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Navigating Complexities: Leadless Pacemaker Management in Proton Therapy for a Pacemaker-Dependent Bilateral Breast Cancer Patient

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ABSTRACT

This case study explores the strategic decision-making and safety considerations in managing a unique scenario where a pacemaker dependent patient, requiring adjuvant radiotherapy for bilateral breast cancer. The conventional pacemaker was located entirely within the treatment target, without the option for transposition because of the bilateral chest treatment, resulting in significant risk of malfunction caused by exposing it to the full prescribed dose. Consequently, the decision was made to replace the conventional pacemaker with a leadless device Micra implanted directly into the heart to mitigate direct device radiation and potential adverse effects of proton therapy on the cardiac device. Following Micra implantation, the patient underwent the proton treatment without complications or serious device malfunctions. This study explores solutions to address the challenges posed by within-the-field cardiac devices and highlights the use of pencil beam proton therapy for individuals with leadless cardiac devices while acknowledging the potential for neutron production and the associated risk of single-event upsets (SEU) in cardiac implantable electronic devices (CIEDs). The findings underscore the significance of strategic decision-making, risk assessment, and continuous monitoring for successful outcomes, particularly in the context of proton therapy for patients with advanced cardiac considerations.

Introduction

Proton therapy has gained recognition for its precision in mitigating radiation exposure to organs at risk distal to the target and notably reducing the integral irradiated volume dose compared to modern photon therapy techniques.[1] Proton beams, generate neutrons, particularly in scattered beams, presenting specific challenges for patients with Cardiovascular Implantable Electronic Devices (CIEDs). It has been reported that scatter proton beams (SPB) for thoracic tumors results in a neutron dose of 1.10 ± 0.55 Sv and an elevated incidence of CIED malfunction.[2] Consequently, it is recommended to exclude pacing-dependent patients from undergoing proton therapy.[2] In scenarios where the CIED faces the prospect of receiving doses exceeding 5 Gy during radiotherapy, or when radiation techniques inevitably give rise to neutron production, the imperative may arise to consider explanting the CIED.[3] American Association of Physicists in Medicine (AAPM) Task Group Report 203 (TG-203) recommends explanting a CIED in case it is directly irradiated or obstructs the target volume.[3] In such instances, this decision becomes complex, particularly when patients heavily rely on their CIEDs.

Fortunately, the emergence of innovative leadless cardiac devices has opened new avenues for the radiotherapy of patients with thoracic tumors by allowing replacement of traditional pacemakers when needed. The leadless pacemaker (Micra MC1VR01, Medtronic, Minneapolis, MN) is directly implanted into the heart's right ventricle through a minimally invasive catheter-based procedure, eliminating the need for traditional leads. It is smaller in size, 1.75 g, 0.8 cc and 25.9 mm in length, (Figure 1) compared to conventional pacemakers and has potential advantages such as a reduced risk of lead-related complications. As the adoption of leadless devices continues to grow, a compelling and immediate need arises for comprehensive information and insights regarding the management of patients undergoing radiotherapy, particularly those with CIEDs situated within the treatment target. Despite these advancements, current risk categories pertaining to radiotherapy (RT) remain, as of, closely aligned with those of conventional CIEDs, in adherence to the guidelines established by the

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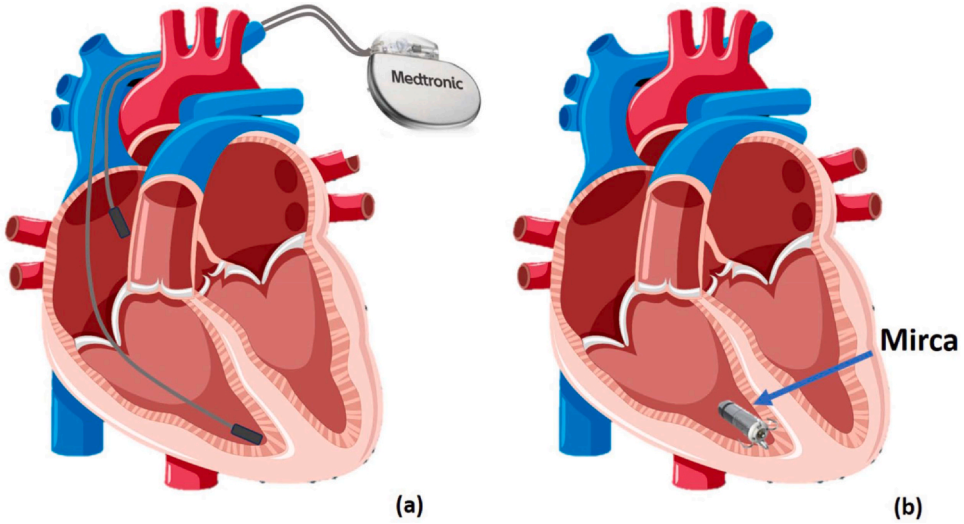


Figure 1. Actual size of traditional pacemaker (a) compared to leadless pacemaker (b). [This figure has been designed using Medtronic brochure and assets from Freepik.com].

