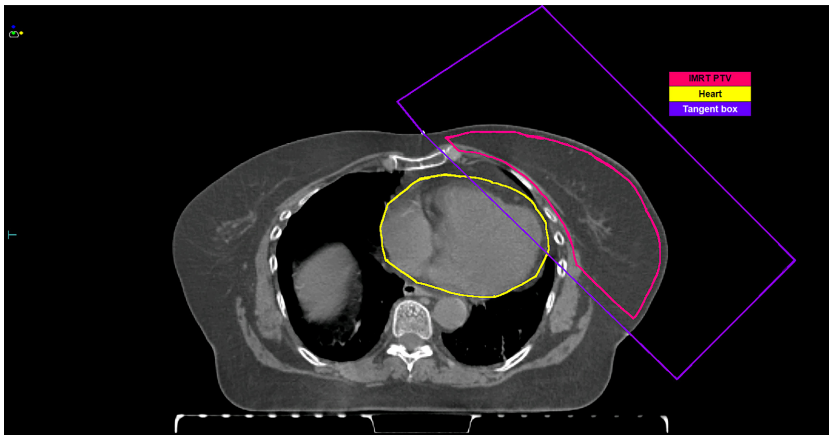

Figure 1. *PTVeval* prior to modification.

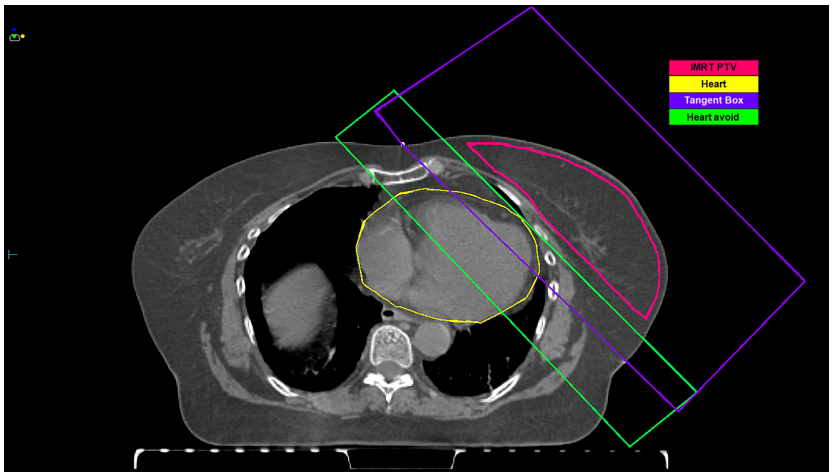

Figure 2. *PTVeval* post-modification with green heart avoidance structure and volume no longer wrapping around the chest wall adjacent to the heart.

A 2.5-cm flash extension was applied to the properties of the breast *PTVeval* structure to ensure that the optimisation and fields covered the anterior aspect/apex of the breast sufficiently (2 cm anteriorly, accounting for the 0.5 cm that the *PTVeval* has been clipped inside the skin) to provide appropriate coverage and to allow for daily setup variation and patient motion.[7,11]

Inverse planning in Monaco is a two-phase process: in the first phase it optimises the beams to generate a plan with the best match to the prescription and in the second phase the system completes segmentation of the beams resulting in a deliverable IMRT plan. It is not uncommon for there to be a difference between the optimised and segmented plans. Little plan degradation was seen between the optimised and segmented plans. The Monaco system plans with a hybrid approach (an open field combined with a portion of the beam inversely optimised). Most of the monitor units (MUs) are delivered through an open field, then subsequent smaller segments which modulate the dose are delivered with a lower number of MU. In order to decrease and control the number of segments, step and shoot segmentation was used rather than dynamic multi-leaf collimation.[12] In consultation with the physics department a minimum segment size of 9 cm^2 was applied with a minimum difference of 20 cm^2 between consecutive segments. The minimum number of MU per segment was set to five.

