Early postoperative complications and patient-reported quality of life following breast-conserving surgery with intraoperative radiotherapy: A prospective cohort study

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Abstract. The present study aimed to evaluate the incidence of short-term complications and health-related quality of life (HRQoL) in patients with breast cancer undergoing breast-conserving surgery (BCS) with intraoperative radiotherapy (IORT), and to identify associated influencing factors. The study prospectively analyzed clinical data from women who underwent BCS with IORT at Tianjin Medical University Cancer Institute and Hospital (Tianjin, China) between March 2021 and June 2023. Telephone follow-up was conducted within 3 months post-surgery to assess surgery- and radiotherapy-related complications. HRQoL was evaluated using the BREAST-Q BCS module and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30. Statistical analyses were performed using SPSS 27.0. Among 102 enrolled patients, common complications included incision site sclerosis (84.3%), pain (58.8%) and skin indentation (44.1%). Severe complications such as infection (7.8%) and delayed healing (12.7%) were less frequent. Grade I-II acute radiation dermatitis occurred in 73.5% of patients. Univariate analysis revealed that larger applicator size was significantly associated with higher-grade skin toxicity, skin indentation and irritation ($P<0.01$). Older age was a risk factor for incision infection and delayed healing ($P<0.05$). Larger tumor size (T stage) adversely affected satisfaction with breasts and chest physical well-being scores ($P<0.01$). The study concluded that, in patients with early-stage breast cancer treated with BCS plus IORT, 3-month postoperative complications are predominantly mild localized tissue reactions with rare severe events. Applicator size, age and tumor stage are significantly associated with early complications and acute-phase QoL, informing preoperative counseling and perioperative management optimization. However, this study only reflects acute recovery outcomes; long-term follow-up of the cohort is ongoing to evaluate late toxicities, cosmetic results and sustained QoL.

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Abbreviations: APBI, accelerated partial breast irradiation; BCS, breast-conserving surgery; EBRT, external beam radiotherapy; HRQoL, health-related quality of life; IORT, intraoperative radiotherapy; PRO, patient-reported outcome; QoL, quality of life; RTOG, Radiation Therapy Oncology Group; WBI, whole-breast irradiation

Key words: breast cancer, BCS, IORT, complications, QoL, BREAST-Q

Introduction

Breast-conserving surgery (BCS) followed by adjuvant whole-breast irradiation (WBI) represents the standard of care for early-stage breast cancer, providing equivalent survival rates to mastectomy while preserving the breast (1). The addition of radiotherapy after BCS markedly reduces the risk of local recurrence (2,3). However, conventional postoperative WBI typically requires 3-6 weeks of daily treatment, which imposes a logistical burden on patients and healthcare systems.

Accelerated partial breast irradiation (APBI) has emerged as an alternative for selected low-risk patients, aiming to deliver radiation to the tumor bed (where most recurrences occur) over a shorter timeframe (4). Intraoperative radiotherapy (IORT), a form of APBI, delivers a single, precise dose of radiation directly to the tumor bed during surgery. This approach offers several potential advantages, including maximal target accuracy, immediate treatment completion,

and reduced radiation exposure to surrounding healthy tissues such as the heart, lungs and contralateral breast (5,6). IORT is increasingly utilized internationally, both as a sole modality for APBI and as a tumor bed boost (7,8).

The clinical efficacy of IORT, particularly using low-energy X-rays, has been evaluated in several randomized trials. The TARGIT-A trial reported the non-inferiority of IORT (as a boost or alone) compared with external beam radiotherapy (EBRT) in selected patients with early-stage, low-risk breast cancer, with a notably lower non-breast cancer mortality rate and reduced toxicity (9). Similarly, the ELIOT study, utilizing electrons, demonstrated equivalence in overall survival but a higher ipsilateral breast tumor recurrence rate with IORT compared with WBI (10). These findings underscore the critical importance of careful patient selection for IORT (11).

While oncological outcomes are paramount, a primary goal of breast-conserving therapy is to maintain or improve cosmetic outcomes and quality of life (QoL) (12). Current evidence on patient-reported outcomes (PROs) and short-term complications following IORT remains less comprehensive compared with data on oncological safety. Some studies suggest favorable cosmetic results with IORT (13), yet others report concerns regarding specific complications, such as fat necrosis and fibrosis, which may impact long-term aesthetics and patient satisfaction (14,15). A systematic assessment of early surgical- and radiotherapy-related toxicities, coupled with validated PRO measures such as the BREAST-Q (16), is necessary to fully understand the treatment's impact on recovery and early QoL (17).

