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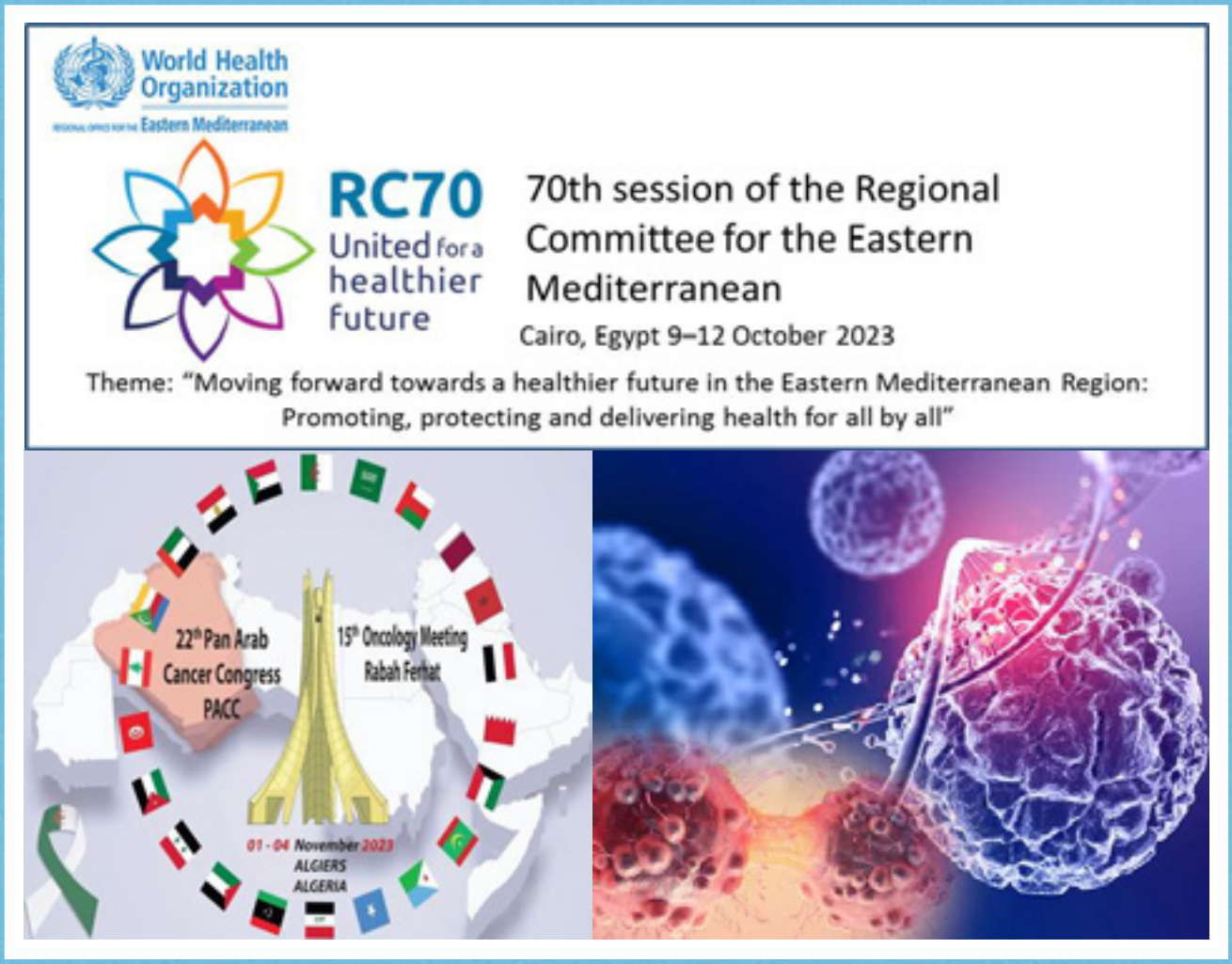

The Official Journal of the Gulf Federation For Cancer Control

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Original Article

Outcomes of Breast Intraoperative Electron Beam Radiotherapy (IOeRT) : Case Series of Single Institute Experience in Saudi Arabia

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Abstract

Introduction: 85–90% of local recurrences after breast–conserving surgery occurs within the index quadrant. Intraoperative radiotherapy may be a good alternative for eligible patients avoiding long course of adjuvant radiation.

Patients and methods: Eligible patients were early stage node negative at least 50 years at time of inclusion, unicentric less than 30mm in diameter any hormone receptor status.

21 Gy was delivered intraoperatively, biologically equivalent to 58 to 60 Gy in standard fractionation using electron beam to 90% isodose line. Cosmetic, Oncological and Patient Satisfaction Evaluation of treated Patients between March 2018 and August 2020 at the King Khalid university hospital, using the IOeRT (Mobetron®). Evaluation done at a combined clinic between surgical and radiation oncology teams at the end of the follow up period before publication.

