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Concomitant Boost Radiotherapy after Conservative Breast Surgery in Early Breast Cancer

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Abstract

Background: Radiation therapy after breast conserving surgery is a standard part of treatment for invasive breast cancer. Based on radiobiological models, it was found that shorter radiation schedules offered the promise of equivalent local control to standard radiation therapy by giving larger doses per fraction in shorter period of time. Methods: This study included 36 female patients with operable invasive stage I-II breast cancer. These patients underwent microscopic wide local excision of the primary tumor and lymph node dissection. They received adjuvant radiotherapy. The radiation dose was 40 Gy total dose in 15 fractions for whole breast and additional dose of 9 Gy in three consecutive fractions was delivered to tumour cavity simultaneously. Results: Mean age was 52 years (range: 30 - 67); most patients were of stage II disease and Grade II was the most common one. Invasive ductal carcinoma was reported in 94.4% and 72.2% of patients were hormone receptor positive. After median follow-up of 52 months, all patients were alive and ipsilateral local recurrence was reported in 1 case only. Grade IV radiation toxicity was not observed; moist desquamation was the most common acute reaction (61%) with grade III in 5.5% followed by dry desquamation in 55.6% of grade I only. Grade I erythema was recorded in 41.7% and grade II in 11%. Fibrosis was the most frequent late reaction (44.3%) with grade II in 11% followed by telengectesia then pigmentation (41.7%, 33.3% respectively). Conclusion: The regimen used in this study appears promising with acceptable acute toxicities and convenient for our patients and has the advantage of economic use of radiation facilities. However, larger number of patients and longer period of follow-up are needed for further evaluation.

Keywords

Conservative Breast Surgery, Radiotherapy, Concomitant Boost, Breast Cancer

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1. Introduction

Breast conserving surgery (BCS) is often preferred by patients as it provides improved cosmosis and decreased psychological trauma. BCS is considered as the standard of care for patients with stage I-II disease [1]. The addition of whole-breast irradiation (WBI) to BCS results in a significant reduction in the risk of death due to breast cancer and local recurrence [2] [3].

BCS consisted of resection of the primary breast tumor (lumpectomy, segmental mastectomy or wide local excision) followed by WBI with total radiation dose of 45 - 50 Gy to the entire breast over 5 - 6 weeks (1.8 - 2 Gy per fraction). In most patients, 10 - 16 Gy boost to the tumor bed is added [4].

However, 30% of patients who undergo BCS do not receive adjuvant radiotherapy (RT) [5]. These may be contributed to many issues: as long time (7 - 8 weeks) of RT, lack of transportation, poor ambulatory status of the patients, significant shortage of radiation therapy equipment and busy radiation centers [6] [7]. So the possibility of delivering adjuvant RT in a shorter period of time could help in solving this problem.

Randomized trials have proved that hypofractionated WBI is equivalent to more conventional WBI with respect to local recurrence and cosmotic outcome [8]-[10].

Simultaneous boost dose, concomitant or integrated, has been started in clinics by using 3-D conformal RT or intensity-modulated RT in order to intensify treatment [11] [12].

The purpose of this study was to evaluate toxicity (acute and late) and local disease-free survival (DFS) of a hypofractionated three weeks WBI schedule with the addition of a concomitant boost dose delivered to tumor bed once a week in patients with early breast cancer undergoes BCS and sentinel node dissection.

2. Patients and Methods

This study included 36 female patients with operable invasive stage I-II breast cancer (as defined by AJCC 2002) referred to Clinical Oncology and Nuclear Medicine department, Mansoura University Hospital in the period between January 2010 to June 2014.

Other eligibility criteria included: Female patients >18 years; underwent microscopic wide local excision of the primary tumor and lymph node dissection, no previous RT or chemotherapy and normal hematological, liver and kidney function.

18 patients underwent inferior pedicle therapeutic mammoplasty, 7 patients round block technique was done and in these all 25 patients the tumour bed was marked by clips, 8 patients lateral mammoplasty was performed and the other 3 patients just wide local excision without any plastic procedures. In these 11 patients no clips markings as the tumour bed was under the scare. Level 1 and 2 axillary dissection was done for all patients.

