Novel method of radiotherapy planning to improve the dose homogeneity at the junction region for breast cancer

Suyan Bi1 | Qian Wang2

1 Department of Radiation Oncology, Shenzhen Center, Cancer Hospital Chinese Academy of Medical Sciences, Shenzhen, China
2 Clinical Oncology Center, The University of Hong Kong-Shenzhen Hospital, Shenzhen, China

Correspondence
Bi Suyan, Department of Radiation, Oncology, Cancer Hospital Chinese Academy of Medical Sciences, Shenzhen Center, Shenzhen 518116, China.
Email: bsh@hku-szh.org

Abstract

Objectives: This article introduces a new method to design the radiation therapy planning after radical surgery for breast cancer in order to provide a better homogeneity of the dose distribution in the junction region between the supra clavicular fossa and chest wall.

Methods: A total of 15 women who received supra clavicular and chest wall irradiation therapy for breast cancer after radical surgery at Cancer Hospital Chinese Academy of Medical Sciences, Shenzhen Center, Shenzhen, China, between 1 October 2018 and 30 November 2019 were included. The prescription dose was 50 Gy/25 fractions. We designed a new plan on the basis of the original plan for each patient on an Varian Eclipse 13.6 planning system, which added two subfields to each tangential opposing field to change the dose distribution at the junction region. Statistical analysis of the target dose distribution – homogeneity index, conformal index, and irradiation doses to the ipsilateral lung, contralateral lung, heart, left-side breast, and spinal cord – was carried out for the two groups and the differences were compared.

Results: When comparing the two plans, the planning target volume minimum dose \( P = 0.04 \) and planning target volume of the junction region, which was defined as the target in the junction region minimum dose \( P = 0.04 \), homogeneity index \( P = 0.02 \), and conformal index \( P = 0.01 \) for the new method plan were better than those for the original plan. However, there was no statistically significant difference in all dosimetric parameters of the organs at risk \( P > 0.05 \) between the new and traditional method plans.

Conclusion: Both plans by new and traditional methods for breast cancer after radical surgery can meet the clinical requirements. The prescription dose coverage, conformal index, and homogeneity index for the target in the new method plan were better than those in the traditional method plan. The new method plan provided a better homogeneity of the dose distribution in the junction region, but had no obvious effect on the dose distribution of the organs at risk. As a result, this new planning method can be used in clinical settings.
INTRODUCTION

Breast cancer is one of the most common malignant tumors in women, ranking first in female tumors. Radiotherapy plays an important role in breast cancer treatment, because it is able to not only reduce the local recurrence rate, but also improve the survival rate of patients with cancer. There are many radiotherapy techniques for breast cancer, such as volume intensity modulated radiotherapy, intensity-modulated radiotherapy (IMRT) and 3-D conformal radiation therapy (3D-CRT). However, in some situations, we need to use a special technique to design the plan. For example, when the target is so large that it includes the clavicle region and whole chest wall, we usually need to use a hybrid IMRT technique to carry out the goal. To be specific, we need to design a IMRT or volume IMRT plan for the clavicle region, and also need to use two tangential intensity-modulated fields (field-in-field) combining two IMRT fields for the chest wall region. In fact, although these techniques have been widely used in a variety of tumor radiotherapy treatments, when we think about breast cancer patients’ breathing, hybrid IMRT and field-in-field techniques are usually preferred over volume IMRT and IMRT techniques. However, when dealing with a large target that includes the clavicle region and whole chest wall in the clinical planning process, we found that the dose distribution and the conformal index (CI) of the planning target volume (PTV) in the junction region are always poor. Therefore, we designed a new method to improve the dose distribution, and evaluated the advantages and disadvantages of these two plans.

METHODS

The experimental scheme design of this study included three steps: (i) case selection; (ii) plan design; and (iii) result analysis.

Case selection and general information

A total of 15 women who received SC and chest wall irradiation therapy for breast cancer after radical surgery at the Cancer Hospital Chinese Academy of Medical Sciences, Shenzhen Center, China, between 1 October 2018 and 30 November 2019 were selected. The patients were aged 25–50 years, with a median age of 30 years. The functions of the liver, kidney, heart, and lung were normal; none of these patients had autoimmune diseases, cardiovascular diseases, diabetes, hypertension, rheumatic diseases, trauma, or other acute or chronic diseases that were contraindications for radiotherapy. There were no significant differences in the clinical data. This study was approved by the institutional review board at Cancer Hospital Chinese Academy of Medical Sciences, Shenzhen Center, and all the patients provided voluntary informed consent to participate in the study.

