Radiotherapy in Patients With a Cardiac Implantable Electronic Device

Ardalan Sharifzadehgan, MD, MPH[a,b], Marc Laurans, MD[c], Marine Thuillot, MD[a], Andres Huertas, MD[b,c], Pierre Baudinaud, MD[a,b], Kumar Narayanan, MD[b,f], Mariana Mirabel, MD, PhD[b,d], Jean-Emmanuel Bibault, MD, PhD[b,c], Pierre Frey, MD[e], Victor Waldmann, MD, MPH[a,b], Emilie Varlet, MD[a], Denis Amet, MD[a], Christophe Juin, MD[a], Thomas Lavergne, MD[a,b], Xavier Jouven, MD, PhD[a,b], Philippe Giraud, MD, PhD[b,c], Catherine Durdux, MD[b,c], and Eloi Marijon, MD, PhD[a,b,*]

Recently, the Heart Rhythm Society published recommendations on management of patients with cardiac implantable electronic device (CIED) who require radiotherapy (RT). We aimed to report the experience of a teaching hospital, and discuss our practice in the context of recently published guidelines. We identified all consecutive CIED recipients (12,736 patients) who underwent RT between March 2006 and June 2017. Among them, 90 (1%) patients (78.2 ± 10 years, 73% male) had a CIED: 82 pacemakers and 8 implantable cardioverter-defibrillators. Two patients required CIED extraction prior to RT for ipsilateral breast cancer (no device replacement in 1 patient). Four patients (5%) were considered at high-risk, 35 (39%) at intermediate-risk, and the remaining 50 (56%) at low-risk for CIED dysfunction. Overall, only a minority of patients followed recommended local protocol during RT delivery (31%) and during follow-up (56%). CIED malfunction was detected in 5 patients (6%), mainly back-up mode resetting (80%), with 4 (including 3 pelvic cancer location) patients initially classified as being at intermediate-risk and 1 at low-risk. Four out of the 5 patients with CEID malfunction had received neutron producing beams. In conclusion, our findings underline the lack of rigorous monitoring of patients undergoing RT (though CIED malfunction appears to be rare and relatively benign in nature), and emphasize the interest of considering neutron producing beam for risk stratification as recommended in recent guidelines. Optimization of patient's management requires a close collaboration between both CIED clinicians and radiation oncologists, and more systematic remote CIED monitoring may be helpful. **(Am J Cardiol 2020;128:196−201)**

Because of substantial progress in the fields of both cardiology and oncology, the prevalence of patients with cardiac electronic implantable device (CIED), such as pacemaker (PM) or implantable cardioverter-defibrillator (ICD), who also require radiotherapy (RT) for cancer is now increasing dramatically.[1−3] Globally speaking, out of the 3.4 million new cancer cases diagnosed in European countries in 2012, half would have received at least 1 course of RT.[4]

Although not addressed in the most recent cardio-oncology expert consensus and guidelines, RT can affect significantly the electronic components of CIED resulting in malfunction and/or damage, especially among those who are totally pacing dependent or at high-risk of ventricular arrhythmias. This involves a substantial concern in daily practice requiring a multidisciplinary discussion to balance benefits and risks of RT.[5,6] Since the first guidelines published by the American Association of Physicists in Medicine in 1994, several have been published and more recently the Heart Rhythm Society (HRS) (2017).[7−10] In the present paper, we aimed to report the experience of a teaching hospital, and discuss our practice in the context of recently published guidelines.

Methods

This was a retrospective observational monocentric study, carried out at the European Georges Pompidou Hospital (Paris, France), between March 2006 and June 2017. We identified all consecutive patients who underwent RT, with a PM or an ICD. Detailed information on RT plan, as well as CIED characteristics at baseline and during regular follow-up were collected.

Regarding RT plan, information on the tumor location, the number of fractions, the type of external beam radiation (photons, electrons), and energy range (units of megavolt, MV) were collected. A radiation course can range from a single fraction to 8 to 9 weeks of daily treatment, depending

[a]Unité de Rythmologie, Département de Cardiologie, Hôpital Européen Georges Pompidou, Paris, France; [b]Université de Paris, PARCC, INSERM, F-75015 Paris, France; [c]Service de Radiothérapie, Hôpital Européen Georges Pompidou, Paris, France; [d]Unité de Cardio-Oncologie, Hôpital Européen Georges Pompidou, Paris, France; [e]Service de Cardiologie, Centre Hospitalier Annecy Genevois, France; and [f]Medicover Hospitals, Hyderabad, India. Manuscript received March 21, 2020; revised manuscript received and accepted April 27, 2020.

