# Short-Time Outcome of Intraoperative Radiotherapy (IORT): A Study on Side-Effects and Quality of Life in the Treatment of Early Breast Cancer

Caroline Page[a,*], Pierre-Alain Brioschi[b] and Jacques Bernier[c]

[a]*Lausanne University, Lausanne, Switzerland*

[b]*Department of Gynecology, Clinique de Genolier, Genolier, Switzerland*

[c]*Department of Radiation Oncology, Clinique de Genolier, Genolier, Switzerland*

**Abstract:** Early prospective studies recently demonstrated the non-inferiority of intraoperative radiotherapy compared to protracted external radiotherapy in selected patients. The present study aims at analyzing, in a cohort of 80 women, the distribution and incidence of short-time side-effects induced by intraoperative radiotherapy as well as its impact on patient's quality of life in the months following the treatment. No side-effect was found in the majority of patients (n: 46; 58%). Out of those 32 patients experiencing side-effects after IORT, 26 cases (81%) were found to develop only mild effects. More than 94% of the patients declared to consider IORT as a clear advantage over external radiotherapy in the armamentarium of breast cancer treatment.

**Keywords:** Breast Cancer, Intraoperative radiation therapy, Radiation therapy, Side-effect, Cosmetics.

## INTRODUCTION

In Switzerland, breast cancer is a common pathology affecting 1 in 10 women. With about 5,000 new cases diagnosed each year, breast carcinoma is the first cancer affecting women and accounts for more than 1,400 deaths every year [1]. The local treatment of the disease constantly evolved over the years: in patients presenting with early disease, Halsted's or Patey's mastectomy, the main surgical option until the 70's, was progressively replaced by conservative surgery techniques (quadrantectomy, tumorectomy) followed by 5-7 weeks of external radiotherapy [2]. In the eighties a number of studies had indeed compared the outcomes of radical mastectomy and conservative surgery followed by radiotherapy. These randomized trials showed that survival rates were similar in the two patient groups [3-7]. Nowadays postoperative external radiotherapy, considered as the "conventional" approach, uses to deliver 45-50 Gy to the entire breast in 5 weekly sessions of 1.80 to 2.25 Gy. In a second phase, a boost of 10-16 Gy is usually delivered to the surgical bed [2].

More recently, various institutions investigated, in selected cases, the feasibility and safety of a conservative surgery combined to intraoperative radiotherapy, denoted here as IORT. Early prospective studies indeed demonstrated the non-inferiority of IORT compared to protracted external radiotherapy in patients presenting with early breast cancer and favorable anatomo-pathological factors [8-9]. In a first randomized trial addressing the role of IORT in selected cases, Vaidya and colleagues showed that, while the number of complications between external and intraoperative radiotherapy was similar in the two patient groups, the RTOG (Radiation Therapy Oncology Group) grade 3 and 4 toxicities were significantly less often observed after IORT than after conventional adjuvant radiotherapy [9].

So far, in Switzerland, IORT has been used only in a few hospitals. Among them, the Clinic of Genolier was, in that country, the first institution to deliver IORT treatment with electrons. In the cohort of patients treated at Genolier since July 2009, the follow-up time interval is by far too short to analyse treatment outcomes in terms of efficacy but an analysis of the clinical short-time effects induced by IORT is certainly of interest, as well as the impact of treatment on patient's daily life activity as demonstrated by Reimer and colleagues who showed in a review published recently, that quality of life is actually a useful measurement for the choice of a treatment in breast cancer [10].

The present study reports on both the short-term side-effects induced by IORT and impact of this procedure on patient's quality of life in the months following the treatment.

