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Original Article

Synchronous bilateral breast irradiation with helical tomotherapy: A single institute experience

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Purpose: Synchronous bilateral breast cancer (SBBC) occurs in less than 3% of patients with breast cancer. Radiation delivery using conventional techniques leads to poor dose coverage and high toxicity. With improved radiation techniques, such as helical tomotherapy, favorable dose coverage and low toxicity profiles can be achieved.
Methods: From February 2011 to February 2014, 3 patients were diagnosed with SBBC and treated with synchronous bilateral whole breast irradiation (SBWBR). The characteristics, radiation planning parameters, and treatment toxicity (acute and late) data of these patients were collected.
Results: All 3 patients received bilateral breast-conserving surgery followed by chemotherapy and SBWBR. The average irradiation volume was 1215.4 cm^3. The average dose to breast tissue was 50.4 Gy. Only grade 1 acute skin toxicity was reported. After a median follow-up time of 48.7 months, all patients were alive without long-term toxicity.
Conclusion: Helical tomotherapy is a feasible radiation treatment for patients with SBBC suited to SBWBR. Its advantages include favorable dose coverage, low skin toxicity, and no long-term side effects.

Keywords: Bilateral breast cancer, synchronous breast cancer, tomotherapy, radiotherapy, intensity-modulated radiotherapy (IMRT)

Introduction

Breast cancer is among the most common cancers in women worldwide. In Taiwan, approximately 10,000 new cases of breast cancer are diagnosed each year [1]. The prevalence of synchronous bilateral breast cancer (SBBC) ranges from 0.7% to 3.0% [2-4]. Patients with SBBC tend to have a less favorable prognosis and an increased distant metastatic rate when compared with patients with other breast cancer types [3]. Whole breast irradiation following breast-conserving surgery has been the standard treatment for unilateral breast cancer for decades. Whole breast irradiation with

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intensity-modulated radiotherapy (IMRT) leads to improved dose coverage and organ protection, as well as decreased acute skin toxicity, when compared with conventional tangent field radiotherapy [5]. No consensus has been reached regarding the treatment of SBBC. Physicians tend to treat SBBC in a similar manner to unilateral breast cancers. Therefore, for patients receiving bilateral breast-conserving surgery, adjuvant synchronous bilateral whole breast irradiation (SBWBR) is often suggested [6,7].

SBWBR poses potential technical challenges. Conventionally, the field matching technique has been used. Applying field matching to radiotherapy increases uncertainties, such as cold and hot spots. Many other methods have been described, including static or rotational IMRT and electron arc therapy [8,9]. Helical TomoTherapy (HT) (Accuray Inc., Sunnyvale, CA, United States) is a linear accelerator mounted on a ring gantry, which delivers IMRT using a fan-beam collimator system. Wadasadawala et al. suggested that HT be used to deliver SBWBR, to reduce mean doses to the total lung and heart and maintain acceptable dose coverage [10]. In one study, increased clinical toxicities of SBWBR using HT were reported. However, there were only a small number of patients included [11]. Few studies have discussed this issue. We report our experience from a single institute in delivering SBWBR, including dosimetric results and acute and late toxicities.

Materials and Methods

We retrospectively searched our institutional database for patients who had received whole breast irradiation using HT from January 2011 to December 2014. Three patients were identified. The medical records of these 3 patients were reviewed.