See page 200 for disclosure information.

*Corresponding author: Tel: +33 6 62 83 38 48; fax: +33 1 56 09 30 47.
E-mail address: eloi_marijon@yahoo.fr (E. Marijon).

0002-9149/
https://doi.org/10.1016/j.amjcard.2020.04.045

on the condition being treated. Currently, RT is mainly delivered by a medical linear accelerator, using photons and/or electrons beams. Secondary neutron producing beam includes 18-MV photons, whereas non-neutron producing include 6- or 10-MV photons, electrons only, and Cyberknife. Cumulative dose to the tumor and at the CIED were both estimated prior to RT. The unit of measurement for absorbed radiation dose (i.e., energy deposited) is the Gray (1 Gy = 1 J of absorbed energy from ionizing radiation per 1 kg of matter). When multiple regions were irradiated, the maximal prescription dose and associated fractionation were recorded. For clinical purposes, we divided the radiation exposure into 3 zones: zone 1 includes the head and the neck, zone 2 includes chest and pectoral regions, zone 3 includes abdomen and pelvic regions.

Regarding CIED information, data collected at baseline (pre-RT) included the type of device (PM, ICD), device location, device manufacturer, the number of leads, the primary indication for implantation, PM dependency (defined as intrinsic rhythm $\leq$ 30 bpm), and history of ventricular arrhythmias (for ICD recipients).[11,12]

All CIED follow-up data were systematically collected from medical reports, including overlying skin's condition, frequency of device interrogation, battery characteristics (residual voltage and impedance), lead parameters (impedance and pacing/sensing thresholds), and arrhythmia events using electrogram recording when available. Malfunction of the device included lead dysfunction, premature battery depletion, CIED reset in back-up mode or complete device failure, and inappropriate ICD therapy (as shocks or antitachycardia pacing).

We established a local protocol in 2006 in order to improve patient safety during RT.[13,14] All patients were systematically evaluated prior to RT initiation including CIED interrogation. CIED patients were classified as low-, intermediate- or high-risk.

Low-risk patients were those that fulfilled all of the 3 following criteria: (i) estimated cumulative dose to CIED <2 Gy; (ii) intrinsic rhythm >30 bpm (i.e., not pacing dependent) and (iii) without an ICD. Patients deemed as being intermediate-risk did not fulfill one of the former criteria but had no high-risk criteria. We classified as high-risk, patients whose cancer was in close proximity to the CIED device and/or receiving a cumulative CIED dose $\geq$ 5 Gy. In high-risk patients, repositioning of the device prior to RT was considered systematically. After CIED repositioning, patients could be subsequently reclassified, as low- or intermediate-risk. Monitoring protocols differed according to risk stratification.

During RT sessions, it was recommended that all patients have audiovisual and ECG monitoring as well as physicians' presence. Furthermore, a cardiologist or CIED clinician was available within a 10 minutes reach and an automatic external defibrillator was available on site. In addition, for intermediate- and high-risk patients, it was advised to systematically apply a magnet over the CIED to avoid any external interference leading to pacing inhibition or inappropriate ICD therapy, as well as to perform an ECG before and after each session.

Regarding follow-up, CIED interrogation was planned to be performed at the end of the RT treatment course, and at 1, 3, and 6 months post-RT follow-up visits. In addition, for intermediate- and high-risk patients, a systematic device interrogation was planned on a weekly basis regardless of the RT scheme.

Categorical data were reported as numbers and proportions. Continuous data were reported as mean $\pm$ standard deviation (SD) or median [IQR], when appropriate. All data were analyzed using R Project for Statistical Computing software (v 3.3.2). The authors had full access to and take full responsibility for the integrity of the data.

Results

Over the 11-year period, a total of 12,736 patients underwent RT in our center. Ninety (1%) patients had a CIED, including 82 PMs and 8 ICD. Principal indications for pacing were high-level atrioventricular block in 23 (31%), and sinus node dysfunction in the remaining patients (Table 1).