Therefore, this prospective study focuses on the acute postoperative recovery phase within 3 months after surgery, to evaluate the incidence and spectrum of early complications of BCS combined with IORT, assess early health-related QoL using standardized PRO instruments, and identify potential clinical and treatment-related factors influencing these acute-phase outcomes. The follow-up window was set within 3 months and before the initiation of any adjuvant therapy in order to avoid the confounding effects of subsequent systemic or local treatment on complications and QoL. The findings are intended to provide a detailed profile of early recovery after BCS combined with IORT, supplementing existing data to inform preoperative patient counseling and perioperative clinical management.

Materials and methods

Patient population and clinical data. The present study prospectively analyzed data from women with stage I-II breast cancer who underwent BCS combined with IORT at Tianjin Medical University Cancer Institute and Hospital (Tianjin, China) between March 2021 and June 2023. The inclusion criteria were as follows: i) Age ≥18 years; ii) pathological confirmation of invasive ductal carcinoma, invasive lobular carcinoma or ductal carcinoma *in situ*; iii) a tumor size ≤5 cm (pTis-T2); and iv) the completion of BCS and IORT as the primary local treatment. Exclusion criteria included: i) A prior history of ipsilateral breast radiotherapy; ii) the presence of distant metastases at diagnosis; iii) the inability to complete the follow-up or questionnaire assessment; and iv) receipt of neoadjuvant systemic therapy (including chemotherapy, endocrine therapy or targeted therapy) before surgery. A total of 120 consecutive patients were initially enrolled. After excluding 18 patients who were lost to follow-up, 102 patients were included in the final analysis. Clinical characteristics, including age, body mass index (BMI), baseline comorbidities (diabetes, hypertension and cardiovascular disease), tumor location, pathological stage according to the American Joint Committee on Cancer 8th edition Tumor-Node-Metastasis staging system (18), molecular subtype and applicator size, were collected from medical records. The study was approved by the Institutional Review Board of Tianjin Medical University Cancer Institute and Hospital, and written informed consent was obtained from all participants.

Treatment protocol. The surgical and radiotherapeutic procedures were standardized. BCS aimed to achieve complete tumor excision with negative microscopic margins, confirmed by intraoperative frozen-section analysis of specimens from all six directions of the surgical cavity (superior, inferior, medial, lateral, anterior and posterior). A sentinel lymph node biopsy or axillary lymph node dissection was performed based on preoperative clinical staging. IORT was delivered immediately after tumor resection, prior to wound closure, using the INTRABEAM® system (Carl Zeiss AG). A spherical applicator, selected to fit snugly within the surgical cavity with its surface within 1 cm of the skin, was positioned. A single dose of 20 Gy was prescribed to the surface of the applicator. Following irradiation, the cavity was irrigated with iodine solution. The breast parenchyma and subcutaneous tissues were then meticulously approximated in layers, and the skin was closed subcuticularly. A single suction drain was routinely placed.

Postoperative management protocol. All enrolled patients received standardized postoperative management according to a uniform institutional protocol as follows: i) The suction drain was removed when the drainage volume was <20 ml/24 h; ii) standardized wound dressing and disinfection were performed by specialized breast surgery nurses; iii) prophylactic antibiotics were not routinely used, and antibiotic use was strictly based on unified clinical indications; and iv) all patients received uniform postoperative health education and follow-up reminders. Routine ambulatory follow-up was performed at 1-month post-surgery for all patients, with consistent examination and assessment procedures.

