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Original article

Immediate breast reconstruction with prostheses after conservative treatment plus intraoperative radiotherapy. Long term esthetic and oncological outcomes

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ABSTRACT

Electron intraoperative radiotherapy (ELIOT) has been introduced for breast conservative treatment (BCT) with promising oncological outcome. Thus, immediate breast reconstruction with prosthesis after BCT became possible due to minimal radiation effect on local tissue from ELIOT. We reported oncological and esthetical results of 29 BCT patients who had immediate implant reconstruction plus 21 Gy-ELIOT as the sole radiation treatment. All patients had prosthesis in ipsilateral breast and had simultaneous contralateral augmentation for symmetrical procedure. The average age was 52.3 years. There were stage Ia thirteen cases, stage Ib seven cases, stage IIa six cases and stage IIIb one case and two cases of intraepithelial neoplasia. From 54.2 (36–88) months follow up, the capsular contracture grading in the reconstructed breast from ELIOT-side is comparable with non-irradiated contralateral side. There was one patient who developed local recurrence (LR) and later on dead with breast related event (LR = 0.76% per year). There was no primary ipsilateral carcinomas and distant metastasis.

Background

Breast conservative treatment (BCT) has been verified as a gold standard treatment for patients with small breast tumors.[1–3] Regardless to the additional axillary procedure, BCT itself has to be conventionally followed by external radiation therapy, which can cause acute and late local side effects. Therefore, implant related reconstruction in this group of patients remains controversial in view of unfavorable outcome, higher complications and capsular contraction rate.[4–11]

The oncological benefit and safety of ELIOT have been described with promising results.[12–19] Since 1999, more than 2000 patients had received electron intraoperative radiotherapy (ELIOT) at European Institute of Oncology (EIO) which broadens its clinical applications.[20–25] In 2006, Rietjens et al., reported a satisfactory short term result at 6 months after implant reconstruction for BCT plus ELIOT.[26] With an electron linear accelerator, the radiation dose is delivered only to the glandular tissue around the tumor bed, therefore avoiding the radiation of skin, subcutaneous tissue and pectoral muscle and overcoming the adverse radiation effects of external conventional radiotherapy.

In this study, we inclusively and systemically described the long term outcome of BCT with full-dose 21 Gy-ELIOT plus immediate implant reconstruction procedures. Hence, the advantage is the possibility of implement of implant reconstruction for BCT and avoiding unsatisfactory results due to conventional external radiation while maintaining the maximum oncologic benefit of ELIOT to these specific patients.

Methods

We enrolled unilateral breast cancer candidates for BCT and received 21 Gy-ELIOT as the sole radiation treatment. Eligibility criteria included patients aged between 35 and 75 years, affected by a unicentric breast invasive carcinoma with a maximum diameter of 25 mm. Exclusion criteria were locally advanced tumors (T3 and T4), the presence of a contralateral synchronous or metachronous tumor, non invasive neoplasia (including Paget disease), other breast malignancies apart from carcinoma, multifocality or multicentricity of the disease, previous surgical biopsy and previous oncological history. At the beginning of our experience, we enrolled all patients within a trial protocol to access the

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oncological safety of the procedure. Afterward, we became familiar with the procedure and we achieved the promising preliminary results so we recruited also patients with in situ cancer lesion. A breast thickness of more than 3 cm from the skin to the tumor is considered a technical contraindication, since it is impossible to deliver energy of more than 9 MeV with the present ELIOT machines. No particular tumor locations are excluded, but the close proximity of the tumor to the skin, pectoral major muscle and axillary region are considered relative contraindications.[21] Neither previous preoperative radiation nor post operative radiotherapy was given. All of the study populations were immediately reconstructed with prosthesis related procedures. The prosthetic associated complications and overall esthetic score were systematically evaluated.

Every patient has given inform consent and this study was conducted under the institutional review board approval. All patients who underwent simultaneous contralateral breast augmentation or prosthesis substitution had proposed for the procedure by themselves. We systemically explained the pros and cons of each procedure to them individually also with the breast surgeons and the medical oncologists.