*Address correspondence to this author at the Lausanne University, Lausanne, Switzerland; Tel: +41216475864; Fax: +4122.362.50.10;
E-mail: page.caroline12@gmail.com

ISSN: 1929-2260 / E-ISSN: 1929-2279/13 

## METHODS

IORT uses to deliver, immediately after the tumor resection, a unique dose of 21 Gy, which is radiobiologically equivalent to 60 Gy ($\alpha/\beta$ ratios of ~10 Gy and ~3 Gy for breast carcinoma and normal mammary tissues, respectively) delivered in 6 weeks of 30 fractions, of 2 Gy each [11]. Under the supervision of the surgeon, an applicator is inserted into the cavity after a lead disk has been placed between the mammary gland and the pectoralis major muscle, in order to protect deep-seated normal tissues as ribs and lung parenchyma. In the same way, this irradiation technique allows to spare completely the skin and subcutaneous tissues. As an alternative to definitive IORT, the so-called "partial IORT", combines a lower dose (12 Gy) to a subsequent external radiotherapy treatment of about 30 Gy over 2.5 weeks, for instance in peri-menopausal patients or in post-menopausal patients with intermediate risks of recurrence.

This study is based on information retrieved from both the clinical charts and questionnaires sent to the patients. Informed consent was obtained from the patients and the study was approved by the hospital and local ethic committee.

Patients were not eligible for IORT if: a) conservative surgery was not possible (besides nipple skin sparing mastectomy); b) the disease was already metastatic at diagnosis; c) they had previously received a systemic treatment; d) the size of the tumor was more than 25 mm; or e) a skin infiltration was clinically or radiologically suspected. The use of IORT was therefore restricted to patients with early breast cancer with favourable pathological risk factors, as recommended by ASTRO (American Society for Radiation and Oncology) and ESTRO (European Society for Radiotherapy and Oncology).

The study analyzes the side-effect distribution and incidence in a cohort of 80 women (two of them treated with a bilateral IORT), aged from 30 to 90 years old, who received intraoperative radiotherapy, from July 2009 to April 2011, at La Clinique de Genolier. Table **1** lists the patient characteristics and tumor patterns and Table **2** the treatment features.

**Table 1: Patient Clinical Characteristics and Tumor Patterns**

| | | |
|---|---|---|
| **Age (nb):**<br>Average: 63 years<br>• < 50 years: 8<br>• 50-65 years: 38<br>• 66-80 years: 30<br>• >80 years: 4 | **Menopausal status:**<br>• Pre: 6%<br>• Peri: 16%<br>• Post: 78% | **Tumor localisation:**<br>• Upper-outer quadrant: 50%<br>• Lower-outer quadrant: 6%<br>• Upper-inner quadrant: 8%<br>• Lower-inner quadrant: 4%<br>• Central: 4%<br>• Upper quadrants junction: 8%<br>• Inner quadrants junction: 1%<br>• Outer quandrants junction: 15%<br>• Lower quadrant junction: 4% |
| **Type of IORT (nb)**<br>• Exclusive: 55<br>• Partial: 19<br>• PAM: 4<br>• Cancelled: 4 | **Grade:**<br>• I: 23%<br>• II: 59%<br>• III: 18% | **Tumor diameter (mm):**<br>• Average: 15.2<br>• Tumor > 25mm: 1 |
| **pN:**<br>• N0: 87%<br>• N1mic: 5%<br>• N1a: 8% | **pSN:**<br>• Not done: 6%<br>• Negative: 86%<br>• Between 0.2-2mm: 3%<br>• >2mm: 5% | **pT:**<br>• pT1a: 8%<br>• pT1b: 31%<br>• pT1c: 45%<br>• pT2: 8%<br>• pTis: 8% |
| **Sentinel node status:**<br>• Negative: 87%<br>• Positive: 13% | **Hormonal Receptors:**<br>• RO +: 93%<br>• RO neg: 7%<br>• RP +: 87%<br>• RP neg: 13% | **Risk factors:**<br>Her2 mutation: 15%<br>Ki67 >20%: 16% |

**Table 2: Treatment Features**

| | | |
|---|---|---|
| **Axillary lymph node dissection:**<br>• Number: 10<br>• Percentage: 12% | **Dose:**<br>• 12 Gy: 24%<br>• 16Gy: 5%<br>• 19Gy: 5%<br>• 21Gy: 66% | **Electron beam energy (Mev):**<br>• 4: 4%<br>• 6: 47%<br>• 8: 25%<br>• 9: 1%<br>• 10: 23% |
| **Treatment depth:**<br>• <10mm: 5%<br>• 10 à <20mm: 42%<br>• 20 à <30mm: 44%<br>• 30mm and more: 9% | **Lead shield diameter:**<br>• 50mm: 6%<br>• 60mm: 31%<br>• 70mm: 46%<br>• 80mm: 17% | **Level of prescribed isodose:**<br>• 85%: 1%<br>• 90%: 87%<br>• 95%: 6%<br>• 100%: 6% |
| **Aplicator size:**<br>• 40mm: 18%<br>• 50mm: 41%<br>• 60mm: 35%<br>• 70mm: 6% | | **Other Treatment:**<br>• Hormonal therapy: 85%<br>• Chemotherapy: 26% |

