European Journal of Radiology 79 (2011) e7–e10

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Mammography findings following electron intraoperative radiotherapy or external radiotherapy for breast cancer treatment

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ARTICLE INFO

Article history:
Received 17 June 2009
Received in revised form
10 November 2009
Accepted 11 November 2009

Keywords:
Breast cancer
Breast conserving surgery
Mammography
ELIOT
RT
Radiotherapy

ABSTRACT

Radiotherapy following breast cancer conserving surgery decreases the risks of local recurrence. Because 85% of breast cancers relapse in or around the surgical bed there has been some debate on the need for irradiating the whole breast. Electron intraoperative radiotherapy (ELIOT) has been used as a viable alternative for conventional external radiotherapy (RT). While the former requires a single dose of 21 Gy in the tumoral bed, the latter requires 5–6 weeks of irradiation with a total dose of 50 Gy and a boost of 10 Gy that irradiates the surgical bed. Herein, we investigated whether any significant differences exist between the mammography findings obtained from patients submitted to one of the two techniques. Two groups of 30 patients each were included in this study. All patients had mammographies taken at 12 and 24 months after finishing treatment. The mammography findings evaluated were: cutaneous thickening (>2 mm), architectural distortion secondary to fibrosis, edema, calcifications (both benign and malignant), and fat necrosis. For all variables studied, there was no statistical difference between the two groups. This indicates that the mammography findings obtained in either 12- or 24-month follow-up periods after breast cancer conserving surgery are similar, regardless of which of the two radiotherapy techniques (ELIOT or RT) is employed as a treatment for breast cancer.

1. Introduction

Breast conserving surgery is now a current practice in patients with early stages of breast cancer. Studies have shown that radiotherapy following breast conserving surgery decreases the risks of local recurrence. However, because 85% of breast cancers relapse occur in or around the surgical bed there has been some debate on the need for irradiating the whole breast [1,2]. Electron intraoperative radiotherapy (ELIOT) has been used as a viable alternative for conventional external radiotherapy (RT). While the former requires a single dose of 21 Gy in the tumoral bed, performed during the conservative breast surgery [3] the latter requires 5–6 weeks of irradiation with a total dose of 50 Gy and a boost of 10 Gy that irradiates the surgical bed [4].

The mammography findings that are obtained after performing conservative surgery with RT have been widely described. Conversely, only one study has shown the mammography and echography changes that are induced by ELIOT [5].

To investigate whether any significant differences exist between the mammography findings obtained with the two techniques, we compared the mammography changes of a series of patients submitted to RT with the changes observed in patients submitted to ELIOT.

2. Materials and methods

Our study was done between January 2004 and December 2007 at the Serviço de Mastologia e Radiologia do Hospital São Lucas da Pontifícia Universidade Católica de Porto Alegre, Rio Grande do Sul, Brazil. All 60 patients signed the consent form; the study was approved by the IRBs of the two institutions involved with the study (Hospital São Lucas de Porto Alegre and Instituto de Radiologia do Hospital das Clínicas da Universidade de São Paulo).

Patients were selected according to the following criteria: be at least 45 years old, have a single tumor smaller than 3 cm according to the clinical, mammography, and echography

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0720-048X/$ – see front matter © 2010 Published by Elsevier Ireland Ltd.
doi:10.1016/j.ejrad.2009.11.009

Table 1
Patients characteristics.

Patients	RT ($n = 30$)		ELIOT ($n = 30$)	
Age	54.33 ± 8.79 (45.0–52.5–76.0)		64.13 ± 8.88 (47.0–63.0–80.0)	
Tumor diameter (mm)	10–28 (15.5)		3–29 (14.1)	
Tumor location				
Lower lateral quadrant	0	0.0%	4	13.3%
Lower medial quadrant	2	6.7%	2	6.7%
Upper lateral quadrant	19	63.3%	8	26.7%
Upper medial quadrant	6	20.0%	2	6.7%
Junction of lateral quadrants	1	3.3%	6	20.0%
Junction of lower quadrants	0	0.0%	2	6.7%
Junction of upper quadrants	2	6.7%	5	16.7%
Retroareolar	0	0.0%	1	3.3%
Histological type				
Invasive ductal carcinoma	21	70.0%	25	83.3%
Invasive lobular carcinoma	3	10,0%	3	10.0%
Invasive ductal + lobular carcinoma	2	6,6%	0	0.0%
Invasive carcinoma other subtype	1	3,3%	1	3,3%
Ductal carcinoma in situ	3	10,0%	1	3,3%

RT = conventional external radiotherapy; ELIOT = intraoperative electron radiation; n = sample size.

exams available, and have a follow-up period of at least 12–24 months.