Results: 15 female patients were evaluable with mean follow up period 33.8 months (19–48 months). Mean Age 56.4 years (50–65 years). Mean tumor size 1.213 cm. Majority of patients were T1. 2 patients showed Sentinel lymph node positive.21 Gy was delivered intraoperatively.4 Patients (26.7%) received adjuvant postoperative external beam radiation therapy (EBRT). 2 patients due to being in Caution group due to positive extensive Ductal carcinoma in situ (DCIS). External beam radiation was 40 Gy/15 fractions/3 weeks using three dimensional radiation therapy (3DCRT). Cosmetically, Apart from one patient score 9 due to presence of keloid scar formation, most patients were in range of 0–3 according to physician evaluation and Modified Hollander's score otherwise, No more than score 3 in any of the patients was detected. Oncologically, Till the time of publication no local or distant relapses was detected. As a patient experience, 100 % of patients were satisfied.

Conclusion: Breast IOERT is a convenient, safe and a valid treatment modality as an option for patients who are otherwise appropriate candidates for APBI. Proper patient selection should focus on clinicopathologic factors predictive of negative nodes and negative margins. Careful assessment of preoperative mammographic and other imaging studies for features, such as extent of calcifications, may be helpful.

Keywords: Intraoperative radiotherapy, Breast cancer, Radiation. IOeRT.

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Introduction

85–90 % of local recurrences after breast–conserving surgery occurs within the index quadrant. Intraoperative radiotherapy may be a good alternative for eligible patients avoiding long course of adjuvant radiation.

Patients and Methods

This is a retrospective cohort analysis of prospectively recorded data involving patients with early stage breast cancer who underwent Intraoperative electron beam radiotherapy (IOeRT) as an anticipated boost over the period from March 2018 to August 2020 in King Khalid University hospital, King Saud University medical city, Riyadh, Saudi Arabia after discussion in tumor board and obtaining written informed consent.

Inclusion criteria :

Parameters to identify eligible patients are as follows:

- European Society of radiotherapy and oncology (ESTRO): >50 years, invasive ductal carcinoma (IDC) / other favorable histology (IDC), T1–2 (≤3 cm), N0, any hormone receptor status, M0.
- American society for radiation oncology (ASTRO): ≥60 years, IDC, T1, N0, positive estrogen hormone receptor status, M0.

Patients were under regular follow up. Cosmetic, Oncological and Patient Satisfaction was evaluated at a combined clinic between surgical and radiation oncology teams at the end of the follow up period before publication.

From the cosmetic evaluation we used 2 scoring systems.

- **First:** A 5 grades physician evaluation scale scoring for each of the breast size, breast shape, skin color, location of nipple and areola and shape of nipple and areola. Scores of 0,1,2,3,4 for no difference, small, moderate, large and non–evaluable difference respectively.
- **Second:** *Modified Hollander scale* which evaluates the surgical scar for six parameters with score 0 or 1 if absent or present respectively. These parameters are step–off border, contour irregularities, margin separation, edge inversion, excessive distortion and overall appearance with total score 0 to 6 .

For evaluating the experience from patient perspective:

At the end of our last evaluation session we evaluated patient experience and asked them a direct question *"If there is a new patient candidate for the technique, would you recommend it for her from patient perspective or not?"*

Results

We studied 15 patients treated over the period from March 2018 to August 2020 after discussion in the tumor board and obtaining written informed consent with mean follow up period 33.8 months (Range 19–48 months).

Mean Age of patients was 56.4 years (Range 50–65 years) .All of them were females. Mean tumor size was 1.213 cm. Almost equally distributed between right and left sided breast cancer cases. After histopathological evaluation 2 (13.3%) were T1a, Most of them, 6 patients (40%), were T1b,5 patients (33.3%) were T1c and 2 patients (13.3%) were T2. All patients were clinically and radiologically node negative but 2 patients showed Sentinel lymph node positive.

21 Gy was delivered intraoperatively, biologically equivalent to 58 to 60 Gy in standard fractionation. Electron beam 9 or 12 MeV (Figure 2) was used and mean cone size of 47.69 mm (Range 35–60) (Figure 1) bolus of 5 mm thickness was used in 2 patients (13.3%) cases. 2 patients (13.3%) cases showed postoperative to be HER2 overexpressing .

4 Patients (26.7%) received adjuvant postoperative external beam radiation therapy (EBRT). 2 patients due to being in Caution group due to positive extensive Ductal carcinoma in situ (DCIS). External beam radiation was 40 Gy/15 fractions / 3 weeks using three dimensional radiation therapy (3DCRT).

