ORIGINAL ARTICLE

Radiation therapy in patients with cardiac implantable electronic devices

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KEY WORDS
cardiac resynchronization therapy, cardiac implantable electronic device, implantable cardioverter-defibrillator, pacemaker, radiotherapy

ABSTRACT

BACKGROUND The number of patients with cardiac implantable electronic devices (CIEDs) treated with radiation therapy (RT) as an oncological treatment is expected to increase.

AIMS The aim of the study was to assess whether cancer treatment with radiation therapy is associated with any device dysfunctions and device-related threats in patients with CIEDs.

METHODS The risk of all patients with CIEDs undergoing RT was assessed according to guidelines. Device interrogations were performed before the first and after the last RT session. In patients at high risk and / or with an implantable cardioverter-defibrillator or cardiac resynchronization therapy with defibrillator (CRT-D), all sessions were supervised by a cardiologist, and device interrogations were performed before and after every single RT session. Device parameters and events were monitored during the whole treatment.

RESULTS The study included 157 patients with CIEDs who had palliative (n = 71) or radical (n = 86) RT. Pacemakers were implanted in 113 patients, implantable cardioverter-defibrillators in 36, and CRT-D in 8. During the 2396 RT sessions (median [interquartile range], 5 [5–28] per patient) with cumulative dose up to 78 Gy per patient for the whole RT treatment and maximum energy beam up to 20 MV, 2 events potentially related to radiation were recorded.

CONCLUSIONS Radiation therapy in patients with CIEDs is not associated with substantial risk to the patients assuming the patients' management follows current guidelines.

INTRODUCTION The prevalence of cancer and the use of cardiac implantable electronic devices (CIEDs) remains high.[1,2] The number of patients with CIEDs and indications for radiation therapy (RT) due to cancer is expected to increase in the near future. In the last years, RT in patients with CIEDs was reported to be safe and rarely associated with CIED dysfunctions or health risk.[3-5] However, RT may be associated with device malfunction as an effect of both electromagnetic interference or ionizing radiation.[3,6] Dysfunctions such as altered stimulation or sensing, inhibition of stimulation, inadequate shock therapy, battery depletion, loss of telemetry or loss of function, reset, or reprogramming the device are rarely associated with any clinical consequences. The risk is supposed to be higher when a higher radiation dose and / or higher beam energy is used. Thus, documents published by manufacturers recommend the inactivation of anti-tachycardia therapies to avoid inappropriate shocks. According to the manufacturers' instructions, using lead shields on the device area and limiting the maximal radiation dose and energy is also suggested. However, some inconsistencies regarding maximal pacemaker / implanted cardioverter-defibrillator (ICD) radiation dose or device shielding may be found, as these procedures are recommended by Biotronik and Boston Scientific but not by Medtronic (technical instructions published by manufacturers). There are also guidelines and

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WHAT'S NEW?

According to the designed algorithm, the evaluation of patients with cardiac implantable electronic devices was performed in all consecutive patients qualified for treatment in a tertiary radiation therapy center. All patients with implantable cardioverter-defibrillators and cardiac resynchronization therapy defibrillators were supervised by the cardiologist during each radiation therapy to monitor possible temporary arrhythmias or dysfunctions of cardiac implantable electronic devices. Some patients and cardiac implantable electronic devices were exposed to beam energy exceeding 6 MV and / or doses higher than 2 Gy per device. Moreover, new radiation therapy techniques in patients with CIEDs were evaluated, including stereotactic radiosurgery and tomotherapy. No events associated with radiation were recorded, encouraging other radiation therapy centers to implement the algorithm into clinical practice.

experiences published by societies and experts in the field, which provide valuable suggestions.[3-11] There is constant progress in RT methods, such as the introduction of volumetric modulated arc therapy, respiratory gating or stereotactic body radiotherapy, and construction of devices such as helical tomotherapy or accelerators integrated with magnetic resonance scanners.[12,13] Similar advances are observed regarding CIEDs with upgraded devices and leads as well as new software features for implantation available almost every year.[14] For that reason, there is a need to monitor the RT effects on CIED functions regarding modern RT methods and modern CIEDs. The purpose of the study was to monitor and register all possible complications or threats in patients with CIEDs treated with RT.