For each patient, the pre-operative work-up included a mammography, an axillary ultrasound, an MRI, a PET-CT and a micro-biopsy with lympho-scintigram. Radiotherapy was delivered at Genolier using a small, mobile accelerator (LIAC-SORDINA). Low-energy electrons (from 4 to 10 MeV) were delivered in less than 2 minutes.

The cohort of patients treated with IORT at La Clinique de Genolier can be divided in 3 subgroups, namely exclusive IORT, partial IORT, and IORT to the areolar plaque after nipple skin sparing mastectomy (PAM). The distribution of the tumor stages and cases among these 3 subgroups is figured out in Table **1**.

The following side-effects were taken into consideration in the current analysis: haematoma, seroma, infection, fibrosis, radiation-induced skin reactions (according to RTOG grading), liponecrosis, lymphedema, scar retraction and scar dehiscence. Were considered to have:

- mild side-effects, those patients experiencing: haematoma, seroma or liponecrosis if limited/partial and not associated to one another; grade I fibrosis, lymphedema (of arm or breast) if early and limited in time, grade I skin erythema, keloids, or two mild side-effects.

- moderate side-effects, those patients with: infection, side-effect associated to an infection, grade II fibrosis, grade II skin erythema, extensive lymphedema or 3 mild side-effects.

- severe side–effects, those patients who developed more than 3 side-effects, persistent lymphedema, grade III-IV skin eyrthema (skin breakdown or healing toxicity).

Regarding the status after treatment, patients were contacted by phone in order to explain the purpose of the study and obtain their approval to be sent a questionnaire by mail. The questions were based on the EORTC QLQ-BR23 questionnaire [12], and included a) satisfaction indices on the treatment; b) the type of feed-back from their medical insurance; c) the time interval before the patient went back to her usual activity; and d) the length of hospitalisation. Answers were scaled from 1 to 10. Results were stratified in four groups: not at all (1), mild (2-3), moderate (4-6) and important impairment (7-10). The EORTC questionnaires are developed to assess patient's quality of life while they are treated for their cancer. We selected those questions entering the framework of intraoperative radiotherapy, and, to complete the evaluation, we added a number of issues relevant to the post-treatment phase.

The cohort of patients from Genolier is nevertheless small and any comparative statistical analysis generated on the basis of this sample size would be underpowered. Side effects rates were calculated by dividing the number of events by the total number of patients in each group of IORT (Exclusive, Partial, PAM). On the basis of the answers from the questionnaire, satisfaction rates were calculated by dividing numbers in each group index (not at all, mild,

moderate, important) by the number of patients who answered each question.

## RESULTS

Only 4 IORT procedures were cancelled at the time of surgery, for the following reasons: insufficient resection margin, high-grade DCIS (ductal carcinoma *in situ*) around the tumor, presence of disseminated microcalcifications, and suspicion of multiple axillary metastases.

In 95% of the cases, the hospitalization time ranged between 4 and 6 days.

There were 4 carcinologic events in the cohort of patients treated at La Clinique de Genolier. While one of them was a local failure at the site of irradiation, two others were considered as a nodal recurrence and a new primary tumor, respectively. Another patient died from another cancer.

### a) Short-Term Side-Effects

As figured out in Table **3**, no side-effect was found, whatever the type of IORT applied, in the majority of patients (n: 46; 58%). Out of those 32 patients experiencing side-effects after IORT, 26 cases (81%) were found to develop only mild effects which did not impact significantly on quality of life. Sixty-two percent of the patients who received exclusive IORT at a dose of 21 Gy, had no side-effects, while mild and moderate complications were found in 33% and 3.6% of them, being severe. As shown in Table **3**, the only patient with severe complications actually developed mild to moderate side-effects (haematoma with super-infection, liponecrosis), which delayed the healing process and led to a scar dehiscence and moderate fibrosis.

