REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY 22 (2017) 277–283

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/rpor

Original research article

Adjuvant intraoperative radiotherapy for selected breast cancers in previously irradiated women: Evidence for excellent feasibility and favorable outcomes

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ARTICLE INFO

Article history:
Received 15 May 2016
Received in revised form
14 October 2016
Accepted 25 February 2017

Keywords:
Breast cancer
Reirradiation
Intraoperative radiotherapy

ABSTRACT

Background: The present report provides preliminary outcomes with intraoperative radiotherapy delivered to women with breast cancer included in a re-irradiation program.
Materials and methods: From October 2010 to April 2014, thirty women were included in a re-irradiation protocol by exploiting IORT technique. The median time between the two irradiations was 10 years (range 3–50). All patients underwent conservative surgery, sentinel lymph node excision and IORT with electron beam delivered by a mobile linear accelerator. Primary endpoint was esthetic result and consequential/late toxicity; secondary endpoints were local control (LC), disease free survival (DFS) and overall survival (OS).
Results: With a median follow up of 47 months (range 10–78), we analyzed 29 patients (1 lost at follow up). Twenty-seven patients (90%) had presented breast cancer local relapse or a new primary cancer in the same breast after a previous conservative surgery plus radiation treatment; three patients (10%) had previously received irradiation with mantle field for Hodgkin Lymphoma. Esthetic result was excellent in 3 pts (10%), good in 12 pts (41%), fair in 8 pts (28%) and poor in 6 pts (21%). 12 (41%) patients showed subcutaneous fibrosis at the last follow-up. LC, DFS and OS at five years was 92.3%, 86.3% and 91.2%, respectively.

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http://dx.doi.org/10.1016/j.rpor.2017.02.009

Conclusion: Although we analyzed a small number of patients, our results are satisfactory and this approach is feasible even if it could not be considered the standard treatment. Further clinical trials exploring IORT are needed to identify possible subgroups of patients that might be suitable for this type of approach.

1. Background

Breast conservative surgery and adjuvant whole breast radiation therapy are considered the standard care for early breast cancer (BC). Nevertheless, breast relapse may occur in a small proportion of patients.[1] A significantly greater risk of developing breast cancer (BC), compared to the general population, has been demonstrated in women treated with chest radiotherapy (RT) at a younger age for Hodgkin lymphoma (HD) or other neoplasms.[2] In all the clinical situations where radiotherapy was already delivered on site and a new irradiation may be strongly correlated with severe late effects, the standard approach is mastectomy alone that results in a loco-regional control rate up to 90%.[3,4] This radical approach is often not well accepted by patients because of the emotional and physical distress related to mutilating surgery. A novel therapeutic option is treating these patients after re-resection of the recurrent tumor with partial breast irradiation (PBI), assuming that re-irradiation to a limited volume will be effective with limited side effects. Intraoperative radiotherapy (IORT) is one modality of these PBI options which allows to deliver high doses to a small area where microscopic tumor cells may be left after the conservative surgery. The present report provides preliminary favorable outcomes with intraoperative radiotherapy (IORT) delivered to a series of women with breast cancer included in a re-irradiation program.

2. Materials and methods

From October 2010 to April 2014 thirty women affected by early breast cancer were included in a re-irradiation protocol by exploiting IORT technique. All the women had already received radiation therapy for other neoplasms, patients with previous breast cancer received 50 Gy in 25 fraction followed by a sequential boost of 10 Gy in 5 fractions and patients with previous HD, 40 Gy in 22 fractions (median dose: 50 Gy, range: 40–60 Gy); as regard systemic therapy, if indicated, patients received CMF or ABVD based chemotherapy for breast cancer or HD, respectively. The median age at first cancer diagnosis was 57 years (range 24–74) and 68 years (range 48–82) at the second cancer occurrence. In 5 breast cancer patients, recurrence occurred within 5 years since first radiotherapy. The median time between the two irradiations was 10 years (range 3–50). Seventeen patients (57%) were affected by right and thirteen (43%) by left breast disease, all of which but one were postmenopausal at second diagnosis. At the time of second diagnosis, the majority of the tumors were classified as invasive ductal carcinoma (21 patients – 70%), lobular carcinoma (3 patients – 10%), mucinous carcinoma (1 patient 3.3%), clear cell carcinoma (1 patient 3.3%) and DCIS (4 patients – 13.4%); twelve pts (67%) had the same histology of the first tumor. All histology had been included, also lobular carcinoma and DCIS because the patients refused standard treatment (mastectomy) and, following ASTRO guidelines,[5] accelerated partial breast irradiation (aPBI) may be considered cautionary in this group. In seventeen patients (57%), the second cancer was in the same quadrant as in the previous surgery. Axillary lymph nodes metastasis was confirmed in four patients (13%): 2 patients underwent lymph node dissection and one of them also, subsequent node radiotherapy (40 Gy in 16 fractions), in the remaining 2 patients no other additional procedures had been done as micrometastasis in only one node was detected. Characteristics of patients treated were presented in Table 1. Tumors were classified according to molecular characteristics as shown in Table 2.

Table 1 – Patients' characteristics at second diagnosis.

Features	No	%
Age (yrs)		
<50	1	3
50–59	3	10
>60	26	87
Histology		
Ductal ca	21	70
DCIS	4	13.4
Lobular ca	3	10
Mucinous	1	3.3
Clear cell carcinoma	1	3.3
Tumor size (cm)		
<0.5	4	13
0.5–1	9	30
1–2	13	43
Not evaluable	4	13
Surgical margins		
Positive	2	7
Close	3	10
Negative	24	80
Not evaluated	1	3
Grading		
G1	3	10
G2	24	80
G3	2	7
Not evaluable	1	3

2.1. *Intraoperative radiotherapy*

All patients refused mastectomy, despite being informed that this was considered the treatment of choice. Karnofsky index > 80%; signs of multicentric invasive growth pattern and distant metastasis were considered exclusion criteria for the