

# New generation implantable cardiac rhythm devices allow safe radiotherapy treatments: A large single centre study

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**INTRODUCTION:** Many patients requiring radiotherapy for malignancies have an already implanted cardiac rhythm device. Previous studies reported a variety of device dysfunctions related to high dose radiation. Aim of this study was to assess the impact of current optimal radiotherapy treatment guided by computed tomography on current generation implantable devices.

**METHODS:** Consecutive patients with implanted pacemakers (PMK) and implantable cardioverter defibrillators (ICD) referred for radiotherapy treatment in any district were enrolled at our Centre and followed prospectively with device interrogation before and just after each radiotherapy cycle. A magnet was positioned on the device in patients with implanted defibrillators or pacemaker-dependency.

**RESULTS:** Overall, 48 patients (74.8 years (9.3), 39 males (81.3)) with implantable devices underwent radiotherapy (29 pacemakers and 19 ICDs). Interval between device implant and start of radiation therapy was 2.9 (1.6) years. Radiotherapy was performed under computed tomography guidance, and a mean of 73.5 (45.0) Gy were administered with a mean of 24.8 (14.6) fractionated doses. About half of the patients underwent thoracic radiotherapy, and 9 were treated for a left thoracic malignancy ipsilateral to the implanted device. No device failures were observed at post-treatment device interrogation, nor changes in electrical parameters, inappropriate shocks, device reprogramming or memory reset. None of the patients experienced premature battery failure or other unexpected anomalous findings at the end of the radiation therapy cycle.

**CONCLUSION:** Radiation therapy for malignancies is safe among patients with implanted current generation cardiac rhythm devices.

**Key Words:** Radiotherapy; Pacemaker; Defibrillator; Cardiac rhythm devices

## INTRODUCTION

Radiotherapy is an effective and established treatment for a large number of patients suffering from malignancies; current application is increasing overtime, due to the increasing prevalence of diagnosed cancer diseases (1). Meantime, cardiac rhythm devices such as permanent pacemakers (PM), cardiac resynchronization devices (CRT) and implantable cardioverter defibrillators (ICD) are widely used for the treatment of sinus node dysfunction, atrioventricular conduction disturbances and prevention of sudden cardiac death (2,3). Due to the same age profile of patients suffering from degenerative cardiac diseases requiring device implantation and patients suffering from malignancies, during the recent years a significant number of patients carrying implantable devices require treatment with radiation therapy for primitive or secondary malignancies.

In this setting, some reports using old generation radiotherapy machines and old implanted devices described the occurrence of a wide spectrum of failures following radiation therapy treatment. Malfunctions ranged from mild errors such as memory reset, up to potentially severe events such as asynchronous stimulation, inhibition of stimulation, altered sensing or inadequate shock therapy, till fatal errors such as permanent setting reset or loss of function (4-6). These reports led to the development of guidelines that suggested intensive monitoring before and after each radiotherapy session aiming to premature detection of any dysfunction, along with limiting the radiation dose close to the device district and device reprogramming; device repositioning in considered indicated in very selected cases (7,8). However, it should be noted that those recommendations were based on studies including patients with older devices and catheters, while the most recent are characterized by technological amendments aimed at preventing external interferences and potential damage. Additionally, radiotherapy equipment and energy sources are now more advanced and can limit the unwanted exposition to the device (9).

We performed the presents single Centre, prospective study aiming to assess the incidence of device damages related to the radiotherapy treatment, in a population of patients with cardiac rhythm devices undergoing focused radiotherapy in various districts malignancies.

## METHODS

Consecutive patients with an already implanted cardiac device, such as PM,

CRT/D or ICD, referred to the Radiotherapy Division of our Hospital for the full cycle treatment of primitive or secondary malignancies, were prospectively enrolled between September 2016 and April 2017. Device interrogation was performed by dedicated Electrophysiologists at the Arrhythmology Division of our Hospital, aiming to detect any change in catheters or battery electrical parameters, programmed stimulation mode, event memory or other dysfunctions.

Inclusion criteria were: any kind of implantable device (PM, CRT or ICD); radiotherapy treatment in any district following the diagnosis of a malignancy; participation to all the scheduled device interrogations. Exclusion criteria were: age below 18 years; inability to begin the radiotherapy treatment; refusal to undergo the scheduled device interrogations.

Radiotherapy was performed according to current recommendation, under computed tomography guidance, following the appropriate scheme for each pathology. The employed machines and protocol, selected case by case, were conformational radiation therapy, intensity-modulated radiation therapy (TomoTherapy) and volumetric modulated arc therapy (RapidARC).

Device interrogations were performed by the Electrophysiologists according to current optimal practice, using the dedicated programmer of each manufacturer (Biotronik, Boston Scientific, Medtronic, Sorin, St. Jude Medical) before and after each treatment cycle. Data concerning device type, manufacturer, model, electrical parameters of the device and catheters were searched for during each interrogation. During each treatment cycle, a magnet was applied on ICD and CRT-D devices, aiming to prevent inappropriate shocks; no persistent temporary changes in programming mode were performed in any device before the treatment, but a magnet was applied on PM devices in patients with PM-dependency during the treatment (defined as absence of stable completely spontaneous heart rhythm with a device stimulation programmed as VVI 40 bpm), aiming to prevent oversensing and inhibition of stimulation.