Exclusion criteria were: evidence of distant metastasis, presence of serious co-morbidities that could preclude RT as cardiovascular or psychiatric diseases, positive margin, and presence of active connective tissue disease. All patients had provided written informed consent before assigned to treatment, and according to the St. Gallen Consensus Conference [13] low risk patients was started RT immediately after BCS while in high risk patients; RT was started sequentially after chemotherapy.

2.1. Systemic Therapy

Patients with tumor size >1 cm or with lymph node involvement received chemotherapy. Patients with positive estrogen or progesterone receptors received hormonal therapy after end of RT and/or chemotherapy while those with HER-2 positive received trastuzumab.

2.2. Radiotherapy

The patients were planned with CT scan and CT cuts were performed in the supine position, using breast board, transferred to planning system (Precise Plan), 3D breast planning was done with two tangential fields using of 6 MV photon. CTV include whole breast tissue, CTV boost includes the tumour bed with clips inside or the area of seroma if clips not present with 5 mm margin to create PTV. Irradiation to supraclavicular L.N was done when indicated. (**Figure 1**, **Figure 2**).

The radiation dose is 40 Gy total dose in 15 fractions for whole breast and additional dose of 9 Gy in three consecutive fractions was delivered tumour cavity simultaneously.

Follow-up of the patients was carried out weekly during RT and monthly after that till 3 months after RT to

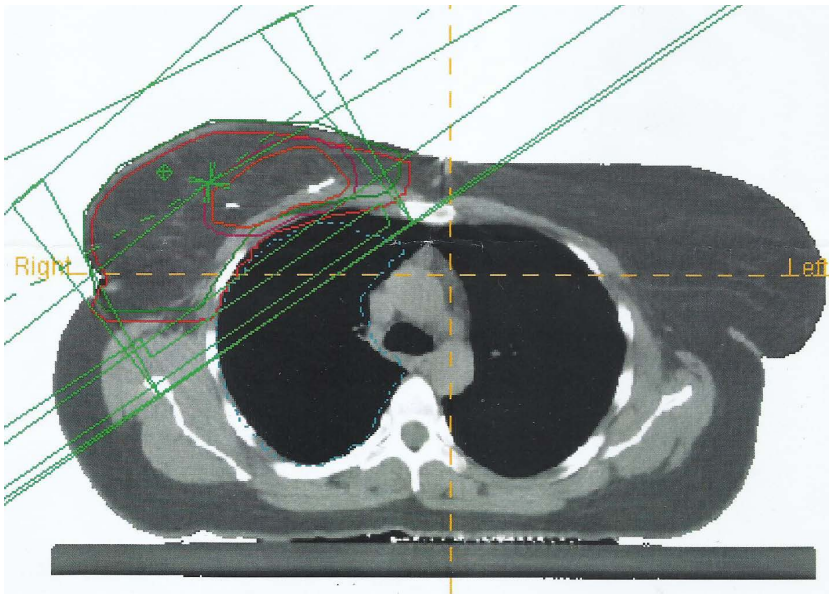

Figure 1. CTV & PTV of the breast and tumor bed with clips in the tumor bed.

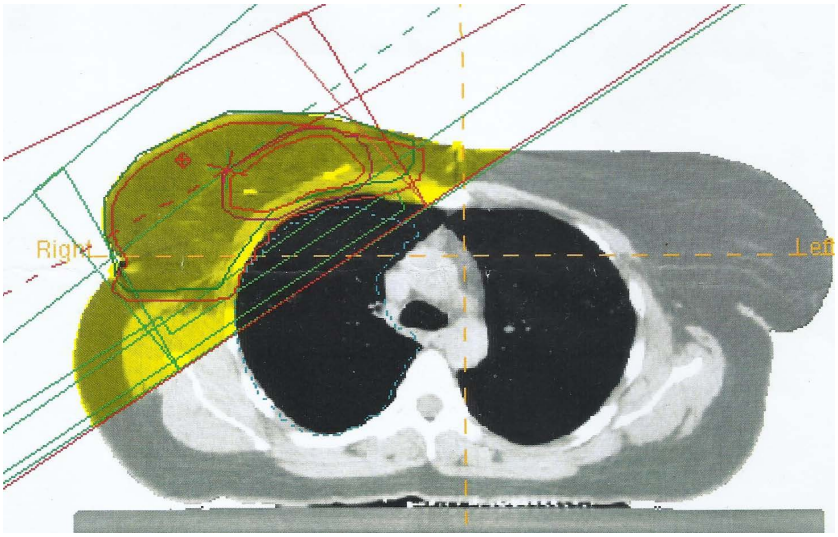

Figure 2. Two tangential fields arrangement for PTV.

evaluate acute toxicity. Then every 3 months to evaluate late toxicity or local recurrence for first year then every 6 months for 2 years then yearly. The RTOG/EORTG scoring system for radiation reactions were used to score radiation toxicity [14]. Local DFS was calculated from date of diagnosis of ipsilateral tumor recurrence either invasive or insitu carcinoma in the operated breast or overlying skin.