From September 2003 to September 2007, we recruited 29 patients who were planned for BCT and ELIOT with prosthesis reconstruction. Their average age was 52.3(37–66) years. There were twenty patients with bilateral prosthetic augmentation and nine patients with bilateral prosthetic substitution due to previous cosmetic augmentation. In the latter group, the prosthesis which they have been inserted subglandularly for the cosmetic augmentation was removed and we inserted new prosthesis submuscularly for breast reconstruction and contralateral symmetrical procedure. In this group the previous cosmetic breast augmentation was performed in an average of 14.2 (3–30) months before these oncoplastic procedures. The textured silicone cohesive gel implants were used in all cases.

The pathological T staging of tumors were; pT1 twenty-two cases, pT2 five cases and pTis 2 cases (one Ductal Intraepithelial Neoplasia and one Lobular Intraepithelial Neoplasia). The pathological N staging of tumors were pN0 twenty cases, pN1 eight cases and pN3 1 case. For axillary procedures, there were twenty-three patients who had sentinel node dissection and six patients who had axillary node dissection. None of them received neoadjuvant therapy but six patients received adjuvant chemotherapy.

The average volumes of prosthesis were 195.8 (100–335) cc. and 177.0 (80–325) cc. for the ipsilateral-ELIOT and the contralateral healthy breasts, respectively. In average, there was an 18.8 cc implant volume difference between the healthy and the disease breasts where quadrantectomy was performed.

The patient characteristics are demonstrated in Table 1.

Surgical technique

The quadrantectomy was performed through a periareolar incision or radial incision, and axillary procedure was performed either through the same incision or a separate one. The tumor was confirmed with histological free margins and the nodal procedure was up to the absence or presence of nodal metastasis.

The glandular tissue nearby the defect was undermined over the pectoralis major muscle and a lead disk and aluminum disk were positioned on the surface of the pectoralis major muscle to prevent muscular and chest wall irradiation. Before delivering ELIOT, the glandular flaps were temporarily approximated to close the quadrantectomy defect (clinical target of irradiation) and the skin was

Table 1
Patient characteristics.

Patient code	Age	FU (month)	Pathological TMN staging[a]			Location		Axillary procedure	Event
Augmentation									
1	57	84	T_1	N_0	M_0	L	SM	SNB	–
2	44	76	T_1	N_{1a}	M_0	R	SL	AND	–
3	66	69	T_{1b}	N_0	M_0	L	IM	SNB	–
4	53	16	T_2	N_0	M_0	L	SM	SNB	LR[b]
5	57	65	T_1	N_0	M_0	L	IL	SNB	–
6	49	64	T_{1c}	N_{1mi}	M_0	L	IL	SNB	–
7	37	59	T_{is}	N_0	M_0	R	SM	SNB	–
8	58	57	T_{1c}	N_0	M_0	R	SM	SNB	–
9	46	55	T_{1c}	N_0	M_0	R	SL	SNB	–
10	52	54	T_{1c}	N_{1a}	M_0	L	IL	AND	–
11	56	54	T_2	N_{3a}	M_0	L	SL	AND	–
12	57	53	T_2	N_0	M_0	L	SL	SNB	–
13	48	50	T_{1c}	N_{1mi}	M_0	L	SM	AND	–
14	49	49	T_{1b}	N_0	M_0	R	SL	SNB	–
15	44	48	T_1	N_0	M_0	L	IM	SNB	–
16	53	36	T_{1a}	N_0	M_0	L	SL	SNB	–
17	54	38	T_{1c}	N_0	M_0	R	SL	SNB	–
18	52	41	T_{1b}	N_0	M_0	R	SM	SNB	–
19	49	40	T_2	N_0	M_0	L	SL	SNB	–
20	42	41	T_{1b}	N_{1mi}	M_0	L	IM	SNB	–
Substitution									
1	62	88	T_{1c}	N_{1mi}	M_0	R	SM	SNB	–
2	48	85	T_{1c}	N_0	M_0	L	SL	SNB	–
3	61	60	T_{1c}	N_0	M_0	R	SL	SNB	–
4	46	46	T_{1c}	N_{1mi}	M_0	R	SL	AND	–
5	62	36	T_2	N_0	M_0	L	SL	SNB	–
6	61	38	T_{1b}	N_{0iso}	M_0	R	SM	SNB	–
7	48	38	T_{is}	N_0	M_0	R	SL	SNB	–
8	56	41	T_{1c}	N_0	M_0	L	IM	SNB	–
9	50	43	T_{1b}	N_{1mi}	M_0	R	SM	AND	–