AAPM and The Heart Rhythm Society (HRS) until new information and literature are available.[3,4]

In this context, a valuable case study by Wang et al. reported the successful treatment of a patient with triple negative left breast invasive ductal carcinoma status post lumpectomy and sentinel node biopsy.[5] Based on this report, the patient underwent the replacement of a conventional CIED with the Medtronic leadless pacemaker, Micra, providing increased flexibility to minimize the dose to the pacemaker (101 ± 5 cGy for the entire course of breast RT treatment) while achieving optimal target coverage using intensity-modulated radiotherapy (IMRT) technique.[5] In another challenging case, an 85-year-old male with a Micra leadless pacemaker (Medtronic-Ibérica S.A., Spain) underwent radiation treatment for a sizable mediastinal mass. Despite partial overlap with the radiation field, the device received a total dose below 1500 cGy during the combined proton and high-energy photon (6 MV and 15 MV) treatment without any significant malfunction.[6]

The current case report explores the complexities and decision-making processes involved in managing a patient with bilateral breast cancer requiring pencil beam scanning (PBS) proton therapy while having a pre-existing conventional pacemaker. Although PBS proton therapy significantly reduces neutron exposure compared to scattering beams[7], it can still lead to a risk of device malfunction, especially when the CIED is within the radiation field, receiving the full proton treatment dose, and the patient is dependent on the device. Additionally, the increased treatment uncertainties and x-ray imaging artifacts introduced by the presence of metal components in the preexisting CIED, further compounded the complexities of the case. Following comprehensive discussions with a multidisciplinary team, the decision was made to replace the conventional pacemaker with a leadless pacemaker. This case study offers valuable insights into the management of in-field pacemakers during PBS proton therapy, especially in scenarios with limited available information.

Case presentation

A 56-year-old perimenopausal female was diagnosed with bilateral breast cancer. The patient received a diagnosis of triple-negative breast cancer (TNBC) and underwent bilateral breast-conserving surgeries