METHODS

The study was conducted thanks to cooperation of a tertiary high-volume cardiology center and a oncology center. Initially, the management of the patients with CIEDs followed in-house regulations based mainly on German (German Society of Radiation Oncology / German Society of Cardiology [DEGRO/DGK]), Dutch (Dutch Society of Radiotherapy and Oncology [NVRO]), and Polish (Polish Society of Oncological Radiation Therapy [PTRO]) guidelines and own experience.[3,4,9] The management policy was updated after the publication of new seminal papers in the field, including the Heart Rhythm Society (HRS) statement release.[9] Our approach based on the risk stratification was eventually described in detail in the expert opinion of the Heart Rhythm Section of the Polish Cardiac Society and the Polish Society of Radiation Oncology.[15] The algorithm is presented in TABLE 1.

During the first consultation before RT, a detailed assessment was performed, including symptoms and signs of coronary artery disease, heart failure, and arrhythmias. CIEDs were assessed in each patient to record all essential parameters, including alerts, pacing settings, and battery voltage. In our study, we defined pacemaker dependency as lack of heart rhythm during VVI stimulation at a rate of 30 bpm. In the case of single heartbeats, pacing was inhibited to ensure that no heart rhythm was suppressed by the stimulation. Based on the assessment and RT parameters obtained from the radiation oncologist, a patient was assigned to one of the 3 risk groups: low, medium, or high (TABLE 1).[15]

Similar follow-up visits with CIED assessment took place after completing the RT course to compare with baseline CIED parameters. Moreover, RT sessions in high-risk patients and / or patients with ICD / CRT-D were supervised by a cardiologist, and CIED assessments were made before and after each RT fraction to register CIED parameters. In the case of pacemaker dependency, pacing was changed to the asynchronous mode before the RT session, and the change was reversed after the session. Such an approach might be considered as excessive caution. However, in our settings, no technicians or nurses were available to supervise sessions in patients with ICD / CRT-D (in such a case, inactivation of ventricular tachycardia / fibrillation therapies with magnet application was required). All CIED parameters were monitored during the whole RT.

Informed consent was obtained from all patients. The approval of the bioethics committee was not obligatory, as guidelines and recommendations were published before.

Statistical analysis The normality of the continuous variables was tested using the Shapiro–Wilk test. Variables with normal distribution were presented as means and SD and those with skewed distribution as medians and interquartile ranges (IQR). Categorical variables were shown as percentages. All statistical analyses were performed using TIBCO Statistica 13 software (Palo Alto, California, United States).

The study's preliminary results were presented as an abstract during the European Heart Rhythm Association 2018 Congress in Barcelona.[16]

RESULTS

There were 157 patients who underwent RT between November 2016 and December 2018. The mean (SD) age was 73 (9) years; 77% of patients were men, 22% of patients with CIED were pacemaker-dependent, and 54% underwent radical RT. Most CIEDs (84%) were implanted in 2011 or later. Characteristics of CIEDs and RT are presented in TABLE 2. No changes in the battery lifetime or capacitors charging time (ICD / CRT-D) occurred. A total of 22 patients were treated with beam energy exceeding 6 MV, and 15 with that exceeding 10 MV. The location of the tumor treated with RT was presented in FIGURE 1. In the preliminary interrogation before RT, 2 elective replacement indicators were found, and the patients were referred for CIED exchange.