All the data concerning radiation therapy subtype, site, cumulative dosage and fractions were collected in the dedicated database. Data concerning device type, age, date of implantation, electrical parameters of the generator and catheters, programming, data retrieved from the device memory were retrieved from each interrogation and collected in the same database.

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## STATISTICAL ANALYSIS

Continuous variables are reported as mean  $\pm$  standard deviation, or median (range), and categorical variables as number (percentage). In case of device dysfunction detection, continuous data of the two groups (dysfunction vs. normal) were compared by one-way ANOVA test; categorical variables were compared in cross-tabulation tables by Pearson's chi-square test.

All tests of significance were two-tailed, and a p value  $<0.05$  was considered statistical significant. All analyses were performed using SPSS 21.0 (IBM, Armonk, NY, USA).

## RESULTS

Overall, 48 patients (74.8 years (9.3), 39 males (81.3)) with implantable devices undergoing radiation therapy treatment at our Institution from September 2016 to April 2017, were included in this study. Twenty-nine had a single or dual chamber PM, while 19 had dual chamber ICD or CRT-D devices. The interval between device implant and start of radiation treatment was 2.9 (1.6) years. Patients' characteristics are reported in Table 1.

TABLE 1

## Baseline characteristics of the included population stratified according to the device type

	Overall	PM	ICD/CRT-D
Population, n (%)	48 (100)	29 (60.4)	19 (39.6)
Age, years (SD)	74.8 (9.3)	76.6 (9.9)	72.2 (7.8)
Males, n (%)	39 (81.3)	23 (79.3)	16 (84.2)
Weight (Kg)	74.6 (5.6)	75.2 (5.1)	73.9 (5.8)
Generator duration, years (SD)	2.9 (1.6)	3.1 (1.9)	2.6 (1.5)
PM, single-chamber, n (%)	2 (4.1)	-	-
PM, dual-chamber, n (%)	27 (56.3)	-	-
ICD, single-chamber, n (%)	0 (0)	-	-
ICD, dual-chamber, n (%)	15 (31.3)	-	-
CRT-D, n (%)	4 (8.3)	-	-
Biotronik, n (%)	10 (20.8)	6 (20.7)	4 (21.0)
Boston Scientific, n (%)	8 (16.7)	5 (17.2)	3 (15.8)
Medtronic, n (%)	14 (29.2)	8 (27.6)	6 (31.6)
Sorin, n (%)	2 (4.1)	2 (6.9)	0 (0)
St. Jude Medical, n (%)	14 (29.2)	8 (27.6)	6 (31.6)

Concerning radiation therapy treatment, a mean of 73.5 (45.9) Gy were administered with a mean of 24.8 (14.6) fractionated doses; about half of the patients underwent thoracic radiotherapy, and 9 patients were treated for a left thoracic malignancy, ipsilateral to the implanted device. The calculated dose absorbed by the device was 3.1 (2.1) Gy for thoracic malignancies, while patients with extra-thoracic treatment received 1.01 (0.8) Gy on the device. Complete details concerning radiation therapy schemes, energy, doses and irradiated districts are reported in Table 2.

Following each radiotherapy treatment cycle, the enrolled patients underwent additional device interrogation, aiming to detect any major or minor dysfunction. Among the entire population, no device failures were observed, nor changes in electrical parameters, inappropriate shocks, device reprogramming or memory reset. None of the patients experienced premature battery failure or other unexpected anomalous findings at the end of the radiation therapy cycle. Complete details on electrical parameters of the devices and malfunctions are reported in Table 3.

## DISCUSSION

The present study provides insight in the safety profile of current generation of cardiac devices in patients undergoing radiotherapy. The main result of the study is that radiation therapy is feasible, and no significant device malfunction was detected; device monitoring throughout the radiotherapy and interrogation before and after each treatment cycle should be performed.

In experimental settings, investigating the effect of direct high dose radiation exposure to functioning devices positioned on *in vitro* phantoms, showed a large variety of anomalous responses; anomalies become manifest when very high radiation dosages were directly delivered to the devices (10,11).