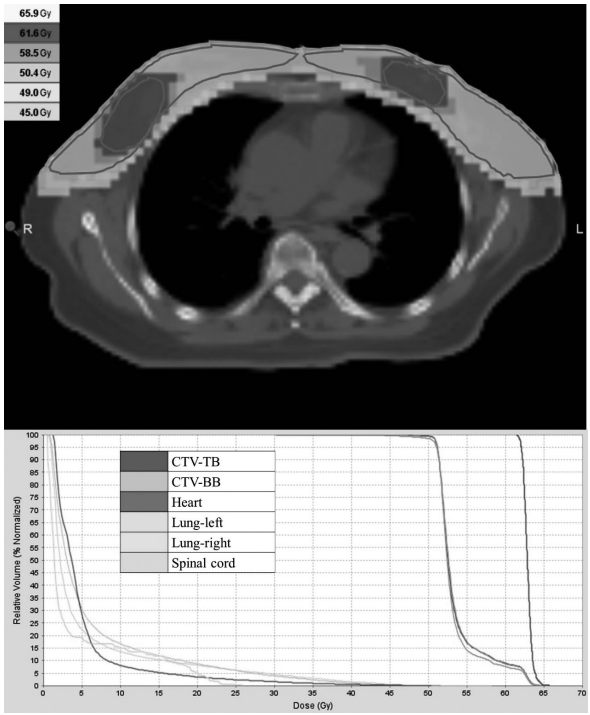

Figure 1. Dosimetric coverage by HT. CTV-TB: clinical tumor volume of the tumor bed; CTB-BB: clinical target volume including the bilateral breasts.

Acute and late adverse events were recorded using the Common Terminology Criteria for Adverse Events (CTCAE V4.0).

All patients received computed tomography (CT) simulation for treatment planning. Patients were immobilized with vacuum cushions in a supine position with arms held overhead. The irradiated volume included bilateral breasts with simultaneous boosts to the tumor beds. Prophylactic supraclavicular lymph node irradiation was delivered according to the patient's risk of disease recurrence. The clinical target volume (CTV) included the bilateral tumor bed (CTV-TB), which was contoured according to

Table 1. Radiation target volumes.

Patient	Primary target				Lymphatic target	
	left whole breast	right whole breast	left tumor bed	right tumor bed	left supraclavicular	right supraclavicular
case 1	Yes	Yes	Yes	Yes	Yes	Yes
case 2	Yes	Yes	Yes	Yes	No	No
case 3	Yes	Yes	Yes	Yes	No	Yes

Table 2. Patient characteristics and cancer treatments.

Patient	Side	TNM	Luminal type	Surgery	Chemotherapy	Hormone therapy
case 1	Left	pT1N0(sn)	A	lumpectomy + SLNB	CMF * 6	Tamoxifen/ Letrozole
	Right	pT1N0(sn)	A	lumpectomy + SLNB		
case 2	Left	pT1aN0(sn)	A	lumpectomy + SLNB	TC*6	Letrozole
	Right	pT2N1	A	partial mastectomy+ ALND		
case 3	Left	pT1cN0(sn)	A	lumpectomy + SLNB	EC*5	Tamoxifen
	Right	pT2N1	A	partial mastectomy+ ALND	followed by dT *4	

sn: sentinel lymph node biopsy; SLNB: sentinel lymph node biopsy; ALND: axillary lymph node dissection; CMF: cyclophosphamide, methotrexate, and fluorouracil; TC: paclitaxel and cyclophosphamide; EC: epirubicin and cyclophosphamide; dT: docetaxel.

Table 3. Prescribed radiation doses.

Patient	Primary Treatment (Gy)			Lymphatic Target (Gy)	
	left whole breast	right whole breast	tumor bed boost	left	right
case 1	50.4	50.4	56	50.4	50.4
case 2	50.4	50.4	61.6	No	No
case 3	50.4	50.4	61.6	No	50.4

Note: All patients received 28 fractions for every treatment field.

the surgical clips marked by the surgeons. The CTV of the bilateral breast tissues was denoted as CTV-BB. The CTV of the supraclavicular region (unilateral or bilateral) was denoted as CTV-SC. The treated volumes of individual patients are summarized in Table 1. The organs at risk, including the heart, bilateral lungs, and spinal cord, were contoured. All treatment plans were devised using Hi-Art TomoTherapy (version 2.2.4.1, TomoTherapy, Inc., Madison, WI, United States) (Fig. 1). The prescribed dose was intended to cover at least 95% of the irradiated volume to meet the quality criteria of our institute. The prescription dose, constraints of the organs at risk, and irradiated volumes were recorded.

