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Risk factors for seroma evacuation in breast cancer patients treated with intraoperative radiotherapy

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ABSTRACT

Background: Novel techniques in oncology provide new treatment opportunities but also introduce different patterns of side effects. Intraoperative radiotherapy (IORT) allows a shortened overall treatment time for early breast cancer either combined with whole breast radiotherapy (WBRT), or alone. Although the early side effects of IORT are well known, data on clinically important late side effects, which require medical intervention, are scarce.

Aim: In this study, we analyze risk factors for seroma evacuation more than 6 months after IORT.

Materials and methods: We evaluated 120 patients with a mean follow-up of 27.8 months (range: 7–52 months). Fifty-one patients received IORT only and 69 were additionally treated with WBRT.

Results: Seroma evacuation was performed 6–38 months after IORT. Two (3.9%) events were observed in the IORT group and 14 (20%) in the IORT + WBRT group. Univariate (Kaplan–Meier) analysis showed that addition of WBRT to IORT increased the risk of seroma evacuation [hazard ratio = 5.5, 95% confidence interval: 2.0–14.7, $P = 0.011$]. In a multivariate analysis (Cox proportional hazards regression), WBRT and axillary lymph node dissection were significant risk factors for seroma evacuation (model P value = 0.0025).

Conclusions: WBRT applied after IORT is associated with increased risk of seroma evacuation, which might be considered as a late side effect.

1. Background

Breast cancer is the second most common cancer worldwide and the most frequent cancer among women. It is estimated that about 1.67 million new breast cancer cases were diagnosed in 2012 (25% of all cancers).[1] Currently, most cases of breast cancer are treated with multiple modalities. Depending on tumor stage, molecular profile, and in certain cases patient preference, treatment options include

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surgery, chemotherapy, hormonal therapy, targeted therapy, and radiotherapy.

The role of adjuvant radiotherapy in the treatment of early-stage and locally advanced breast cancer has been demonstrated.[2,3] Whole breast radiotherapy (WBRT) is part of breast conservative treatment (BCT) and improves local control and overall survival.[3,4] WBRT with additional radiation dose to the tumor bed improves local control, although with moderately poorer cosmetic effect.[5–8] The risk of WBRT side effects depends on the volume of irradiated breast tissue, the dose given to the heart, lung, lymph node areas.[9–11] Omitting irradiation of the whole breast and delivering high-dose radiation only to the lumpectomy bed, with a 1- to 2-cm margin, in a shorter period of time, may reduce the risk of these side effects without compromising curability in selected patients. This concept of accelerated partial breast irradiation (APBI) after a lumpectomy has led to the development of various radiotherapy techniques (balloon catheter brachytherapy, multi-catheter interstitial brachytherapy, conformal external beam radiotherapy, and intraoperative radiotherapy) and dedicated equipment allowing delivery of the radiation dose in 1–7 days.

Intraoperative radiation therapy (IORT) is one of the APBI techniques that delivers a single fractional dose of radiation with megavoltage electrons (Mobetron, Sunnyvale, CA, USA; Novac, LIAC, Sordina IORT Technologies, SpA, Vicenza, Italy) or kilovoltage photons (Intrabeam, Carl Zeiss, Oberkochen, Germany) directly to the tumor bed during surgery. The technique and its clinical application were described by Vaidya.[12,13] IORT given as a boost is an effective option for breast-conserving treatment.[14] Data gathered in the Targeted Intraoperative radiotherapy (TARGIT) and Intraoperative radiotherapy with electrons (ELIOT) trials support the idea that some patients with breast cancer can be offered APBI as a sole radiation modality in BCT.[15–17] Recommendations for the selection of patients for APBI have been proposed by the American Society for Radiation Oncology (ASTRO) and the European Organisation for Research and Treatment of Cancer (EORTC).[18,19]

When introducing novel techniques such as APBI, we are faced with new data in imaging modalities[20–22] and different patterns of side effects.[23–26] Frequently reported side effects related to IORT are seroma, delayed wound healing, and fibrosis.[20,23,26–31] In mammography and breast ultrasonography, the most frequently reported side effects are hematoma or seroma, fat necrosis (manifesting as oil cysts), unspecific dystrophic calcifications, and parenchymal scarring (architecture distortions).[21,22] Most of these side effects are reported irrespective of the time of occurrence. It is widely accepted that side effects appearing later than 3–6 months after radiotherapy are considered as late. In our institution, seroma is the most frequently observed side effect that needs medical intervention.

2. Aim

The aim of the present study was to analyze the risk factors for seroma evacuation more than 6 months after IORT.

Table 1 – Eligibility criteria for APBI.

Factor	Criterion
Patient factors	
Age	≥50 years
Pathologic factors	
Histology	NST, tubular, mucinous
Tumor size	≤20 mm
Margins	>2 mm
LVSI	No
ER status	Positive
Her-2 status	No overexpression
Pure DCIS	<5% within tumor
EIC	Not allowed
Nodal status	No

LVSI, lymphvascular space involvement; NST, no special type; ER, estrogen receptor; Her-2, human epidermal growth factor receptor 2; DCIS, ductal carcinoma in situ; EIC, extensive intraductal component.

3. Materials and methods

3.1. *Characteristics of patients and follow-up*

The research protocol was accepted by Bioethical Committee of Polish Chamber of Physicians and Dentists in Szczecin (Decision Number 08/KB/V/2015). The study is a retrospective medical records analysis of radiotherapy side effects and the data were analyzed and reported anonymously, thus, it did not require additional patients' informed consent.

One hundred and twenty-seven patients with breast cancer were treated in our institution using IORT from April 20, 2010 to February 19, 2014 based on the decisions of a multidisciplinary team. The criteria for APBI were in accordance with the ASTRO and EORTC recommendations (Table 1).[18,19] After APBI, patients were consulted by the multidisciplinary team and qualified for further treatment. Indications for WBRT included findings that did not match the criteria in Table 1. Two patients in the APBI group refused WBRT. Patients with sentinel lymph node metastasis were offered axillary lymph node dissection (ALND). Fifteen of 18 patients with sentinel lymph node metastasis underwent ALND, but it was omitted in three patients with micrometastasis. Enrolment for systemic treatment (chemotherapy, hormonal therapy, or other therapy) followed international recommendations.[18,19,32–34] Fourteen patients were given chemotherapy before WBRT. Eighty three patients were treated with tamoxifen, while 27 with aromatase inhibitors, 1 with LHRH analog and 9 patients did not receive hormonal therapy.

The patients were followed up prospectively every 3 months for 2 years and every 6 months thereafter. The data were collected in relation to treatment results and side effects using a modified LENT-SOMA scale (Late Effects in Normal Tissues Subjective, Objective, Management and Analytic scores). Seven patients were lost to follow-up. This analysis included 120 patients with a mean follow-up of 27.8 months (range: 7–52 months, median: 24 months). Fifty-one patients received APBI only and 69 were additionally treated with WBRT.