Equipment and scanning parameters

All patients were placed on a positioning couch that was made up of carbon fiber in a supine position, with an appropriate headrest, and both arms above the head. A breast bracket plus fixed lower limb foam plate were used on the affected side of the patients. The crossbar was held, and the inclination angle of the breast bracket was adjusted. At the same time, the foam plate with the appropriate angle and thickness was cushioned under the limb of the affected side to keep the patients stable, and expose the axillary and breast areas. In addition, functional training needs to be provided for those patients who could not keep their arms raised for a long time. A GE Discovery RT (Discovery LS; GE Medical System, Waukesha, WI, USA) computed tomography instrument was used for scanning under calm breathing. The scanning layer was 0.5 cm, with a voltage of 120 kV, and electric current of 200 mA. The scanning ranged from the annular cartilage to the breast folds or 2 cm below the drainage port. The images were transferred to the Varian’s Eclipse treatment-planning system (version 13.6; Varian Medical Systems, Palo Alto, CA, USA).

Target and organs at risk delineation

The doctors treating the participants contoured the target area based on computed tomography imaging. The clinical target volume (CTV) included the ipsilateral clavicle, chest wall, and lymphatic drainage area. If the primary tumor is located in the center of the breast, when no adjuvant trastuzumab treatment is indicated, the breast area needs to be covered. The PTV was a clinical target area of 5-mm extension in three dimensions from the CTV no less than 3mm from the skin surface. Patients with modified radical surgery will not need to pay attention to the skin distance of the PTV, but, in genera, a 0.5-cm compensation material is required during planning. We also defined the target as PTV_J. PTV_J was the volume of the junction region, which was 1-cm cranial and 1-cm caudal to the isocenter in PTV. The endangered organs were the heart, lung, healthy breast, and spinal cord. Contouring was carried out according to the window width and window position on the computed tomography image.
2.4 Planning design

2.4.1 Planning design of hybrid IMRT

The target area of the breast was irradiated with an 80% dose of the prescription in the tangential fields planning and a 20% dose of the prescription in the IMRT planning. The aim was to adjust the uniformity of the target area. We could move the target position so as to use only one side of the jaw to control the tangential field planning. The upper boundary of the jaw in the mammary gland area was located in the interface of the upper and lower target areas, as shown in Figure 1. We ensured the angle of the collimator was 0° degrees and the tangential opposing fields passed through the lung with minimal volume on the beam eye view. We also aimed to avoid the heart and contralateral breast exposure. The jaw on the outer line of the patient’s breast was opened 2 cm more to avoid underdose caused by respiratory movement. We added two fields to IMRT planning based on the tangential opposite fields, which increased by 10–15° to cover the whole target area.
The upper clavicle IMRT planning design also used half the jaw to control the dose distribution; the lower boundary was located in the isocenter position. Four or five fields were used in this IMRT planning with the spacing between two fields greater >20°, and the angle of the field range was from 290 to 180°.

2.4.2 New planning design

After adding the tangential opposing fields, we needed to adjust the design method to form a dose gradient at the junction, as shown in Figures 1 and 2. Two subfields were given for each main field, and multileaf collimation (MLC) shielding of 1 cm and 2 cm was carried out along the junction field. Each subfield was set at 10 MU. The upper bound of the jaw in the chest wall fields was the same as that of the tangential fields. We also needed to keep the other conditions the same with the traditional method.

A comparison of the dose distribution of the penetrating fields by the two methods is shown in Figure 3. The dose distribution changed significantly such that the conventional method had no obvious dose gradient at the junction, whereas the new method formed an obvious dose gradient through MLC shielding.

2.4.3 Planning optimization and dose limit

Both method plans use the AAA algorithm for optimization, and the optimization parameters were based on the prescription dose, as shown in Table 1. We need to keep the parameters the same as those in the first optimization when optimizing. The optimization process also needs to be adjusted to keep the dose of the organs at risk (OARs) as low as possible until the optimal value is reached while ensuring that the target area meets the requirements.

### Table 1: Dose limits of the breast cancer target and organs at risk

| Structures               | Optimization limit |
|--------------------------|--------------------|
| PTV                      | $V_{95\%} \geq 95\%$ |
| D_max                    | $\leq 109\%$      |
| Ipsilateral lung         | $V_{20\text{Gy}} \leq 20\%$ |
| D_mean                   | $\leq 15\text{ Gy}$ |
| Contralateral lung       | $V_{20\text{Gy}} \leq 10\%$ |
| Heart                    | $D_{\text{mean}} \leq 15\text{ Gy}$ (left breast cancer) |
|                          | $D_{\text{mean}} \leq 5\text{ Gy}$ (right breast cancer) |
| Contralateral breast     | $D_{\text{mean}} \leq 1\text{ Gy}$ |
| Spinal cord              | $D_{\text{max}} \leq 40\text{ Gy}$ |

$D_{\text{max}}$, maximum dose; $D_{\text{mean}}$, mean dose; $V_{20\text{Gy}}$, (percentage volumes receiving at least XGy of prescribed doses); $V_{95\%}$, (percentage volumes receiving at least X% of prescribed doses).

