

RESEARCH ARTICLE

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Comparison of Different Radiotherapy Planning Techniques for Breast Cancer after Breast Conserving Surgery

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Abstract

Objectives: To compare different radiotherapy planning techniques for breast cancer after breast conserving surgery. **Materials and methods:** Eighteen patients with breast cancer who underwent breast conserving surgery were selected. For each patient four different whole breast irradiation techniques including Tan, fIMRT, iIMRT and VMAT were compared to the conventional tangential technique (Tan). **Results:** Mean maximum point dose (Dmax) for Tan, fIMRT, iIMRT and VMAT were 110.17% (± 1.87), 105.89% (± 1.13), 106.47% (± 0.92) and 106.99% (± 1.16) ($p < 0.001$). Mean minimum point dose (Dmin) from Tan was 84.02% (± 3.68) which was significantly higher than those from fIMRT, iIMRT and VMAT which were 76.57% (± 11.4), 67.69% (± 19.20) and 80.69% (± 7.06) ($p < 0.001$). Only the mean V95 of fIMRT was significantly less than Tan ($p = 0.01$). Mean percentage of volume receiving ≥ 20 Gy (V20Gy) and mean doses of the ipsilateral lung were 17.09% and 953.05 cGy, 16.60% and 879.20 cGy, 14.79% and 772.26 cGy, 15.32% and 984.34 cGy for Tan, fIMRT, iIMRT and VMAT. Only iIMRT had a significantly lower mean V20Gy and the mean dose to ipsilateral lung in comparison with Tan. Significantly, high mean doses to the contralateral breast (498.07 cGy, $p < 0.001$) were observed in VMAT. **Conclusion:** The conventional tangential technique provides adequate dose coverage but resulted in high dose-volumes. The iIMRT and fIMRT had significantly smaller high dose-volumes and better conformity. VMAT demonstrated excellent dose homogeneity and conformity but an increased low-dose volume outside the target should be of concern.

Keywords: Breast cancer- radiotherapy planning technique- IMRT- VMAT- conventional tangential technique

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Introduction

Breast cancer is one of the most common cancers in women worldwide with an estimated rate of 37: 100,000. The age-standardized incidence rate (ASR) of breast cancer in Thailand in 2004–2006 was 25.6:100,000 which had an increasing trend with age. There were about 37.5% (Attasara et al., 2011) of all cancers in Thai woman with the highest incidence at ages 45 – 49 years. In general, treatments of breast cancer consist of surgery, as major modality, and adjuvant treatments including chemotherapy, radiotherapy, hormonal and targeted therapy. Recently, cosmetic outcome from these treatments modalities has become of more concern resulting in widespread using of breast conserving therapy (BCT) in which patients do not have to lose their breast from the treatment procedure. This provides a more satisfactory outcome than radical surgery. Several studies demonstrate good outcomes of breast conserving therapy in comparison to radical mastectomy (Bhatti et al., 2014; Fisher et al., 2002; Veronesi et al., 2002). With breast conserving therapy, the patient has

a better quality of life and self-image perception as shown in several studies (Acil and Cavdar, 2014; Curran et al., 1998). Surgery and radiotherapy are the foundations of breast conserving therapy. Patients with favorable early stage breast cancer can be treated conservatively by lumpectomy, followed by postoperative irradiation to the breast.

The techniques commonly used with standard external beams for whole breast irradiation are medial and lateral tangential approaches combined with wedges to obtain more homogeneous distribution of radiation dose. The advantage of using the medial and lateral tangential field technique is lower doses to lung and heart. Some areas of irradiated breast still received high radiation doses from this technique, resulting in poor cosmetic outcome due to fibrosis and shrinkage of breast tissue regardless of surgical factors. The dose homogeneity produced by the tangential technique is much affected by variations of size and shape of patient's breasts. In cases with left-side disease, the heart also receives a high radiation dose which can lead to future cardiac morbidity. Factors that

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influence cosmetic results after BCT have been reported in the study of Taylor et al., (1995) which demonstrated radiation factors that affect cosmetic outcomes of BCT were treatment volume (tangential breast fields only vs. three or more fields), the whole breast dose in excess of 50 Gy, and total dose to tumor site > 65 Gy, as well as optimum dose distribution with compensating filters. Modern radiation techniques have developed to get better dosimetric results in treatment of breast cancer such as intensity-modulated radiotherapy (IMRT) and volumetric-arc modulated radiotherapy (VMAT) which can improve radiation conformity and homogeneity. Many studies reported that modern radiation techniques had significant improvements in the dose coverage, dose homogeneity, dose conformity and cosmetic outcome.