TABLE 1 The algorithm of risk stratification in patients with cardiac implantable electric devices qualified for radiation therapy (modified from Tajstra et al)[15]

Risk	Conditions	Pacemaker / CRT-P	ICD / CRT-D
Low	• No pacemaker dependency AND • Radiation energy <10 MV AND • Dose for CIED <5 Gy	• Intervention protocol • (Temporary) disabling of the "R" function, automatic measurement, and setting safe stimulation impulses (with a margin of at least 1 V above the stimulation threshold) • Staff trained in RT in patients with CIED • Continuous monitoring of ECG and SpO_2 • Availability for external stimulation and defibrillation, ECG, arterial pressure monitor, SpO_2, programmer • CIED control every 2 weeks after completing RT and 1, 3, and 6 months after completing RT	Low risk not possible, see below
Medium	• Pacemaker dependency AND • Radiation energy <10 MV AND • Dose for CIED <5 Gy	Recommendations as for low risk, and: • Staff trained in the diagnosis and treatment of VT/VF and asystole (BLS) • CIED control every week • Presence of a cardiologist proficient in the use of CIED during the 1. fraction of radiotherapy is required • Setting stimulation to a frequency other than the default frequency of a reset device	• Staff trained in the diagnosis and treatment of VT / VF and asystole (BLS) • CIED control every week • Presence of a cardiologist proficient in the use of CIED during the first fraction of radiotherapy is required • To temporarily disable VT / VF detection / therapy, it is recommended that the magnet is placed above the device during each RT fraction.
High	• Radiation energy ≥10 MV AND / OR • Dose for CIED ≥5 Gy	Recommendations as for medium risk, and: • If CIED remains within the radiation beam, consider CIED relocation. • Presence of a cardiologist is recommended during RT and CIED control immediately before and after completing the RT fraction.	Recommendations as for medium risk, and: • If CIED remains within the radiation beam, consider CIED relocation. • Presence of a cardiologist is recommended during RT and CIED control immediately before and after completing the RT fraction.

Abbreviations: BLS, basic life support; CIED, cardiac implantable electric device; CRT-D, cardiac resynchronization therapy with a defibrillator; CRT-P, cardiac resynchronization therapy with a pacemaker; ECG, electrocardiography; Gy, Grey; ICD, implantable cardioverter-defibrillator; MV, megavolts; RT, radiation therapy; SpO_2, oxygen saturation; VF, ventricular fibrillation; VT, ventricular tachycardia

TABLE 2 Techniques of radiation therapy with regard to the cardiac implantable electric device type

Radiation therapy technique	Number of patients	Number of fractions	Pacemaker	ICD	CRT-D	Max beam energy	Max estimated dose on CIED
Linear accelerator	139	2296	100	31	8	20 MV	8 Gy
Stereotactic radiosurgery	15	63	11	4	-	6 MV	<2 Gy
Tomotherapy	3	36	2	1	-	6 MV	<2 Gy
Overall	157	2396	113	36	8	-	-

Abbreviations: max, maximal; see TABLE 1

During 2396 RT sessions (median [IQR], 5 [5–28] per patient) and maximum cumulative dose during a RT treatment reaching 78 Gy per patient, 2 significant events were recorded.

In the first case, the pacing mode was switched from DDI to DDIR, and the right ventricular pacing lead threshold temporarily increased from 0.5 V at 0.5 ms before the RT session to 2.0 V at 0.5 ms after the session (medium risk; RT of the prostate; energy, 6 MV; after the third of 38 RT doses; ICD Medtronic Protecta DR; the event took place 2 months after generator replacement).

There was also a single episode of T-wave oversensing in ICD (medium risk; the neck area; energy, 6 MV; before the 25th of 30 RT doses; ICD-VR Medtronic Evera II) during paroxysmal atrial tachycardia, which caused inappropriate VF detection and inadequate shock therapies (FIGURE 2). Despite the fact that the episode took place when a patient entered the linear accelerator (LINAC) room a few minutes after the previous RT, there is no direct proof that the event was associated with radiation. The episodes of paroxysmal atrial tachycardia were recorded before, but T-wave oversensing has not been observed. The sensitivity of the RV lead was adjusted from 0.3 mV to 0.6 mV to avoid T-wave oversensing during the following RT. The remaining sessions of RT were conducted, and further episodes or shocks were recorded. Moreover, there were 2 deaths before the last RT session, which were not related to RT nor CIEDs.

