High Tangent Radiation Therapy With Field-in-Field Technique for Breast Cancer

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ABSTRACT

PURPOSE: We evaluated whether the field-in-field (FIF) technique improves the homogeneity of the target in high tangent radiation therapy (HTRT).

MATERIALS AND METHODS: This study included 30 patients. In total, 3 HTRT plans were created: 1 with conventional opposed fields (Conv-p), 1 with the FIF technique (FIF-p), and 1 with FIF technique using lung-blocked subfields (FIF-LB-p).

RESULTS: The maximum dose of the breast and planning target volume (PTV) was significantly lower for FIF-p and FIF-LB-p than Conv-p. Homogeneity index of PTV was also significantly lower for FIF-p and FIF-LB-p than Conv-p. Homogeneity index of the breast or PTV was significantly better for FIF-p than FIF-LB-p. The volumes of the breast or the PTV receiving 95% and 90% of the prescribed dose were also significantly better for FIF-p, indicating the advantages of FIF-p.

CONCLUSIONS: The FIF technique was useful in HTRT and improved homogeneity in the target.

KEYWORDS: Breast cancer, axillary lymph node dissection, sentinel lymph node biopsy, high tangent radiation therapy, field-in-field technique

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Introduction

Most patients with early-stage breast cancer are given breast-conserving treatment consisting of wide excision and postoperative radiotherapy. Similar to mastectomy, postoperative radiotherapy reduces the risk of local recurrence and results in long-term survival.[1–3] Patients with positive axillary sentinel lymph node biopsy (SLNB) specimen often undergo axillary lymph node dissection (ALND). The American College of the Surgeons Oncology Group (ACSOG) Z0011 trial revealed that among patients with limited sentinel lymph node metastatic breast cancer treated with breast conservation and systemic therapy, the use of sentinel lymph node dissection alone compared with ALND did not result in decreased survival.[4] The European Organization for Research and Treatment of Cancer (EORTC) 10981-22023 After Mapping of the Axilla: Radiotherapy or Surgery (AMAROS) trial also showed that there was no significant difference in axillary recurrence rate between the SLNB group and the ALND group.[5] Therefore, attempts have been made to omit ALND even for SLNB-positive patients if certain conditions are met. As a replacement to this procedure, high tangent radiation therapy (HTRT) that intentionally irradiates the axillary lymph node region was examined.

The field-in-field (FIF) technique has become a widely preferred method for administering tangential whole-breast radiotherapy. Several studies have reported that the use of the FIF technique facilitates better control of dose homogeneity. The FIF technique was reported to be useful in reducing hot regions as well as cold regions.[6–9] The dual-energy FIF technique, whose energy of subfields is high, improves the homogeneity even in large-breast patients.[10] Moreover, the impact of respiratory motion is smaller with the FIF technique than with physical wedges.[11] In HTRT, the shape of the target becomes more complicated than with tangential whole-breast radiotherapy. Because HTRT involves the axilla region, the difference in body thickness of the target is large, and the dose inhomogeneity increases. However, the usefulness of the FIF technique in HTRT has not been sufficiently evaluated. The purpose of this study was to evaluate whether the FIF technique improves the homogeneity of the target in HTRT.

Materials and Methods

This study included 30 patients with breast cancer: 11 with right-sided and 19 with left-sided breast cancer. All patients had undergone breast-conserving surgery. This study was conducted with the approval from our institutional review board. All patients provided informed written consent. Computed tomography (CT) images were obtained using a scanner with

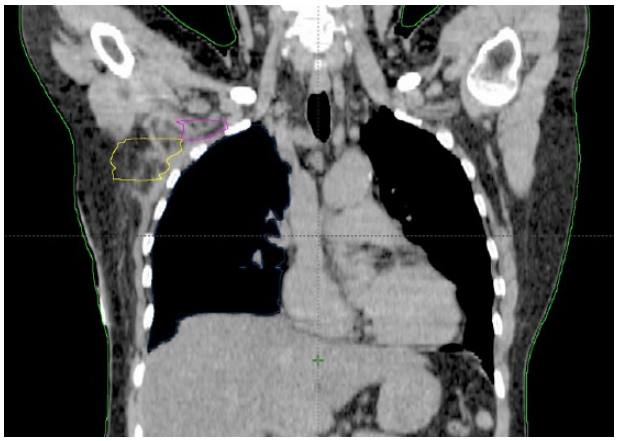

Figure 1. The typical contouring of axilla levels I and II. The axilla levels I and II are presented in magenta and yellow, respectively.