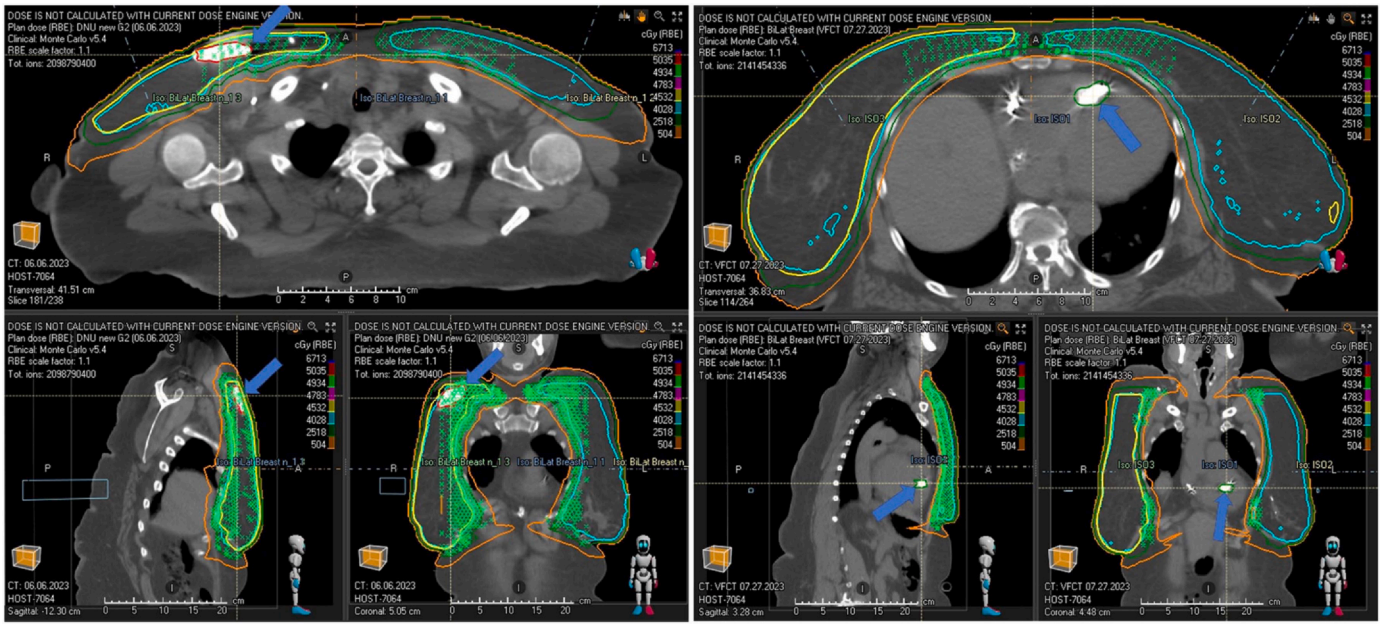


Figure 2. The high-density object pointed by the blue arrows indicates the conventional pacemaker (left panel) and Micra (right panel).

(BCTs) and sentinel lymph node biopsies (SLNB). Notably, the patient underwent atrioventricular (AV) nodal ablation 15 years ago due to third-degree heart block, rendering the patient completely pacemaker-dependent for life. As such, the patient's ventricles no longer receive signals to contract from the atria. Without these pacing signals, the ventricular base rate of contraction is only approximately 30–40 beats per minute, which is incompatible with life, making the pacemaker a life-preserving device situated within the treatment target. The presence of the conventional pacemaker within the treatment area presented a multifaceted challenge as it created concerns about potential serious device damage, and uncertainties related to proton therapy and its impact on the treatment quality.

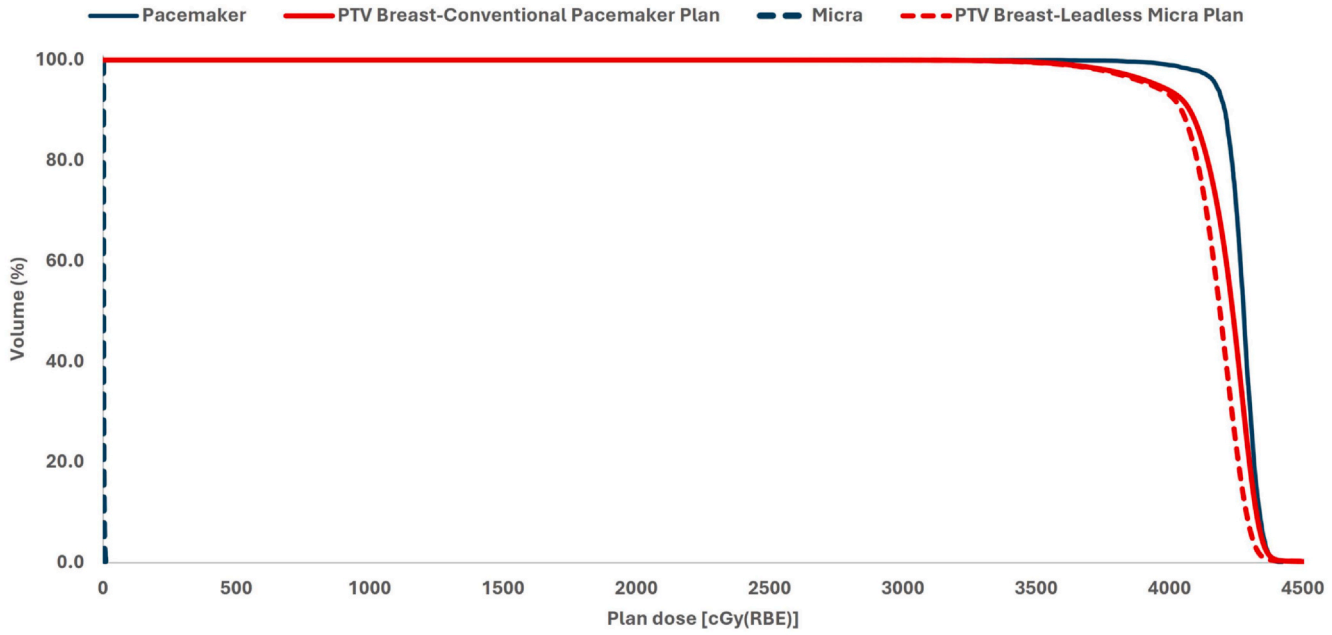
This case used a 3 field beam arrangement (anterior-posterior, right anterior oblique, and left anterior oblique) typical in bilateral breast PBS treatment plans. Based on the initial treatment plan, the original pacemaker would receive an average dose of 42.73 Gy (RBE) (Relative Biological Effectiveness). This information provides valuable insight into the potential radiation exposure that could be delivered to the device during treatment. Potential alternatives to the leadless CIED were considered, such as the use of a removable cardiac vest. However, after careful consideration of factors such as the fact the patient could not remove the vest even for treatment (as she would be completely dependent on the vest for life-supported pacing), patient discomfort, additional uncertainties in proton therapy, and practical issues associated with day-to-day patient immobilization and vest removal related to positional changes of the vest and other activities of daily living requiring the removal of the vest, the best alternative remained to replacement the existing device with a leadless Mirca CIED.

