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Particle therapy

Intensity modulated proton therapy for postmastectomy radiation of bilateral implant reconstructed breasts: A treatment planning study

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ABSTRACT

Background and purpose: Delivery of post-mastectomy radiation (PMRT) in women with bilateral implants represents a technical challenge, particularly when attempting to cover regional lymph nodes. Intensity modulated proton therapy (IMPT) holds the potential to improve dose delivery and spare non-target tissues. The purpose of this study was to compare IMPT to three-dimensional (3D) conformal radiation following bilateral mastectomy and reconstruction.

Materials and methods: Ten IMPT, 3D conformal photon/electron (P/E), and 3D photon (wide tangent) plans were created for 5 patients with breast cancer, all of whom had bilateral breast implants. Using RTOG guidelines, a physician delineated contours for both target volumes and organs-at-risk. Plans were designed to achieve 95% coverage of all targets (chest wall, IMN, SCV, axilla) to a dose of 50.4 Gy or Gy (RBE) while maximally sparing organs-at-risk.

Results: IMPT plans conferred similar target volume coverage with enhanced homogeneity. Both mean heart and lung doses using IMPT were significantly decreased compared to both P/E and wide tangent planning.

Conclusions: IMPT provides improved homogeneity to the chest wall and regional lymphatics in the post-mastectomy setting with improved sparing of surrounding normal structures for woman with reconstructed breasts. IMPT may enable women with mastectomy to undergo radiation therapy without the need for delay in breast reconstruction.

Recent studies of women with breast cancer have demonstrated an increase in the rate of elective mastectomy, prophylactic contralateral mastectomy, and immediate implant reconstruction [1,2]. However, the delivery of post-mastectomy radiation therapy (PMRT) following breast reconstruction represents a distinctive challenge to treatment planning, often requiring removal or manipulation of the implant for optimal delivery of radiation, due to the positioning and limited deformability of the reconstructed breast. Many practitioners elect to delay breast reconstruction until after radiation therapy to avoid suboptimal radiation planning however, delays can also impair psychological recovery and limit available reconstructive options to complex surgeries with higher risks of side effects [3–7]. Therefore, there is a need to improve radiation dose delivery for women with reconstructed breasts in the post-mastectomy setting.

Prior treatment planning studies have demonstrated impaired dose optimization using conventional radiation techniques for women with immediate breast reconstruction [8]. Improvements in dose distribution and delivery with both intensity-modulated radiation therapy (IMRT) and proton beam radiation have previously been reported, but are not widely utilized [9].

With the advent of intensity modulated proton therapy (IMPT), there is a potential to improve dose delivery further and better spare non-target tissues without limitations due to complex anatomy. A recently published comparison of IMPT versus both IMRT and 3D conformal plans for breast cancer patients treated with either breast conserving therapy or mastectomy demonstrated a significant benefit in dose sparing for both the heart and lung [10]. However, this study did not include patients who had undergone breast reconstruction.

Therefore, the primary objective of this treatment planning study was to determine whether IMPT following bilateral mastectomy and reconstruction could optimize radiation planning compared to standard 3D conformal radiation. We hypothesized that post-mastectomy treatment plans utilizing intensity modulated proton therapy would result in better dose coverage of target

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structures, in particular, the regional lymph nodes, while decreasing dose to avoidance structures including the heart and lung.

Methods and materials

10 IMPT, 10 3D conformal photon/electron (P/E), and 10 conformal photon plans utilizing wide tangents (5 left chest wall, 5 right chest wall) were created de novo for the purposes of this study using the planning CT scans of 5 women who underwent either breast conserving surgery after a prior cosmetic breast implant placement ($n = 2$) or double mastectomy with immediate implant reconstruction ($n = 3$) and required adjuvant radiation therapy as part of their cancer care. Therefore, all treatment plans were based upon virtual assumptions of necessary lymph node coverage and not the patient's actual disease stage. Patients were immobilized in the supine position with both arms raised above their heads using a breast board. Non-contrast CT scans were performed in this position to encompass the cricoid cartilage to mid-abdomen in 2.5 mm slices. A single physician delineated all relevant contours based on RTOG breast atlas guidelines. These contours were then independently reviewed and verified by a second radiation oncologist. Target structures included the chest wall, internal mammary nodes (IMN), supraclavicular fossa (SCV), and three levels of the axilla. Organs-at-risk included the heart and lungs. For the purposes of this study, the breast implant was contoured, but was considered neither a target nor an organ-at-risk. Consequently, the chest wall was defined as the skin and subcutaneous tissue of the chest wall minus the volume of the implant.