Prior to RT and according to our local protocol, 50 (56%) patients were assessed as being at low-risk of CEID dysfunction, 35 (39%) were classified as intermediate-risk and 4 (5%) patients were considered as high-risk. Two patients were originally classified in high-risk group, requiring PM extraction prior to RT for ipsilateral breast cancer. In 1 of those 2 patients, device replacement was not deemed necessary and was then excluded of the evaluation; the PM had been initially inserted for sinus node dysfunction with subsequently permanent atrial fibrillation with preserved atrioventricular conduction. The second patient required contralateral CIED reimplantation prior to RT, and was then reclassified in the intermediate-risk group. All patients in high-risk group received a cumulative dose to the CIED device of more than 5 Gy.

Overall, the median total dose delivered to the tumor was 49.5 [31.5;66.0] Gy with a median cumulative dose to the CIED device of 0.0 [0.0;0.7]. Neutron producing beams were delivered in 49 (55%) patients and non-neutron producing beams in 40 (45%). In the latter group, 1 received electron-only treatment, 2 received a combination of photons and electrons, and 2 treated by Cyberknife. Systematic cardiac monitoring during RT delivery was provided for all patients, and electrocardiograms (before and after radiation exposure, as recommended in the local policy) during RT were performed in 12 of the intermediate-and high-risk patients (31%). Only 3 patients in the intermediate-risk group and none in the high-risk group received magnet over the device during the RT sessions (3 out of 39, 8%). No significant clinical event was detected during and immediately after RT delivery.

CIED evaluation was available for 87 patients (97%). Overall, 56% had appropriate surveillance during follow-up. In high- and intermediate-risk groups, weekly CIED interrogations during RT were carried out as recommended by our local policy in 22 out of 39 (56%) patients. In addition, 20 of the 50 low-risk patients (40%) were followed on a weekly basis, though not required by our local protocol.

The follow-up at 1 month was available in 73 patients (91%), at 3 months in 66 (87%), at 6 months in 65 (81%) and at 12 months in 55 (79%). Overall, CIED malfunction occurred in 5 patients (6%), during a mean period of 21.5 $\pm$ 16.7 days from the start of RT. Of the 5 patients with CIED

Table 1
Patients CIED and RT characteristics

Variable	n = 90
Age (years)	78.1 ± 10.3
Men	66 (73%)
CIED characteristics	
Manufacturer	
Biotronik	8 (9%)
Boston Scientific	9 (10%)
Medtronic	19 (21%)
St Jude Medical / Abbott	8 (9%)
Sorin / Liva Nova / Microport	19 (21%)
Data not available	27 (30%)
Device type	
Implantable cardioverter defibrillator	8 (9%)
Pacemaker	82 (91%)
Cardiac resynchronization therapy	9 (11%)
PM dependency	35 (39%)
Level of risk (local policy)	50 (56%)
Low-risk group*	
Intermediate-risk group	35 (39%)
High-risk group	4 (5%)
Time of CIED in patient (years)	5.1 ± 6.2
RT characteristics	
Radiation exposure zone**	
1	18 (20%)
2	31 (34%)
3	41 (46%)
Neutron producing beam***	49 (55%)
Number of RT fractions	11.5 [1.0;25.0]
Total dose delivered to tumor (Gy)	49.5 [31.5;66.0]
Cumulative dose delivered to the CIED**** (Gy)	0.0 [0.0;0.7]
1	0.6 [0.0;2.7]
2	0.4 [0.1;1.0]
3	0.0 [0.0;0.0]
CIED interrogation during RT	
Weekly interrogation	42 (48%)

CIED = cardiac electronic implantable device; RT = radiotherapy treatment.

Values are expressed as mean ± SD, median [IQR] or n (%).

* Cumulative dose to CIED less than 2 Gy, not pacing dependency, without an ICD.

** Zone 1 includes the head and the neck, zone 2 includes chest and pectoral regions, zone 3 includes abdomen and pelvis region.

*** Neutron producing includes 15- or 18 MV photons, non-neutron producing includes 6- or 10-MV photons, electrons only, Cyberknife and Gamma Knife.

**** Cumulative dose delivered to the CIED planned with CT scan pretreatment evaluation.

malfunction, 1 had been classified as low-risk and 4 as intermediate-risk. None of them had permanent device damage (Table 2). CIED reset to back-up mode was observed in 4 cases, symptomatic in only 1 case (exercise-induced dyspnea). When weekly CIED interrogation was carried out (Cases 1, 3 and 4), the evaluations preceding the malfunction diagnosis were normal. During the median follow-up of 24 [3;102] months, no case of sudden cardiac death was reported in the entire population.