[a] Abbreviations: 1mi = Micrometastasis, S = Superior, I = Inferior, M = Medial, L = Lateral, SNB = Sentinel node biopsy, AND = Axillary node dissection, IS = In situ, LR = Local recurrence.
[b] Infraclavicular recurrence, death at 16 months after surgery.

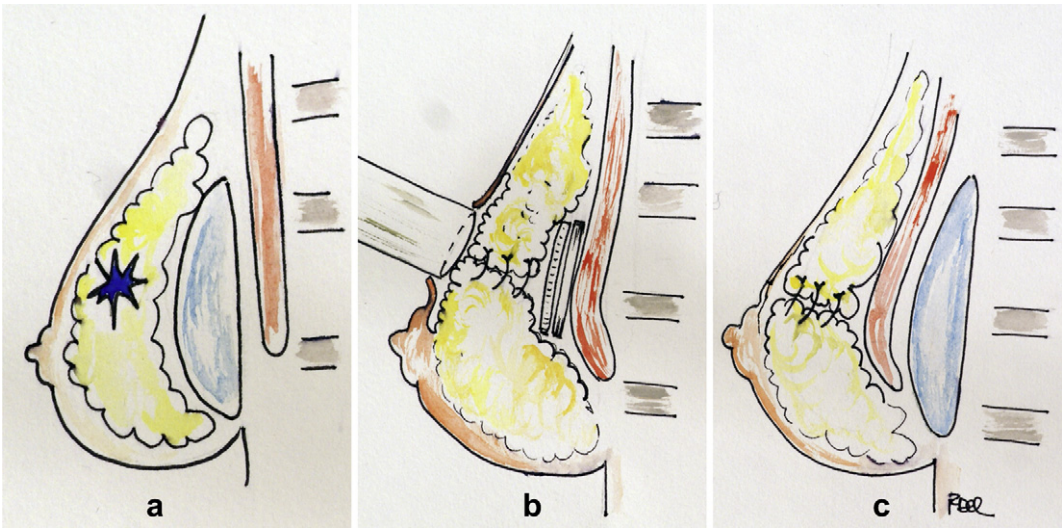

Fig. 1. (a): Tumor in previous augmented breast (subglandular layer) (b): ELIOT delivery and (c): Completion of prosthetic reconstruction and substitution (subpectoral layer).

retracted to avoid its irradiation.[27,28] The irradiation collimator was placed directly over the target zone and connected to the articulated arm of the miniaturized linear accelerator machine (either Novac 7: Hitesys, Italy or LIAC: Info&Tech, Italy). An electron beam radiation was delivered with a dose of 21 Gy which was equivalent to prescription at 90% isodose using electron beams 9 MeV energy.

A submuscular pocket was later undermined under the pectoralis major muscle and an implant was placed. The glandular flaps were sutured together to close the quadrantectomy defect and to achieve a satisfactory reshape of the breast.

For those cases of previous prosthetic cosmetic augmentation breast, the procedure began with the oncologic resection and followed by ELIOT. Afterward, the implant was removed and the submuscular pocket was created for a new implant replacement and accomplished glandular flaps reshaping in the same fashion as the previous group as shown in Fig. 1.

In both group, the contralateral breast augmentation or substitution or mastopexy-augmentation was performed in every case. The implant model was individually determined for the best esthetic breast figure and symmetry.