Each patient's data set was run with the standard template initially; minor adjustments were made as required to produce a clinically acceptable plan that achieved the aims of the protocol. Plan acceptability was initially assessed on visual inspection of breast tissue coverage and the position of hot and cold spots. Subsequently, data including coverage of PTV*eval* (D2-near maximum and D95), dose homogeneity (D95/D5), overall maximum and organs at risk (OAR) dose information for both treatment plans (IP-IMRT and FP-IMRT) were collected and recorded to enable a comparison between the current and proposed treatment techniques. Mean, standard deviation and range were calculated for each parameter to determine the significance of the collated results. Treatment plans were compared using Student's paired *t*-test; $P < 0.05$ was considered significant.

This work met the criteria for a Quality Improvement project and was reviewed by the NCNSW Human Resource Ethics Committee.

Results

The treatment plans of 20 patients with early stage breast cancer were analysed, 10 of each laterality. The average tangential separation from medial edge to post-edge (clinical borders) was 21.7 cm, with a minimum separation of 18.5 cm and a maximum of 27 cm. The *PTVeval* structures varied widely in volume with a minimum of 415 cm^3, a maximum volume of 1636 cm^3 and an average volume of 932 cm^3 (SD = 364.7 cm^3).

PTV coverage

The inverse plans easily met the D95 ≥ 38.05 Gy planning constraint with a mean D95 of 38.18 Gy (Table 1). For the forward-planned cases, the mean D95 was 36.08 Gy, significantly lower than for IP-IMRT ($P = 0.005$), with only 91% of the *PTVeval* covered by 95% of TD. The variation in doses covering 95% of the PTV in the forward-planned cases was much higher than the range seen in the inverse-planned cases. If the *PTVeval* had been in place during the FP-IMRT planning, this variation may have been less significant.

The D2 < 42.85 Gy planning aim (maximum dose to 2% of the PTV*eval* to be less than 107% of the prescribed dose) was achieved in all except one of the IP-IMRT patients. Lower doses were seen for D2 in the FP-IMRT cases (42.08 Gy vs. 42.52 Gy for IP-IMRT; $P = 0.0001$) although the variation was higher in the former group (SD: 0.36 vs. 0.23).

IP-IMRT resulted in a more homogeneous plan with a smaller range. The average homogeneity index (HI) was 0.908 for IP-IMRT and 0.861 for the FP-IMRT cases, and this was a statistically significant difference ($P = 0.010$).

Organ at risk doses

The ipsilateral lung mean and V20 doses were comparable, on average, between the two techniques ($P > 0.05$; Table 2). Average mean ipsilateral lung doses for IP-IMRT and FP-IMRT were 3.7 Gy (SD: 1.3, range: 0.91–5.67) and 3.9 Gy (SD: 1.3, range: 1.01–6.72) respectively. The average V20 was 7.3% (SD: 3.6, range: 0.16–12.5) for IP-IMRT and 7.6% (SD: 3.3, range: 0.28–13.9) for FP-IMRT. All of the patients in this study

Table 1. Dosimetric comparisons for breast IMRT: *PTVeval* coverage.

Characteristic	Forward-planned IMRT	Inverse-planned IMRT	*P*-value
D95%[1]	36.08 (3.02)	38.18 (0.28)	0.005
D2%[2]	42.08 (0.36)	42.52 (0.23)	0.0001
HI[3]	0.861 (0.074)	0.908 (0.006)	0.010

Data presented as means in Gy (SD). IMRT, intensity modulated radiation therapy; PTV, planning target volume.
[1]D95% is the dose received by 95% of *PTVeval* – near minimum.
[2]D2% is the dose received by 2% of *PTVeval* – near maximum.
[3]Homogeneity index (HI), calculated as D95/D5 to *PTVeval*.

Table 2. Dosimetric comparisons for breast IMRT: organs at risk.