16 detector arrays (LightSpeed Xtra; GE Healthcare, Waukesha, WI, USA), with patients in the supine position on a breast board with both arms above their heads. Radiopaque markers were placed at the midline, the mid-axillary line, and 1 cm below the infra-mammary fold. Scanning was performed in 2.5-mm slices from the hyoid bone to the mid-abdomen during free breathing. All CT images were transferred to a computer with Eclipse External Beam Planning 8.6 software (Varian Medical Systems, Palo Alto, CA, USA). The clinical target volume consisted of the remaining whole breast and axilla levels I and II. The axilla levels I and II were delineated by referring to the contouring atlas of breast cancer provided by the Radiation Therapy Oncology Group (Figure 1).[12] The planning target volume (PTV) was obtained by adding 5-mm margins and removing 5 mm of the build-up region from the skin surface of the breast (PTVeval). Each patient's plan was normalized to a reference point at the interface of the breast and pectoralis major muscle at the level of the nipple. None of the reference points was on the lung parenchyma or the border between the lung and chest wall. A 6-MV energy photon beam was used. The prescribed dose was 50 Gy in 25 fractions. The dose calculation algorithm used was the analytic anisotropic algorithm.

The radiotherapy plan was generated as follows: 2 opposed tangential fields were created according to the clinically determined borders, and the gantry angles and beam weight were optimized (Conv-p) (Figure 2). Leaf margin of 2 cm was added to the skin side and leaf margins of 3 mm to the other side. The method used to create the FIF plan (FIF-p) has been reported previously.[13] The medial fields were copied as the first subfield. Using multileaf collimators (MLCs) for blocking, the dose to the first subfield was 1% to 3% lower than the maximum dose on the beam's eye view. After dose calculation, the beam weight was shifted away from the original field to the first subfield until the dose cloud disappeared. The lateral field was copied as the second subfield. Again using MLCs for blocking, the dose to the second subfield was 2% to 4% lower than the dose blocked in the first subfield, and the beam weight was shifted

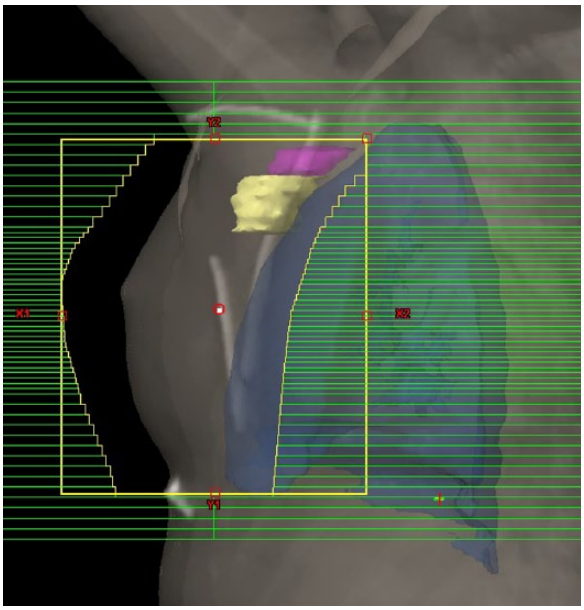

Figure 2. Beam's eye view of a typical high tangent field. The axillary lymph node region was intentionally included. The axilla levels I and II are presented in magenta and yellow, respectively.