Assessment of complications and QoL. Patients were systematically assessed for short-term (≤3 months post-surgery) complications related to surgery and radiotherapy. Surgery-related complications were assessed with pre-defined standardized operational criteria consistent with the Radiation Therapy Oncology Group (RTOG) acute morbidity scoring criteria (19) and international breast surgery norms, including: i) RTOG grade 1 incision site pain (mild pain not requiring analgesics); ii) incision site sclerosis (defined as palpable localized hardening of the incision and surrounding breast parenchyma, reported by patients and confirmed by photo-assisted assessment during follow-up); iii) skin indentation (defined as visible localized depression of the breast skin at the surgical site); iv) incision edema; v) delayed wound healing (defined

as unhealed surgical incision with exudation for >2 weeks postoperatively); vi) fat necrosis (defined as hypoechoic mass with calcification on breast ultrasound, or pathologically confirmed fat necrosis in patients with secondary surgery); vii) incision infection (mastitis, defined as redness, swelling, heat and pain of the breast with positive bacterial culture or requiring antibiotic treatment); and viii) symptomatic hematoma/seroma requiring puncture aspiration or surgical intervention. Radiotherapy-related complications were graded according to the RTOG criteria for acute radiation morbidity, with a focus on skin reactions. Health-related QoL (HRQoL) was evaluated using two validated PRO instruments: The BREAST-Q (Breast-Conserving Therapy Module) (16) and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (20). To minimize the confounding effects of all subsequent adjuvant therapies (including chemotherapy, endocrine therapy, targeted therapy and supplementary EBRT), all follow-up assessments were completed strictly within 3 months after surgery, and before the initiation of any adjuvant systemic or local treatment.

Follow-up procedure. A structured telephone follow-up was conducted by a designated, professionally trained research coordinator at 1 and 3 months post-surgery. The interview was based on a pre-tested standardized case report form with uniform descriptive guidelines for each complication item, to guide patients to report their conditions accurately. To mitigate the potential reporting bias of telephone follow-up, the following quality control measures were adopted: i) Patients were required to provide photos of the surgical site during follow-up to assist the objective assessment of physical signs such as skin indentation and sclerosis; ii) all follow-ups, data entry and questionnaire scoring were completed by the same fixed coordinator throughout the study to eliminate inter-observer bias; and iii) patient-reported results were cross-validated with the medical records of their 1-month routine in-person ambulatory follow-up.

Statistical analysis. Statistical analysis was performed using SPSS software (version 27.0; IBM Corp.). Descriptive statistics are presented as the mean ± standard deviations for continuous variables and as n (%) for categorical variables. Univariate analyses were conducted to explore associations between patient/treatment characteristics and outcomes (complications and BREAST-Q scores). The χ^2 test or Fisher's exact test was used for categorical variables, and the independent samples t-test was used for continuous variables, as appropriate. Baseline confounding factors, including BMI and relevant comorbidities, were evaluated in univariate analysis. Detailed results are presented in Table SI. No statistically significant associations with postoperative complications or BREAST-Q scores were observed (all P>0.05). Variables with P<0.1 in the primary univariate analyses were further included in multivariate regression models. For dichotomous complication endpoints (presence vs. absence of events), binary logistic regression was used to calculate odds ratios and 95% confidence intervals (CIs). For continuous BREAST-Q scale scores, multiple linear regression was used to calculate unstandardized coefficients (β) and 95% CIs. Two-tailed P<0.05 was considered to indicate a statistically significant difference.

