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Postoperative radiotherapy following mastectomy for patients with left-sided breast cancer: A comparative dosimetric study

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ABSTRACT

The purposes of this article were to compare the biophysical dosimetry for postmastectomy left-sided breast cancer using 4 different radiotherapy (RT) techniques. In total, 30 patients with left-sided breast cancer were randomly selected for this treatment planning study. They were planned using 4 RT techniques, including the following: (1) 3-dimensional conventional tangential fields (TFs), (2) tangential intensity-modulated therapy (T-IMRT), (3) 4 fields IMRT (4F-IMRT), and (4) single arc volumetric-modulated arc therapy (S-VMAT). The planning target volume (PTV) dose was prescribed 50 Gy, the comparison of target dose distribution, conformity index, homogeneity index, dose to organs at risk (OARs), tumor control probability (TCP), normal tissue complication probability (NTCP), and number of monitor units (MUs) between 4 plans were investigated for their biophysical dosimetric difference. The target conformity and homogeneity of S-VMAT were better than the other 3 kinds of plans, but increased the volume of OARs receiving low dose (V_5). TCP of PTV and NTCP of the left lung showed no statistically significant difference in 4 plans. 4F-IMRT plan was superior in terms of target coverage and protection of OARs and demonstrated significant advantages in decreasing the NTCP of heart by 0.07, 0.03, and 0.05 compared with TFs, T-IMRT, and S-VMAT plan. Compared with other 3 plans, TFs reduced the average number of MUs. Of the 4 techniques studied, this analysis supports 4F-IMRT as the most appropriate balance of target coverage and normal tissue sparing.

Introduction

Radiotherapy (RT) is one of the main treatments for patients after mastectomy. Postmastectomy RT (PMRT) can effectively reduce the recurrence rate in local area, improve the tumor-specific survival rate, and disease-free survival rate; however, the total survival rate is insignificant.[1] Cardiovascular injury has been implicated as the reason that, although adjuvant RT improved breast cancer–specific survival, no improvement in overall survival was demonstrated in meta-analyses that included randomized RT trials.[2] Especially, anthracycline-based chemotherapy, trastuzumab, and both in combination were being used increasingly in the adjuvant therapy of patients with invasive breast cancer. These agents alone or in combination with RT may cause later cardiac morbidity.

There have been various RT techniques proposed to patients with breast conservation surgery (BCS), Teh *et al.*[3] reported that the conventional opposed tangential fields (TFs) technique (3-dimensional–conformal RT [3DCRT]) delivers too much radiation to a large volume of the ipsilateral lung and heart in breast-conserving therapy. Meanwhile, tangential intensity-modulated therapy (T-IMRT) was reported by Rongsriyam *et al.*[4] having better target dose homogeneity and conformity and sparing normal tissue, such as the heart and the ipsilateral lung for patients undergoing adjuvant RT after BCS. However, Yin *et al.*[5] showed another significant result that intensity-modulated arc RT performed better in target conformity and can reduce high-dose volume in the heart and the left lung in treatment of BCS.

Some reports[6,7] also suggested that different planning target volume (PTV) size may lead to different results in using various irradiating techniques in RT with breast cancer. If the PTV includes only the breast, such as treatment of BCS, then the technique typically consists of 2 TFs placed medially and laterally to the

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breast. This field arrangement attempts to minimize the amount of underlying normal tissue irradiated. However, if the PTV also includes chest wall (CW), anterior supraclavicular area (SA) and internal mammary node (IMN), then simple TFs usually do not offer the best solution. Then volumetric-modulated arc therapy (VMAT) as a new RT technology has dynamic parameters, including variations of dose rate, gantry rotation speed, leaf motion speed, and gantry position. However, for the target of PMRT that is located on the chest and next to the lung and the heart, whether these dynamic parameters could produce ascendant results should also be reconsidered.

The purpose of this planning study was to evaluate and compare 4 RT (TF, T-IMRT, 4 fields IMRT [4F-IMRT], and single arc VMAT [S-VMAT]) techniques in the treatment of patients with left-sided breast cancer following mastectomy.