Organ at risk	FP-IMRT	IP-IMRT–modified PTV	IP-IMRT–original PTV
Heart mean dose	1.05 (0.45)	0.96 (0.39)	1.88 (0.84)[3]
Heart V20 dose[1]	0.71 (0.95)	0.11 (0.32)	2.04 (1.85)
Lung mean dose	3.80 (1.31)	4.03 (1.60)	N/A
Lung V20 dose[2]	7.52 (3.16)	5.34 (2.73)	N/A

Data presented as means in Gy (SD). IMRT, intensity modulated radiation therapy; PTV, planning target volume; N/A, not applicable.
[1]Volume of heart receiving 20 Gy.
[2]Volume of lung receiving 20 Gy.
[3]Significantly different to FP-IMRT, $P = 0.009$.

achieved the Radiation Therapy Oncology Group (RTOG) dose guideline of a V20 less than 15%.[13]

Heart doses were also comparable, with the IP-IMRT plans resulting in slightly lower mean and average doses. Prior to modification of the PTV*eval* structure adjacent to the heart, mean and V20 heart doses were higher than the forward-planned option ($P = 0.009$; Table 2). This is due to the inclusion of cardiac shielding in the forward-planned fields. Even prior to modification though, the doses to this structure were still acceptable within the RTOG 1005 protocol guidelines.[13]

Plan parameters

The MU and number of segments were consistently higher in the IP-IMRT plans. The average MU for the FP-IMRT option was 249.8 (SD 8.9) versus 287.0 (SD 30.0) for IP-IMRT ($P = 0.0001$). On average FP-IMRT plans had five segments per plan (SD: 1.12) and IP-IMRT had nine (SD: 2.23).

Quality assurance

Departmental process is that all IMRT plans are checked with MapCHECK (Sun Nuclear Corp., Suntree Blvd, Melbourne, FL) using gamma criteria of 3 mm and 3%. All of the plans were measured and met quality assessment criteria, with the lowest pass of 99.7% on a singular tangent field.

Optimisation and calculation time

The time taken to produce the final plan had not been formally measured during the forward planning of our subject patients, but typically required approximately 0.5–1 h of radiation therapist (RT) time. Using our Monaco inverse planning template it took, on average, 15–20 min of RT time to achieve the final plan. This time did not include the contouring and preparation for each patient, only the planning component. However, the ROs who were creating the PTV*eval* found that, with practice, this process took very little more time than simply putting on the tangent beam required for FP-IMRT.

Discussion

Intensity modulated radiation therapy employing tangential photon beams is a well-established technique for adjuvant breast radiotherapy. We wished to continue using a tangential beam arrangement as this is well proven and avoids extensive irradiation of non-target tissues.[8] The results of the present study suggest that we can generate clinically acceptable IP-IMRT plans using a template-based approach in Monaco while contributing minimal doses to OAR. We were also able to improve the plan consistency and homogeneity in this group of patients using this technique.

There are a number of methods described in literature for the delineation of a whole breast CTV/PTV structure; however, their results highlight the variability between users. We chose to use the auto-margin tool for generation of the breast PTV*eval*, as it produced volumes consistent with those outlined in RTOG 1005, were simple and provided a clinically relevant structure for optimisation and evaluation.[13,14] By clipping the PTV*eval* 0.5 cm inside the skin, penumbra is accounted for in statistical analysis. Using the tangent box in combination with clinical borders and an auto-margin tool it was also an efficient method to create a standardised structure with less variability than using manually drawn contours, particularly at the lateral extents of breast tissue.

This study was conducted retrospectively, using FP-IMRT plans that had been deemed 'optimal' for clinical use as the control. Breast contours were not used and planning aims were not as prescriptive for these plans; therefore they were assessed based on visual inspection of breast tissue (and tumour bed) coverage by the 95% isodose line, hotspot size and location, as well as heart and lung dose volume histogram statistics. The statistical plan assessment criteria were developed from existing relevant literature for the purpose of this study.

The difference in coverage between the FP-IMRT and IP-IMRT PTV*eval* could be attributable to the defined coverage goals used in the optimisation in the latter group. The scope of this project was not to improve the dose coverage, but rather to develop a template for use with the inverse planning algorithm that could generate comparable, clinically acceptable plans. The use of IP-IMRT avoids the iterative process used in FP-IMRT, and can therefore reduce the variation between planners. Our results demonstrated that a template could be used

to generate an ideal clinical plan and that this coverage could potentially be increased without compromising OAR or dose homogeneity.