Discussion

In our series, we observed that severe CEID malfunction during and after RT were infrequent. The most frequent event was a resetting in back-up mode which was most often asymptomatic. Our findings also illustrate the inadequate adherence of physicians to local policies to detect potential adverse events in a timely fashion, and support the need for a more practical protocol as suggested by the recent 2017 HRS recommendations.

Several factors influence CIED malfunction associated with RT delivery. First, maximum cumulative dose to the CIED device is important and cutoffs have been proposed since the 1980s, with a 2 Gy threshold mentioned in the first guidelines supported by the American Association of Physicists in Medicine in 1994.[9,10,13,15] In line with our findings, where majority of CIED malfunctions occurred with very low cumulative dose delivered to the device, the 2 Gy cutoff remains debated and is no longer part of the recent HRS recommendations.[10] Second, a correlation between dose rate (defined as the absorbed dose per unit of time, Gy/min) and CIED malfunction has been proposed by Mouton et al[16] Nevertheless, Rodriguez et al reported dysfunctions due to dose rate to be mostly transient and reversible.[17] Third, more recent studies have focused on the importance of stochastic effects related to interactions with ionized particles, with especially neutrons produced from high energy beams (energy > 10 MV) recently being identified as the strongest predictor of dysfunction.[18–21] Neutrons are generated mainly in linear accelerator head through interactions of photons with nuclei of high atomic number materials.[22] Grant et al reported in a retrospective clinical study that all CIED malfunctions occurred with high-energy particles producing neutrons.[23] Although counter intuitive, the occurrence of CIED malfunction in patients undergoing pelvic RT, by definition far from the device, is explained by the secondary production of neutrons with high-energy particles.[23] In our study, 3 out of the 5 patients with CIED malfunctions had pelvic RT with 18 MV photon beam. Finally, in addition to the direct effect of radiation, the level of electromagnetic interference may play a role in the occurrence of transient oversensing, which could cause pacing inhibition or inappropriate ICD therapies (not observed in our study); however, this mechanism appears to be rare.

The infrequency of CIED malfunction (6%) reported in our study is in line with the largest published series of CIED patients undergoing RT.[9,19,21] Zaremba et al reported 3.1% CIED malfunctions, most frequently transient resetting, and Brambatti et al reported 1.5% CIED malfunctions with a median absorbed dose of 1.0 Gy [2.90;29.5].[19,21] Several national guidelines have been proposed in different countries.[3,8,9,24–26] Although existing algorithms differ to variable extents, the main criteria usually considered for risk stratification are (i) location of the CIED, (ii) maximal cumulative dose to the CIED (usually > 2 Gy), (iii) pacing dependency or presence of an ICD. In these patients, continuous monitoring during RT delivery is usually recommended with a CIED clinician available within a 10 minutes reach, as well as weekly CIED interrogation during follow-up.[24]

Recently, Indik et al under the auspices of the HRS have published a North-American consensus statement for better standardization.[10] Similar to previous guidelines, CIED relocation is not recommended for devices expected to receive a maximum cumulative incident dose <5 Gy. By

Table 2
CIED and RT characteristics in patients with CIED malfunction

Variable	Case 1	Case 2	Case 3	Case 4	Case 5
Age (years)	76.2	89.4	75.2	66.1	83.9
Sex	Female	Female	Male	Male	Female
Type of CIED malfunction	Reset in back-up mode	Reset in back-up mode	Ventricular oversensing in device event counter	Reset in back-up mode	Reset in back-up mode
Type of the device	PM	PM	PM	PM	ICD
Device manufacturer	Sorin	St Jude Medical	St Jude Medical	Biotronik	Biotronik
Time in patient (years)	1.9	1.2	1.0	7.8	5.1
Pacing dependency	No	Yes	Yes	Yes	No
Intermediate-risk group	No	Yes	Yes	Yes	Yes
Treatment site	Breast	Esophagus	Prostate	Prostate	Anal
RT Energy, MV	10	18	18	18	18
Neutron producing beam	No	Yes	Yes	Yes	Yes
Total delivered dose (Gy)	50	36	74	74	36
Cumulative dose delivered to the CIED (Gy)	NA	0	NA	0	0
Time to malfunction diagnosis (days)	39	2	11	39	18
Clinical symptoms	0	Bradycardia	0	0	0
Weekly CIED interrogation	Yes	No	Yes	Yes	No

