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Case Report

Targeted Intraoperative Radiotherapy Is a Safe Approach for Patients with Pacemakers: A Case Study and Literature Review

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Keywords

Breast cancer · Cardiac implantable electronic device · Intraoperative radiation therapy · Pacemaker · Targeted intraoperative radiotherapy

Abstract

Case reports detailing the effects of targeted intraoperative radiation therapy (IORT) on patients with cardiac pacemakers (PMs) are rare. This growing population sub-group requiring IORT and lack of standardized guidelines necessitate more practical published research. An 81-year-old patient with clinical stage II, T1 N0 grade III, triple-negative invasive ductal carcinoma and an implanted single-lead chamber PM (VVIR mode, model: Biotronik, type Effecta SR) received targeted intraoperative radiotherapy at the time of wide local excision and sentinel lymph node biopsy. It presents the shortest distance between the outer diameter of the PM and IORT applicator in literature. Target IORT was performed utilizing an Intrabeam device (50 kV, Carl Zeiss Surgical, Oberkochen, Germany). This case elucidates the successful use of targeted IORT for breast-conserving surgery in a patient with a single ipsilateral chamber VVIR mode PM. No device failure or malfunction was reported for the PM before, during, or after the procedure. These findings support the use of targeted IORT for patients diagnosed with early-stage breast carcinomas who have a PM implanted. However, further research is needed to understand the safety of other methods and devices for IORT patients with cardiac implantable electronic devices.

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Introduction

We present a rare case consisting of the shortest radial distance between the intraoperative radiation therapy (IORT) applicator and cardiac pacemaker (PM) in the open literature, demonstrating the safety of this technique.

Globally, over 14 million new cancer cases were confirmed in 2012, and breast cancer was the second most frequently diagnosed cancer [1]. IORT is commonly used for the treatment of early-stage breast carcinomas due to its tissue preservation benefits [2, 3]. In 2004, over 3 million people worldwide were reported to be living with various types of cardiac PMs [4], with annual installations increasing from 600,000 in 2002 to 900,000 in 2016 [1, 4, 5]. The increasing overlap between these two groups in an aging population is likely to lead to an increase in the frequency of cases involving patients with PMs and breast cancer [5].

The available evidence suggests that the short-range kilovoltage energy sources reduce the radiation dose to normal tissues by eliminating the electromagnetic radiation and scattered radiation typical of EBRT [6, 7]. Nonetheless, manufacturers are less likely to perform cardiac implantable electronic device (CIED) testing with various IORT devices due to the large number of devices available compounded with types of IORT devices in operation. Hence, case studies expanding the effects of IORT on cardiac PMs are critical.

Case Report

An 81-year-old woman presented with a self-detected suspicious palpable mass in the central portion of the right breast. Core biopsy of the palpable mass revealed clinical stage I, T1 (20 mm) N0 grade III, triple-negative invasive ductal carcinoma. She had a history of hyperlipidemia, hypothyroidism, hypertensive heart disease with diastolic dysfunction, sick sinus syndrome, and an implanted single-lead chamber PM (VVIR mode, model: Biotronik, type Effecta SR). The patient's first PM was implanted 28 years ago, which was replaced with the current unit 5 years ago. The PM was programmed to ventricular rate modulated pacing (VVIR) of 60 bpm and hysteresis of 55 bpm in single chamber mode. Anatomically the PM was located in the subcutaneous tissue pocket in the upper pole of the right breast.

The condition of the patient was discussed at the multidisciplinary meeting. Given the aggressiveness of the tumor, its anatomical proximity to the PM, and the frailty and comorbidities of the patient, it was collectively decided to offer wide local excision, sentinel node biopsy, and IORT using the targeted intraoperative radiotherapy (TARGIT) technique, which involves delivering IORT via a spherical applicator placed in close proximity to the tumor bed for periods of up to 52 min, depending on the diameter of the applicator (30–50 mm) [8]. The pre-anesthetic assessment found that the patient was fit with no contraindications for surgery. A full cardiac assessment by a cardiologist prior to surgery was also performed, which indicated a possible need for mode switching during the IORT procedure if any device malfunction was noted.