Till the time of publication no local or distant relapses was detected.

From the cosmetic evaluation we used 2 scoring systems

First: A 5 grades scoring for each of the breast size, breast shape, skin color, location of nipple and areola and shape of nipple and areola. Scores of 0,1,2,3,4 for no difference, small, moderate, large and non–evaluable difference respectively.

Apart from one outlier value of 9 due to presence of kelid scar formation, most patients were in range of 0–3.

Second: *Modified Hollander scale* which evaluates the surgical scar for six parameters with score 0 or 1 if absent or present respectively. These parameters are step–off border, contour irregularities, margin separation, edge inversion, excessive distortion and overall appearance with total score 0 to 6. No more than score 3 in any of the patients was detected

Age	Mean	56.4
	Median	**56**
	Mode	**52**
	Range	**50–65**
Follow up period	Mean 33.8	Range (19–48 months)
Sex	15 females	
Radiation Dose and Technique		
Dose	21 Gy to 90 % isodose line	
Beam Energy	9 or 12 Mev	
Cone Size	47.69 mm	Range (35–60)
Bolus 5 mm	2 (13.3 %)	
Caution group patients	2	
External beam radiation	4	2 positive nodes and 2 due to falling in caution group
Adjuvant Chemotherapy + Trastuzumab	2	13.3%
Histopathological findings		
Tumor size	T1a	2 (13.3%)
	T1B	6 (40%)
	T1c	5 (33.3%)
	T2	2 (13.3%)
Node positive On (pathological paraffin blocks)	N1mi	2 (13.3%)
Average tumor size	1.213 cm	0.3–2.1 cm
Laterality	Right	7 (46.7%)
	Left	8 (44.4%)
HER2 overexpressing	2	
Bilateral cases	1	Metachronous with 10 years interval
Double malignancy	1	Synchronous T3 N1 colon cancer
Late Complications and fibrosis / cosmetic outcome		
Physician evaluation score	Apart from one outlier value of 9 due to presence of kelid scar formation , most patients were in range of 0=3	
Modified Hollander Score	None more than score 3	
Oncological Outcome		
DFS	No relapses was detected	
Patient Experience		
100 % of patients do recommend it for candidate patients if they were asked to give their recommendation		

Table 1: Results

King Saud University Medical City
Radiation Oncology
Medical Physics
IOERT Dose Calculation & Treatment Record
Mobetron 2000, SN 51
Date

Patient Name:		Patient Number	
Treatment Site	RT BREAST	Tumor Type	
Radiation Oncologist	Dr. A.ALSUHABANI	Surgeon	Prof. A.ALSAF
Medical Physicist	Dr. GHOZLAN/Dr. Fisal	Nurse in Charge	

Parameters	Field 1	Field 2	Field 3
Dose (cGy), **D**	2100		
Treatment Depth (mm)	29.5		
Cone Diameter (mm)	60		
Cone Bevel angel (deg)	0		
Gantry Tillt (deg)			
Head Tilt (deg)			
Head Vertical Position			
Longitudinal Position			
Isodose Line (%), **L**	0.9		
Bolus (mm)			
Total Depth (mm)	29.5	0	0
Cone Factor, **F**	1.41		
Output (cGy/MU), **Op**	1.035		
Air Gap, G (mm)	0	0	0
Gap Factor, **GF**	1	1	1
Beam energy	9		
Calculated MU's	1598.885348	#DIV/0!	#DIV/0!
Delivered MU's			
Remainig MU's			
Lead Sheet Removed			

Gap Factor equation: GF = [500/(500+G)]^2

MU calculation eqnation: MU's = D / (F * GF * L * Op)

Radiation Oncologist	
Medical Physicist	
Medical Physicist (2nd Check)	

Figure 1: Calculations of one of the cases treat

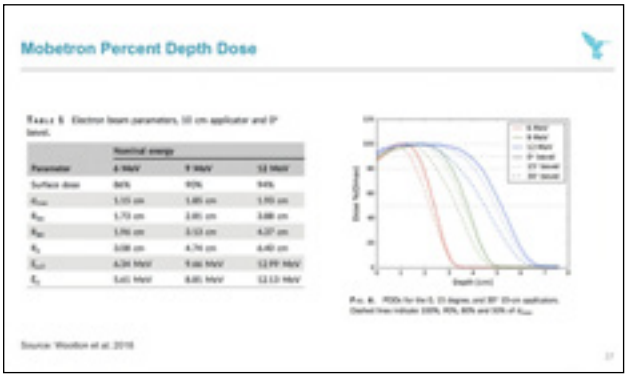

Figure 2: Percent Depth Dose of Machine us

Discussion:

Breast–conserving surgery followed by radiotherapy is the standard treatment option for most women with clinical stage I/II invasive breast cancer[1, 2].

