CASE REPORT

Pacemaker malfunction associated with proton beam therapy: a report of two cases and review of literature—does field-to-generator distance matter?

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Abstract

It is well known that radiotherapy causes malfunctions of cardiac implantable electronic devices such as pacemaker (PM) and implantable cardioverter-deﬁbrillator because of incidental neutron production. Here, we report our experience with two cases of PM reset among seven patients with PM who underwent proton beam therapy (PBT) from January 2011 to April 2015 at our centre. Our experience shows PM reset can occur also with abdominal PBT. In both cases, PM reset was not detected by electrocardiogram (ECG) monitoring but was rather discovered by post-treatment programmer analysis. Our cases suggest that PM malfunction may not always be detected by ECG monitoring and emphasize the importance of daily programmer analysis.

INTRODUCTION

It is well known that ionizing radiation can damage cardiac implantable electronic devices (CIEDs) due to incidental neutron production by nuclear fragment reaction, which may result in a loss of cardiac function [1, 2]. In photon radiotherapy, it has been reported that beam energy and the locations of tumours are risk factors for device malfunction [3]. However, there have been no large clinical studies to investigate the inﬂuence of proton beam therapy (PBT) on CIED malfunction. Therefore, CIED-dependent patients with malignancies may face unexpected clinical challenges from PBT. In this context, we report our experience with two cases of pacemaker (PM) reset that occurred during PBT.

CASE REPORT

The characteristics of seven patients with PMs who underwent PBT at our centre from January 2011 to April 2015 are presented in Table 1. Among these, we experienced 2 (28.6%) PM resets during PBT.

Case 1

This patient was an 87-year-old male diagnosed with primary lung carcinoma in the right lower lobe with a clinical Tumor-Node-Metastasis (TNM) stage of T2bN2M1a according to the Union for International Cancer Control (UICC); he underwent PM implantation (EnRhythm™; Medtronic, MN, USA) in the left infraclavicular region for sick sinus syndrome (SSS) at the age of 83 years (Fig. 1).
The pacing mode was AAIR$\leftrightarrow$DDDR. The pacing rate was low with an atrial sense–ventricular sense (AS–VS) of 77.2%, atrial sense–ventricular pacing (AS–VP) of <0.1%, atrial pacing–ventricular sense (AP–VS) of 22.7% and atrial pacing–ventricular pacing (AP–VP) of <0.1%.

Before treatment, we performed a phantom simulation using the same PM model as that implanted in our patient and measured neutron dose (Fig. 2). The measured neutron dose (154.6 mSv) was within the estimated values at simulation (158.4 mSv), and we found no abnormality in PM function. A total of 66 GyE was administered in 10 fractions at three different angles in 210-MeV proton beams (Fig. 3). The pacing leads were partially irradiated with one proton beam. We monitored the electrocardiogram (ECG) throughout irradiation during every treatment but found no abnormality.

After the completion of PBT, a change in the PM mode from AAIR$\leftrightarrow$DDDR to VVI was detected through programmer analysis on the final treatment day. Retrospectively, the date of the mode change corresponded to the time of irradiation (Treatment Day 8), although no ECG change was observed pre- or post-treatment in the recorded waveforms (Fig. 4). This patient remained asymptomatic after PM reset.

Case 2

This patient was a 72-year-old male with pancreatic cancer (UICC TNM stage T3N0M0). We planned 50 GyE in 25 fractions from two different angles to deliver proton beams of 210 and 150 MeV (Fig. 5). This patient also had a previous history of SSS and implantation of PM (IDENTITY® ADx; St. Jude Medical, CA, USA) via the left subclavian approach 6 years ago. The PM mode was originally programmed to DDD. He was not completely dependent on pacing (AS–VS, 61%; AS–VP, 1%; AP–VS, 34% and AP–VP, 4.8%). We simulated a phantom study in the same way as performed in Case 1. The measured dose of neutrons (96.4 mSv) fell well within the estimated values (103.2 mSv), and a PM reset occurred in the simulation. Accordingly, we performed programmer analysis during each step of treatment, which revealed that the reset of the device occurred after Treatment Day 13. Progmmmer message indicated a reset of the device. As with the first case, there was no change in the ECG pattern of this patient (Fig. 6). Because this was an emergency event, the patient was transported to a cardiac specialty hospital and returned to our centre with the PM settings recovered. After a discussion with
the attending cardiologists, we continued the treatment regimen and experienced no problems with PM; we then completed the planned schedule.

**DISCUSSION**

Although we confirmed the safety of PMs in these patients through phantom studies and monitored ECGs during treatment, PM reset occurred and we did not realize the mode change of PM for an entire 2 days in the first case. In the second case, we prepared for PM reset during treatment through the simulation, and one actually happened. We believe our simulation to expect the PM reset is effective. However, in both cases, PM malfunction was not detected by ECG monitoring but was rather discovered by programmer analysis. Fortunately, neither of the patients experienced a severe event as both had sustainable heart rates.

Moreover, neither experienced an additional reset event during the remaining treatments, and both PMs continued functioning properly after reprogramming.

There is little information about the effect of PBT on PM function. Oshiro et al. reported that minor PM malfunction occurred in 2 of 8 patients (25%) receiving high-energy PBT [4]. In addition, Gomez et al. reported that the frequency of CIED reset was ~20% among patients receiving PBT to the thorax [5]. In our series, PM malfunction occurred in 28.6% (2/7) of the cases, which was higher than that reported by Zaremba et al. who encountered malfunctions in 10 (2.5%) PMs and 4 (6.8%) implanted cardiac defibrillators from 453 patients after radiotherapy using photons or electrons [3]. Thus, the incidence of PM malfunction in PBT may be higher than that in photon radiotherapy.

In our cases, neutrons scattered by collimators or the patient’s body might have accidentally collided with PM. Therefore, we

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**Figure 3:** PBT plan for Case 1. The patient experienced PM reset on the eighth day of 52.8 GyE of a total 66 GyE. A dose–volume histogram (DVH) is shown in the lower right. The volume of 95% of the prescribed dose (V95%) for the gross tumour volume (GTV), clinical target volume (CTV) and planning target volume (PTV) was 100, 100 and 95%, respectively. The maximum dose of the PM chamber was negligible.

**Figure 4:** ECG of Case 1 on PBT Day 8 showing no change between pre- and post-treatment.
emphasize the importance to recognize the risk of PM malfunction during PBT, even with devices located at a distance from the target of the irradiated field. Further data about the field-to-generator distance are needed. In the future, pencil beam scanning will possibly be able to reduce the neutron impact on PMs [4]. Zaremba et al. reported that beam energy plays a considerable role in inducing CIED malfunctions in photon radiotherapy [6]. There is a possibility that beam energy of proton might have an impact. Larger-scale study would be needed to verify that low-energy PBT might be safer in PM patients.

Both our patients experienced PM malfunction that resulted in a mode change to VVI, which is the safety back-up programme to support infrequent pacing when necessary and might prevent severe PM malfunction. We believe that PBT is feasible for patients who are not completely PM dependent if adequate precautions are considered.

We reported two cases of PM malfunction associated with PBT. There is a possibility that the incidence of PM malfunction in PBT is higher than that in photon radiotherapy. It is difficult to accurately predict a PM reset event associated with PBT by
simulation or ECG monitoring as both might be insufficient as measures for safe PBT in patients with PMs. Our experience emphasizes the importance of daily programmer analysis after every treatment session.

CONFLICT OF INTEREST STATEMENT
None declared.

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ETHICAL APPROVAL
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CONSENT
Informed consent was obtained from these patients.

GUARANTOR
T.U. will act as guarantor.

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