Methods and Materials

Clinical data selection

Treatment planning was performed retrospectively on 30 patients with left-sided breast cancer previously treated from February 2013 to July 2013 in Hangzhou Cancer Hospital, Hangzhou City, Zhejiang Province, P.R. China. The ages of patients ranged from 44 to 63 years with the median age being 56 years. The stage of disease was $T_{4a\text{-}4c}N_3M_0$, and all patients received a course of chemotherapy before RT. Written informed consents were obtained from all patients or their families. All procedures of this study were approved by the Ethical Committee of Hangzhou Cancer Hospital.

Target and normal tissue delineation

The PTV included CW, SA, and IMNs. It was created by adding a 7-mm expansion in all directions around the clinical target volume, and another 8 mm was added on the surface of the CW skin for the purpose of compensation of movement. All 30 cases were delineated by the same senior radiation oncologist based on the computed tomography (CT) image. The contours of all the involved organs at risk (OARs), including the contralateral breast, heart, coronary artery (CA), and left and right lung were outlined by the treating physician. All targets and OARs were outlined slice by slice in the CT image in the treatment planning system (TPS) and then the 3D contour was reconstructed automatically.

Treatment plan

All plans were completed in 3D Oncentra TPS (Nucletron BV, Veenendal, Netherlands). The TPS determined homogeneous media and density in the body based on the CT density calibration curve and calculated the dose with collapse cone convolution, which took into account the calibration of the homogeneous medium. The Elekta Axesse linear accelerator with 6-MV photon energy was used. The PTV was prescribed 50 Gy given in 25 fractions within 5 weeks, and the optimization constraint is that ensuring 95% isodose line encompasses 95% of PTV ($V_{95\%} \geq 47.5$ Gy). The detailed method was as follows:

The TF plan used 2 opposite half beam, which included whole PTV and avoided direct exposure to the contralateral breast. The arrangement of gantry angle was 300° and 120°. The T-IMRT plan was created with same angle of the conventional TF plan.

4F-IMRT plan added the other opposite half beam based on the T-IMRT plan and the gantry angle was 300°, 320°, 120°, and 140°.

S-VMAT, in which arc direction is such that beam enters the breast before exiting through the lung, may increase the dose volume of the lung and contralateral breast. The VMAT plan used a single arc field in which starting angle and ending angle were respectively the same as the 4F-IMRT beam angle, and the degree of the subfield interval of 4° was used.

For the IMRT and VMAT plans, the optimization objective listed in Table 1 was used. Collapsed cone (graphics processing unit) algorithm optimization was applied to optimize plans. The minimum field size and monitor unit (MU) of subfield were restricted to 2 cm^2 and 2 MU.

The different treatment techniques have been applied to the patients' data set without any clinical application. This activity does not require an ethical approval according to our institution's rules.

Table 1
The optimization objective applied in IMRT and VMAT planning

Structure	Planning aim (weight)
PTV	$V_{53\ Gy} \leq 1\%$ (70), $V_{50\ Gy} \geq 95\%$ (80), and $V_{49\ Gy} \geq 98\%$ (80)
Left lung	$V_{5\ Gy} \leq 45\%$ (10), $V_{20\ Gy} \leq 25\%$ (10), and $V_{30\ Gy} \leq 18\%$ (10)
Contralateral breast	$D_{max} \leq 5$ Gy (8)
Heart	$V_{20\ Gy} \leq 18\%$ (10) and $V_{10\ Gy} \leq 22\%$ (10)
CA	$V_{10\ Gy} \leq 27\%$ (12), $V_{20\ Gy} \leq 18\%$ (12), and $V_{30\ Gy} \leq 8\%$ (12)