Likewise, only 47% of the patients (n: 11) treated with partial IORT or IORT after nipple skin sparing mastectomy developed side-effects in the immediate follow-up of the treatment (Table **3**), none of them being severe. Only 3 patients among the partial IORT and nipple skin sparing mastectomy subgroups were considered to have moderate side-effects. In the group treated with partial IORT, the complementary phase of external radiotherapy induced cutaneous side-effects such as skin retraction and actinic reaction only in a limited number of patients (2 and 5 patients respectively). These side-effects were not elicited in the exclusive IORT subgroup (Table **3**).

**Table 3: Distribution of the Patients According to the Side-Effect Grades in the 3 IORT Subgroups (n=78)**

| Complications | Exclusive IORT N=55 | Partial IORT N=19 | IORT after PAM N=4 |
|---|---|---|---|
| No side-effect | 34 (62%) | 10 (53%) | 2 (50%) |
| Mild | 18 (33%) | 7 (37%) | 1 (25%) |
| Moderate | 2 (3.6%) | 2 (10%) | 1 (25%) |
| Severe | 1 (1.8%) | 0 | 0 |
| Haematoma | 7 (12.3%)<br>Mild: 5<br>Moderate: 2 | 0 | 0 |
| Seroma | 0 | 2 (10.5%) | 0 |
| Fibrosis | 5 (9.1%)<br>Mild: 4<br>Moderate: 1 | 2 (10.5%)<br>Mild: 2 | 0 |
| Liponecrosis | 3 (5.5%)<br>Mild: 2<br>Moderate: 1 | 1 (5.3%)<br>Mild: 1 | 2 (50%)<br>Mild: 2 |
| Lymphedema | 7 (12.7%)<br>Mild: 7 | 4 (21.1%)<br>Mild: 4 | 0 |
| Dehiscence | 2 (3.6%) | 0 | 0 |
| Skin retraction | 0 | 2 (10.5%) | 0 |
| Actinic reaction | 0 | 5 (26.3%) | 1 (25%) |
| Keloid | 3 (5.5%) | 0 | 0 |

Overall, the most frequent side-effect was lymphedema, which was found in 7 cases treated with exclusive IORT and in 4 others after partial IORT group (Table **3**). Of the eleven events, only one was located in the patient's arm. The other ten developed in the breast. All of them were of mild significance. Lymphedema was observed in 3 out of the 10 patients who had undergone an axillary dissection.

Nine percent of the patients developed fibrosis, of mild significance in all cases but one in the IORT exclusive group. Two patients in the partial IORT group