Two groups of 30 patients each were included in this study and each group was submitted to one of the two techniques, ELIOT or RT. Patients submitted to ELIOT were on average 64.13 years old, and 83.33% were at T1 stage. The most frequent histological type was invasive ductal carcinoma (in 83.3% of the patients), mostly (25 patients) located in the lateral upper quadrant. Average age of patients submitted to RT was 54.33 years old and of those 63.33% were at T1. Invasive ductal carcinoma was also the most frequent type in this group of patients (found in 76.6% of the patients) (Table 1).

ELIOT was performed using a conventional Philips SL75/10 linear accelerator [Philips, England]. In this study, we applied as treatment a rate of 360 cGy/min. The total radiotherapy dose applied was 21 Gy, with the necessary energy varying between 8 and 10 MeV, according to the thickness of the mammary gland.

All patients in the study had mammographies taken at 12 and 24 months after finishing treatment. All mammographies were taken in the radiology department at the Hospital São Lucas de Porto Alegre, with an analog mammography system (Senographic 800T, General Electric Medical System/Instrumentarium, Tuusula, Finland), during routine exams (craniocaudal and medial lateral oblique). Additional mammography views (compression and magnification) were taken when necessary.

Mammographies from patients in the two groups were evaluated blindly by two radiologists with extensive experience (10 and 13 years) in radiological breast imaging. The level of concordance between readings was calculated using the Kappa and Kendall coefficient. The level of concordance approached 1 for all variables, showing that no significant differences were detected between the two physicians. Thus, we only considered in our analysis the readings done by one of the specialized physicians.

The mammography findings evaluated in this study were: skin thickening (the normal skin thickness is 2 mm; following radiation therapy it may increase to 1 cm [6]); architectural distortion secondary to fibrosis; edema (diffuse increased density and trabecular thickening [7,8] when compared to the other breast); calcifications (both benign and malignant); and fat necrosis (oil cyst either associated or not associated to calcifications).

To compare the two groups and the findings obtained for each variable during the two follow-up periods (12 and 24 months) we used chi-square or the Fisher's exact test, and calculated the odds ratio considering the respective confidence intervals.

3. Results

In the ELIOT group, 60% of the patients presented skin thickening in the 12-month follow-up and 33% at 24 months. As for the RT group, the presence of skin thickening lowered from 40% in the 12-month follow-up to 13% at 24 months (Table 2). No difference was observed in the presence of architectural distortion in either 12- or 24-month follow-up periods, with fewer patients showing distortions (19 patients against 23) in the 24-month follow-up period. The presence of edema in the 12-month follow-up slightly decreased in the two groups in the 24-month follow-up (57–40% in the RT group and 37–27% in the ELIOT group), but no significant difference was observed (Table 3). Fat necrosis, with or without calcification, was more pronounced in the ELIOT group in the 12-

Table 2
Presence of cutaneous thickening in the two groups after 12 and 24 months of treatment.

Cutaneous thickness	Group		p	OR	CI 95% for OR
	RT ($n = 30$)	ELIOT ($n = 30$)			
12 months					
No	18	12	0.196	2.250	[0.801;6.321]
Yes	12	18			
24 months					
No	26	20	0.125	3.250	[0.888;11.899]
Yes	4	10			

RT = conventional external radiotherapy; ELIOT = intraoperative electron radiation; n = sample size; $p \leq 0.05$; OR = odds ratio; CI = confidence interval of 95% for odds ratio.

Table 3
Presence of edema in the two groups after 12 and 24 months of treatment.

Edema	Group		p	OR	CI 95% for OR
	RT ($n = 30$)	ELIOT ($n = 30$)			
12 months					
No	13	19	0.195	0.443	[0.157; 1.247]
Yes	17	11			
24 months					
No	18	22	0.412	0.545	[0.183;1.623]
Yes	12	8			

RT = conventional external radiotherapy; ELIOT = intraoperative electron radiation; n = sample size; $p \leq 0.05$; OR = odds ratio; CI = confidence interval of 95% for odds ratio.