The primary end points were acute and late radiation reactions while the secondary end-point was ipsilateral tumor recurrence.

3. Results

Patients, tumor and treatment characteristics are given in **Table 1**. Mean age was 52 years (range; 30 - 67), most patients were of stage II disease. Grade II was the most common. Invasive ductal carcinoma was reported in 94.4% and 72.2% of patients were hormone receptor positive.

After median follow-up of 52 months; all patients were alive and ipsilateral local recurrence was reported in 1 case only.

Table 1. Patients characteristics.

Character	N	%
Age		
Mean (range)		
52 (30 - 67) years		
Stage		
I	8	22.8
II	28	77.8
Grading		
I	3	8.3
II	24	66.7
III	9	25
Histology		
Invasive ductal	34	94.4
Invasive lobular	1	2.8
Medullary	1	2.8
Hormonal status		
ER and/or PR positive	26	72.2
ER and/or PR negative	10	27.8
Chemotherapy		
Yes	30	83.3
No	6	16.3
HER-2 receptor		
Positive	8	22.2
Negative	28	77.8

Acute Radiation Reactions

As shown in **Table 2**; no grade IV acute radiation toxicity was observed. Moist desquamation was the most common one (61%) with grade III in 5.5% followed by dry desquamation in 55.6% of grade I only. Grade I erythema was recorded in 41.7% and grade II in 11%.

Table 3 showed the incidence of late radiation reactions. No grade IV toxicity and grade III telengectesia occurred in 3 patients (8.3%) only. Fibrosis was the most frequent one (44.3%) with grade II in 11% followed by telengectesia then pigmentation (41.7%, 33.3% respectively).

4. Discussion

Based on radiobiological models, it was found that shorter radiation schedules offer the promise of equivalent local control to standard radiation therapy by giving larger doses per fraction in shorter period of time [15]. Our study demonstrated local recurrence in 1 case only but it is very early to make conclusion about this parameter at this time as longer follow-up period and larger number of patients are needed.

Our study revealed reasonably good feasibility in terms of acute toxicity as no grade IV reaction was found and grade III was reported in 3.3% only which is comparable to other studies [16]-[18].

Results of retrospective studies of hypofractionated RT in early breast cancer suggest satisfactory outcomes as regard tumor control and late adverse events [19] [20].

The initial our results of late effects appears promising as no grade IV toxicity and grade III telengectesia in 8.3% and higher percentage of reactions was of grade I. Fibrosis was the most frequent occurred late event, this

Table 2. Acute radiation toxicity.

Toxicity	Grade							
	I		II		III		IV	
	N	%	N	%	N	%	N	%
Radiation pneumonitis	2	5.5	0	0	0	0	0	0
Erythema	15	41.7	4	11	0	0	0	0
Dry desquamation	20	55.6	0	0	0	0	0	0
Moist desquamation	13	36	7	19.5	2	5.5	0	0

Table 3. Late radiation toxicity.

Toxicity	Grade							
	I		II		III		IV	
	N	%	N	%	N	%	N	%
Radiation pneumonitis	2	5.5	0	0	0	0	0	0
Fibrosis	12	33.3	4	11	0	0	0	0
Pigmentation	9	25	3	8.3	0	0	0	0
Telengectasia	7	19.5	5	13.9	3	8.3	0	0
Pain	3	8.3	1	2.7	0	0	0	0

is similar to that reported by Guenzi *et al*. [21]. Ciammella *et al*. [22] and Scorsetti *et al*. [23] also concluded that 3-week hypofractionated postoperative radiotherapy with boost is safe and acute toxicity is acceptable.

5. Conclusion

The regimen used in this study appears promising with acceptable acute toxicities and convenient for our patients and has the advantage of economic use of radiation facilities as well as saving time in our busy radiotherapy units. However, larger number of patients and longer period of follow-up are needed for further evaluation.

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