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Original Article

A Dosimetric Comparison of Breast Radiotherapy Techniques to Treat Locoregional Lymph Nodes Including the Internal Mammary Chain

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Abstract

Aims: Radiotherapy target volumes in early breast cancer treatment increasingly include the internal mammary chain (IMC). In order to maximise survival benefits of IMC radiotherapy, doses to the heart and lung should be minimised. This dosimetry study compared the ability of three-dimensional conformal radiotherapy, arc therapy and proton beam therapy (PBT) techniques with and without breath-hold to achieve target volume constraints while minimising dose to organs at risk (OARs).

Materials and methods: In 14 patients' datasets, seven IMC radiotherapy techniques were compared: wide tangent (WT) three-dimensional conformal radiotherapy, volumetric-modulated arc therapy (VMAT) and PBT, each in voluntary deep inspiratory breath-hold (vDIBH) and free breathing (FB), and tomotherapy in FB only. Target volume coverage and OAR doses were measured for each technique. These were compared using a one-way ANOVA with all pairwise comparisons tested using Bonferroni's multiple comparisons test, with adjusted P-values ≤ 0.05 indicating statistical significance.

Results: One hundred per cent of WT(vDIBH), 43% of WT(FB), 100% of VMAT(vDIBH), 86% of VMAT(FB), 100% of tomotherapy FB and 100% of PBT plans in vDIBH and FB passed all mandatory constraints. However, coverage of the IMC with 90% of the prescribed dose was significantly better than all other techniques using VMAT(vDIBH), PBT(vDIBH) and PBT(FB) (mean IMC coverage $\pm$ 1 standard deviation = 96.0% $\pm$ 4.3, 99.8% $\pm$ 0.3 and 99.0% $\pm$ 0.2, respectively). The mean heart dose was significantly reduced in vDIBH compared with FB for both the WT ($P < 0.0001$) and VMAT ($P < 0.0001$) techniques. There was no advantage in target volume coverage or OAR doses for PBT(vDIBH) compared with PBT(FB).

Conclusions: Simple WT radiotherapy delivered in vDIBH achieves satisfactory coverage of the IMC while meeting heart and lung dose constraints. However, where higher isodose coverage is required, VMAT(vDIBH) is the optimal photon technique. The lowest OAR doses are achieved by PBT, in which the use of vDIBH does not improve dose statistics.

Key words: Heart-sparing radiotherapy; internal mammary chain radiotherapy; proton beam therapy for breast cancer

Introduction

The 2014 Early Breast Cancer Trialists' Collaborative Group systematic overview reported a significant reduction in breast cancer mortality associated with post-mastectomy locoregional breast radiotherapy irrespective of the number of lymph nodes involved and systemic therapies used [1].

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Two recently reported randomised trials of breast/chest wall ± locoregional lymph node radiotherapy (including the internal mammary chain [IMC]) reported disease-free survival benefits in the locoregional lymph node radiotherapy group [2,3]. Subsequently, the Danish Breast Cancer Group IMC study, which compared outcomes in right breast-affected patients (who had the IMC irradiated) versus left breast-affected patients (who did not have the IMC irradiated), showed an overall survival benefit for IMC irradiation of 4.4% in all node-positive patients and 7.4% in those patients with a medial or central tumour and/or a minimum of four positive lymph nodes [4]. Following publication of these data, the UK Royal College of Radiologists issued guidance that IMC irradiation should be considered in patients at higher risk of locoregional recurrence [5].

In long-term breast cancer survivors treated with radiotherapy, fatal radiation-induced heart disease is the main competing cause of mortality. Standard radiotherapy techniques to treat the IMC (using wide tangents [WT] with matched photon-electron fields in free breathing [FB]) have previously been shown to deliver mean heart doses (MHD) of around 9 Gy [6]. A case–control study suggested that the rate of radiation-induced major coronary events increases linearly with dose (7.4%/Gy) and that there is no apparent threshold below which patients are safe [7–9]. Therefore, reducing the heart dose in patients undergoing IMC radiotherapy is of vital importance.