CIED = cardiac electronic implantable device; ICD = implantable cardioverter defibrillator; PM = pacemaker; RT = radiotherapy treatment.

contrast, the energy beam is considered very early in the risk stratification algorithm (Figure 1). A non-neutron producing treatment is preferred, and if not possible, RT should be performed with asynchronous pacing (in pacing dependent patients) and/or ICD therapies deactivated and a weekly CIED interrogation during the course of RT is recommended.[8,24] Authors have published a checklist for allowing both electrophysiologists and RT physicians to better evaluate patient risk prior to RT (Figure 2). Considering our data, 62 (69%) patients would have required weekly follow-up according to 2017 HRS recommendation versus the 39 (43%) recommended using our local policy.

With regard to these current guidelines, availability of CIED clinicians and the public health resources needed for implementation in routine clinical practice need to be considered. In fact, a more sensitive risk stratification with frequent device monitoring could increase the workload for CIED clinicians and pose difficult organizational challenges for both cardiology and RT departments. This would explain why half of all patients in the intermediate-risk group in our study were not followed weekly as recommended while, a high proportion of patients in the low-risk group were followed closer than recommended.[27] In the future, remote CIED monitoring appears to be a safe

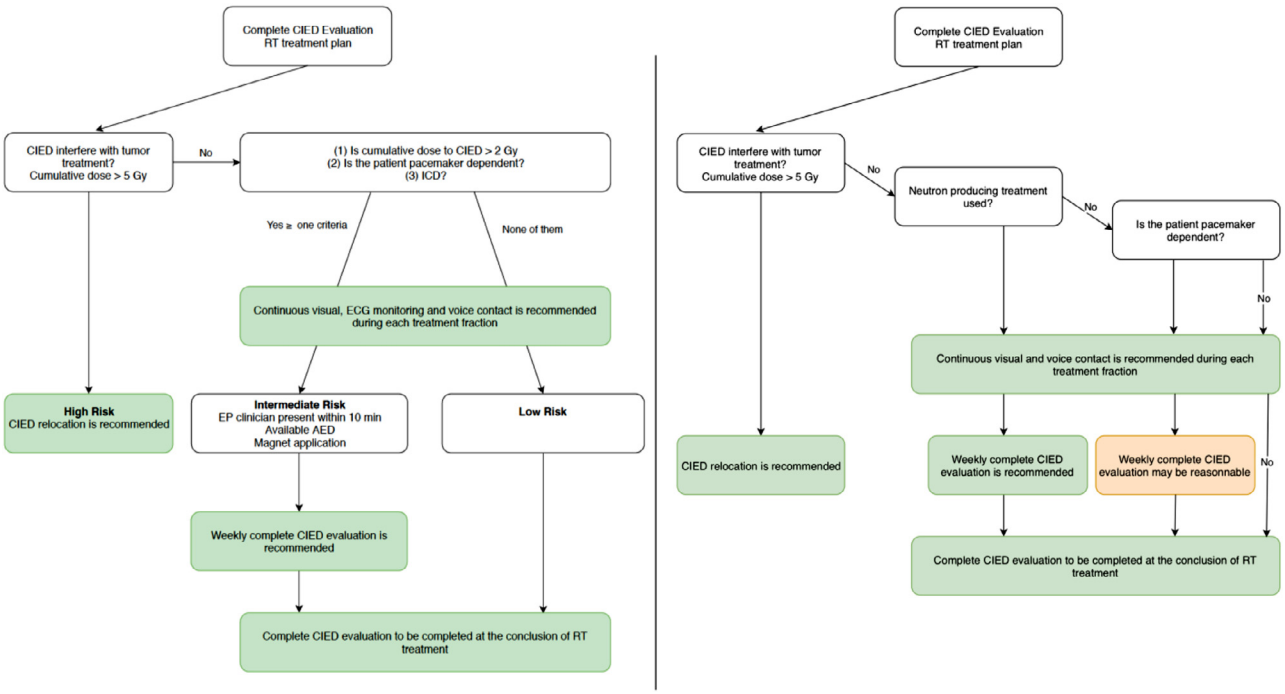

Figure 1. Comparative risk stratification algorithm for patients with CIED undergoing RT. *Left panel*: Algorithm at our Hospital Local Algorithm. *Right panel*: HRS 2017 Guidelines.[10]