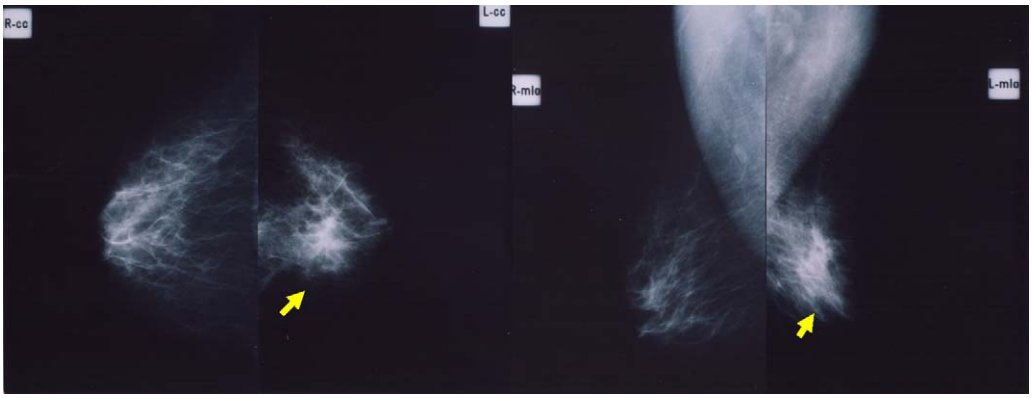

Fig. 1. Presence of edema (yellow arrows) during the 12-month follow-up period.

month follow-up (20% of ELIOT patients against 7% of RT patients) and in the 24-month follow-up (33.3% of ELIOT patients against 13.3% of RT patients) (Fig. 1A and B). Cutaneous retraction was more pronounced in ELIOT patients, especially in the 24-month follow-up. Interestingly, the cutaneous retraction showed opposite behaviors depending on the treatment. While it decreased from 37% (12-month follow-up) to 23% (24-month follow-up) in patients submitted to RT, it increased from 43% to 47% in those submitted to ELIOT, during the same follow-up period. No statistic significance was observed, though.

Benign calcifications were more common in the ELIOT group (60% in the 24-month follow-up against 47% in the RT group during the same period). A patient in the RT group presented suspicious calcification in the 24-month follow-up. The biopsy revealed a