The capsular contracture grading was evaluated according to Spear and Baker classification.[30] As all patients have bilaterally implant placement, we compared the capsular contracture grading of the reconstructed breast in ELIOT-side to those own contralateral side without any irradiation. Therefore, the contralateral side of each individual patient was referred as a control.

The questionnaire was completed by the individual patient and the plastic surgeon. Though, the plastic surgeon who rated the questionnaire is the single surgeon who has not performed any of those interventions. The aspects of evaluation comprised of breast symmetry, breast shape, scar and defect at lumpectomy site, nipple areolar complex symmetry and overall esthetic satisfaction. Each category was assessed by visual analog scale, the score ranged from 0 = worst to 10 = best satisfaction. The individual and total score summary were analyzed and calculated.

Results

Finally we enrolled all 29 patients who underwent BCT plus 21 Gy-ELIOT and were immediately reconstructed with prosthesis in ipsilateral breast and had simultaneous contralateral augmentation for symmetrical procedure.

During an average period of 54.2 (36–88) months follow up; immediately there was one case of hematoma which required secondary surgical evacuation. There were four minor liponecrosis which occurred in ELIOT introduced breast and healed spontaneously without any corrective intervention. There was neither infection nor wound dehiscence in the entire procedures.

The capsular contracture of the ipsilateral-ELIOT and the contralateral healthy breasts was found as grade I–II in 25 and 27 breasts, respectively (86.2% versus 93.1%), whilst grade III–IV in 4 and 2 breasts, respectively (13.7% versus 6.8%). The results were shown in Table 2.

For the questionnaire scores, we were able to obtain complete scores from only 27 out of 29 patients. One patient died at 16 month after surgery and one patient developed local recurrence after 29 months of intervention and proceeded for total mastectomy, then none of them were excluded from questionnaire scores. The completed scores were summarized and calculated as in Table 3.

All the average score of breast symmetry and shape, scar and defect at lumpectomy site, nipple areolar complex symmetry and

Table 2
Capsular contracture.

	Ipsilateral side with ELIOT	Contralateral side without ELIOT
Baker I	20 (8)	23 (8)
Baker II	5 (1)	4 (1)
Baker III	2 (0)	2 (0)
Baker IV	2 (0)	0 (0)

The numbers in the bracket show the Baker capsular contracture from subgroup of prosthesis substitution.

Table 3
Esthetic questionnaire score.

Category	Evaluator	
	Patient	Surgeon
Breast symmetry[a]	6.24	8.10
Breast shape[a]	6.70	8.05
Scar and defect at lumpectomy site[a]	6.81	8.05
Nipple areolar complex symmetry[a]	6.85	7.95
Overall esthetic satisfaction[a]	6.63	8.12
Total score summary (score out of 50)	33.24	40.26
Total score average (score out of 10)	6.65	8.05

[a] Scale score ranges from 0–10 (worst to best satisfaction).

overall esthetic satisfaction found lower score from patient than surgeon evaluation as shown. The average of esthetic score were 6.65 and 8.05 (out of full score 10) from patients and surgical team, respectively.

These questionnaires were subjective evaluations, so that, there were major variations in scoring. Two patients scored zero for all categories as the surgeon scored at average of 6–7. The following are sample photographs of patients who underwent bilateral prosthetic augmentation (Fig. 2) and bilateral prosthetic substitution (Fig. 3).

There was one patient who developed local recurrence and later on dead with breast related event (0.76% per year).

Discussions

The surgical techniques and results of ELIOT have been firmly established since 1999 at European Institute of Oncology.[12–19] So far, more than 2000 patients had received ELIOT with various clinical applications including in particular patients which prostheses were integrated in reconstructive procedures.[20–25] The first report in 2006 by Rietjens et al., showed satisfactory short term result at 6 months after implant reconstruction for BCT plus ELIOT.[26]

The ELIOT procedures were conducted according to the currently standard techniques which were described by Intra et al. and reconstructive procedures were performed as illustrated in methodology.[28]