Figure 2 provides a comparative analysis of the treatment plans for both conventional and leadless devices. The figure illustrates key parameters, such as differences in radiation dose distribution and x-ray imaging artifact reduction within the treatment volume. The use of a Mirca leadless CIED allowed the proton radiation dose received by the pacemaker to be reduced from 42.73 Gy RBE to an average of 1 cGy RBE, posing negligible malfunction risk. This visual representation aids in understanding the impact of device type and placement on the treatment plan and informs decision-making in the context of patient care.

Treatment planning (to be revised/continued by Dosimetrist)

Following the successful replacement of the pacemaker, the patient underwent compute tomography (CT) simulation. Four-dimensional CT images acquired during regular breathing cycle and average CT images used for treatment planning. The Micra was shown as radiopaque on kV-CT, a high-density metal object located in the right ventricle and carefully contoured (Figure 2). Treatment planning was performed using RayStation version 12A SP1 (RaySearch Laboratories, Stockholm, Sweden). The treatment plan involved robust optimization of three proton beams, comprising two lateral scanning beams and one anterior-posterior scanning beam. The prescribed dose was 42.5 Gy (RBE) administered in 16 fractions with a dose of 2.65 Gy (RBE) per fraction. Daily kV portal images, weekly cone-beam computed tomography (CBCT) and verification CTs on week 2 and week 3 were performed following the start of radiation treatment.

Figure 3 presents the dose volume histograms (DVH) for both treatment plans, clearly illustrating a notable difference in the radiation dose received by the Micra leadless device compared to the traditional device, which would have received full target dose, (42.5) Gy (RBE), from proton therapy. Remarkably, the treatment planning DVH indicates that the Micra device would receive an average proton dose of approximately 1 cGy (RBE) throughout the entire treatment course. It is crucial to highlight the challenges encountered in assessing dose from portal imaging and CBCT during treatment, primarily due to kV imaging dose not calculated by the treatment planning system and the specific location of the Micra device. Our CTDI phantom study



			Dose[cGy(RBE)]						
	ROI	ROI vol(cm3)	D99	D98	D95	Average	D50	D2	D1
Conventional	Pacemaker	19.86	3999	4088	4175	4271	4279	4371	4381
	PTV Breast	6961.94	3633	3763	3955	4206	4236	4366	4383
Leadless	Micra	5.53	0	0	0	1	0	6	8
	PTV Breast	6933.96	3615	3742	3913	4166	4189	4334	4352

Figure 3. Dose Volume Histogram (DVH) comparison for conventional (left) and leadless device (right) treatment plans. The red curve indicates the pacemaker, and the green curve is the planning target volume (PTV) breast.

Patient Name:

Medical Record #:

PHYSICS PRELIMINARY REPORT
Cardiac Implantable Electrical Device

Attending Physician:

Date of Service:

Anticipated treatment modality:

Distance from CIED to are of treatment is expected to be:

Based on distance and the modality of treatment, the dose to the CIED will be:

Information:

Table 1: Patient risk-categories: cumulative dose to the CIED and pacing independent versus pacing-dependent. Neutrons are considered present when protons or photons with energy > 10 MV are used. Here, risk relates to the probability of a negative patient incident due to CIED malfunction.

Patient	Dose region and risk category			
	< 2 Gy	2-5 Gy	> 5 Gy	Neutrons present
Pacing independent	Low risk	Medium risk	High risk	≥ Medium risk
Pacing dependent	Medium risk	Medium risk	High risk	≥ Medium risk

Ref: Management of radiotherapy patients with implanted cardiac pacemakers and defibrillators: a report of AAPM TG-203.

Figure 4. Exemplary policy form based on TG-203 highlighting cardiac safety measures.

measurements shows that the dose resulting from a full arc CBCT is about 1-2 cGy dose. This dose will be accumulated during the course of treatment and will be absorbed by the device in higher probability due to elevated photoelectric interaction. AAPM Task Group 180 provides detailed information regarding the imaging dose during treatment and recommends a variety of techniques available to reduce the imaging dose.[8] Consequently, to mitigate potential radiation exposure from imaging procedures during treatment, the frequency of CBCT imaging was strategically reduced to once per week. This adjustment aims to strike a balance between maintaining necessary imaging information and minimizing the cumulative dose to the Micra device.