Results

From January 2011 to December 2014, 3 patients received SBWBR at our institute. Two patients were 59 years old and 1 patient was 45 years old. One patient had bilateral stage I breast cancers, while the other 2 patients had stage I breast cancer on the right side and stage III cancer on the left side. All patients received bilateral breast-conserving surgery followed by chemotherapy. Patient characteristics and cancer treatments are listed in Table 2.

All 3 patients received SBWBR with simultaneous boost to the tumor bed using HT (Fig. 1). One patient received no regional node irradiation, 1 patient received regional nodal irradiation over the right side, and 1 patient received bilateral regional nodal irradiation. The average dose to the tumor bed was 59.73 Gy. The mean prescribed dose to the bilateral breasts was 50.4 Gy (Table 3). The average irradiated volume was 1215.4 cm^3. The average mean doses to the lungs, heart, and spinal cord were 11.39, 16.04 and 24.55 Gy, respectively. Dose prescriptions and doses to the organs at risk are listed in Table 4.

Regarding acute toxicity, all 3 patients experienced grade 1 radiation dermatitis. After a median follow-

Table 4. Dosimetric parameters.

Patient	Left Lung V20	Left Lung D_{mean}	Right Lung V20	Right Lung D_{mean}	Heart Dmean	Spinal Cord D_{max}
case 1	20%	16.77 Gy	20%	16.07 Gy	26.84 Gy	27.12 Gy
case 2	8%	5.63 Gy	8%	6.42 Gy	5.09 Gy	20.67 Gy
case 3	10%	11.36 Gy	13%	12.07 Gy	16.18 Gy	25.85 Gy

V20: Percentage of the normal organ receiving at least 20 Gy; D_{mean}: the mean dose to the normal organ; D_{max}: the maximum dose to the normal organ.

up period of 48 months, all patients were alive without any late toxicity.

Discussion

Whole breast irradiation has been proven to improve locoregional control and survival in patients with early stage breast cancer [12]. Dosimetric studies have shown that whole breast irradiation using IMRT, instead of a conventional tangent field technique, improves the homogeneity index (HI) and conformity index (CI), and reduces doses to the heart, contralateral breast, and lungs [5,13-15]. These dosimetric benefits translate into favorable patient-reported outcomes such as those related to acute and late skin toxicities. A Canadian phase III study showed that the rate of grade 3 and 4 acute skin dermatitis was reduced from 36.7% to 27.1% [16]. Reduced rates of chronic skin telangiectasia and improved cosmetic outcomes were also reported from long-term follow-up data of randomized control studies using IMRT [17]. Donovan et al. demonstrated a reduced late effect in "change of breast appearance" from 58% to 40% using IMRT for breast irradiation [18]. IMRT is now a standard treatment for patients receiving breast irradiation.

HT, a type of IMRT delivery system, is unique. Mechanically, it lacks a flattening filter. Instead, a narrow fan-beam delivery is used to increase shielding of the collimator. Unlike conventional linear accelerators, an HT unit is similar to a CT machine. The patient is treated on a moving couch, with a helical pattern of IMRT delivered from a rotating gantry. Many studies have shown that HT effectively improves the HI and CI of target volumes, while simultaneously reducing doses to the organs at risk [19]. Early studies of HT have demonstrated that it is superior to conventional IMRT for large treatment volumes, multitarget irradiation, simultaneous concomitant boost, and critical organ protection [20-23]. Liem et al. reported their experience of using HT to treat patients with breast cancer after breast-conserving surgery. Almost full target coverage was achieved with relatively low doses to the heart and the ipsilateral lung, demonstrating that HT is a feasible technique for these patients [24]. Wojcieszynski et al. also showed that patients administered HT experience tolerable skin acute toxicity and favorable target coverage [25]. Based on dosimetric studies, HT improves target coverage and decreases doses to the heart, contralateral breast, and ipsilateral lung [26-29]. Therefore, for SBBC, with a target that is twice as large as usual for whole breast irradiation, HT is advantageous.