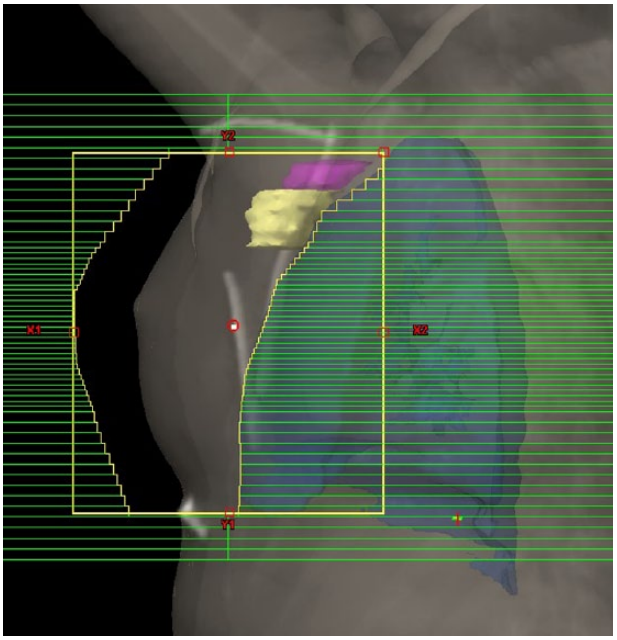

Figure 3. Beam's eye view of the lung-blocked subfield. Multileaf collimators were manipulated to shield the lung parenchyma on beam's eye view. The ipsilateral lung is presented in dark blue.

as described above. If the maximum dose was over 107% of the prescribed dose, the medial field was copied again as the third subfield. The MLCs were not allowed to block within 1 cm of the reference point. The minimum monitor unit of each subfield was 5. Finally, the plan with lung-blocked subfields (FIF-LB-p) was created. Another main field was copied again, and the MLCs were set to block the ipsilateral lung area (Figure 3). The beam weight of the lung-blocked subfield was set at approximately one-tenth of the main field.

Table 1. The average of D95%, D90%, and Dmean of the axilla level I and II (mean ± SD).

	LEVEL I			LEVEL II		
	CONV-P	FIF-P	FIF-LB-P	CONV-P	FIF-P	FIF-LB-P
D95%	43.6 ± 1.7	43.7 ± 1.7	42.2 ± 1.8	38.5 ± 1.5	38.5 ± 1.5	38.6 ± 1.5
D90%	44.4 ± 1.6	44.5 ± 1.6	43.0 ± 1.7	40.0 ± 1.4	40.0 ± 1.4	40.0 ± 1.4
Dmean	46.8 ± 1.5	46.8 ± 1.8	45.7 ± 1.5	42.6 ± 1.3	42.6 ± 1.3	42.7 ± 1.3

D95% and D90%, the doses administered to 95% and 90% of the axilla region; Dmean, the mean dose to the axilla region; FIF, field-in-field; SD, standard deviation.

Table 2. The average of V95%, V90%, Dmax, and HI of the breast and PTVeval (mean ± SD).

	BREAST			PTVEVAL		
	CONV-P	FIF-P	FIF-LB-P	CONV-P	FIF-P	FIF-LB-P
V95%	96.1 ± 2.6	95.9 ± 2.5[a]	91.5 ± 4.0[a]	87.5 ± 5.8	87.5 ± 5.6	76.8 ± 7.3[a]
V90%	99.7 ± 0.4	99.6 ± 0.5	98.3 ± 1.6[a]	95.5 ± 1.9	95.6 ± 1.9[a]	91.2 ± 4.1[a]
Dmax	56.1 ± 1.6	53.1 ± 0.5[a]	53.1 ± 0.5[a]	56.1 ± 1.7	53.1 ± 0.5[a]	53.1 ± 0.5[a]
HI	0.155 ± 0.036	0.116 ± 0.017[a]	0.146 ± 0.023	0.234 ± 0.029	0.189 ± 0.027[a]	0.208 ± 0.025[a]

V95% and VD90%, the volumes of the breast or the PTVeval receiving 95% and 90% of the prescribed dose; Dmax, the maximum dose to the breast or PTVeval; FIF, field-in-field; HI, homogeneity index; SD, standard deviation.
[a]Significantly smaller than that in Conv-p, FIF-p, or FIF-LB-p.

Table 3. The average of V20 Gy and Dmean of the ipsilateral lung (mean ± SD).

	CONV-P	FIF-P	FIF-LB-P
V20 Gy	10.6 ± 1.8[a]	10.5 ± 1.9[a]	9.8 ± 2.0
Dmean	20.2 ± 4.4[a]	20.2 ± 4.5[a]	19.7 ± 4.5

V20 Gy, the volumes of the ipsilateral lung receiving 20 Gy; Dmean, the mean dose to the ipsilateral lung; FIF, field-in-field; SD, standard deviation.
[a]Significantly larger than in FIF-LB-p, Conv-p, or FIF-p.