Biophysical dosimetric evaluation

The biophysical dosimetric evaluation metrics were chosen for each structure, and the same metrics were used to evaluate all plans. Dose-volume histograms (DVHs) were calculated for all involved structures, including the target volume, left lung, heart, CA, and contralateral breast. For each target volume, the mean dose, $D_{2\%}$ and $D_{98\%}$ (dose corresponding to 2% and 98% target volume); $V_{95\%}$, and $V_{110\%}$ (volume of the target received 95% and 110% prescription dose); conformal index (CI)[8]; and homogeneity index (HI)[9] were tabulated and reviewed. For the normal tissues, metrics included the mean dose for each structure. For the left lung, the values for the percentage of left lung that received 5 Gy (V_5), 20 Gy (V_{20}), and 30 Gy (V_{30}) were chosen; for the heart and CA, values for the percentage of heart and CA that received 5, 10, 20, and 30 Gy (V_5, V_{10}, V_{20}, and V_{30}, respectively) were both chosen; and for the contralateral breast, values for the percentage of contralateral breast that received 5 and 10 Gy were obtained. Other metrics included tumor control probability (TCP) for PTV and normal tissue complication probability (NTCP) for the left lung and the heart. The CI, HI, TCP and NTCP are described later.

The CI and HI were defined to describe the quality of target as follows:

$$CI = \frac{V_{T.ref}}{V_T} \times \frac{V_{T.ref}}{V_{ref}}$$

where V_T represents target volume, $V_{T.ref}$ represents the target volume wrapped by reference isodose curve face, and V_{ref} represents all the volume wrapped by reference isodose curve face. A higher CI value, ranging from 0 to 1, represents better conformity.

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{mean}}$$

where $D_{2\%}$ represents the dose corresponding to 2% target volume as shown in DVH and can be deemed as the maximum dose; $D_{98\%}$ represents the dose corresponding to 98% target volume as shown in DVH, and can be deemed as the minimum dose.

LQ-Poisson model was used to calculate the TCP for PTV[10]:

$$TCP_{PTV} = \exp\left\{-N_0 \exp\left(-n\left(\alpha d + \beta d^2\right)\right)\right\}$$

where N_0 is the number of tumor cells about clone source. α is the probability of cell injury by a single ionizing particle strike to DNA, and β is the probability of cell injury by double ionizing particles strike to DNA. α/β Ratio was 3 for PTV. These tumor-specific parameters were cited from a study by Webb.[11]

The NTCP-Lyman model was used to calculate the NTCP of the left lung as follows[12,13]:

$$NTCP_{\text{left lung}} = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{t} EXP\left(-\frac{x^2}{2}\right) dx$$

$$t = \frac{D_{max} - D_{50\ (v)}}{m \times D_{50\ (v)}}$$

$$D_{50\ (v)} = D_{50\ (v\ =\ 1)} \times V^{-n}$$

where m is the slope of 50% complication probability in the curve of dose effect (m = 0.18), and $D_{50\ (v)}$ is the tolerance dose for 50% complication probability. The tissue-special parameters were based on the Lyman model (AAPM No.166).[14]

The NTCP-RSM (relative seriality [RS]) model was accepted as the most suitable biological model to calculate the NTCP for the heart.[15] This model is based on Poisson statistics, and it accounts for the architecture of the organ through the parameter of RS. The RS is derived from the ratio of serial subunits to all subunits in the organ.

$$NTCP_{Heart} = \left\{1 - \prod_{i=1}^{N} \left[\left(1 - p(D_i)^s\right)\right]^{\Delta V_i}\right\}^{1/s}$$

$$p(D_i) = 2^{-\exp(e \cdot \gamma \cdot (1 - D_i/D_{50}))}$$

The 50% dose response and the maximal relative slope, γ, were used to describe the dose-response curve. $\prod$ Is related to the parameter m of the probit formula, where N is the number of calculation subvolumes in the dose calculation volume, D_i is the dose in the subvolume considered, and $\triangle V_i = V_i/V$ where V_i is the volume of each subvolume in the DVH and V is the total volume of the organ. p (D) Is the Poisson dose-response relationship. The tissue-special parameters were based on the RS model.[15]