SBBC is rare, accounting for less than 3.0% of the entire breast cancer population [2-4]. Kuo et al. studied more than 1000 Taiwanese women with early stage breast cancer. Their results showed that the risk of death for overall bilateral breast cancer is 2.5 times higher than that for unilateral breast cancer. Among all patients with bilateral breast cancers, those with SBBC have a 1.12-fold higher risk of death, whereas those with metachronous breast cancer have a 6.11-fold higher risk of death [30]. Carmichael et al. reported that patients with SBBC have significantly worse overall survival when compared with those with metachronous bilateral or unilateral breast cancer [31].

Little research has been conducted on the treatment of SBBC including randomized control studies comparing radiation techniques for administering SBWBR. Wadasadawala et al. compared radiation techniques for SBWBR, including the conventional

bitangential radiotherapy technique, conventional field-in-field IMRT, rotational HT, and HT with TomoDirect technique. Acceptable target coverage was achieved with each technique. With HT, there was significantly greater reduction in hot spots than conventional bitangential radiotherapy technique. HT with simultaneous boost to the tumor bed markedly reduced mean doses to the heart and bilateral lungs. Accordingly, the simultaneous boost technique should be considered for SBWBR with HT [10].

Researchers at the University of North Carolina reported their experience using HT for SBBC from August 2011 to January 2016. Four of 9 patients had recurrent disease. Among these 4 patients, 2 previously received unilateral breast irradiation. Four of 9 patients received SBWBR, 3 patients received bilateral chest wall irradiation, and 1 patient each received whole breast irradiation to one side and chest wall irradiation to the other side. All patients underwent regional lymph node irradiation in diverse areas (internal mammary and/or axillary and/or supraclavicular). The prescribed dose was 50 Gy with standard fractionation or 1.25 Gy delivered twice daily for patients requiring retreatment. Eight of 9 patients received a boost dose to the tumor bed following HT. The mean dose to the heart was 20 Gy and the average V20 (percentage of the normal lungs receiving at least 20 Gy) of the lungs was 29%. Significant clinical toxicities were observed, including skin desquamation in all 9 patients, dysphagia in 5 patients, fatigue in 4 patients, and nausea and weight loss in 1 patient [11].

Ekici et al., in a study of 2 centers, analyzed the data of 14 patients who underwent bilateral breast cancer treatment with HT between January 2011 and October 2014. In their study, those with a previous history of radiation treatment of the chest wall or the breast were excluded. Six patients underwent bilateral chest wall irradiation, 7 patients underwent SBWBR, and 1 patient underwent definitive radiotherapy for inoperable disease. Among those who received bilateral conserving surgery, another boost to the tumor bed after SBWBR was provided with 8–10 Gy in 4–5 fractions. The median irradiated volume was 2070 cc^3. Median V20 to the lungs was 18.5 % and median V25 to the heart was 6%. Seventy-two percent of the patients had grade 1 acute skin toxicity, whereas 14% had grade 2 acute skin toxicity. Forty-three percent experienced grade 1 esophageal acute toxicity [32].

In our study, all 3 patients underwent bilateral breast-conserving surgery and received SBWBR with simultaneous boost to the tumor bed. Compared with the results of previous studies, irradiated volume for bilateral whole breast was relatively small (average: 1215.4 cm^3), which reflected the typically small breast size among women in Asian populations. Due to the administration of simultaneous boost, our average prescribed dose was higher than that in the literature (average: 59.73Gy). The average mean doses to the lungs, heart, and spinal cord were 11.39, 16.04, and 24.55 Gy, respectively. Furthermore, only grade 1 acute skin toxicity was observed in all patients. There was a significantly lower prevalence of acute skin toxicity when compared with previous studies. Although the number of patients was small, from our experience SBWBR with simultaneous boost and HT is well tolerated.

Conclusion

SBWBR using HT is a feasible method for treating patients with SBBC. The simultaneous boost technique should be considered when applying HT to SBWBR. Further studies and long-term follow-up are required to understand the late toxicity profile of patients receiving SBWBR with HT.

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