2.5 Definition of conformity index and homogeneity index

Dose Volume Histogram (DVH), dose statistics, and isodose distribution graphs of the planning are often used to evaluate the pros and cons of a planning. The DVH shows the target coverage and exposure dose of the OAR as a whole. The dose statistics table can give the average exposure dose of the OARs and the specific dose we need to pay attention to in order to compensate for the deficiency of DVH. The isodose distribution curve directly shows the relative relationship of the reference dose on the target area. In addition, the conformal index (CI) and uniformity index (HI) of the PTV and PTV_J are also important parameters for evaluating plan quality, as defined in equations (1) and (2), respectively:

$$CI = \frac{V_{\text{ref}}}{V_1 \cdot V_{\text{ref}}}$$  (1)
TABLE 2  Dose comparison of planning target volume of the two methods

| Targets       | Traditional planning | New method planning | P-value |
|---------------|----------------------|---------------------|---------|
| PTV           |                      |                     |         |
| D_{max} (Gy)  | 57.58 ± 1.8          | 56.66 ± 1.05        | 0.08    |
| D_{min} (Gy)  | 29.72 ± 8.7          | 32.61 ± 6.74        | 0.04    |
| HI            | 1.09 ± 0.02          | 1.08 ± 0.02         | 0.10    |
| CI            | 0.73 ± 0.04          | 0.74 ± 0.06         | 0.77    |
| PTV_J         |                      |                     |         |
| D_{max} (Gy)  | 56.56 ± 1.51         | 56.02 ± 1.07        | 0.41    |
| D_{min} (Gy)  | 36.57 ± 7.09         | 41.96 ± 6.09        | 0.04    |
| HI            | 1.14 ± 0.06          | 1.09 ± 0.03         | 0.02    |
| CI            | 0.75 ± 0.11          | 0.88 ± 0.09         | 0.01    |

Data presented as the mean ± SD. P-value, CI, the conformity index; D_{max}, maximum dose; D_{min}, minimum dose; HI, uniformity index; PTV_J, planning target volume of the junction region.

In formula (1), V_t was the volume of the target, V_{t,ref} was the volume of the target covered by the reference isodose surface, and V_{ref} was the volume of the 3-D space covered by the reference isodose surface. The CI values ranged from 0 to 1; the larger the value the better the CI.

\[ HI = \frac{D_{5\%}}{D_{95\%}} \]  \hspace{1cm} (2)

In formula (2), D_{5\%} and D_{95\%} were the doses accepted by 5% and 95% of the target volume, respectively, with better uniformity of the target for HI values closer to 1.

2.6 Statistical analysis

In the comparative analysis of the two technologies, the targets in the two planning programs were evaluated according to PTV and PTV_J. The maximum dose, the minimum dose, and HI and CI of the PTV were also compared.

The V_5, V_{20}, and V_{30} of the ipsilateral lung were compared, which represent the volume percentage when the ipsilateral lung accepted doses of 5 Gy, 20 Gy, and 30 Gy, respectively, and the mean dose (D_{mean}), V_20 and D_{mean} of the contralateral lung, D_{mean} of the heart, V_{20} and D_{mean} of the contralateral lung, and maximum dose of the spinal cord were compared for two groups of the plans.

Statistical analysis was carried out using IBM SPSS Statistics for Windows, version 17.0 (IBM Corporation, Armonk, NY, USA). Quantitative data were expressed as the mean ± SD, and Shapiro–Wilks normality tests were carried out for the differences in volume dose or dose volume between the conventional plan and new plan for the target and OARs. Paired-sample t-tests were carried out for normal distribution. The test level was α = 0.05 (two-tailed).

TABLE 3  Dose comparison of organs at risk of the two methods

| OARs              | Traditional planning | New method planning | P-value |
|-------------------|----------------------|---------------------|---------|
| Ipsilateral lung  |                      |                     |         |
| V_5 (%)           | 63.06 ± 17.25        | 61.37 ± 15.95       | 0.27    |
| V_{20} (%)        | 24.18 ± 3.39         | 23.51 ± 4.01        | 0.26    |
| V_{30} (%)        | 18.66 ± 3.19         | 17.66 ± 3.87        | 0.26    |
| D_{mean} (Gy)     | 13.98 ± 1.84         | 13.8 ± 1.78         | 0.39    |
| Contralateral lung|                      |                     |         |
| V_20 (%)          | 1.43 ± 1.09          | 1.45 ± 1.04         | 0.85    |
| D_{mean} (Gy)     | 4.06 ± 5.86          | 4.06 ± 5.96         | 0.97    |
| Heart             |                      |                     |         |
| D_{mean} (Gy)     | 1.57 ± 1.43          | 1.85 ± 1.35         | 0.15    |
| Contralateral breast|                    |                     |         |
| V_{20} (%)        | 8.47 ± 12.3          | 8.47 ± 13.67        | 0.99    |
| D_{mean} (Gy)     | 3.12 ± 1.2           | 2.64 ± 0.77         | 0.09    |
| Spinal cord       |                      |                     |         |
| D_{max} (Gy)      | 36.36 ± 5.74         | 35.09 ± 4.5         | 0.37    |