Materials and Methods

Eighteen patients with early stage breast cancer who underwent breast conserving surgery were studied using computed tomography (CT) simulation and post-operative whole breast irradiation at Srinagarind Hospital between September 2012 and November 2013.

Simulation

All patients underwent a non-contrast computed tomography (CT) simulation using a helical 16-slice CT scanner (Phillips Brilliant Big-bore 16). Patients were placed in the supine position and immobilized by a breast board. Image data were transferred to the Eclipse Planning System version 10.0 (Varian Medical system, Palo Alto, CA) for the planning process. The body contours, target volumes and organs at risk were delineated and reconstructed into three-dimensional images.

Volumes of interest contouring

Regions of interest including ipsilateral lung, contralateral lung, involved breast, contralateral breast, heart, liver and spinal cord were delineated by the same physician, slice by slice. All targets and organs at risk were then reconstructed into three-dimensional structures.

Breast and PTV

The involved breast and contralateral breast were outlined by the definition of the Radiation Therapy Oncology Group (RTOG) according to the recommendations for target volume in the International Commission on Radiation Units and Measurements (ICRU) Report 62. The planning target volumes (PTV) were defined as the volume that is tangentially irradiated excluding 5 mm from skin surface to avoid under dosage due to a build-up effect. Lungs, heart and liver were also excluded.

Organs at risk (OAR)

The heart, ipsilateral lung, contralateral lung, liver and spinal cord were outlined manually using contouring tools in the treatment planning system. The heart included all myocardium and pericardium from apex to the infundibulum of right ventricle, right atrium and auricle, excluding the roots of all great vessels. The lung and spinal

cord were contoured using a bucket tool and interpolation. The liver was outlined by CT reference.

Planning

Four different planning techniques were used for each patient including a standard 2D-tangential plan (Tan), forward-planned IMRT (fIMRT), inverse-planned IMRT (iIMRT) and VMAT. The radiation doses were planned and calculated by using a 6 MV photon beam to the PTV with the Eclipse External Beam Planning version 10.0. The prescribed dose to PTV was 5000 cGy in 25 fractions for all cases.

Conventional tangential plan

The conventional tangential plan included two opposing half beams combined with a pair of appropriate dynamic wedges covering the whole PTV. The locations of radio-opaque wires were used as the references of the field boundaries. The boundaries of tangential fields according to following landmarks were: midline at the interclavicular space to xyphoid process, mid-axillary line, 2.0 cm below inframammary fold and inferior border of medial clavicular head. The anterior margin was extended for a 2 cm fall-off from the skin to ensure the encompassing of the target volume. The reference point for 100% dose normalization was placed near chest wall.

fIMRT

Two opposite half beams without wedges used in the conventional tangential plan were used in fIMRT planning. The percent isodose line of maximum point dose (Dmax) was identified. Subfields were added to each tangential field by manual manipulation of the multileaf collimator (MLC) in order to block volumes of high dose and organs at risk. Each subfield was adjusted to the dose weight to reduce Dmax by steps of 1-2% until Dmax reached 105 – 106% and 95% isodose covering the whole PTV.

iIMRT

Two opposite half beams without wedges used in the conventional tangential plan were used in iIMRT planning. The initial dose constraints and priorities were added during plan optimization and adjusted until Dmax reached 105 – 106% and a 95% isodose covering the whole PTV. Whenever there were some unacceptably high dose areas, virtual organs could be created and added for further dose optimization.

VMAT

Two partial arcs were used to prevent unnecessary radiation doses to normal tissues. Start and stop angles of both arcs were 10 degrees beyond the tangential beam angle. The subfield interval used was 4 degrees. The most acceptable parameters which resulted in good dose distribution were developed and saved in the template library for further use as initial optimization in the next cases.

All plans were reviewed in terms of a dose-volume histogram and dose distribution slice by slice. The best plan of each technique was selected for comparisons of

PTV coverage, Dmax, minimum point dose (Dmin), conformity index, homogeneity index and dose to OARs.