Wide local excision with sentinel node harvesting was performed, achieving macroscopically clear margins. Thereafter, TARGIT was performed utilizing a 50-kV Intrabeam device (Carl Zeiss Surgical, Oberkochen, Germany) (Fig. 1). Using a 35-mm applicator, IORT was administered, delivering approximately 20 Gy to the surface of the surgical margin in direct contact with the applicator and 6 Gy to an area 10 mm from the surface at a total duration of 17 min and 27 s, respectively, as estimated from the potential depth dose curve. Radiation levels at the PM were estimated using the isodose curve, as shown in Figure 2. The team utilized a minimum safe distance of 80 mm between the outer tangent of the PM and the

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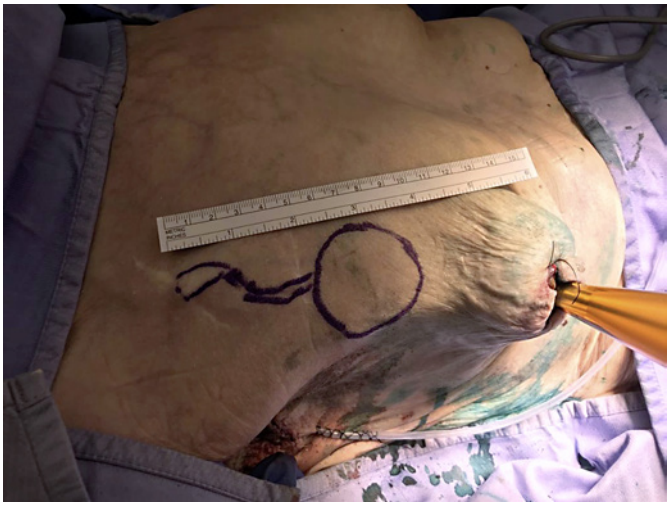

Fig. 1. The pacemaker is marked by a circle on the patient's skin. The ruler and blue surgical markers provide relative dimensions.

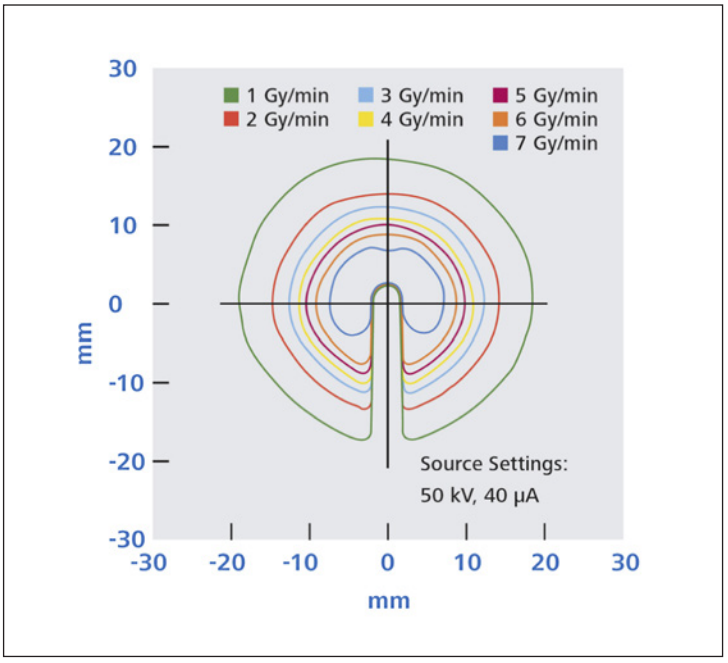

Fig. 2. Isodose line for the Intrabeam device (Carl Zeiss Surgical, Oberkochen, Germany). Profiles of the isodose lines between the radial locations (millimeter) and the IORT applicator wall for radiation exposures of 1–7 Gy/min in increments of 1 Gy/min for a 50-kV, 40-µAmp applicator. The diagram has been reproduced from Intrabeam System from ZEISS Technical Specifications 2017; http://yourrad.se/wpcontent/uploads/en_30_010_0158iv_intrabeam_system_technical_specifications.pdf.

spherical IORT applicator (35 mm in size), yielding a calculated threshold of less than 1 Gy. Direct measurements of the radiation levels at the PM site were not made.

A film diode was placed vertically above the applicator on the skin. The distance between the shaft of the Intrabeam applicator and the nearest edge of the PM was 45 mm. At this distance, the calculated incident radiation dose to the PM was 0.42 Gy, which was well below the recommended safe limit of 1 Gy. We were not able to directly measure the amount of radiation to the PM as our measurement devices provided mixed results upon calibration, and an alternative thermoluminescent dosimeter could not be sourced in time for the scheduled IORT.

The surgery and TARGIT were completed successfully. No malfunction, failure, or mode switching of the cardiac PM was detected by the technician who monitored it intraoperatively and the hemodynamic parameters remained stable throughout the radiation. The patient tolerated the procedure well, recovered completely, and was discharged 2 days later. No

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Table 1. Summary of prior IORT cases of patients with implanted cardiac pacemakers and phantom cases