A dose volume histogram was calculated for each patient. The doses administered to 95% (D95%) and 90% (D90%) as well as the mean dose (Dmean) of axilla levels I and II were calculated. The maximum dose (Dmax) to the breast or PTVeval and the volumes of the breast or the PTVeval receiving 95% and 90% of the prescribed dose (V95% and V90%, respectively) were also calculated. The homogeneity index (HI) was calculated as follows: HI = D2% – D98%)/prescribed dose, where D2% and D98% are the doses administered to 2% and 98% of the breast or PTVeval. The Dmean and the volumes of the ipsilateral lung receiving 20 Gy (V20 Gy) were calculated. Dosimetric parameters were compared using the Wilcoxon signed rank test. A *P* value less than .05 was considered to indicate a statistically significant difference.

Results

The mean age of the patients was 54 (range: 26-76) years. The mean (±SD) volumes of the axilla levels I and II were 35.5 (±16.8) and 14.6 (±5.0) mL, respectively. The mean (±SD) volume of the breast was 352.8 (±193.6) mL. Because the enrolled patients were Asian females, the mean breast volume was relatively small. The mean (±SD) volume of the PTV was 511.7 (±220.6) mL. The mean (±SD) volume of the ipsilateral lung was 1197.7 (±249.5) mL.

The investigated methods were statistically significant but showed very small differences in the D95%, D90%, and Dmean of the axilla levels I and II (Table 1). About 90% of the axilla level I received approximately 44 Gy in any plan, and the mean dose was approximately 46 Gy in any plan. About 90% of the axilla level II received approximately 40 Gy in any plan, and the mean dose was approximately 43 Gy in any plan.

The Dmax values of the breast and PTVeval were significantly lower for FIF-p and FIF-LB-p than Conv-p. The HI of the PTVeval was also significantly lower for FIF-p and FIF-LB-p than Conv-p (Table 2). The HIs of the breast or PTVeval were significantly better for FIF-p than FIF-LB-p. V95% and V90% of the breast and PTVeval were also significantly better for FIF-p, indicating the advantages of FIF-p. The dose to the ipsilateral lung was significantly lower with FIF-LB-p than with other plans (Table 3).

Discussion

The ACSOG Z0011 trial analyzed 891 patients with clinical T1 and T2 invasive breast cancer and 1 to 2 sentinel lymph nodes with metastases. All patients underwent lumpectomy and tangential whole-breast radiotherapy. Those with sentinel lymph node metastases identified by SLNB were randomized to undergo ALND or no further axillary treatment. The 5-year overall survival and 5-year disease-free survival were not significantly different between the 2 groups.[4] Jagsi et al[14] pointed

out that more than half of the patients treated in Z0011 were irradiated with a high tangent field in both arms. The EORTC 10981-22023 AMAROS trial analyzed 1425 SLNB-positive patients with T1 and T2 invasive breast cancer. In total, 744 patients were randomly assigned to receive ALND followed by tangential whole-breast radiotherapy, and 681 patients received HTRT without ALND. The 5-year axillary recurrence rate was 0.43% after ALND and 1.19% after HTRT. Both ALND and HTRT in SLNB-positive patients provide excellent and comparable axillary control.[5] However, the planned noninferiority test was underpowered because of the low number of events. Lymphedema in the ipsilateral arm was noted significantly more often after ALND than after HTRT at 1, 3, and 5 years. Therefore, attempts have been made to omit ALND even for SLNB-positive patients if certain conditions are met. As a replacement to this procedure, HTRT that intentionally irradiates the axillary lymph node region was examined. In the National Comprehensive Cancer Network guidelines, patients with 1 or 2 positive sentinel lymph nodes are not recommended to undergo axillar dissection under certain conditions (eg, existence of T1 or T2 tumor, whole-breast radiation therapy planned, no preoperative chemotherapy administered).[15] It is speculated that the opportunities to perform postoperative irradiation in patients with 1 or 2 positive sentinel lymph nodes who do not undergo axillary dissection will increase in the near future. High tangent radiation therapy would be appropriate in these populations.