	CIED CLINIC CHECKLIST
1	CIED implantation date:
2	CIED implant indication:
3	Device manufacturer and model:
4	Pacing-dependent *(intrinsic HR<40 bpm)*: Yes [ ] No [ ]
5	Complete weekly CIED evaluation recommended*: Yes [ ] No [ ]
6	System features: Pacemaker/CRT-P [ ] ICD/CRT-D [ ] Pacing mode: _____ Minimum pacing rate: _____ Maximum tracking rate: _____ Maximum sensor rate: _____ Measurements of the pacing system function and parameters are stable†: Yes [ ] No [ ]
7	CIED evaluation following completion of radiation therapy: Measurements of the pacing system function and parameters are stable†: Yes [ ] No [ ] Comments: _____
	RADIATION CLINIC CHECKLIST
8	Type of radiation course: Neutron-producing‡: Yes [ ] No [ ] CIED location might interfere with adequate tumor treatment§: Yes [ ] No [ ] Maximum expected cumulative incident dose <5 Gy‖: Yes [ ] No [ ]

HR = heart rate; CRT-P = cardiac resynchronization therapy-pacemaker; CRT-D = cardiac resynchronization therapy with implantable cardioverter defibrillator; CIED = cardiac implantable electronic device.
*It is recommended to perform a weekly CIED evaluation for patients undergoing neutron-producing treatment and might be reasonable for pacing-dependent patients undergoing non-neutron producing treatment;
† Device function pacing output, pacing thresholds, sensing of T and P waves, lead impedance, battery voltage and impedance;
‡ Non-neutron producing radiation is preferred (neutron producing: > 10 mV photons, protons, electrons ≥ 20 MeV);
x CIED relocation is recommended if it will interfere with adequate tumor treatment;
II CIED relocation is not recommended for devices receiving a max cumulative incident dose of <5 Gy.

Figure 2. Checklist prior to radiation treatment (from HRS 2017 Guidelines).[10]

solution for patients requiring weekly CIED interrogation, simplifying and optimizing the follow-up for patients and clinicians without increasing significantly their workload.

Although data on CIED and RT are scarce, we need to acknowledge several limitations of our study. First, it is an observational retrospective study. Second, it is a single center experience providing data on a relatively small number of patients with an even smaller event rate, not allowing further analysis of factors associated with CIED malfunction. Finally, some proportion of patients were lost to follow-up. However, no sudden cardiac death occurred, making undetected late severe CIED malfunction unlikely.

In conclusion, our findings underline the lack of rigorous monitoring and follow-up of CIED patients undergoing RT, although CIED malfunction remains a rare event, relatively benign in nature. Optimization of local policies, especially the consideration of the energy beam type, could potentially simplify monitoring without compromising patient safety. In this setting, a close collaboration between CIED clinicians and radiation oncologists, and finally, more systematic use of remote CIED monitoring may be of substantial value.

Authors' contribution

Ardalan Sharifzadehgan: Conceptualization, Data curation, Methodology, Software, Writing and Editing; Marc Laurans: Data curation, Reviewing; Marine Thuillot: Visualization, Investigation, Reviewing; Andres Huertas: Visualization, Investigation; Pierre Baudinaud: Visualization, Investigation; Mariana Mirabel: Reviewing; Jean-Emmanuel Bibault: Reviewing; Pierre Frey: Reviewing; Victor Waldmann: Visualization, Investigation; Emilie Varlet: Visualization, Investigation; Denis Amet: Visualization, Investigation; Christophe Juin: Visualization, Investigation; Thomas Lavergne: Visualization, Investigation; Xavier Jouven: Supervision; Philippe Giraud: Supervision; Catherine Durdux: Supervision, Reviewing; Eloi Marijon: Supervision, Conceptualization, Methodology, Writing and Editing.

Disclosures

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.

