

# Targeted Intraoperative Radiotherapy During Breast-conserving Surgery for Breast Cancer in Patients After Implant Augmentation

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**Abstract.** *Background/Aim:* Targeted intraoperative radiotherapy (TARGIT IORT) is an option during breast-conserving surgery (BCS). No data have yet been published regarding the safety of TARGIT IORT with implants *in situ*. TARGIT IORT is an attractive option in this context because of the risk of capsular fibrosis following external beam radiotherapy (EBRT) in such patients. *Patients and Methods:* We are reporting a retrospective analysis of 16 patients who received TARGIT IORT during BCS for early breast cancer after previous implant-based breast augmentation. TARGIT IORT was performed using the Intrabeam™ method. *Results:* Follow-up varied from 98 to 5 months. There were no procedure-related complications. One patient developed local recurrence after 36 months of follow-up. Among the remaining patients (15/16), no breast-cancer-related events occurred. *Conclusion:* This series of patients with TARGIT IORT during BCS after implant-based breast augmentation revealed no safety concerns and gives some confidence in discussing this option with selected patients.

Since the results of the TARGIT A trial demonstrating non-inferiority of targeted intraoperative radiotherapy (TARGIT

IORT) compared to external beam radiotherapy (EBRT) in selected patients with early breast cancer have been presented (1), TARGIT IORT has become an option during breast conserving surgery in over 350 centers in 35 countries and over 20,000 patients have been treated. In cases where TARGIT IORT seems not appropriate due to an increased risk of recurrence, the technique is often used as an anticipated boost. The oncological safety of this concept has also been demonstrated (2, 3). In addition to non-inferiority regarding local control, a positive impact of intraoperative radiotherapy on overall survival has been proposed. In the TARGIT A trial, the effect of TARGIT IORT on overall survival had an enhancing trend and in a retrospective analysis of patients after neoadjuvant chemotherapy who received TARGIT IORT as an anticipated boost, this effect was statistically significant (2). A recent meta-analysis confirmed the survival benefit of targeted radiotherapy (3).

A growing number of women are undergoing breast augmentation with implants. In the United States in 2016, over 310,000 breast augmentations were performed, representing an increase of over 200% compared to 1996 (4). The growing demand for breast augmentation will increase the number of patients with breast cancer and implants *in situ*. In cases with implant breast augmentation, breast conserving surgery and whole breast irradiation have been associated with capsular contracture rates as high as 65% (5). We were aware of the fact that in TARGIT centers TARGIT IORT was offered in selected cases of patients with breast cancer and implants *in situ* in order to avoid this complication. Here, we are presenting a series of 16 cases and discuss the feasibility and safety of TARGIT IORT in patients with implants.

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Table I. Patient characteristics.

ID	ER/PR/ HER2	Grade	Sentinel nodes	Tumor size (mm)	Distance implant to tumor (mm)	EBRT after IORT	Age at time of surgery to IORT (years)	Time from augmentation	Implant position (months)	Implant type	Follow-up time
1	Pos/pos/neg	2	pN1mi(sn)	9	5	No	52	4	Prepectoral	Silicone	62
2	Pos/neg/neg	2	pN0(sn)	19	12	Yes	56	13	Prepectoral	Silicone	54
3	Pos/pos/neg	3	pN0(sn)	0.8 + DCIS	5	Yes	45	20	Subpectoral	Not reported	32
4	Pos/pos/neg	2	pN0(sn)	6	11	No	49	4	Prepectoral	Silicone	15
5	Pos/pos/neg	3	pN0(sn)	7	1	Yes	50	3	Prepectoral	Silicone	14
6	Pos/pos/neg	1	pN0(sn)	5	15	No	49	16	Subpectoral	Saline	14
7	Pos/pos/neg	2	pN0(sn)	7	Not reported	No	43	Unknown	Subpectoral	Saline	37
8	Pos/pos/na (DCIS)	1	N/A	15	Not reported	No	55	Unknown	Subpectoral	Silicone	98
9	Pos/pos/neg	2	pN0(sn)	15	Not reported	No	75	2	Subpectoral	Silicone	25
10	Pos/neg/neg	1	pN0(sn)	14	4	No	46	10	Prepectoral	Silicone	52
11	Pos/pos/neg	2	pN0(sn)	9	1	No	63	20	Prepectoral	Saline	28
12	Pos/pos/neg	2	pN0(sn)	7	5	No	49	25	Prepectoral	Silicone	18
13	Pos/pos/neg	1	pN0(sn)	8	Not reported	No	57	Unknown	Subpectoral	Saline	5
14	Pos/pos/neg	2	pN0(sn)	7	Not reported	No	60	10	Subpectoral	Saline	6
15	Pos/pos/neg	2	pN0(sn)	17	Not reported	No	48	Unknown	Subpectoral	Saline	72
16	Pos/pos/na (DCIS)	2	N/A	2	Not reported	No	47	6	Subpectoral	Silicone	84

## Patients and Methods

This is a retrospective analysis of 16 patients from centers of the TARGIT group in Germany, Italy, New Zealand and the USA who had breast conserving surgery for early breast cancer, had undergone breast augmentation with implants before and wanted their implants to stay *in situ*. All patients were informed that no published data existed regarding TARGIT IORT over implants and gave their informed consent for this individual approach. The project of collecting data in this indication from centers of the TARGIT group worldwide was submitted to the local ethics committee in the corresponding author's institution on March 5, 2017, and approved by the committee. Patients have given their written informed consent.