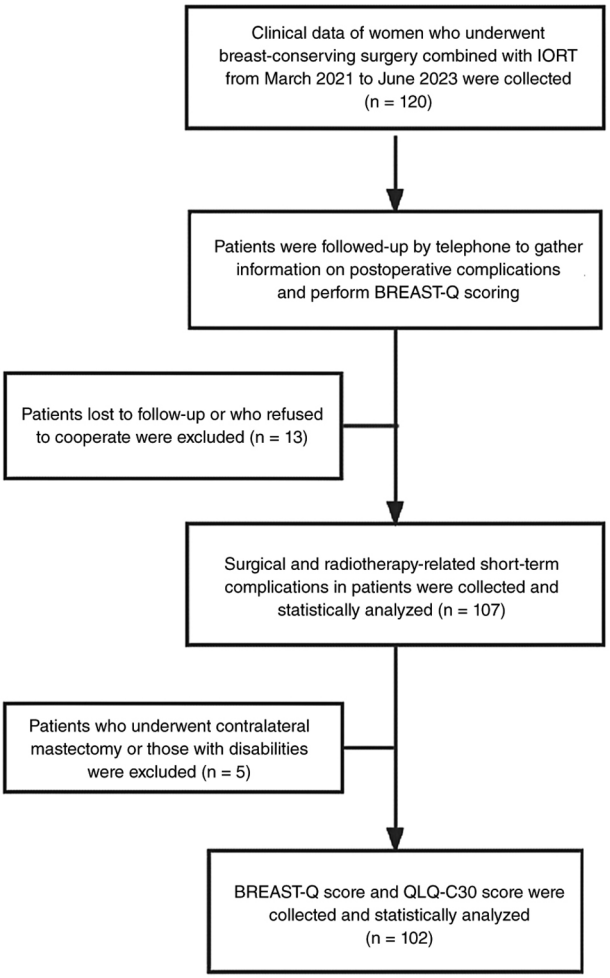

Figure 1. Study flow diagram. Among 120 consecutively enrolled patients who underwent breast-conserving surgery with IORT, 18 were excluded: 13 were lost to follow-up or refused to cooperate, and 5 underwent contralateral mastectomy or had disabilities. Complications were analyzed in 102 patients, and quality of life was assessed in the 92 patients who completed the questionnaires. IORT, intraoperative radiotherapy; QLQC30, Quality of Life Questionnaire-Core 30.

Results

Patient characteristics and study flow. Between March 2021 and June 2023, a total of 120 consecutive patients who underwent BCS with IORT were initially enrolled. Of these, 13 patients were lost to follow-up and 5 patients were excluded due to other reasons (contralateral mastectomy or disability), resulting in 102 patients being included in the final analysis. Among these, 92 patients completed the QoL assessment and were analyzed for PROs. The study flow is summarized in Fig. 1. The baseline clinical and pathological characteristics of the 102-patient cohort are detailed in Table I. The median age was 45 years (range, 29-78), with 55 patients (53.9%) aged <45 years. Invasive ductal carcinoma was the most common pathological type (78.4%). Most patients had early-stage disease: pTis/T1 tumors accounted for 74.5% (76/102), and 77.5% (79/102) had node-negative (pN0/pNsn) disease. The majority of patients (90.2%) underwent axillary lymph node dissection. The most frequently used applicator sizes were 4.5-5.0 cm (74.5%).

Table I. Baseline clinical and pathological characteristics of the study cohort (n=102).

Characteristic	n (%)
Age, years	
<45	55 (53.9)
≥45	47 (46.1)
Affected breast	
Left	55 (53.9)
Right	47 (46.1)
Primary tumor location	
Outer upper quadrant	42 (41.2)
Outer lower quadrant	32 (31.4)
Inner upper quadrant	21 (20.6)
Inner lower quadrant	7 (6.9)
Pathological type	
Invasive ductal carcinoma	80 (78.4)
Ductal carcinoma *in situ*	18 (17.6)
Invasive lobular carcinoma	4 (3.9)
pT stage	
Tis	18 (17.6)
T1	58 (56.9)
T2	26 (25.5)
pN stage	
N0/Nsn	79 (77.5)
N1	21 (20.6)
N2	2 (2.0)
Axillary surgical procedure	
Axillary lymph node dissection	92 (90.2)
Sentinel lymph node biopsy only	10 (9.8)
Molecular subtype	
Luminal A	47 (46.1)
Luminal B	19 (18.6)
HER-2 overexpression	15 (14.7)
Triple-negative	21 (20.6)
Applicator size, cm	
2.5-3.0	4 (3.9)
3.5-4.0	22 (21.6)
4.5-5.0	76 (74.5)

Nsn, sentinel lymph node biopsy without additional dissection; pT, pathological tumor stage; pN, pathological nodal stage.

Surgery-related complications. The incidence of various surgery-related complications within 3 months post-operation is presented in Table II. The most common complications were incision site sclerosis (84.3%) and surgical site pain (58.8%). All reported pain was mild (grade 1 per RTOG acute morbidity criteria) and manageable without routine analgesic use. Skin indentation (44.1%) and symptomatic seroma/hematoma (32.4%) were also frequently observed. Severe complications such as delayed incision healing (12.7%), fat necrosis (11.8%) and incision infection (7.8%) occurred less frequently.

Table II. Incidence of surgery-related complications within 3 months after breast-conserving surgery with intraoperative radiotherapy (n=102).