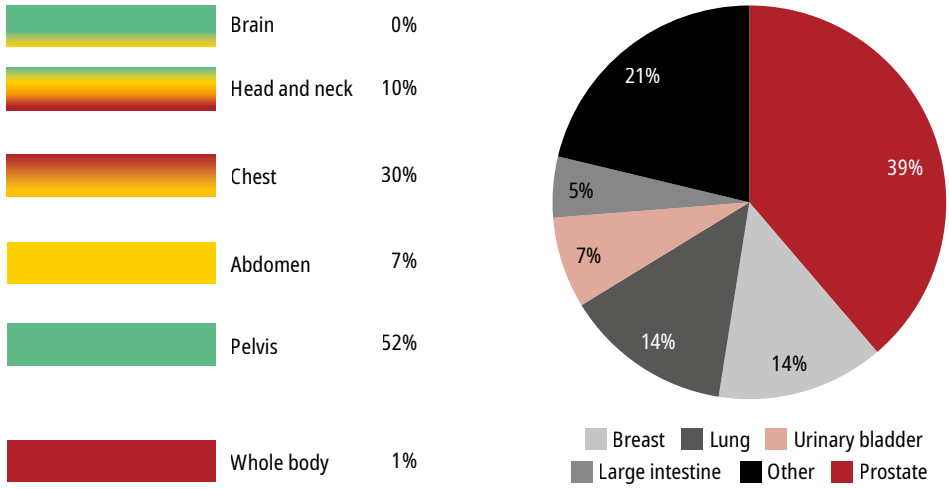
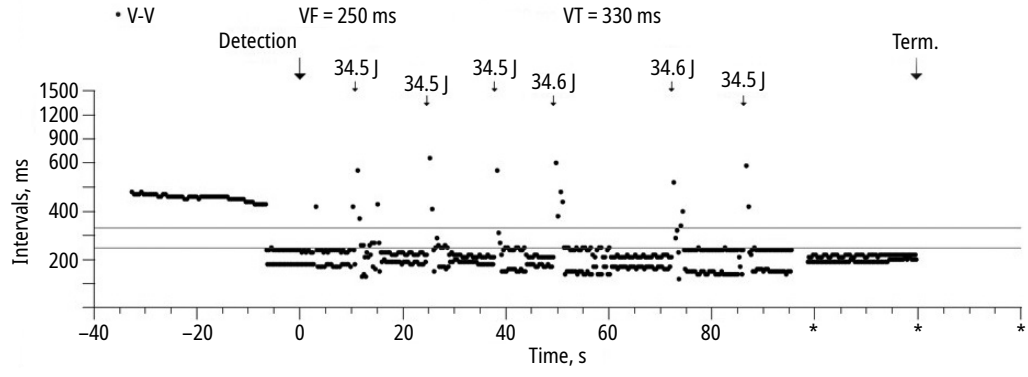


FIGURE 1 The proportion of body areas (left) and location of the tumor (right) treated with radiation therapy. The color of body area on the image on the left is associated with the distance between radiotherapy beam and the device, which is consistent with the risk of radiotherapy; red indicates the highest risk, and green, the lowest.