All patients received TARGIT IORT using the Intrabeam™ 50 kV X-ray device delivering 20 Gy at the surface of the tumor bed. In 15 cases, TARGIT IORT was performed during the initial breast conserving surgery; one case was performed at a re-excision. After breast conserving surgery, all patients were presented to their local multidisciplinary tumor boards. Three patients received additional EBRT after TARGIT IORT because of the presence of extensive intraductal component or lymphovascular invasion. Patients were included if a basic dataset including immunohistochemistry, grade, nodal status and tumor size was available and at least one follow-up was documented.

## Results

Patient characteristics are shown in Table I. Follow-up varied from 98 months to 5 months. Fourteen patients presented with invasive breast cancer. Two patients were diagnosed with ductal carcinoma *in situ* (DCIS). There were no procedure-

related complications and none of the patients needed their implant to be removed. One patient (ID 7) was diagnosed with a local recurrence in a distant quadrant after 36 months of follow-up. In 15/16 patients no breast-cancer-related events occurred.

## Discussion

Cases of patients with implants and breast-conserving therapy for breast cancer have initially been reported more than 30 years ago when the standard surgical therapy was still considered to be mastectomy (6). Since then, there have been individual approaches of de-escalation in cases of breast cancer after breast augmentation. Although the high incidence of capsular contracture after whole breast irradiation is a well-known risk in augmented patients, small case series with up to 20 patients showed that breast conserving surgery with consecutive radiotherapy is feasible (7, 8). However, smaller series describe an increased risk of cosmetic failure after EBRT with as many as 8 out of 11 patients in one series rating their cosmetic result as moderate or even worse (9). The risk of cosmetic failure was demonstrated to be even higher in patients receiving not only whole breast irradiation but also a boost to the tumor bed (10). The use of a brachytherapy boost instead of an external boost yielded favorable cosmetic outcomes even though patients received additional whole breast irradiation (11). A report on partial breast irradiation after implant-based breast augmentation comprised 16 patients treated with external

beam accelerated breast irradiation (38.5 Gy in 10 fractions over 5 days) after breast conserving surgery (12). Follow-up varied from 1.2 to 58 months. Patients were satisfied with individual cosmetic results, reported no pain and remained disease-free during the follow-up period. Another retrospective analysis from a single center comprised 250 augmented patients who received interstitial brachytherapy. With follow-up of up to 20 years, fewer than 5% of patients experienced new-onset or worsening capsular contracture (13). However, tumor control, survival rates, cosmetic outcomes, and toxicities other than capsular contracture in this series have not been reported.

Our data represent the sole results of follow-up after partial breast irradiation using a 50 kV X-ray-source to give targeted intraoperative radiotherapy in the context of breast-conserving surgery for breast cancer after implant-based breast augmentation. There were no procedure-related complications and no cases that had loss of implant or needed exchange of the implant. We are aware of the limitations of our analysis, such as the inhomogeneous follow-up between 5 and 98 months, the small dataset due to the retrospective nature of our data from four different health systems and the small number of patients. However, the fact that there were no safety signals, neither complication-related nor breast cancer-related, facilitates discussing the option of TARGIT IORT with selected patients on an individual basis and warrants efforts for increasing the existing database including a prospective evaluation of cosmetic satisfaction and disease-free survival.

## Conclusion

This series of patients with TARGIT IORT during breast-conserving surgery for early breast cancer after breast augmentation with implants *in situ* revealed no safety concerns and gives some confidence in discussing this option among suitable patients. To expand this series, we are gathering details about other cases from the whole TARGIT group worldwide.

## Conflicts of Interest

Dr. Kolberg reports personal fees from Carl Zeiss meditec, personal fees from Theraclion SE, personal fees from Genomic Health, personal fees from Novartis, personal fees from Pfizer, personal fees from Roche, non-financial support from LIV Pharma, personal fees from TEVA, personal fees from Riemser, personal fees from Janssen-Cilag, personal fees from Astra Zeneca, outside the submitted work. Dr. Uhl has nothing to disclose. Dr. Massarut reports other from Carl Zeiss meditec, outside the submitted work. Dr. Holmes has nothing to disclose. Dr. Kolberg-Liedtke has nothing to disclose. Dr. Whineray Kelly reports other from Focus Radiotherapy, outside the submitted work. Dr. Lövey has nothing to disclose. Dr. Vaidya reports personal fees and non-financial support from Carl Zeiss meditec, outside the submitted work.

## Authors' Contributions

HCK, VU and JSV developed the idea of this analysis. HCK, VU, SM, DH, GL, EWK contributed in the data collection. HCK, VU, SM, DH, GL, EWK, CKL and JSV contributed in analyzing the data and writing the manuscript.

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