Categorization and monitoring

The selection of a pencil beam proton and the placement of the pacemaker within the heart allowed for exceptional flexibility in designing an optimal plan while effectively sparing the heart and other organs at risk. Even though the pacemaker DVH showed negligible dose in the treatment plan, the patient was still categorized as high risk based on the manufacture information, AAPM Task Group Report 203, HRS2017 guidelines and institutional policy as demonstrated in our sample policy form (Figure 4),[3,4] Based on this category, the patient needed electrocardiography (ECG) monitoring during the treatment, and device interrogation immediately after treatment. This high-risk categorization primarily stemmed from neutron production and pacing dependency as well as the importance of monitoring and managing the potential risks associated with this complex case. Neutrons, produced during proton therapy, can impart energy to electronic components, potentially causing malfunctions such as induced single event upsets (SEUs) in CIEDs. These events are of great concern due to their potential impact on patient safety and device functionality. Notably, there is a reduction in neutron yield between passive scatter and proton PBS by an order of magnitude respectively.[7] PBS protons does not rely on physical scatters and collimators in the path of the beam, significantly reducing neutron production in the treatment room. Despite having both modalities available, PBS is the preferred modality when treating patients with CIEDs, for the previously mentioned reasons. This precautionary measure aligns with our commitment to ensuring the safety and well-being of patients with implanted electronic devices during proton therapy.

Radiation treatment/cardiovascular implantable electronic device monitoring

The proton beams (Ion Beam Applications (IBA) Proton Therapy, Belgium) were delivered as planned, and the patient's condition was closely monitored by CIED trained staff during the treatment. Throughout the treatment period, the patient underwent weekly monitoring in Cardiology clinics as well as evaluated immediately following the course of radiation treatment. At treatment day 11, an alert indicated an "Electrical Reset" in the pacemaker. Since the patient was in the middle of treatment, the radiation therapy team coordinated with the cardiology team to promptly call the patient in for a reboot. Subsequently, 27 days after the treatment finished, another electrical reset alert required a visit to the cardiology department for a thorough pacemaker evaluation. Outside of these two noncritical CIED reboot events, the treatment concluded successfully, without causing any serious malfunctions or adverse effects on the leadless pacemaker. Follow-up screening conducted approximately 6 weeks after the completion of the radiation course revealed the patient's recovery with no cardiac-related concerns.

Discussion and future implications

Proton therapy for patients with CIEDs is classified as high-risk according to the risk assessment criteria outlined in TG-203. This classification stems from concerns regarding the scattering of secondary neutrons beyond the treatment field, which could potentially impact CIEDs. In this context, pencil beam proton therapy is favored due to its substantially diminished neutron doses in comparison to scattering proton beams. It has been shown that neutron doses at distances up to 200 cm from the proton field range from 1 μSv/Gy to 2 mSv/Gy, with this variability attributed to factors such as higher energy and/or closer proximity to the field.[9–15] Moreover, for patients with cancer risk, Micra devices have many advantages when installed in lieu of traditional CIEDs such as improved CT artifacts and reduction in radiation exposure to critical life support, especially in pacing-dependent patients. These improvements are made most evident by the DVH in Figure 3. In line with recommendation provided by TG-203 for managing patient classified as high-risk, it is crucial to perform device interrogation within both one month and six months after radiotherapy. The success of this case underscores the significance of interdisciplinary collaboration and the need for tailored approaches in managing complex cases involving radiation therapy and electronic devices. Caution is advised when administrating neutron generating radiation with CIEDs.

Conclusion

This case study highlights the challenges of managing patients with leadless pacemakers during proton therapy. It emphasizes the importance of meticulous decision-making, precise treatment planning, and rigorous verification and monitoring protocols to ensure the safety and effectiveness of treatment.

Author Contributions

M.S., H.G., M.A., T.W., J.P., E.B.,P.J.: Conceptualization, M.S., H.G.: Data curation, M.S., H.G., M.A.: Formal Analysis, M.S., H.G., M.A., T.W.: Investigation, M.S., H.G., M.A., T.W., J.P., E.B., P.J.: Methodology, M.S., H.G., M.A.: Visualization, M.S.: Writing – original draft, M.S., H.G., M.A., T.W., J.P., E.B., N.G., A.S., P.J.: Writing – review and editing.

Declaration of Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability Statement

The data presented in this article is available upon request from the corresponding author.

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