In this series, the complication rate of liponecrosis occurred in four cases (13.7%) and hematoma recorded in one case (3.4%). All of the complications occurred in ELIOT-side whilst the contralateral healthy side showed no complication. Our complications were comparable to those prior reports by Luini et al., who reported pilot trial on 101 ELIOT patients after mean follow up of 41 months, and there were 4% of liponecrosis and 3% of hematoma.[29] Intra et al. reported over 1000 cases of ELIOT with 3% mild fibrosis and 0.2% localized severe fibrosis which developed 6 months after treatment and lasted for another 6 months before it spontaneously disappeared.[28]

Despite the fact that our ELIOT breasts are associated with implant placement which may tend to increase the complications, the complications in our study group are still low and minor, even comparable to other previous large series.[19,28,29]

The prosthetic contracture rates in high risk group especially with conventional radiotherapy were reported to be extremely high and emerged up to 70%.[3–11] In contrast, the Baker's grade III–IV capsular contracture rate in ELIOT breast was observed only 13.7% in this present series. Concomitantly, the healthy contralateral side has Baker's grade III–IV capsular contracture rate at 6.8% which can be regarded as the control data. Therefore, we compared the results of ELIOT-side to those own individual contralateral side without ELIOT. Both sides have undergone exactly the same reconstructive procedures which some patients had only minor differences in prosthesis model and volume. However, the average volumes of prosthesis were 195.8 (100–335) cc. and 177.0 (80–325) cc. for the ipsilateral-ELIOT and the contralateral healthy breasts, respectively. This was only 18.8 cc different on average, which is considered as a minor factor.

Therefore this minor increase of capsular contracture rate in ELIOT sides could be from more extensive surgery on those sides. In fact, the disease breast with ELIOT needed superficial and deep plane undermining and also accompanied with sentinel node biopsy or axillary dissection. As a result, these more extensive interventions can cause seroma formation, local fibrosis, local tissue reaction and eventually the capsular contracture.

There were two cases in which ipsilateral-ELIOT-side had suffered from severe capsular contracture and had undergone surgical correction with capsulotomy plus mastopexy and prostheses substitution at 31 and 12 months after primary reconstructive procedures. However, their contralateral breasts also developed severe capsular contracture which required simultaneous capsulotomy plus mastopexy and prostheses substitution at the same corrective interventions.

With the appropriate protection of pectoralis muscle and limitation of the radiation area only to the surrounding tumor related breast parenchyma, the introduction of ELIOT can significantly reduce the prosthetic capsular contracture while maintain the oncological control and the advantages of implant reconstruction. Moreover, in esthetic aspect ELIOT also adds the benefit of reducing unfavorable effect on skin and scar appearance on the whole breast.

There are other publications which emphasized on feasible cosmetic outcome after ELIOT and brachytherapy.[30–35] Nevertheless, our series not only shows the satisfied cosmetic results after ELIOT, but all of our cases also underwent prosthetic reconstruction and we can acquire the higher satisfaction rates.

We also observed that the areolar dislocations due to scar retractions were more frequent in those patients with radial skin incisions compared to periareolar incisions plus separated axillary incisions. Slight superior lateral retraction toward axilla was remarked in the radial skin incision patient and caused nipple areolar complex shape, size and level asymmetry.

Nipple projection after ELIOT was satisfied in most of the cases and there is no major retraction follow ELIOT procedure. Concomitantly, the color of the ELIOT nipples was detected faintly different from those without ELIOT. However, none of them need corrective procedure such as nipple areolar reconstruction or tattooing.

