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Original research article

Frequency of whole breast irradiation (WBRT) after intraoperative radiotherapy (IORT) is strongly influenced by institutional protocol qualification criteria

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ARTICLE INFO

Article history:
Received 24 July 2017
Received in revised form
20 September 2017
Accepted 26 November 2017

Keywords:
Breast cancer
Accelerated partial breast irradiation
Intraoperative radiotherapy
Whole breast irradiation

ABSTRACT

Background: Accelerated partial breast irradiation (APBI) is a promising method of adjuvant radiotherapy for select patients. Intraoperative radiotherapy (IORT) is a form of APBI, and appropriate patient selection is important.

Aim: The aim of our study was to analyse the influence of our protocol on the frequency of WBRT after IORT and our protocol's correlation with the reported use of WBRT according to TARGIT guidelines. We also aimed to verify how changes in our protocol influenced the frequency of WBRT.

Material and methods: Between April 20, 2010 and May 10, 2017, we identified 207 patients irradiated with IORT for APBI.

Results: Ninety-one patients (44%) met the criteria for APBI only, while 116 (56%) should have been offered additional WBRT. Retrospective analysis showed that WBRT was applied statistically significantly less frequently compared with strict protocol indications: 99 patients (47.8%) received APBI only and 108 (51.2%) underwent adjuvant WBRT ($p < 0.0001$). Applying the TARGIT trial guidelines, 69 patients (33.4%) should have been offered WBRT ($p < 0.0001$), which is twice the number of patients treated with WBRT in our study. Changing the protocol to less restrictive criteria would have statistically significantly decreased the number of patients (95, 46%) offered WBRT ($p < 0.0001$).

Conclusions: Following international guidelines, 46% of patients should receive WBRT after IORT, which is 1.5–2 times more than for the TARGIT criteria. In our analysis, a high percentage of patients (19%) did not receive WBRT after IORT despite the protocol recommendations. The chosen protocol strongly influences the frequency of adjuvant WBRT.

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https://doi.org/10.1016/j.rpor.2017.11.003

1. Background

The value of whole breast radiotherapy (WBRT) after breast-conserving surgery (BCS) for invasive breast cancer (IBC) has been confirmed in multiple clinical trials and meta-analyses.[1–3] Based on these studies, all patients should be offered adjuvant radiotherapy after BCS for IBC. However, the disadvantages of adjuvant WBRT include exposure of healthy tissue to irradiation (lung, heart, chest wall) and the time needed to conduct at least 15 fractions (3 weeks).[4] Considering the limitations of WBRT and the biology of IBC, researchers began irradiating only the primary tumour and surrounding healthy tissue, which is called accelerated partial breast irradiation (APBI).

Several scientific societies have published recommendations for patient qualification for APBI, including the European Organisation for Research and Treatment of Cancer (ESTRO) and the American Society for Radiation Oncology (ASTRO).[5,6] These societies divide candidates for APBI into three groups: "suitable", "cautionary", and "unsuitable", depending on the histological tumour type, diameter, presence of ductal carcinoma in situ (DCIS), excision margin, oestrogen receptor-positive status, lymphatic vessel invasion, lymph node status, age, and BRCA1 gene status.

The advantages/disadvantages of APBI have been evaluated in randomised trials using different methods and different groups of patients. Linear accelerator-based APBI was evaluated in two trials with conflicting results. Conformal radiotherapy appeared to induce unacceptable cosmetic effects,[7] while intensity-modulated radiotherapy (IMRT) showed comparable efficacy to WBRT with better cosmetic effects.[8] Recently, brachytherapy (either high-dose rate or pulsed-dose rate) was confirmed as an acceptable alternative to WBRT in "suitable" patients with IBC.[9] Both IMRT and brachytherapy can be used after BCS when all risk factors are known, and the qualification procedure is relatively simple.

Intraoperative radiotherapy (IORT), applied at the time of BCS, enables localised irradiation precisely in the tumour cavity and is biologically optimal.[10] However, certain factors are unknown when using APBI, including histological tumour type, DCIS status, excision margin, lymphatic vessel invasion, and lymph node status. Currently, two systems of IORT are available: electron-based: (Mobetron; Sunnyvale, CA, USA, and a mobile dedicated accelerator, Novak LIAC; Sordina IORT Technologies, SpA, Vicenza, Italy), or kilovoltage photon-based (INTRABEAM; Carl Zeiss, Oberkochen, Germany). Studies evaluating electron-based IORT were among the first to be published.[11] One trial confirmed that APBI is an acceptable treatment option for "suitable" candidates and that its use in other groups of patients should be carefully considered.[12]

The targeted intraoperative radiotherapy (TARGIT) trial verified the value of kilovoltage photon-based IORT for APBI.[13] The advantage of the method is that it can be followed with WBRT.[14,15] The TARGIT trial protocol recommends using WBRT after IORT in cases of extensive intraductal component, resection margins <1 mm, and lobular cancer. In the trial, each participating centre was able to apply its own recommendations, and overall, 15.2% of patients in the TARGIT trial received WBRT after IORT.[13]

2. Aim

The aim of our study was to analyse how our protocol influenced the frequency of WBRT use after IORT and to assess our protocol's correlation with WBRT use following the TARGIT guidelines. We also aimed to verify how changes in the protocol influenced the frequency of WBRT use.

3. Materials and methods

This was a retrospective medical record analysis. The data were analysed and reported anonymously; therefore, no additional patient informed consent was required.

Beginning in April 2010, IBC patients in our hospital have been treated with the INTRABEAM system (INTRABEAM; Carl Zeiss Surgical, Oberkochen, Germany). The criteria for APBI were defined according to the ESTRO and ASTRO recommendations (Table 1).[5,6] Patients who did not meet these criteria did not qualify for APBI. Patients were consulted in two multidisciplinary team (MDT) meetings: before and after operation. BCS included tumour resection, intraoperative radiological specimen analysis, sentinel lymph node biopsy, and APBI. During the second MDT meeting, WBRT indications were assessed. If pathological report findings did not meet eligibility criteria for APBI only (Table 1), patients were qualified for WBRT. If the only criteria for WBRT qualification was age, patients between 50 and 60 years were given the option to decline WBRT.

Between April 20, 2010 and May 10, 2017, 207 patients received irradiation according to the APBI protocol. Of these, 99 patients (47.8%) underwent APBI only, while 108 (51.2%) received adjuvant WBRT after IORT. Group characteristics are presented in Table 2.

IORT was performed using INTABEAM system, which emits low-energy photons (30–50 kV) with a steep fall-off in soft tissues. After the resection of tumour, the cavity was examined and the applicator was installed. The diameter of applicator was chosen depending on cavity volume. The specimen of resected tissue was verified for margins with the Trident specimen radiography system (Hologic, Inc., Malborough, USA). 50 kV photons were used and the dose of 20 Gy was prescribed on the surface of applicator. Irradiation time depended on the

Table 1 – Eligibility criteria for APBI based on the West Pomeranian Oncology Center protocol.

Tumour type	Ductal, tubular, mucinous carcinoma No lobular, medullar carcinoma
ER	Positive
Her-2	No overexpression
Tumour size	≤20 mm
Margins	>2 mm
LN status	pN0
LVI	No
DCIS	<5% in tumour, no outside of the tumour
Age	Above 60

APBI, accelerated partial breast irradiation; ER, oestrogen receptor; LN, lymph node; LVI, lymphatic vessel invasion; DCIS, ductal carcinoma in situ.