Complication	n (%)
Incision site sclerosis	86 (84.3)
Pain at surgical site	60 (58.8)
Not requiring analgesics	60 (58.8)
Requiring analgesics	0 (0.0)
Skin indentation	45 (44.1)
Symptomatic seroma/hematoma	33 (32.4)
Managed conservatively	23 (22.5)
Requiring aspiration	10 (9.8)
Breast edema	20 (19.6)
Delayed incision healing	13 (12.7)
Fat necrosis	12 (11.8)
Incision infection	8 (7.8)
Mastitis	2 (2.0)

Table III. Patient-reported radiotherapy-related adverse events within 3 months as assessed by the BREAST-Q breast-conserving therapy module (n=92).

Adverse event	Total, n (%)	Mild, n (%)	Severe, n (%)
Pigmentation changes	81 (88.0)	72 (78.3)	9 (9.8)
Dry skin	54 (58.7)	45 (48.9)	9 (9.8)
Skin thickening	51 (55.4)	44 (47.8)	7 (7.6)
Telangiectasia	38 (41.3)	35 (38.0)	3 (3.3)
Skin sores/pain	25 (27.2)	15 (16.3)	10 (10.9)
Skin irritation	21 (22.8)	16 (17.4)	5 (5.4)

Radiotherapy-related adverse events. Acute radiation skin reactions (graded by RTOG acute morbidity criteria) were observed in 75 patients (73.5%), all of which were mild to moderate: 67 patients (65.7%) had grade I reactions and 8 patients (7.8%) had grade II reactions. No grade ≥3 severe acute radiation dermatitis was observed in the entire cohort. Patient-reported radiotherapy-related adverse events from the BREAST-Q are detailed in Table III. Pigmentation changes (88.0%) and dry skin (58.7%) were the most commonly reported issues. Severe events were reported by a minority of patients across all categories.

Quality of life outcomes. HRQoL was assessed with the BREAST-Q scale (0-100 scoring range, with higher scores representing better QoL and greater patient satisfaction). The mean ± standard deviation scores of the 92 evaluable patients were: Satisfaction with breasts, 54.69±19.56; psychosocial well-being, 64.37±25.74; and chest physical well-being, 60.99±23.47 (Table SII).

Univariate analysis of influencing factors. Three clinical and treatment-related factors were identified to be significantly

Table IV. Univariate analysis of associations between patient/treatment characteristics and patient-reported radiotherapy-related adverse events[a].

Characteristic	Grade of radiation skin injury	Pigmentation changes	Dry skin	Skin thickening	Telangiectasia	Skin sores/pain	Skin irritation
Age (<45 vs. ≥45 years)	0.963	0.250	0.178	0.364	0.658	0.250	0.374
Affected side (left vs. right)	0.632	0.864	0.581	0.582	0.154	0.850	0.154
Tumor quadrant	0.864	0.649	0.640	0.163	0.895	0.679	0.895
Tumor T stage	0.338	0.851	0.356	0.495	0.924	0.851	0.154
Applicator size	<0.01[b]	0.556	0.093	0.628	0.741	0.556	<0.01[b]

[a]Data are presented as P-values. [b]P<0.05.

Table V. Univariate analysis of associations between patient/treatment characteristics and surgery-related complications within 3 months[a].

Characteristic	Pain	Symptomatic seroma/ hematoma	Sclerosis	Skin indentation	Breast edema	Delayed healing	Fat necrosis	Incision infection	Mastitis
Age (<45 vs. ≥45 years)	0.172	0.154	0.250	0.178	0.364	<0.05[b]	0.304	<0.05[b]	0.625
Affected side (left vs. right)	0.152	0.895	0.850	0.581	0.582	0.154	0.250	0.748	0.172
Tumor quadrant	0.444	0.924	0.649	0.640	0.163	0.895	0.850	0.586	0.152
Tumor T stage	0.701	0.070	0.556	0.093	0.628	0.481	0.851	0.356	0.878
Applicator size	0.308	0.585	0.107	<0.01[a]	0.152	0.154	0.250	0.178	0.192

[a]Data are presented as P-values. [b]P<0.05.