High tangent radiation therapy considers the cranial border of the irradiation field to be within 2 cm of the humeral head that receives high tangents.[16] The coverage of the axillary region is better in HTRT than in whole-breast tangential radiotherapy both in 2-dimensional (2D)-based plans and 3-dimensional (3D)-based plans.[17,18] However, the doses to the ipsilateral lung were also high in HTRT. Alço et al[19] reported that the coverage of the axillary region was better in 3D-based plans than that in 2D-based plans for HTRT. The doses to the ipsilateral lung were also high in the 3D-based plans. Ohashi et al[20] also reported that the doses to the axillary region were higher in 3D-based plans than in 2D-based plans for HTRT. There was no significant difference in doses to the breast between 2D and 3D-based plans. Sanuki et al[21] reported that the 3D-based HTRT improved axillary control compared with 2D-based HTRT.

Thus, HTRT improves the dose to the axillary region. However, the problem with HTRT is that it results in higher doses to the ipsilateral lung.

In this study, we compared 3D-based HTRT with or without the FIF technique. In HTRT, the shape and thickness of the target differ considerably depending on the part, compared with normal tangential whole-breast radiation therapy; that is, it is more difficult to control dose homogeneity in HTRT than in normal tangential radiation therapy. We conducted this study to confirm whether dose homogeneity of the target could be controlled in HTRT using the FIF technique. These methods provided comparable axillary dose coverage. About 90% of the axilla level I was received approximately 44 Gy in any plan, and the mean dose was approximately 46 Gy in any plan. About 90% of the axilla level II was received approximately 40 Gy in any plan, and the mean dose was approximately 43 Gy in any plan. These values were thought to have a certain effect on the axillar lesion, which was not detected on the imaging diagnosis. Homogeneity indices of the breast and PTVeval were significantly better in HTRT with the FIF technique (FIF-p and FIF-LB-p) than in HTRT without the FIF technique (Conv-p). The HI, V95%, and V90% were significantly better for FIF-p than FIF-LB-p. These results were suggestive of the advantages of FIF-p. However, the dose to the ipsilateral lung was significantly lower with FIF-LB-p than with the other plans. Lung blocks were useful for reducing the dose delivered to the lungs, but a simultaneous decrease in the breast or PTVeval was observed. The average Dmean and V20 Gy of the ipsilateral lung in FIF-p was 10.5 and 20.2 Gy, respectively. Oetzel et al[22] reported that the recommended mean ipsilateral lung dose to eliminate the risk of grade 2 pneumonitis is 15 Gy. Alternatively, Graham et al[23] reported that the recommended V20 Gy of the ipsilateral lung to eliminate the risk of grade 2 pneumonitis is 22%. Present results were within an acceptable range of both recommendations. However, some of the patients (20%) had V20 Gy of the ipsilateral lung exceeding 22%. These patients might require lung blocks when planning for radiation planning.

In conclusion, the FIF technique was useful in HTRT and improved homogeneity in the target.

Author Contributions

HT, SG, MF, and MM conceived and designed the experiments. HT, MI, TYam, KH, TYaj, MK, and KM analyzed the data. HT, MI, TYam, and SG wrote the first draft of the manuscript. HT, TYam, KH, MK, KM, MF, and MM contributed to the writing of the manuscript. HT, MI, TYam, KH, TYaj, MK, KM, SG, MF, and MM agree with manuscript results and conclusions. HT, KM, SG, MF, and MM jointly developed the structure and arguments for the paper. HT, MI, TYam, KH, TYaj, MK, KM, SG, MF, and MM made critical revisions and approved final version. All authors reviewed and approved the final manuscript.

REFERENCES

1. Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomized trials. *Lancet*. 2005;366:2087–2106.
2. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med*. 2002;347:1233–1241.
3. Sautter-Bihl ML, Sedlmayer F, Budach W, et al. One life saved by four prevented recurrence? update of the early breast cancer trialists confirms: postoperative radiotherapy improves survival after breast conserving surgery. *Strahlenther Onkol*. 2012;188:461–463.
4. Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. *JAMA*. 2011;305:569–575.