The current quality improvement study was not a plan comparison study per se; the focus was on clinical outcomes. The concept was to ensure that we could produce similar plans for the different planning systems using the different methods. The primary measure of an acceptable plan was the visual inspection of 95% isodose coverage and assessment of clinically relevant hotspots. Using two different planning systems as well as techniques made it difficult to find an appropriate normalisation method. FP-IMRT XiO uses a superposition algorithm dosed to a point on the 100% isodose line, resulting in a locus of acceptable dose normalisation points. Monaco uses a Monte Carlo algorithm for dose calculation with IP-IMRT and is dosed to a volume. We recognise that this could influence our statistical results, however in terms of the generation of clinically acceptable plans this is unlikely to change our results.

Planning and treatment time differences between the techniques were considered, but not formally measured for every patient. Preparation and contouring prior to planning initially requires more time for IP-IMRT than FP-IMRT due to the delineation of the *PTVeval* which is not required for FP-IMRT, however this time is offset by the use of the template which produces a plan in less time than manually adjusting segments. Beam on time for both methods are similar, so although the MU are higher and there are more segments (on average 9 per patient) there are small time savings as only two fields need to be loaded as opposed to the average five separate fields of an XiO FP-IMRT plan.

The two patients with the largest tangential separations (27 cm and 24.5 cm) also had the highest doses at D2, 42.81 Gy and 42.96 Gy respectively. The homogeneity indices for these patients also indicated that these plans were the least homogeneous in the cohort. These results are consistent with published data on the effect of breast size, tangent separation and inhomogeneity in radiotherapy planning.[4,9,15,16] It was noted during the study that once a patient's tangential separation reached 22 cm or more with 6 MV photons, the optimiser struggled to provide enough coverage to the volume without resulting in an overall hotter plan with a higher significant maximum. The lower maximum seen in these patients when planned with FP-IMRT could be attributed to the inclusion of a proportion of 15 MV photons in their treatment plan which was not possible in the IMRT planning system at the time this comparison was completed. With a recent upgrade to the planning system, it is now possible to treat using a combination of 6 MV and 15 MV photons, an area that could be investigated in the future.

The heart was excluded from the constraints used for optimisation as it tended to create hotter plans anteriorly, but with poorer coverage of the *PTVeval* and overall a minimal improvement on the dose to this structure. Our results are similar to the study by Landau et al.[8] which found that using a two-field tangential beam arrangement for IP-IMRT did not significantly improve sparing of the heart. Tangential beams alone do not provide the programme with enough options to modulate the beam around OAR. For left breast patients the *PTVeval* structure was adjusted adjacent to the heart in order to minimise cardiac dose. For patients with left breast cancer and with a very medial or lateral tumour bed this technique may not be suitable or the clinician may be required to accept higher doses to the heart. Utilisation of a breath-hold technique may be another option to deliver the desired dose to the target (in combination with IP-IMRT) while minimising the risk of cardiac toxicity, however, this method is not standard clinical practice in our department.

Some authors have raised concerns regarding the effect of breathing motion on IMRT dosimetry due to the 'interplay' effect. However, Richter et al.[17] demonstrated that when delivered over a number of fractions the dose gradient is blurred, resulting in a delivered dose that is at least equivalent to if not better than the planned dosimetry. Therefore, breathing motion may be of minor relevance to breast radiotherapy.[17–19]

Conclusions

IP-IMRT for adjuvant breast radiotherapy is a suitable alternative to FP-IMRT. We have observed improvements in consistency in PTV coverage and increased homogeneity as well as a tendency towards lower lung doses. The study also demonstrated that it is feasible to utilise a template-based planning solution to generate IP-IMRT plans for breast patients. An amount of user intervention will always be required given the variability in the PTV, but this approach provides a reasonable platform to standardise this planning technique. Given the above benefits, this protocol has now been implemented clinically in our department.

Acknowledgements

The authors acknowledge Matthew Hoffmann, Deanna Tune, Kath Dower, Lakshimi Sathianandan and Robyn Martin at the Mid North Coast Cancer Institute for their contribution to the project and publication.

Conflict of Interest

The authors declare no conflict of interest.

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