Type	ATP Seq	Shocks	Success	ID, n	Data	Time, hh:mm	Duration, hh:mm:ss	Avg bpm V	Max bpm V	Activity at onset
VF	0	6	No	736	04-Dec-2017	15:57	:02:40	286	286	Rest



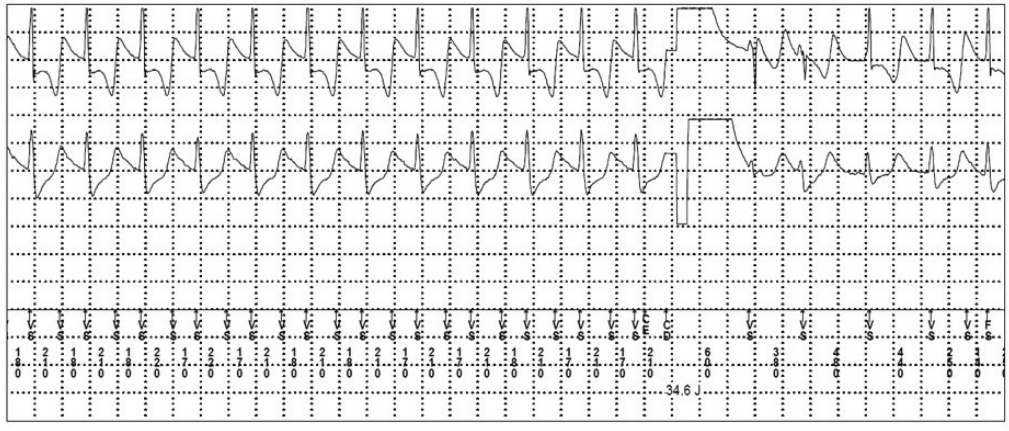


FIGURE 2 Electrogram of a patient with a tumor in the neck area showing the T-wave oversensing episode which resulted in inappropriate ventricular fibrillation detection and shocks delivery
Abbreviations: ATP, antitachycardia pacing; avg, average; max, maximum; term, termination; others, see TABLE 1

DISCUSSION Our study results showed that a cautious and methodical approach for RT in patients with CIEDs might be safe, even in therapies with beam energy exceeding 6 MV. However, some issues need to be addressed. The episode of T-wave oversensing occurred in a patient entering the LINAC room, which resulted in an inappropriate shock delivery. The previous episodes of

similar arrhythmia recorded outside the RT unit were not associated with T-wave oversensing. As the previous session of RT in the LINAC room was performed with energy of 6 MV and the delay after the end of the session was more than 2 minutes, no neutrons in the LINAC room were expected. The minimum delay after the previous session should be considered if beam energy is higher than 6 MV. The energy exceeding 6 MV may result in longer persistence of ionizing radiation in the room.[17] Neutrons produced during the LINAC treatment might generate the CIED dysfunctions only during the radiation, even when no direct exposure to the radiation beam was present.[18] Although no significant photon radiation was found in the chest area during the prostate RT with an energy beam of 15 MV, software malfunctions were found in 52% of ICDs and 18% of pacemakers. Interestingly, the year of CIED manufacturing was not crucial in the pacemaker group, but malfunctions were found more often in older ICD devices.[18]

When preparing the patient and CIED management principles during RT for our study, many CIED manufacturers (Biotronik, Boston Scientific, Medtronic, and St. Jude Medical) recommended shielding the device with a lead shield placed on the CIED.[3] The main intention was to decrease CIED exposition to ionizing radiation and minimize the risk of device dysfunction. Lead shields do not protect CIEDs from neutrons. Moreover, it may be an additional source of scatter radiation and neutrons, potentially increasing the risk of device malfunction. Neutrons may be generated as a result of beam collision with lead. The only potential benefit of CIED shielding may be protection from the direct beam. For that reason, in most cases, lead shields may be harmful and should not be used.

As the CIED malfunctions were described weeks or even months after RT, detailed CIED assessments after the last session and 1, 3, and 6 months after RT's completion will be performed. In high-risk patients (pacemaker-dependent, treated with high energy and/or doses), remote monitoring during and after RT sessions may be considered. It may improve safety and allow to diagnose even asymptomatic device complications.

To conclude, our findings showed that RT in patients with modern CIEDs is not associated with substantial risk to the patients assuming the management follows current guidelines.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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