First author	Tumor site	Patient/ phantom patient	Tumor/ NanoDot site	Device	Total RT dose	Dose at CIED site	Applicator	Distance from PM	Energy	Effects
Keshtgar [18]	Breast	Patient	Tumor	PM	20 Gy	8 cGy	3 cm	9 cm, 8 cGy	50 kV	No malfunctions or failures
Chen [7]	Breast	Phantom	NanoDot	PM	20 Gy	4±0.8 cGy	4.5 cm	5 cm, 159±11 cGy	50 kVp X-rays	No malfunctions or failures
Chen [7]	Breast	Phantom	NanoDot	PM	20 Gy	4±0.8 cGy	4.5 cm	10 cm, 15±1 cGy	50 kVp X-rays	No malfunctions or failures
Chen [7]	Breast	Phantom	NanoDot	PM	20 Gy	4±0.8 cGy	4.5 cm	15 cm, 6.6±0.5 cGy	50 kVp X-rays	No malfunctions or failures
Chen [7]	Breast	Phantom	NanoDot	PM	20 Gy	4±0.8 cGy	4.5 cm	20 cm, 1.8±0.1 cGy	50 kVp X-rays	No malfunctions or failures

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aberrations were noted relating to the functionality of the PM by the cardiology team on the day of the procedure and a few weeks after the surgery.

The final histology confirmed the tumor to be a stage Ib, T1b (9 mm), N0 (0/1), grade III, triple-negative invasive ductal carcinoma associated with high-grade DCIS (15 mm). The surgical margins were clear. Chemotherapy was not offered due to the patient's ECOG status and comorbidities.

Discussion

IORT paired with breast conservation therapy involves the application of a single high dose of radiation directly to the surgical margins immediately after tumor resection, reducing the radiation exposure to the surrounding tissues [3, 9]. Further benefits include breast preservation, increased compliance, shortened treatment time, and reduced journey times with complementary environmental benefits [10].

Cardiac devices that monitor and regulate heart function are generally referred to as CIEDs, which can be subclassified as PMs and implantable cardioverter defibrillators [4, 11, 12].

Architecturally, modern CIEDs utilize complementary metal-oxide silicon (CMOS), allowing the units to be small (30–50 mm in diameter) [10, 13]. The core functions of the CIEDs are stored in the random-access memory, which is susceptible to interference from ionizing radiation [6, 11, 14–16]. The earliest guidelines suggest a conservative approach of limiting the radiation exposure to 2 Gy, while more recent studies categorize exposures over 10 Gy as high risk [11, 13, 17]. A study on the effects of therapeutic radiotherapy on CIEDs from 1994 to 2015 reported a malfunction rate of up to 3%, including both failure and malfunctions (e.g., disruptions or perturbations that do not result in failure) [10].

There is a paucity of literature regarding the use of IORT in patients with CIEDs (Table 1). The first documented case involved an 83-year-old woman diagnosed with invasive ductal carcinoma in the left breast, who also had a St. Jude Medical (St. Jude Medical Inc., St. Paul, MN, USA) dual chamber PM programmed to VVIR 70 bpm and hysteresis 60 bpm in single chamber mode [18]. The PM was located 90 mm from the tumor mass in the upper pole of the left breast and successfully received TARGIT using an applicator of 30 mm diameter, which delivered radiation doses of 20 Gy to the surgical margin and 6 Gy to an area 10 mm from the surgical margin, over a period of 26 min.

The second documented study summarized a collection of phantom cases that revealed an exponential decrease in energy exposure to the PM with increasing radial distance from the source. No device malfunctions or failures of PMs were reported, even after 1–2,000 cGy exposure [7].

Compared to the traditional EBRT, beam scattering is lower in IORT due to direct/close contact with the tumor bed. The generation of an electromagnetic field is also more limited in IORT compared to traditional linear accelerators [6, 18]. The adverse impact of these factors on modern CMOS circuitry has been documented [5, 19]. Despite this theoretical advantage, the effects of traditional EBRT on cardiac PMs have been widely discussed [10, 14, 15, 18], while the effects of IORT on patients with PMs are not well understood [13].

At a minimum for IORT treatment, we recommend further protocols should include methods, device-specific guidelines, and enhanced measures to limit malfunctioning of CIEDs during the IORT procedures with the following proposed enhancements:

- A pre- and post-check of the cardiac PM with a certified cardiac technician.
- A thermoluminescent dosimeter or equivalent radiotherapy dose measurement device to record radiation levels close to the cardiac PM.

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- A full cardiac and anesthetic workup before and after IORT.
- A cardiac technician, as a part of the IORT surgical team, to monitor the cardiac PM function and perform mode switching, if required.

Conclusion

This case elucidates the successful use of targeted IORT for breast-conserving surgery in a patient with a single ipsilateral chamber VVIR mode PM. No device failure or malfunction was reported for the PM before, during, or after the procedure. These findings support the use of targeted IORT for patients diagnosed with early-stage breast carcinomas who have a PM implanted. However, further research is needed to understand the safety of other methods and devices for IORT patients with CIEDs.

Statement of Ethics

Written informed consent to publish this case report was given.

Conflict of Interest Statement

None declared.

Funding Sources

None declared.

Author Contributions

All authors contributed equally to the study.

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