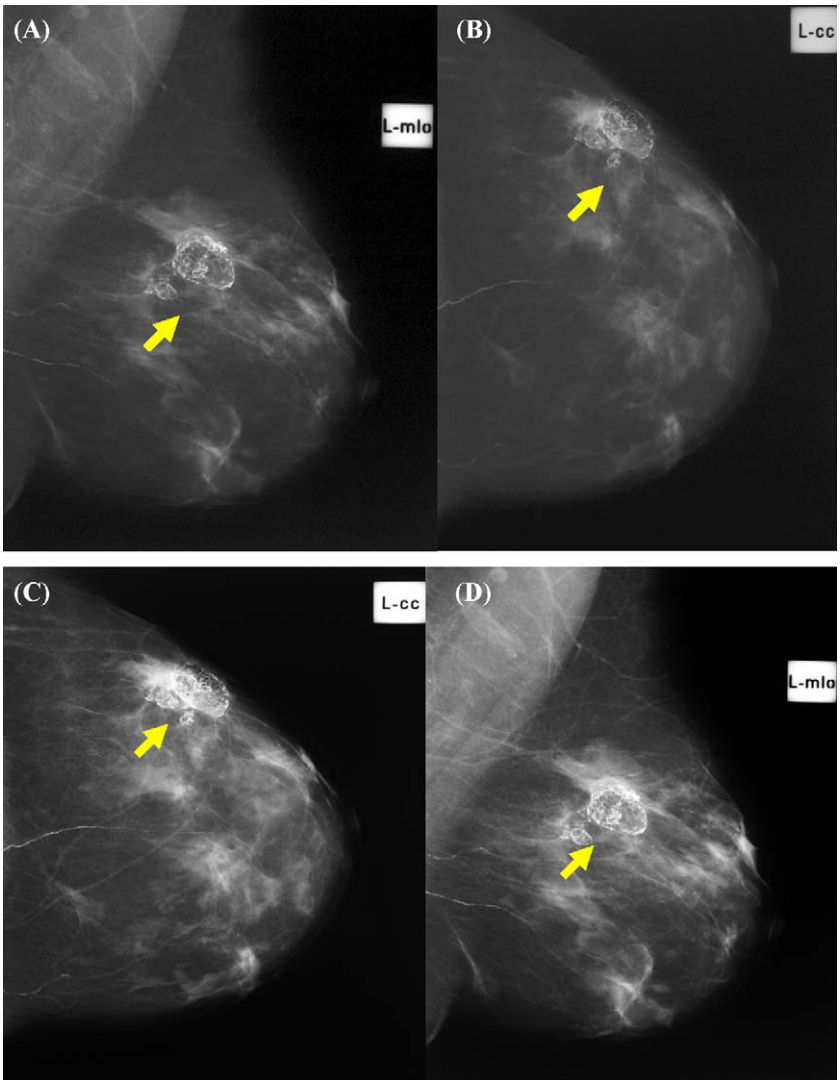

Fig. 2. Presence of fat necrosis (yellow arrows) during the 12-month (A and B) and 24-month (C and D) follow-up periods.

relapse in the surgical bed and she was submitted to mastectomy. For all variables studied, there was no statistical difference between the two groups (Fig. 2).

4. Discussion

The most common finding on post-treatment mammography of women who have undergone breast irradiation is the thickening of the skin, which may be localized or diffuse, and may be secondary to an inflammation in response to radiation [7]. Skin thickness contributes to an impression of diffuse increase in density of the treated breast mammograms [9]. Over time, skin thickness returns from 26% [7,9] to 60% [9]. In our study with 12-month follow-up the skin thickening was found in only 40% of the patients in the RT group and in 60% in the ELIOT group. With the 24-month follow up, these values dropped to 13.3% and 33.3%, respectively. These findings are similar to those of Della Sala et al. [5]. Architectural distortion in the 12-month follow-up period was found in 83.3% of the patients in the ELIOT group and in 76.7% of the patients in the RT group. At the 24-month follow-up the presence of architectural distortion was not only lower (73.3% and 63.3%, respectively) but also less severe. The architectural distortion secondary to fibrosis is located in the surgical bed and is characterized by the absence of a central mass, a changing appearance on different projections [6], and thick, curvilinear spicules [8]. The presence of spiculated lesions early after surgery is suggestive of a scar, as a tumoral relapse is not commonly seen in the 12 or 24 months following surgery [7].

In our study, edema secondary to a mammography was found in 36.6% of the patients submitted to ELIOT, during the 12-month follow-up period, and decreased to 26.7% after 24 months. In patients in the RT group, these findings were of 46.6% and 40%, respectively. This type of edema is formed by an increased density of the parenchyma, which is prone to decrease over time [11]. Edema that increases after stabilization is a suspicious finding [8].

Another finding related to breast conserving surgery is fat necrosis. We found fat necrosis in 6.7% of the patients in the RT group, and in 20% in the ELIOT group, at the 12-month follow-up. These values increased to 13.3% and 33.3%, respectively, at 24 months. In another study [5], fat necrosis was found in 4.4% of the RT patients and in 26% of the ELIOT patients in the same follow-up periods as the ones in our study. In the same study it was also observed that patients submitted to ELIOT presented more pronounced architectural distortions and edemas, if compared to patients in the RT group. The authors applied a higher radiotherapy dose in most patients submitted to ELIOT. Of the 45 patients in their study five received 20 Gy, 20 received 22 Gy, and 20 received 24 Gy. In our study we applied an equal dose of 21 Gy. This may explain the difference, although not significant, observed between the two studies, for the presence of fat necrosis.

In our study we did not find any significant difference for any of the variables analyzed, in the mammography findings obtained during the two follow-up periods considered (12 and 24 months) in the two groups of patients (ELIOT and RT).

The ELIOT technique offers many benefits, as it requires one single irradiation of 21 Gy that is done while the breast conserving surgery is being performed. The benefit of receiving one single irradiation dose in one single session, instead of receiving a weekly external radiation dose for 5 or 6 weeks, has a positive impact in the patient's quality of life, besides representing lower costs. Additionally, the single-dose ELIOT does not interfere with the systemic treatment [4].

5. Conclusions

Our study indicates that the mammography findings obtained in either 12- or 24-month follow-up periods after breast conserving surgery are similar, regardless of which of the two radiotherapy techniques (ELIOT or RT) is employed as a treatment for breast cancer. Therefore, we suggest that that the mammographic follow up should be the same in both cases.

Conflict of interest

This is an original study that has not been published either in part or as a whole, and that we believe will be of great interest to any one interested in exchanging information on the use of radiological imaging combined with interventional techniques, for early breast cancer. This article is not under consideration for publication elsewhere. All authors had full participation in the study and take full responsibility on the information here presented.

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