Data analysis

The parameters obtained by all techniques including Tan, fIMRT, iIMRT and VMAT used in the comparisons were planning target volumes (PTV), Dmax, Dmin, volume enclosed by the 95% isodose (V95), high dose-volume defined as the volume enclosed by the 107% isodose (V107) and volume enclosed by the 110% isodose (V110), radical dose homogeneity index (HI), PTV conformity index (CI), ipsilateral lung percentage of volume receiving ≥ 20 Gy (V20Gy), ipsilateral lung mean dose and contralateral breast mean dose. The heart percentage of volume receiving ≥ 30 Gy (V30Gy) and heart Dmax were compared only in left sided disease.

The differences between any two of the four plans were compared and analyzed with ANOVA at a confidence level of 0.05 ($\alpha=0.05$).

Results

Demographic data

Eighteen patients were included in this study. Nine patients (50%) had right sided breast disease and the other nine patients (50%) had left sided disease. The mean PTV of overall patients was 581.42 cm³ (± 201.52).

Radiation Dose to Planning target volume (PTV), Organs at risk (OAR) and Non-PTV Dmin and Dmax in PTV

From the conventional tangential technique, the mean Dmin was 84.02% (± 1.86) which was statistically higher than other special techniques in the same group of patients. The values of Dmin obtained from VMAT, fIMRT and iIMRT were 80.69% (± 3.53), 76.57% (± 5.70) and 67.69% (± 9.60) ($p < 0.001$) as shown in Table 1.

From the conventional tangential technique, the average Dmax was 110.17% (± 0.94) which was statistically higher than other special techniques in the same group of patients. The values of Dmax obtained from VMAT, iIMRT and fIMRT were 106.99% (± 0.58), 106.47% (± 0.46) and 105.89% (± 0.57) ($p < 0.001$) as shown in Table 1

Dose coverage of PTV

The mean PTV coverage by isodose 95% (V95) by the conventional tangential technique was 98.16%

(± 0.89). Meanwhile, the mean V95s obtained by fIMRT, iIMRT and VMAT were 96.83% (± 0.73), 97.42% (± 0.61) and 98.66% (± 0.52). Only the mean V95 of fIMRT was less than the conventional tangential plan with a statistical significance of ($p=0.01$).

The mean V107 by conventional tangential technique was 13.05% (± 4.91). Meanwhile, the mean V107s obtained by fIMRT, iIMRT and VMAT were 0.38% (± 0.35), 0.25% (± 0.19) and 1.47% (± 1.09). The mean V107s of all special techniques were less than conventional tangential plan with statistical significance ($p < 0.01$).

Conformity index (CI) and Homogeneity index (HI) of PTV

The mean Conformity indices (CI) achieved by VMAT, fIMRT and iIMRT were 0.876, 0.727 and 0.728, all of which were significantly better than the 0.643 of the conventional tangential technique ($p < 0.05$).

For the Homogeneity index (HI), the mean HIs of VMAT, fIMRT and iIMRT were 0.755, 0.723 and 0.636. iIMRT was the only one that was significantly lower than conventional tangential technique (0.626 vs 0.763, $p=0.047$).

Organs at risk (OAR)

Heart

This study focused on the heart only in 9 cases whose breast disease was on the left side located in close proximity to the heart. The dose to the heart that equaled or was more than 30 Gy was defined as V30Gy. The conventional tangential technique had a mean V30Gy of 7.69%. With the advanced techniques, the mean V30Gys were 7.37%, 4.97% and 4.25% for fIMRT, iIMRT and VMAT. The mean Dmax of the heart was also considered. In the conventional tangential plan, the heart received a mean Dmax of 50.3 Gy, which was not significantly different from those of fIMRT (48.8Gy), iIMRT (50.8 Gy) but different from the VMAT (41.5 Gy) ($p < 0.05$) as shown in Table 2.

Ipsilateral lung

The dose to the ipsilateral lung that equaled or more than 20 Gy was defined as V20Gy. The mean V20Gy and mean radiation doses to ipsilateral lung from conventional tangential plan were 17.09% and 953.05 cGy. In comparison to fIMRT, the mean V20Gy and mean radiation dose were 16.60% and 879.20 cGy ($p > 0.05$). For VMAT, the mean V20Gy and mean radiation dose were

Table 1. Comparisons of the Means of Dmax, V95, V107, Dmin on PTV between the Conventional Tangential Technique and fIMRT, iIMRT and VMAT