Following old anecdotic case reports on old devices and radiotherapy machines, small case samples studies described device malfunctions when radiotherapy was performed in a district close to the device site; anomalies ranged between mild dysfunction and severe errors, including noise detection as ventricular fibrillation (12,13). Conversely, Makkar et al. described a very

TABLE 2

## Characteristics of the radiation therapy treatment, including treatment site, radiotherapy scheme and dosage

	Overall (n=48)	PM (n=29)	ICD/CRT-D (n=19)
Malignancy site, head/neck, n (%)	8 (16.7)	6 (20.7)	2 (10.6)
Malignancy site, right thorax, n (%)	12 (25.0)	5 (17.2)	7 (36.8)
Malignancy site, left thorax, n (%)	9 (18.8)	6 (20.7)	3 (15.8)
Malignancy site, abdomen/pelvis, n (%)	19 (39.6)	12 (41.4)	7 (36.8)
Conformational radiotherapy, n (%)	11 (22.9)	6 (20.7)	5 (26.3)
Tomotherapy, n (%)	22 (45.8)	12 (41.4)	10 (52.6)
RapidARC, n (%)	15 (31.3)	11 (37.9)	4 (21.1)
Cumulative dosage, Gy (SD)	73.5 (45.0)	72.0 (39.8)	75.9 (53.8)
Fractions mean (SD)	24.8 (14.6)	24.5 (14.4)	25.3 (15.3)
6 mEV photons beam, n (%)	38 (79.2)	25 (86.2)	13 (68.4)
18 mEV photons beam, n (%)	10 (20.8)	4 (13.8)	6 (31.6)
Device absorbed dosage (thoracic RT), Gy (SD)	3.1 (2.1)	2.9 (2.0)	3.4 (1.9)
Device absorbed dosage (non-thoracic RT), Gy (SD)	1.01 (0.8)	0.97 (0.8)	1.07 (0.9)
Premature radiotherapy interruption (22 Gy), n (%)	4 (8.3)	2 (6.9)	2 (10.5)

TABLE 3

## Device interrogation for any kind of dysfunction at the end of the radiation therapy treatment

	Overall (n=48)
Device failure, n (%)	0
Reset mode, n (%)	0
Inappropriate ICD shocks, n (%)	0
Battery premature failure, n (%)	0
Sensing deficit, n (%)	0
Stimulation deficit, n (%)	0
Programming alterations, n (%)	0
Impedance rise, n (%)	0
Memory reset, n (%)	0
Noise event registration, n (%)	0
Atrial sensing, baseline, mV (SD)	3.1 (1.8)
Atrial sensing, final, mV (SD)	2.9 (2.0)
Ventricular sensing, baseline, mV (SD)	12.1 (4.8)
Ventricular sensing, final, mV (SD)	12.9 (5.2)
Atrial threshold, baseline, V/0.5 ms (SD)	1.2 (0.4)
Atrial threshold, final, V/0.5 ms (SD)	1.2 (0.5)
Ventricular threshold, baseline, V/0.5 ms (SD)	0.8 (0.5)
Ventricular threshold, final, V/0.5 ms (SD)	0.9 (0.5)

limited incidence of device dysfunction following radiation treatment, although referred to a population of patients carrying old generation PM and ICD devices, limited to partial memory reset in cases with great radiation exposure (14).

More recently, larger retrospective studies have been published, reporting a very limited incidence of device severe dysfunction, mainly related to direct radiation exposure of the device or very high cumulative radiation dosage, in particular for old generation devices. Brambatti et al. described a preventive protocol based on device reprogramming in patients with PM dependency and careful monitoring with device interrogation following the radiation treatment, finding 1% of mild device inappropriate function, without any severe dysfunction (15). Two other large series reported a higher incidence of 7% mild device inappropriate function, without severe complication for the device (16,17). In this setting, neutron-producing beam use was associated with higher incidence of dysfunction, compared to standard radiation treatment beams.

In our study the use of a simple algorithm based on device careful monitoring and interrogation before and after radiotherapy, as suggested by recent recommendations (18), including magnet application on the device in selected cases. No mild or severe dysfunctions occurrence following radiotherapy treatment, including patients treated in the left thoracic district with high cumulative radiation dosage. Of note, implanted devices were last

generation, radiation protected PM or ICD generators. Meantime, the use of modern radiation treatment equipment, including positioning of the beam for radiation treatment guided by megavoltage computed tomography, might contributed to reduction of the radiation dose directly received by the device.

In conclusion, modern radiotherapy on patient with current generation cardiac devices is associated to a high safety profile; previously reported severe device malfunctions are not currently seen now-a-days.

**CONCLUSION**

Radiation therapy for malignancies is safe even among patients with implanted new generation PM or ICD. Simple amendments such as careful monitoring without the need of reprogramming are useful to prevent device dysfunction. Modern radiotherapy machines, included detailed tomography guided beam positioning, leads to further improvement in the safety of radiotherapy among these patients.

**LIMITATIONS**

The limited number of patients included in this study is the main limit, although the prospective design and the inclusion of unselected patients from a high-volume Centre warrants significant value to our results. Additionally, due to the limited number of patients, the absence of adverse events could be an underestimation, as these events are usually very rare; however, it should be noted that even all kinds of minor adverse events were searched for, and device monitoring was very strict and careful. Children were excluded from this study; further studies should address safety issues of radiotherapy in children. Finally, larger prospective studies are warranted to confirm on a larger scale the safety of radiation therapy among patients with implanted cardiac devices, and new updated guidelines are needed to uniform the multidisciplinary approach to these patients.

**CONFLICTS OF INTEREST**

The authors have no conflicts of interest to declare.

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