Technical solutions exist for reducing the heart dose associated with breast cancer radiotherapy. The UK HeartSpare IA trial showed that a simple and cost-effective voluntary breath-hold technique (voluntary deep inspiratory breath-hold; vDIBH) could at least halve MHD from 2 Gy to <1 Gy in the context of breast/chest wall radiotherapy alone [10]. Intensity-modulated radiotherapy, volumetric-modulated arc therapy (VMAT) and proton beam therapy (PBT) can also reduce heart doses, but limiting heart doses cannot be achieved in isolation [11–15]. For locoregional pan-lymph node treatments, where the target volume envelops the thorax, multi-field photon beam arrangements can increase low doses to the organs at risk (OAR), potentially increasing the risk of radiation-induced heart disease and secondary cancers [16–18]. PBT has been shown in dosimetry studies to deliver lower cardiac doses compared with photon-based techniques [11,12,14], but the additional benefit of breath-hold to PBT has been less well studied.

The aim of this study was to compare target volume coverage and OAR doses using seven radiotherapy techniques in order to establish optimal solutions for implementation in UK IMC radiotherapy practice.

Materials and Methods

Patient Selection and Volume Delineation

Fourteen patients from a single centre with left-sided breast cancer who had been previously treated within the HeartSpare II trial [19] (by virtue of having any heart within the 50% isodose on the FB computed tomography planning scan) were selected. The patients' median age was 57 years (range 31–68 years). Ten patients had undergone wide local excision, one mastectomy and three mastectomies with deep inferior epigastric perforators flap reconstruction. All patients had undergone two radiotherapy planning computed tomography scans, one in FB and one in vDIBH. Left-sided clinical target volumes ([CTVs] breast, axillary levels 1–4 and IMC) were delineated by a panel of four clinical oncologists based on ESTRO guidelines [20]. The planning target volumes (PTVs) were constructed by adding a 5 mm margin to the CTVs for all photon plans [21]. All PTVs were clipped 5 mm from the skin surface. The PTV IMC excluded lung for all photon techniques except tomotherapy, which was optimised and reported for the whole PTV IMC, reflective of local practice. CTVs were used for proton plan optimisation and evaluation. The following normal structures were contoured: heart, left anterior descending coronary artery (LAD), left lung, right lung, right breast, thyroid gland, oesophagus and brachial plexus.

Treatment Planning

For each patient, seven plans were generated: wide tangents in voluntary deep inspiratory breath-hold (WT(vDIBH)), wide tangents in free breathing (WT(FB)), volumetric-modulated arc therapy in voluntary deep inspiratory breath-hold (VMAT(vDIBH)), volumetric-modulated arc therapy in free breathing (VMAT(FB)), tomotherapy in free breathing (Tomotherapy(FB)), proton beam therapy in voluntary deep inspiratory breath-hold (PBT(vDIBH)) and proton beam therapy in free breathing (PBT(FB)). Planning was carried out across two centres. The Royal Marsden NHS Foundation Trust carried out WT, VMAT and PBT planning and Cambridge University Trust carried out the tomotherapy planning. Optimisation priorities were defined before planning to achieve consistency between inverse planned semi-automated intensity-modulated radiotherapy techniques. All plans were for a fractionation schedule of 40 Gy in 15 fractions. The mandatory target volume constraints for the PTVs and OAR dose objectives are summarised in Table 1.

WT plans were created manually in the Pinnacle^3 v9.10 (Philips, Fitchburg, WI, USA) treatment planning system (TPS) using opposing wide tangential step-and-shoot photon beams with a non-divergent posterior field edge modified to cover the breast or chest wall, IMC and the inferior part of lymph node levels 1–3. A matched anterior field was used to cover the PTVs of lymph node level 4 and the superior part of levels 1–3. Heart and lung shielding was achieved using multileaf collimation. 6 MV photon beams were used for most patients. 10 MV beams were used for the anterior field to achieve coverage of nodal volumes at depth.

VMAT plans were generated using the Pinnacle^3 TPS using Pinnacle's SmartArc optimisation algorithm with 2° control point spacing. A 'bowtie' technique consisting of two partial arcs, as described by Viren *et al.* [22], was used. The two anticlockwise partial arcs each consisted of about 40° (30–50° range) of rotation about the angles used for

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