	Tan	fIMRT	p Value	iIMRT	p Value	VMAT	p Value
Dmax, mean (%)	110.2	105.9	< 0.001	106.5	< 0.001	107	< 0.001
(\pm SD)	(± 0.9)	(± 0.6)		(± 0.5)		(± 0.6)	
Dmin, mean (%)	84	76.6	< 0.001	67.7	< 0.001	80.7	< 0.001
(\pm SD)	(± 1.9)	(± 5.7)		(± 9.6)		(± 3.5)	
V95, mean (%)	98.2	96.8	0.01	97.4	0.533	98.7	0.991
(\pm SD)	(± 0.9)	(± 0.7)		(± 0.6)		(± 0.5)	
V107, mean (%)	13.1	0.3	< 0.001	0.3	< 0.001	1.5	0.001
(\pm SD)	(± 4.9)	(± 0.3)		(± 0.2)		(± 1.1)	

Table 2. Comparisons of the Mean dose to Organs at Risk between the Conventional Tangential Technique and fIMRT, iIMRT and VMAT

	Tan	fIMRT	p Value	iIMRT	p Value	VMAT	p Value
Heart							
Mean V30Gy	7.6	7.4	1	4.9	0.129	4.3	0.94
(±SD)	(±2.0)	(±2.1)		(±1.5)		(±1.2)	
mean Dmax (cGy)	5030.7	4877.3	0.172	5084.7	1	4153.2	0.422
(±SD)	(±85.8)	(±133.5)		(±113.1)		(±561.3)	
Ipsilateral lung							
Mean V20Gy	17	16.6	1	14.7	0.007	15.3	1
(±SD)	(±3.8)	(±3.8)		(±3.8)		(±1.2)	
Mean dose (cGy)	953	879.2	0.156	772.8	<0.001	984.3	1
(±SD)	(±182.6)	(±173.8)		(±141.9)		(±64.1)	
Contralateral breast							
Mean dose (cGy)	51.7	42.2	<0.001	26.6	0.137	498.1	<0.001
(±SD)	(±31.3)	(±29.2)		(±10.3)		(±57.2)	

15.32% and 984.34 cGy ($p>0.05$). Although fIMRT and iIMRT had a trend of decreasing doses to the ipsilateral lung than the conventional tangential plan, only iIMRT was proven to have a significantly lower V20Gy (14.79%, $p=0.007$) and mean radiation dose (772.26 cGy, $p<0.001$) as shown in Table 2.

Contralateral breast

Despite that fIMRT and iIMRT had a reduced mean radiation dose to the contralateral breasts from 51.69 cGy of conventional tangential plan to 42.22 cGy of fIMRT and 26.63 of iIMRT, only fIMRT was shown to be significantly different ($p<0.001$). The mean radiation dose to the contralateral breast from VMAT technique, however, was significantly higher than all other techniques (498.07 cGy, $p<0.001$) as shown in Table 2.

Discussion

Breast conserving therapy consists of non-radical surgery and post-operative radiotherapy. The patients do not have to lose their entire breast which results in a better quality of life (Acil and Cavdar, 2014; Curran et

al., 1998). Evidence has confirmed that breast conserving therapy provides the same efficacy as radical mastectomy. Thus breast conserving therapy becomes the new standard treatment in early stage breast cancer mastectomy (Bhatti et al., 2014; Fisher et al., 2002; Veronesi et al., 2002). Some advanced techniques have been developed and implemented in many institutes to improve and reduce dose homogeneity and conformity to organs at risk resulting in a lower rate of radiation complications whereas good cosmesis can be preserved. Many reports showed that beam intensity modulation by MLC has demonstrated superior results on target coverage and dose homogeneity (Hong et al., 1999; Morganti et al., 2011; Lanea et al., 2012; Mukesh et al., 2013). Using the conventional tangential technique is less time-consuming and doses do not need expert teamwork or modern equipment but can provide acceptable outcome (Fisher et al., 2002). It is quite suitable for developing countries. If it is not well-designed individually, however, then there is a high propensity to cause acute and late complications from dose inhomogeneity and high doses to organs at risk can result (Jean-Philippe et al., 2008). The maximum dose from the conventional tangential technique in this study was as high as 113.5% of the prescribed dose and then might also provide a large high dose volume. From the study of Rongsriyam et al (Rongsriyam et al., 2008), the mean Dmax from the conventional tangential technique was 110.68% and mean V110 was 3.28%. In most cases of this study, volumes of high radiation doses were usually found at the base and apex of the breast.