**Table 4: Quality of Life Indices: Answers to the Questionnaire**

| | |
|---|---|
| **Recovery time before usual activities could be performed again:**<br>• 1 week or less: 24%<br>• > 1 week to 2 weeks: 21%<br>• > 2 weeks to 4 weeks: 26%<br>• > 4 weeks to 8 weeks: 12%<br>• > 8weeks: 17% | **Hospitalisation time:**<br>• 1 day: 0%<br>• 2-3days: 34%<br>• 4-6 days: 61%<br>• A week or more: 5% |
| **Difficulty with heavy lifting:**<br>• Not at all: 27%<br>• A little: 28%<br>• Average: 29%<br>• A lot: 16% | **Fatigue resented 3 months after surgery:**<br>• Not at all: 22%<br>• A little: 27%<br>• Average: 27%<br>• A lot: 24% |
| **Help needed for usual activities one month after surgery:**<br>• Not at all: 88%<br>• A little: 6%<br>• Average: 3%<br>• A lot: 3% | **Limitation in pursuing hobbies one month after surgery:**<br>• Not at all: 30%<br>• A little: 25%<br>• Average: 25%<br>• A lot: 20% |
| **Limitation in pursuing hobbies today:**<br>• Not at all: 83%<br>• A little: 6%<br>• Average: 8%<br>• A lot: 3% | **Pain in the operated breast one month after surgery:**<br>• Not at all: 30%<br>• A little: 20%<br>• Average: 32%<br>• A lot: 18% |
| **Pain in the operated breast 3 months after surgery:**<br>• Not at all: 39%<br>• A little: 32%<br>• Average: 21%<br>• A lot: 8% | **Sleeping problems one month after surgery:**<br>• Not at all: 42%<br>• A little: 23%<br>• Average: 23%<br>• A lot: 12% |
| **Lack of appetite one month after surgery:**<br>• Not at all: 77%<br>• A little: 12%<br>• Average: 6%<br>• A lot: 5% | **Worrying one month after surgery:**<br>• Not at all: 36%<br>• A little: 30%<br>• Average: 22%<br>• A lot: 12% |
| **Feeling depressed one month after surgery:**<br>• Not at all: 49%<br>• A little: 22%<br>• Average: 15%<br>• A lot: 14% | **Physical condition or treatment impacted on family life:**<br>• Not at all: 67%<br>• A little: 17%<br>• Average: 7%<br>• A lot: 9% |
| **Physical condition impairment or treatment impacting on social life:**<br>• Not at all: 73%<br>• A little: 17%<br>• Average: 6%<br>• A lot: 7% | **Physical condition impairment or treatment impacting on professional activities:**<br>• Not at all: 74%<br>• A little: 6%<br>• Average: 9%<br>• A lot: 11% |
| **IORT as an advantage over conventional adjuvant radiotherapy:**<br>• Yes, a lot: 83%<br>• Yes: 12%<br>• Average: 5%<br>• Not at all: 0% | **Insurance reimbursement:**<br>• Yes: 29%<br>• In part: 8%<br>• No: 63% |

developed fibrosis, both associated with an actinic reaction and one with a seroma.

Liponecrosis was the only side-effect found in each subgroup. Liponecrosis was not always found to be along the scar. One liponecrosis occurred above the scar in the exclusive IORT group. As for the PAM group, of the two events, one was located in the areola and the other one in the nipple. Except in one case developing concomitantly a non-infectious collection, liponecrosis was actually a radiological finding with no clinical impact, as confirmed by the answers provided by patients experiencing this type of side-effect.

Skin reactions such as dehiscence (2.5% overall), keloids (3.8%), skin retraction (2.4%) and actinic reaction (7.7%) were infrequently observed, the latter two side-effects being found only in the partial IORT and nipple skin sparing mastectomy subgroups. Skin retraction was associated in one case with lymphedema and in another with liponecrosis. Only grade I and II actinic reactions were observed in our cohort. Of rare occurrence, haematomas, seromas and dehiscence were often associated to other side-effects such as infection, fibrosis or liponecrosis. Only one of the haematomas required a drainage, and one of the two skin dehiscences was associated to infection.

As expected, the side-effect occurrence did not seem to be correlated to age or menopausal status. Less than eight percent of the side effects occurred in the pre-menopausal patients, 18.4 % in the peri-menopausal group and 73.7% in the post-menopausal group, which corresponds to the number of patients within each group 6.4%, 15.4%, and 78.4% respectively. Among the 4 patients of more than 80 years old, 2 had no side-effect at all, and the other two only experienced mild side-effects (one small haematoma and one breast lymphedema, both disappearing within a few days).

Likewise, the lead shield or collimator diameter did not impact on the occurrence of side-effects. Regarding the lead shield diameters, the rate of appearance of side effects was as follows: 2.63% with a diameter of 50mm, 36.8% with 60mm, 44.7% with 70mm and 15.9% with 80mm. The only procedure seeming to play a role was axillary dissection. Indeed, all the patients in whom this surgical procedure had to be performed developed mild to moderate side-effects.

### b) Quality of Life Indices

Eighty-six percent of patients who had received the questionnaire had sent their answers at 3 months. The 11 patients who had not answered were then called back to check their interest in the study. We stopped recording data after a total of 66 fulfilled questionnaires, corresponding to an answer rate of almost 90%. Their results are reported in Table **4** and Figures **1** and **2**.