5. Donker M, van Tienhoven G, Straver ME, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomized, multicenter, open-label, phase 3 non-inferiority trial. *Lancet Oncol*. 2014;15:1303–1310.
6. Lo YC, Yasuda G, Fitzgerald TJ, Urie MM. Intensity modulation for breast treatment using static multi-leaf collimators. *Int J Radiat Oncol Biol Phys*. 2000;46:187–194.
7. Tanaka H, Hayashi S, Kajiura Y, et al. Evaluation of the field-in-field technique with lung blocks for breast tangential radiotherapy. *Nagoya J Med Sci*. 2015;77:339–345.
8. Borghero YO, Salehpour M, McNeese MD, et al. Multileaf field-in-field forward-planned intensity-modulated dose compensation for whole-breast irradiation is associated with reduced contralateral breast dose: a phantom model comparison. *Radiother Oncol*. 2007;82:324–328.
9. Kestin LL, Sharpe MB, Frazier RC, et al. Intensity modulation to improve dose uniformity with tangential breast radiotherapy: initial clinical experience. *Int J Radiat Oncol Biol Phys*. 2000;48:1559–1568.
10. Tanaka H, Kajiura Y, Kitahara M, et al. Usefulness of the dual energy field-in-field technique in breast tangential radiotherapy. *Radiol Med*. 2016;121:323–326.
11. Tanaka H, Hayashi S, Ohtakara K, Hoshi H. Impact of respiratory motion on breast tangential radiotherapy using the field-in-field technique compared to irradiation using physical wedges. *Radiol Oncol*. 2014;48:94–98.
12. Radiation Therapy Oncology Group (RTOG) Foundation INC. *Breast Cancer Contouring Atlas*. https://www.rtog.org/CoreLab/ContouringAtlases/BreastCancerAtlas.aspx. Accessed April 12, 2017.
13. Tanaka H, Hayashi S, Hoshi H. Determination of the optimal method for the field-in-field technique in breast tangential radiotherapy. *J Radiat Res*. 2014;55:769–773.
14. Jagsi R, Chadha M, Moni J, et al. Radiation filed design in the ACOSOG Z0011 (Alliance) Trial. *J Clin Oncol*. 2014;32:3600–3606.
15. National Comprehensive Cancer Network (NCCN). *NCCN guidelines for treatment of cancer by site*, Breast Cancer. https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 19, 2017.
16. Schlembach PJ, Buchholz TA, Ross MI, et al. Relationship of sentinel and axillary level I-II lymph nodes to tangential fields used in breast irradiation. *Int J Radiat Oncol Biol Phys*. 2001;51:671–678.
17. Reznik J, Cicchetti MG, Degaspe B, Fitzgerald TJ. Analysis of axillary coverage during tangential radiation therapy to the breast. *Int J Radiat Oncol Biol Phys*. 2005;61:163–168.
18. Nagar H, Zhou L, Biritz B, et al. Is there a tradeoff in using modified high tangent field radiation for treating an undissected node-positive axilla? *Clin Breast Cancer*. 2014;14:109–113.
19. Alço G, Iğdem SI, Ercan T, et al. Coverage of axilla lymph nodes with high tangential fields in breast radiotherapy. *Br J Radiol*. 2010;83:1072–1076.
20. Ohashi T, Takeda A, Shigematsu N, et al. Dose distribution analysis of axillary lymph nodes for three-dimensional conformal radiotherapy with a field-in-field technique for breast cancer. *Int J Radiat Oncol Biol Phys*. 2009;73:80–87.
21. Sanuki N, Takeda A, Amemiya A, et al. Axillary irradiation with high tangent fields for clinically node-negative breast cancer: can 3-D conformal radiotherapy with an field-in-filed technique better control the axilla? *Breast Care (Basel)*. 2013;8:362–367.
22. Oetzel D, Schraube P, Hensley F, Sroka-Pérez G, Manke M, Flentje M. Estimation of pneumonitis risk in three-dimensional treatment planning using dose-volume histogram analysis. *Int J Radiat Oncol Biol Phys*. 1995;33:455–460.
23. Graham MV, Purdy JA, Emami B, et al. Clinical dose-volume histogram analysis for pneumonitis after 3D treatment for non-small cell lung cancer (NSCLC). *Int J Radiat Oncol Biol Phys*. 1999;45:323–329.