associated with study outcomes in univariate analysis: Patient age, applicator size and tumor T stage. The results of the univariate analyses exploring associations between patient/treatment characteristics and outcomes are shown in Tables IV-VI. Table IV shows that a larger applicator size was significantly associated with a higher grade of radiation skin injury (P<0.01) and more severe skin irritation (P<0.01). Table V shows that older age (≥45 years) was a significant risk factor for delayed incision healing (P<0.05) and incision infection (P<0.05). Larger applicator size was significantly associated with the occurrence of skin indentation (P<0.01). Tumor T stage showed a non-significant trend towards an association with symptomatic seroma/hematoma (P=0.07). Table VI demonstrates that a higher tumor T stage was significantly associated with lower scores in both satisfaction with breasts (P<0.01) and chest physical well-being (P<0.01). No other characteristics showed a significant association with BREAST-Q domain scores. Univariate analysis of baseline BMI and comorbidities revealed no statistically significant associations with postoperative complications or BREAST-Q domain scores; detailed results are presented in Table SI (all P>0.05). Meanwhile, all follow-up assessments were strictly completed before the initiation of any adjuvant systemic therapy, which completely eliminated the confounding effect of subsequent treatment on wound healing and QoL outcomes.

Multivariate regression analysis results. Variables with P<0.1 in the univariate analyses were included in the regression models. These included age, applicator size and tumor T stage for surgery-related complications, applicator size for radiotherapy-related adverse events and tumor T stage for BREAST-Q domain scores. The multivariate analysis showed that none of the included variables were identified as statistically significant independent predictors for postoperative complications or BREAST-Q domain scores (all P>0.05). The detailed results of the binary logistic regression for surgery-related complications, binary logistic regression for radiotherapy-related adverse events, and multiple linear regression for BREAST-Q scores are presented in Tables VII, VIII and IX, respectively. Given the limited sample size of this cohort, the associations identified in univariate analysis should be interpreted with caution, and cannot be inferred as causal relationships.

Discussion

The present study provides a detailed prospective analysis of short-term complications and patient-reported QoL following

Table VI. Univariate analysis of associations between patient/treatment characteristics and BREAST-Q scale scores within 3 months[a].

Characteristic	Psychosocial well-being	Satisfaction with breasts	Chest physical well-being
Age (<45 vs. ≥45 years)	0.178	0.305	0.581
Affected side (left vs. right)	0.581	0.154	0.640
Tumor quadrant	0.640	0.895	0.356
Tumor T stage	0.093	<0.01[b]	<0.01[b]
Applicator size	0.178	0.721	0.964

[a]Data are presented as P-values. [b]P<0.05.

Table VII. Multivariate binary logistic regression analysis of factors associated with surgery-related complications within 3 months after breast-conserving surgery combined with intraoperative radiotherapy (n=102).

Complication endpoint and influencing factor	Odds ratio	95% confidence interval	P-value
Symptomatic seroma/hematoma			
Age (≥45 vs. <45 yrs)	1.42	0.61-3.32	0.412
Tumor T stage	1.76	0.95-3.26	0.072
Applicator size	1.18	0.58-2.41	0.645
Skin indentation			
Age (≥45 vs. <45 years)	1.53	0.69-3.39	0.294
Tumor T stage	1.45	0.81-2.59	0.211
Applicator size	1.87	0.92-3.79	0.082
Delayed incision healing			
Age (≥45 vs. <45 years)	2.35	0.89-6.21	0.085
Tumor T stage	1.21	0.54-2.71	0.643
Applicator size	1.64	0.66-4.08	0.287
Incision infection			
Age (≥45 vs. <45 years)	2.47	0.78-7.82	0.124
Tumor T stage	1.09	0.41-2.90	0.864
Applicator size	1.52	0.51-4.53	0.453

Variable assignment: Age (0, <45 years; 1, ≥45 years); tumor T stage (0, Tis; 1, T1; 2, T2); applicator size (0, 2.5-3.0 cm; 1, 3.5-4.0 cm; 2, 4.5-5.0 cm); all complication endpoints (0, absent; 1, present).

BCS combined with IORT using low-energy X-rays. The findings indicate that while severe complications are infrequent, the overall short-term morbidity profile is notable, with specific factors such as applicator size, tumor stage and patient age influencing outcomes.