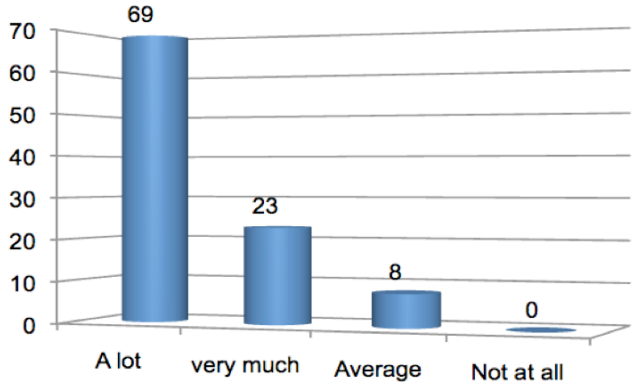


**Figure 1: Global evaluation**

The figure shows the answering distribution pattern (in %) to the question: In general, are you satisfied with your treatment?

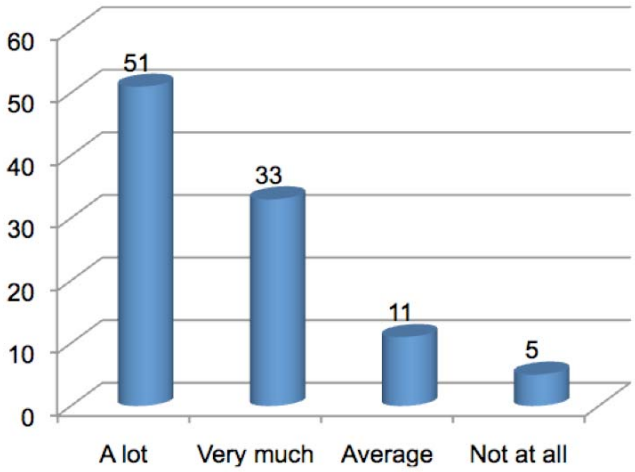


**Figure 2: Cosmetic evaluation**

The figure shows the answering distribution pattern (in %) to the question: Are you satisfied with the esthetic outcome of your treatment?

As expected, a majority of issues addressed in the questionnaire were characterized by broad variations in reporting. For instance, answers to the question “difficulties with heavy lifting” yielded the following distribution: not at all: 27%; a little: 28%; average: 29%; a lot: 16%. The pattern of answers was similar for

questions investigating the evolution at one month after IORT, namely limitations in pursuing hobbies, pain in the operated breast, worries or fatigue.

At a 1-month interval, only few patients felt depressed (14%) or had sleeping problems (12%). Likewise, lack of appetite, difficulties in pursuing hobbies today and usual activities were not reported by more than 75% of the patients. At a 3-month interval, the equivalent figure for residual breast pain was 8%. Less than 18% of patients mentioned that the time to full recovery had exceeded 8 weeks.

In about 90% of the cases, the physical conditions did not impact significantly on family, social life or professional activities. A vast majority of patients (95%) also considered that IORT presented for them a clear advantage over conventional postoperative radiotherapy. The index of satisfaction was also high regarding the cosmetic aspects (85%), and more than 9 patients out of 10 were pleased with the procedure from a global viewpoint. All the patients declared they were satisfied to have opted for IORT, rather than for conventional postoperative radiotherapy.

## DISCUSSION

Intraoperative strategies are aimed at getting a direct access to the tumor bed, decrease the volume of irradiation, and avoid any delay between the surgery and radiotherapy. Last but not least, it is bound to reduce the socio-economical and emotional impact of lengthy treatment periods. It is also postulated that the concept itself of irradiation inside the cavity after the tumor resection should impact favourably on the occurrence and intensity of side-effects, since the skin and subcutaneous tissues are not irradiated during IORT.

While Ruano-Ravina *et al*. found in 2011, that the most frequent short-time side-effects were seroma, wound healing problems and fibrosis, the current study elicits fibrosis, liponecrosis, lymphedema and haematomas as the main issues after exclusive or partial IORT [13].

Intraoperative radiotherapy implies a re-arrangement of the cavity walls after the resection as well as after the insertion of the perspex collimator, the diameter of which often exceeds 5 cm. Compared to tumorectomy, the whole IORT-based procedure might therefore favor the occurrence of haematomas and lymphedema, as a consequence of the cavity walls' distention. Nevertheless, in the present cohort of patients, these side-effects were mild in a majority of patients, except in one case with superinfection.