As a final point, our reason to explain why the individual and average of esthetic scores from patients are lower than those from surgical team is because most of them have high esthetic result

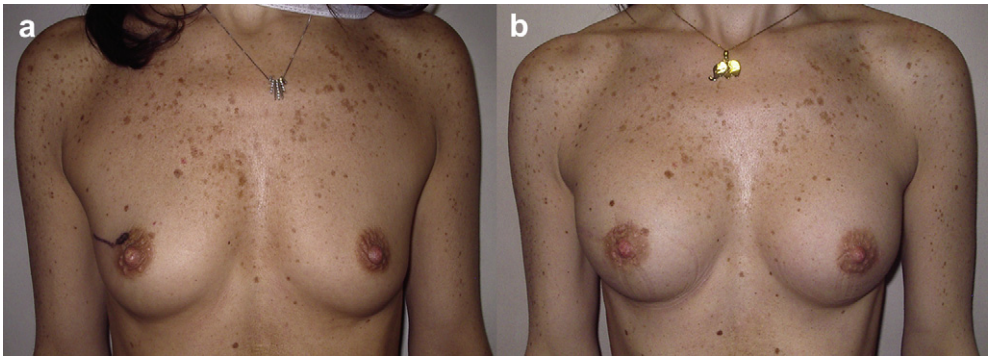

Fig. 2. (a) Pre operative: Bilateral prosthetic augmentation, (b) Post operative: Bilateral prosthetic augmentation (24 months post operation).

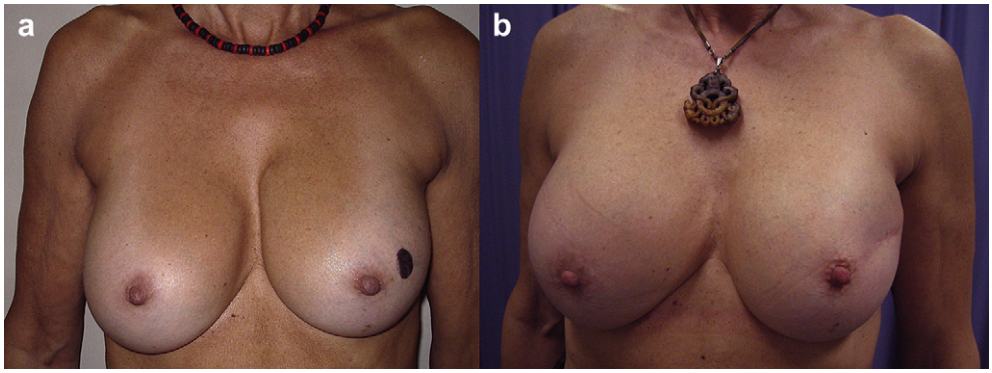

Fig. 3. (a) Pre operative: Bilateral prosthetic substitution, (b) Post operative: Bilateral prosthetic substitution (18 months post operation).

expectation. Even a minor unaesthetic appearance can cause them unsatisfied as their oncological concerns are not the majority.

In oncological view, there was one patient who progressed with local recurrence and received locoregional radiotherapy and finally died at 16 months after primary procedure. In addition, one patient developed local recurrence after 29 months of intervention and proceeded for total mastectomy. In summary for this series developed the local recurrence rate and dead with breast related event is 0.76% per year.

There was one patient with N3 stage who psychologically refused to undergo locoregional radiotherapy as an adjuvant treatment. However she had no relapse after 50 months follow up.

There was neither local recurrence nor metastatic evidence in the rest of the study group. The incidence of local recurrence is comparable to the recent report of our institute (0.76% versus 0.77%, respectively).[36]

ELIOT has proven itself to assign several benefits markedly on safe oncological control and limited tissue radiation exposure along with time-and-cost effectiveness. The new indications and clinical applications of ELIOT have increased recently. So far, the prosthetic reconstruction in ELIOT has never been reported with long term follow up. The evidence from our series showed the safety of prosthetic reconstruction together with the advantages of ELIOT. Nonetheless, larger number of patients and longer follow up period may be required to accentuate the result especially for the long term outcome at over 5 years.

Conclusions

Immediate implant reconstruction in breast conservative treatment plus full-dose 21 Gy-ELIOT is a safe procedure with good satisfactory long term outcomes. The capsular contracture grading in the reconstructed breast from ELIOT-side is comparable with non-irradiated contralateral side and provide better result than in those of conventional external radiation. In addition, the subgroup of previous cosmetic augmentation can also be securely treated with BCT plus ELIOT and implant substitution.

Conflict of interest statement

None declared.

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