The oncological rationale for APBI, including IORT, is strongly supported by evidence that most ipsilateral recurrences after BCS occur in close proximity to the original tumor bed (21). For patients aged ≥45 years with early-stage, low-risk breast cancer (T1 and small T2 ≤3.5 cm, N0-1, M0, suitable for breast-conserving surgery), large randomized trials have established the role of IORT. The TARGIT-A trial demonstrated that risk-adapted IORT yielded comparable long-term local control and overall survival to EBRT, with the additional benefit of reduced non-breast cancer mortality rate and lower toxicity (9). Similarly, the ELIOT trial confirmed equivalent overall survival rates, while noting a higher rate of ipsilateral breast tumor recurrence in the IORT group, thereby underscoring the paramount importance of stringent patient selection criteria (10). This is particularly relevant for specific populations, such as elderly patients with low-risk disease profiles, who may derive substantial benefit from the condensed treatment schedule without compromising oncological safety (22).

When evaluating complications, the current results present a multifaceted picture that aligns with and extends previous observations. Consistent with the ELIOT trial report, the present study observed a low rate of severe acute skin toxicity, corroborating the dosimetric advantage of IORT in minimizing exposure to superficial skin layers (23). However, the reported high incidence of incision site sclerosis (84.3%) and notable rates of fat necrosis (11.8%) and delayed healing (12.7%) resonate with studies indicating that IORT can be associated with increased perisurgical fibrosis and fat necrosis, likely a direct

Table VIII. Multivariate binary logistic regression analysis of factors associated with patient-reported radiotherapy-related adverse events within 3 months after breast-conserving surgery combined with intraoperative radiotherapy (n=92).

Adverse event endpoint	Influencing factor	Odds ratio	95% confidence interval	P-value
Grade of radiation skin injury	Applicator size	1.92	0.94-3.92	0.073
Pigmentation changes	Applicator size	1.15	0.52-2.54	0.731
Dry skin	Applicator size	1.78	0.91-3.48	0.094
Skin thickening	Applicator size	1.08	0.56-2.08	0.821
Telangiectasia	Applicator size	0.94	0.48-1.84	0.852
Skin sores/pain	Applicator size	1.15	0.52-2.54	0.731
Skin irritation	Applicator size	1.98	0.96-4.08	0.064

Variable assignment: Applicator size (0, 2.5-3.0 cm; 1, 3.5-4.0 cm; 2, 4.5-5.0 cm); all adverse event endpoints (0, absent/mild; 1, severe/higher grade for radiation skin injury).

Table IX. Multiple linear regression analysis of factors associated with BREAST-Q domain scores within 3 months after breast-conserving surgery combined with intraoperative radiotherapy (n=92).

BREAST-Q domain	Influencing factor	Unstandardized coefficient (β)	95% confidence interval	P-value
Satisfaction with breasts	Tumor T stage	-4.27	-8.76 to 0.22	0.062
Psychosocial well-being	Tumor T stage	-3.85	-8.94 to 1.24	0.137
Chest physical well-being	Tumor T stage	-4.12	-8.98 to 0.74	0.096

Variable assignment: Tumor T stage (0, Tis; 1, T1; 2, T2); BREAST-Q domain scores were treated as continuous variables (0-100 scale; higher scores indicate better quality of life).

consequence of delivering a high single dose to a confined tissue volume (23,24). Notably, the incidence of sclerosis in the present cohort is consistent with the 78-86% incidence of early postoperative peritumoral fibrosis reported in previous IORT studies using the same INTRABEAM system (25-27), which further validates the consistency of the assessment criteria and results in the present study. A previous single-center study in China also reported high rates of excellent/good cosmetic outcomes (28), and the present detailed patient-reported data complement this by quantifying the spectrum of early physical changes that underlie such ratings.

The findings from the univariate analysis within the present study offer direct clinical insights. Larger applicator size was significantly associated with higher-grade skin toxicity, skin indentation and irritation (all $P<0.01$), driven by larger irradiated volume and reduced applicator-skin distance, highlighting the need for precise applicator selection and cavity closure to reduce acute morbidity and preserve cosmetic potential. Older age was a risk factor for incision infection and delayed healing ($P<0.05$), supporting tailored postoperative care for elderly patients. Higher T stage (larger tumor volume) was linked to worse breast satisfaction and physical well-being ($P<0.01$), reflecting the impact of larger resection volume on early cosmetic and QoL outcomes. These findings refine patient selection for IORT, consistent with the 2024 ASTRO APBI clinical guidelines (29). The present data support prioritizing IORT for Tis-T1 patients with smaller tumor volume, while more cautious evaluation and supportive care are needed for elderly patients and those requiring larger applicators.