While the incidence of side-effects may vary from a study to another, it remains low in most reports. Comparing the present cohort of patients with the patient population treated with IORT at the European Institute of Oncology in Milan, the proportion of cases without any complication was 59 and 79%, respectively. In this latter study published in 2010, Veronesi and colleagues had reported 0.1% of severe fibrosis, this grade being not observed in the current study. They reported the presence of fibrosis in 1.8% of the cases treated by partial IORT, liponecrosis in 4.2%, haematomas in 5.5%, wound infection in 1.3%, and seromas in 12.9% [8].

The pattern of evolution of fibrosis, one of the most frequent side-effects in this cohort of patients, matches pretty well that previously described in the literature on IORT. Fibrosis is shown to increase during the months following the surgical procedure, reaches a peak after about one year, before regressing slowly and disappearing almost completely after around a 24-month period [14]. In his 2010 study, Veronesi reported a 36 month interval before a complete clearance of fibrotic reactions [8].

Other side-effects such as telangiectasia, mastitis or dermatitis, observed in other studies, were not found in the current analysis [13].

Interestingly, Wenz *et al*., showing that chronic skin toxicity (fibrosis, telangiectasia, breast edema, retraction, ulceration, hyperpigmentation) was found in less than 10% of the patients treated by partial IORT, demonstrated that the side-effects increased when external radiotherapy was delivered earlier than 30 days after IORT [15].

In most patients, IORT does not impact on the women's physical conditions and therefore present a significant number of socio-economic advantages allowing them to go back faster to their job, family and friends.

Following adjuvant treatment in breast cancer, persistent pain can represent a major issue in a significant number of patients (25-60%) [16]. Andersen *et al*., comparing IORT with EBRT, showed that the former approach was not a risk factor for developing persistent pain after treatment. Although the results show no significant difference between the two

techniques, the proportion of patients experiencing pain was 34 and 25%, respectively [16].

As far as cosmesis is concerned, Ruano-Ravina and colleagues found that, in 80% of patients, esthetic results were usually good and even excellent [13]. These results were recently confirmed by Leonardi al., who elicited high levels of satisfaction among the women treated with IORT, with rates exceeding 90% [17]. Such excellent indices are found in the current study since 95% of the patients declared that IORT presented a clear advantage over external radiotherapy in the armamentarium of breast cancer treatment. As a matter of fact it has to be kept in mind that some parameters, such as the short hospitalization time and immediate re-insertion into normal life do interact with the final appreciation of this new approach by most patients.

This high index of satisfaction expressed by almost all patients, combined to the confirmation brought by recent clinical trials on the feasibility, safety and efficacy of IORT in patients with favorable prognostic factors, sharply contrasts with the current policy of the health insurances in Switzerland since it turns out from our survey that only 29% of the patients treated with IORT at La Clinique de Genolier were reimbursed by their insurer for the cost of this procedure.

## CONCLUSION

This analysis of the immediate outcome of intraoperative radiotherapy in breast cancer patients presenting with early disease and favorable prognostic factors shows that, whatever the type of IORT applied (exclusive, partial, or after nipple skin sparing mastectomy), the incidence of short-term side-effects is low and their intensity is, in the majority of patients, mild. From the answers to the questionnaire, it results that these short-time side-effects have a limited clinical relevance and, in most of them, do not impact significantly on quality of life. Together with the significant shortening and simplification of the radiotherapy treatment, this favorable outcome, evaluated in the current study by the patient and not by the treating physician, accounts to a large extent to the high indices of satisfaction expressed by the patients in favour of IORT.

## REFERENCES

[1] Ligue Suisse contre le cancer [homepage on the Internet]. Cancer du sein (carcinome mammaire) [cited march 2011]: Available from: http://www.liguecancer.ch/fr/a_propos_du_cancer/types_de_cancer/cancer_du_sein/

[2] Saglier J, Beuzeboc P, Pommeyrol A, Toledano A. Cancer du Sein: Questions et réponses au quotidien, Abrégés. 3rd ed. Masson 2009.