Data are presented as the mean ± SD. D_{max}, maximum dose; D_{mean}, mean dose; V_5, V_{20}, V_{30}, (VX(%), percentage volumes receiving at least X% of prescribed doses)

3 RESULTS

3.1 Dosimetric comparison of targets

Among the 10 patients, the maximum PTV was 877.20 cc, the minimum was 546.00 cc, and the average was 737.91 cc. The maximum PTV_J was 53.50 cc, the minimum was 11.20 cc, and the average was 31.32 cc. Regardless of the size of the target area, both PTV and PTV_J obtained better dose uniformity with statistical significance compared with conventional plans (PTV-CI, P = 0.04; PTV_J-CI, P = 0.01; HI = 0.02). The statistical results are shown in Table 2, and the dose distribution is shown in Figure 3.

The uniformity of the dose distribution of the target PTV_J can be directly seen in Figure 2; Fig. 2a shows the new method, and Fig. 2b shows the conventional method. The dose distribution and the 5000-dose line that wrapped the target area of the new method were better than those of the conventional method, and the uniformity and adaptability of the target area were also better with the new method. The dose line 2000 was lower in the lung than that in the conventional method planning.

3.2 Dosimetric comparison of the OARs

As shown in Table 3, there was no significant difference in OAR dose distribution (P > 0.05). The reason is that only the position of the MLC changed in the junction field compared with the two planning methods. This affected the dose gradient of the junction field, but not the dose distribution in the other areas.
4 | DISCUSSION

Breast cancer is the most common malignant tumor in female cancer patients. Surgery combined with radiotherapy and chemotherapy is one of the main treatment methods, which can effectively improve the clinical symptoms of breast cancer patients and the survival rate. For patients with early-stage breast cancer, partial resection and breast conserving treatment are often used. Compared with modified radical mastectomy, this method has a good therapeutic effect while preserving the breast shape. In China, modified radical mastectomy is still the most commonly used treatment due to the late detection and late staging of many patients.

In the treatment of breast cancer, changes in the target areas of the breast caused by respiratory movements should be considered. To avoid changes in the target areas, 4DCT technique and respiratory gating technique are required for IMRT treatment alone. This improves positional accuracy and protects normal tissue, but at the expense of therapeutic efficiency. In the present study, we used tangential opposing fields planning and IMRT planning to modulate the dose distribution and ensure the target area receives 70–80% of the dose and the uniformity of the target area dose; it was a practical design scheme.

The difficulty in the design of breast and supra clavicular region irradiation is how to deal with the distribution of the dose in the junction field, where a hot dose might cause skin reactions, and too many cold spots might hinder the treatment in the traditional planning. This is a problem that many therapy centers face. According to the analysis of dose distribution at the junction, a very steep dose drop occurred due to 70–80% of the prescription dose given at the chest wall and half-jaw irradiation given at the junction, which made the dose contribution of the supra clavicular field unable to reach the prescription dose in such a short distance. Therefore, we designed a new planning method to create a dose-drop gradient at the junction. In addition, if the distance between the lower boundary drawn by the breast and the treatment center is > 20 cm, the treatment center point should be moved downward to ensure that the lower boundary of the jaw covers the whole target area.

We used the field-in-field technique by changing the MLC in the fields to produce the dose gradient. The method was to add two subfields in each tangent opposing field. In the subfield design, the dose gradient was formed by shielding with MLC leaves. According to the calculation, if 80% of the prescribed dose was given to the main field (~80 MU), then approximately 10 MU would be given to each subfield. A drop dose zone of approximately 30% dose was formed within 2 cm, so that better dose modification could be achieved when the IMRT planning was designed in the supra clavicular region.

In the present study, it was found that the new method improved the dose distribution at the junction region and did not affect the OAR dose (Tables 3, 4; Figure 4). The advantage of the new method for planning the dose gradient is that it can avoid the situation where the MLC cannot be adjusted quickly and accurately due to the excessive dose drop.

As a result, the new method of planning can improve the dose distribution in the junction field and tumor control rate. It also reduces the side-effects by controlling the OAR dose and has value in the clinical setting.

ORCID
Suyan Bi https://orcid.org/0000-0001-7992-4078

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