The use of advanced techniques including fIMRT, iIMRT and VMAT could significantly reduce Dmax and also the high dose-volume of PTV. The Dmax was decreased by 3 – 4%, V107 was decreased by 12 – 13%. No significant differences in Dmax and V107 were found in comparisons between each advanced technique ($p = 0.075 – 0.590$). V110 was rarely shown in fIMRT and iIMRT, but a small volume of V110 sometimes showed in the VMAT technique. These results in fIMRT and iIMRT were comparable to the study of Mihai et al., (2005). The mean V95s from iIMRT and VMAT

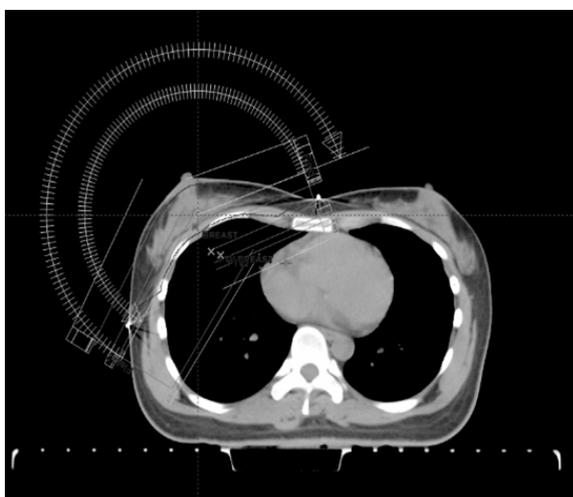


Figure 1. Showing Arcs Orientation in VMAT Plan

97.42% and 98.66% were comparable to the other studies (Liu et al., 2015; Mansouri et al., 2014). Although advanced techniques in this study showed a better result for Dmax, Dmin, however, was difficult to control. For the conventional tangential plan, mean Dmin was 84% whereas those obtained by the advanced techniques ranged from 67.7 to 80.7%. Mean Dmin in this study was measured as the point dose. The study from Morganti (2011), however, showed that mean Dmin from fIMRT was 74.9%, which was comparable to this study. The mean V95 from the conventional tangential technique of this study could cover almost the whole PTV (98.16%). V95 from Tan was significantly more than fIMRT ($p=0.01$), but not significantly different from iIMRT and VMAT ($p>0.05$). V95 coverage from all advance techniques were acceptable together with lower dose to organs at risk. Beside good V95 coverage, all advance techniques also produced significantly better conformity than the conventional tangential plan as well. The homogeneity index from this study was obviously low as compared to the study of Rangsiyam et al., (2008) which could be due to very small value of Dmin or experience in treatment planning. There were no significant differences in HIs between all advance techniques and the conventional tangential technique except iIMRT which could be due to a small sample size.

A study of Darby et al., (2013) reported that ionizing radiation exposure to the heart in breast cancer radiotherapy increases the rate of ischemic heart disease. Fewer cardiac complications could be observed if the heart V30Gy was kept lower than 10% (Gyenes et al., 1997). In 8 cases of left sided disease, this study showed acceptable doses to the hearts in all techniques and especially iIMRT and VMAT with the mean heart V30Gy below 10%. The mean lung dose should be of strict concern in every case of breast irradiation as it may result in lethal morbidity. This study utilized the tangential iIMRT to minimize the dose to the ipsilateral lung. The study of Graham et al., (1999) reported that the radiation dose to the lung more than 20 Gy was related to development of radiation pneumonitis. Yorke et al., (2002) and Kwa et al., (1998) also reported that radiation pneumonitis was associated with a high mean lung dose as well. Thus, the mean dose to the lung should be kept under 20 Gy and V20Gy should not be over 20%. All techniques from this study including the conventional tangential technique can achieve these objectives. Hall and Wu, (2003) estimated that by switching from 3D conformal RT to IMRT in various cancer sites could double the incidence of second malignancy from 1.5 to 3% for patients surviving ten years. Therefore, unnecessary radiation exposure to normal tissues can lead to important in secondary malignancies such as thyroid cancer, lung cancer and soft tissue sarcoma. From this study, the mean radiation dose to contralateral breast in VMAT was significantly higher than in fIMRT and iIMRT ($p<0.001$). This finding should be considered before making the decision of which technique should be selected.

In conclusion, the conventional tangential technique in breast conserving therapy provided adequate dose coverage but resulted in high dose-volumes. The iIMRT

and fIMRT techniques have significantly better conformity and high dose-volume reduction than Tan. Although VMAT demonstrated excellent dose homogeneity and conformity, the increased low-dose volume should be a matter of concern. Whichever technique is used, proper treatment planning can minimize radiation doses to organs at risk.

Conflict of interest

None.

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