[3] Fisher B, Anderson S, Bryant J, *et al*. Twenty-year follow-up of randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002; 347: 1233-41. http://dx.doi.org/10.1056/NEJMoa022152

[4] Horst K-C, Smitt M-C, Goffinet D-R, Carlson R-W. Predictors of local recurrence after breast-conservation therapy. Clin Breast Cancer 2005; 5: 425-38. http://dx.doi.org/10.3816/CBC.2005.n.001

[5] Jolly S, Kestin L-L, Goldstein N-S, Vicini F-A. The impact of lobular carcinoma in situ in association with invasive breast cancer on the rate of local recurrence in patients with early-stage breast cancer treated with breast conserving therapy. Int J Radiat Oncol Biol Phys 2006; 66: 365-71. http://dx.doi.org/10.1016/j.ijrobp.2006.05.070

[6] Poggy M-M, Danforth D-N, Sciuto L-C. *et al*. Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: The National Cancer Institute Randomized Trial. Cancer 2003; 98: 697-702. http://dx.doi.org/10.1002/cncr.11580

[7] Veronesi U, Cascinelli N, Mariani L, *et al*. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002; 347: 1227-32. http://dx.doi.org/10.1056/NEJMoa020989

[8] Veronesi U, Orecchia R, Luini A, *et al*., Intraoperative radiotherapy during breast conserving surgery: a study on 1,822 cases treated with electrons. Breast Cancer Res Treat 2010; 124: 141-51. http://dx.doi.org/10.1007/s10549-010-1115-5

[9] Vaidya JS, Joseph DJ, Tobias JS, *et al*. Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): An international, prospective, randomised, non-inferiority phase 3 trial. Lancet 2010; 376: 91-102. http://dx.doi.org/10.1016/S0140-6736(10)60837-9

[10] Reimer T, Gerber B. Quality-of-life considerations in the treatment of early-stage breast cancer in the elderly. Drugs Aging 2010; 27: 791-800. http://dx.doi.org/10.2165/11584700-000000000-00000

[11] Zurrida S, Leonardi MC, Del Castillo A, Lazzari R, Arnone P, Caldarella P. Accelerated partial breast irradiation in early breast cancer: focus on intraoperative treatment with electrons (ELIOT). Womens Health 2012; 8: 89-98. http://dx.doi.org/10.2217/whe.11.86

[12] Sprangers MA, Groenvold M, Arraras JI, *et al*. The European Organization for Research and Treatment of Cancer breast cancer-specific quality-of-life questionnaire module: first results from a three-country field study. J Clin Oncol 1996; 14: 2756-68.

[13] Ruano-Ravina A, Cantero-Munoz P, Eraso Urien A. Efficacy and safety of intraoperative radiotherapy in breast cancer: A systematic review. Cancer Lett 2011; 313: 15-25. http://dx.doi.org/10.1016/j.canlet.2011.08.020

[14] Bitterman A, Kessner R, Goldman L, Shiloni E, Steiner M. Intraoperative Radiotherapy for Breast Cancer. IMAJ 2012; 14: 256-59.

[15] Wenz F, Welzel G, Keller A, *et al*. Early irradiation of external beam radiotherapy (EBRT) may increase the risk of long-term toxicity in patients undergoing intraoperative radiotherapy (IORT) as a boost for breast cancer. Breast 2008; 17: 617-22. http://dx.doi.org/10.1016/j.breast.2008.05.009

[16] Andersen K, Gärtner R, Kroman N, Flyger H, Kehlet H. Persistent pain after targeted intraoperative radiotherapy (TARGIT) or external breast radiotherapy for breast cancer: A randomized trial. Breast 2012; 21: 46-49. http://dx.doi.org/10.1016/j.breast.2011.07.011

[17] Leonardi C, Ivaldi GB, Santoro L, *et al*. Long-term side effects and cosmetic outcome in a pool of breast cancer patients treated with intraoperative radiotherapy with electrons as sole treatment. Tumori 2012; 98(3): 324-30.

Received on 05-05-2013 Accepted on 02-07-2013 Published on 13-11-2013

DOI: http://dx.doi.org/10.6000/1929-2279.2013.02.04.2