Veronesi et al. (2001) found that 85% of recurrence after Breast Conservative Surgery (BCS) occurs in the scar area and they proposed that whether the whole breast radiotherapy after BCS could be replaced by partial radiotherapy only around the tumor bed[2]. The remaining 15% of relapses occurred in other quadrants with a

likelihood similar to the contralateral breast and therefore must be considered as new primary ipsilateral carcinomas[3]. This is the rationale for partial breast irradiation (PBI) leading to reduction of radiation fields from the whole organ to the involved portion of the breast[4, 5].

Radiobiologically, The RBE of 50 kV electronic brachytherapy sources has been estimated to exceed biological effectiveness by 40–50% over Co60 or Ir192[6]. In the example of IORT for breast cancer, higher RBE for low–energy X–rays may result in higher tumor control rates in the breast tissue in closest proximity to the surgical excision bed and effectively eliminating the "marginal miss". In addition, cell culture data suggest that the RBE decreased at increasing distance, potentially reducing the effective dose to adjacent critical structures including heart and lung[7].

As a dose homogeneity, IOeRT delivers the most homogeneous dose distribution compared to interstitial brachytherapy, Mammosite® (an inflatable balloon with a central high–dose–rate source), Intabeam® (a miniature orthovoltage system), and linac–based electron radiotherapy (IOeRT) when comparing simplified geometric figures[8].

Clinically, intraoperative radiation therapy (IORT) as a modality of partial breast irradiation may be an alternative to whole breast irradiation (WBI) for selected patients with early–stage breast cancer according to The randomized phase III TARGiT trial and ELIOT studies[3, 9].

These two published large prospective randomized controlled trials comparing post lumpectomy standard whole breast irradiation to IORT, one using electrons (ELIOT study)[3], and one using 50 kV photons (TARGIT–A study)[9].

In an Austrian study, Immediate IORT boost yielded excellent local control figures in this prospective investigation and appears to be superior to conventional postoperative boost in a short–term follow–up[10].

The randomized phase III TARGiT trial and ELIOT studies gives the standards for selection criteria for optimal breast IORT candidates and provide the first evidence of outcomes and toxicity when using these techniques. Patient selection is of paramount importance when recommending IORT, as the final pathology is not available at the time of treatment, so in order to avoid the potential use of subsequent whole breast irradiation, careful pre–operative, and intraoperative assessment is mandatory so that the risk of high–risk features such as positive margins or positive sentinel nodes are minimized .

The most important benefit of IORT for a woman with breast cancer is that it allows her to complete her entire local treatment at the time of her operation[11], with lower toxicity being a safe method for breast conservation strategy, avoids the long period of postoperative radiotherapy, reduces the cost of radiotherapy and reducing radiation to normal tissues and organs. Moreover, the daily stress that may be cause of depression during the long external radiotherapy course is solved[12].

A major advantage of an immediate boost during surgery is avoiding artifact by seroma that may enlarge the volume at risk by spherical distension resulting in larger treated volumes and hence increased risk of late effects[13].

Moreover, direct visualization of the target tissue ensuring treatment of the high–risk tissue and eliminating the risk of marginal miss, reducing omission of radiation and the selection of mastectomy for women without access to a radiotherapy facility or unable to undergo several weeks of daily radiation. So, it has radiobiological and clinical advantage[14]. Additional advantage that there is no delay in administering RT in cases that need adjuvant chemotherapy. There is some evidence that the delay of radiotherapy increases the risk of local recurrences, beside lack of advantage to giving Radiation before adjuvant chemotherapy[15, 16].

A delay in delivery of radiotherapy either because of long waiting lists or because chemotherapy is given first, could jeopardize its effectiveness[17].

The portion of the breast (CTV, Clinical Target Volume) that needs to be irradiated is generally an area of 4 to 6 cm in diameter. This field size allows to keep a safe margin around the tumor bed of at least 1–1.5 cm[3]. This goes with our data of the mean applicator size of 47.69 mm Range (35–60).

Usually, peak hazard of local recurrence has passes by year 4 according to TARGIT–A trial[9]. Till time of publication, no local or distant relapses was detected in any patient.

Conclusion

Breast IOERT is a well–established evidence based partial breast irradiation modality as an option for patients who are otherwise appropriate candidates for APBI. Patient selection should focus on clinicopathologic factors predictive of negative nodes and negative margins. Careful assessment of preoperative mammographic and other imaging studies for features, such as extent of calcifications, may be helpful.

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None. Fully used facilities of King Khalid University hospital.

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