Plans were designed to achieve 95% coverage of all targets (chest wall, IMN, SCV, and axilla [levels 1, 2, 3]) to a dose of 50.4 Gy or Gy (RBE) while maximally sparing avoidance structures (heart, lungs). One half to one centimeter synthetic bolus was used on all the plans to assist with target coverage. When target coverage was difficult to achieve according to these constraints, the dose of the target was given priority over homogeneity and normal tissue sparing. A plan was considered optimized when $\geqslant$95% of the target volume received the prescription dose (50.4 Gy) and hot spots were limited to <110% of prescription dose.

Photon and photon/electron plans were generated using forward planning on a CMS planning system (Xio version 4.6). All photon/electron plans consisted of partially wide tangents, a medial anterior oblique field, an optional posterior axillary boost to adequately cover the regional lymph nodes, and an enface electron beam to cover the internal mammary nodes. All photon plans consisted of partially wide tangents and a medial anterior oblique field with the option of a posterior axillary boost. A multi-isocentric technique was employed with couch kicks on the tangential fields to match the tangents and the supraclavicular field. A field-in-field technique was used for both photon and photon/electron plans to improve homogeneity as necessary and to avoid the increased integral dose associated with multi-field IMRT.

IMPT plans were calculated with Astroid, an in-house treatment planning system. Two fields, an anterior–posterior and left/right-anterior oblique (45/315°) were chosen to maximize robustness and to improve plan quality.

A 7 cm thick Lucite range shifter was used for all fields. A range shifter was needed at our facility for the treatment of shallow tumors with pencil-beam scanning because the lowest proton energy available (90 MeV) corresponded to a range in water of approximately 7 cm. Scanning beam energy varied from 100 to 185 MeV. Distal spacing of each beam was equal to 80% of the width of the Bragg peaks; lateral spacing was equal to 1 sigma. The lateral and distal spacing of the spots selected for treatment planning also served as a compromise between homogeneity and deliverability.

All IMPT plans were created with a spot size of about 5 mm for the beam energies used. Spot size is defined as one sigma of the pencil-beam distribution in air and at isocenter. Currently, spot sizes between 9 and 16 mm are available at our facility (for high and low energies, respectively). For the purposes of this study, we utilized a smaller spot size that is expected to be clinically available within two years.

Comparisons of the different techniques were made using a priori determined criteria. These criteria included the mean percent prescription dose, minimum dose, and maximum dose for target coverage of the chest wall and regional lymphatics, as well as, the V5, V10, and V20 for organs-at-risk. Dose volume histograms were generated for all avoidance structures. SAS (version 9.1, SAS Institute, Cary, NC) statistical software was utilized to perform a repeated measure ANOVA with Bonferroni correction to estimate the statistical significance between IMPT, P/E, and wide tangent avoidance structure doses. Two-sided p-values were then generated from pairwise comparisons.

Results

Target coverage

Target doses and dose constraints were achieved for all 10 individual plans (5-left sided, 5 right-sided). Target coverage of the chest wall and regional lymphatics were comparable for IMPT, P/E and wide tangent plans (Table 1), however, IMPT resulted in lower maximum percent doses or "hot spots" and superior homogeneity (Table 2). Plan comparisons are depicted in Fig. 1.

Avoidance structure dose distribution

Repeated measure ANOVA with Bonferroni correction confirmed a significant interaction (p-value < 0.05) between treatment modality and avoidance structure dose for all metrics, except right-sided heart V20 ($p = 0.09$). Pairwise comparisons of the remaining metrics demonstrated that IMPT resulted in significantly lower V5, V10, and V20 left-sided heart and lung doses compared to both P/E and wide tangent plans (Table 3, Fig. 2a). No significant differences were evident between left-sided P/E and wide tangents plans.

Statistically significant improvements were also seen in some right-sided metrics with IMPT compared to P/E or wide tangent plans (Table 3, Fig. 2b). Specifically, ipsilateral lung V5, V10, and V20 were superior with IMPT planning compared to either P/E or wide tangents planning. Additionally, right-sided heart V5 was improved with IMPT planning compared to P/E planning, but was not

Table 1
Target PTV mean percent prescription dose (SD).

Mean % (SD, $N = 10$)	Chest Wall	IMN	SCV	Level I	Level II	Level III
IMPT-5 mm	100 (0.0)	99.9 (0.2)	99.9 (0.0)	99.4 (1.2)	99.3 (2.0)	98.8 (3.0)
Photon/electron (P/E)	97.7 (1.1)	98.7 (1.5)	99.4 (1.0)	99.8 (0.3)	99.8 (0.3)	100 (0.0)
Wide tangents (WT)	99.2 (0.5)	99.8 (0.3)	99.3 (1.2)	99.8 (0.3)	99.9 (0.2)	99.9 (0.3)

SD, standard deviation; IMPT, intensity modulated proton therapy; IMN, internal mammary nodes; SCV: supraclavicular fossa.