In the domain of QoL, the application of the validated BREAST-Q instrument in the present study revealed that larger initial tumor size (T stage) was the most significant factor negatively impacting early scores for satisfaction with breasts and chest physical well-being. This underscores a persistent challenge in breast-conserving therapy in terms of achieving optimal PROs following larger volume resections. It is instructive to compare this with the long-term PROs from the TARGIT-A trial, where IORT was associated with better cosmetic scores and fewer breast symptoms compared with EBRT at later time points (30). The present early-phase data provide a foundational snapshot, suggesting that the initial recovery experience is heavily shaped by tumor-related factors, upon which the longer-term benefits of IORT may subsequently be realized.

The present study has several inherent limitations. First, the 3-month follow-up in this study only covers the acute postoperative recovery phase, and cannot evaluate radiotherapy-related late adverse events (including progressive fibrosis, fat necrosis and long-term cosmetic changes) or the sustained impact of treatment on QoL, which typically develop gradually over months to years after radiotherapy. Notably, this 3-month window was specifically set to complete all assessments prior to the initiation of any adjuvant therapy, to minimize confounding effects of subsequent systemic treatment or supplementary radiotherapy on complications and QoL, and to accurately isolate the independent impact of BCS combined with IORT on early postoperative recovery. To address the gap in long-term outcomes, a 5-year systematic follow-up of this cohort is

ongoing, which includes annual in-person clinical examinations, clinician-rated cosmetic assessments and standardized PRO evaluations; the long-term oncological safety, late toxicities and sustained QoL outcomes will be separately reported once this follow-up is completed. Second, telephone follow-up has inherent limitations in the assessment of objective physical signs; even with photo-assisted evaluation, it is less accurate than standardized in-person clinical examination. A standardized in-person physical examination will therefore be adopted for all patients in the ongoing long-term follow-up to obtain more accurate and robust outcome data. Third, the present study is a single-arm prospective cohort study without a concurrent control group of patients treated with BCS followed by standard WBI, including contemporary hypofractionated WBI regimens that have become the global standard of care (31,32). This design limits the direct comparison and contextualization of the observed complication profile and patient-reported QoL outcomes with current standard-of-care treatment. Prospective head-to-head comparisons between IORT and modern hypofractionated WBI are therefore needed to further clarify the relative risk-benefit profile of IORT in early-stage breast cancer. Fourth, no objective clinician-rated cosmetic assessment was performed during the 3-month acute follow-up period, as the primary endpoints of this study focused on early postoperative complications and patient-reported QoL. To address this, a standardized clinician-rated cosmetic assessment using the Harris cosmetic scoring system will be included in the ongoing 5-year long-term follow-up to comprehensively evaluate the long-term cosmetic outcomes of this treatment regimen (33).

In conclusion, BCS combined with IORT has a manageable early complication profile within 3 months post-surgery, predominantly consisting of mild localized tissue reactions with rare severe adverse events. Applicator size, patient age and tumor T stage are significantly associated with early complications and acute-phase QoL, providing practical reference for preoperative patient counseling and perioperative management optimization. Given the limited short-term follow-up, long-term follow-up of this cohort is ongoing to verify the long-term safety, cosmetic outcomes and sustained QoL impacts of this treatment.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

HH and XL completed the data analysis and wrote the manuscript. QP and JW were responsible for the research design and guided the revision of the manuscript. BZ and JL contributed to data acquisition and clinical interpretation, data curation (extraction of clinical data from medical records and the compilation of the study database) and validation, and performed revision of the manuscript. QP and HH confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

This study was performed in accordance with the Declaration of Helsinki and was approved by the Medical Ethics Committee of Tianjin Medical University Cancer Institute and Hospital (Tianjin, China; initial approval no. bc2021-015; concluding approval no. bc20240265). All participants provided written informed consent prior to enrollment.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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