1. Mond HG, Proclemer A. The 11th world survey of cardiac pacing and implantable cardioverter-defibrillators: calendar year 2009−a World Society of Arrhythmia's project. *Pacing Clin Electrophysiol* 2011;34:1013–1027.
2. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JWW, Comber H, Forman D, Bray F. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. *Eur J Cancer* 2013;49:1374–1403.
3. Möller TR, Brorsson B, Ceberg J, Frödin J-E, Lindholm C, Nylén U, Perfekt R, SBU Survey Group. A prospective survey of radiotherapy practice 2001 in Sweden. *Acta Oncol* 2003;42:387–410.
4. Borras JM, Lievens Y, Dunscombe P, Coffey M, Malicki J, Corral J, Gasparotto C, Defourny N, Barton M, Verhoeven R, Eycken L van, Primic-Zakelj M, Trojanowski M, Strojan P, Grau C. The optimal utilization proportion of external beam radiotherapy in European countries: an ESTRO-HERO analysis. *Radiother Oncol* 2015;116:38–44.
5. Zamorano JL, Lancellotti P, Rodriguez Muñoz D, Aboyans V, Asteggiano R, Galderisi M, Habib G, Lenihan DJ, Lip GYH, Lyon AR, Lopez Fernandez T, Mohty D, Piepoli MF, Tamargo J, Torbicki A, Suter TM, ESC Scientific Document Group. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC committee for practice guidelines: the task force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). *Eur Heart J* 2016;37:2768–2801.
6. Armenian SH, Lacchetti C, Barac A, Carver J, Constine LS, Denduluri N, Dent S, Douglas PS, Durand J-B, Ewer M, Fabian C, Hudson M, Jessup M, Jones LW, Ky B, Mayer EL, Moslehi J, Oeffinger K, Ray K, Ruddy K, Lenihan D. Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol* 2017;35:893–911.
7. Lenarczyk R, Potpara TS, Haugaa KH, Deharo J-C, Hernandez-Madrid A, Del Carmen Exposito Pineda M, Kiliszek M, Dagres N. Approach to cardio-oncologic patients with special focus on patients with cardiac implantable electronic devices planned for radiotherapy: results of the European Heart Rhythm Association survey. *Europace* 2017;19:1579–1584.
8. Gauter-Fleckenstein B, Israel CW, Dorenkamp M, Dunst J, Roser M, Schimpf R, Steil V, Schäfer J, Höller U, Wenz F, DEGRO/DGK. DEGRO/DGK guideline for radiotherapy in patients with cardiac implantable electronic devices. *Strahlenther Onkol* 2015;191:393–404.
9. Zaremba T, Jakobsen AR, Søgaard M, Thøgersen AM, Riahi S. Radiotherapy in patients with pacemakers and implantable cardioverter defibrillators: a literature review. *Europace* 2016;18:479–491.
10. Indik JH, Gimbel JR, Abe H, Alkmim-Teixeira R, Birgersdotter-Green U, Clarke GD, Dickfeld T-ML, Froelich JW, Grant J, Hayes DL, Heidbuchel H, Idriss SF, Kanal E, Lampert R, Machado CE, Mandrola JM, Nazarian S, Patton KK, Rozner MA, Russo RJ, Shen W-K, Shinbane JS, Teo WS, Uribe W, Verma A, Wilkoff BL, Woodard PK. 2017 HRS expert consensus statement on magnetic resonance imaging and radiation exposure in patients with cardiovascular implantable electronic devices. *Heart Rhythm* 2017;14:e97–e153.
11. Lelakowski J, Majewski J, Bednarek J, Małecka B, Zabek A. Pacemaker dependency after pacemaker implantation. *Cardiol J* 2007;14:83–86.
12. Korantzopoulos P, Letsas KP, Grekas G, Goudevenos JA. Pacemaker dependency after implantation of electrophysiological devices. *Europace* 2009;11:1151–1155.
13. Marbach JR, Sontag MR, Van Dyk J, Wolbarst AB. Management of radiation oncology patients with implanted cardiac pacemakers: report of AAPM task group no. 34. American Association of Physicists in Medicine. *Med Phys* 1994;21:85–90.
14. Huertas A, Thuillot M, Bibault J-E, Sharifzadehgan A, Laurans M, Giraud P, Lavergne T, Marijon É, Durdux C. Management of patients with pacemakers or implantable cardioverter defibrillator undergoing radiotherapy. *Cancer Radiother* 2018;22:515–521.
15. Souliman SK, Christie J. Pacemaker failure induced by radiotherapy. *Pacing Clin Electrophysiol* 1994;17:270–273.
16. Mouton J, Haug R, Bridier A, Dodinot B, Eschwege F. Influence of high-energy photon beam irradiation on pacemaker operation. *Phys Med Biol* 2002;47:2879–2893.
17. Rodriguez F, Filimonov A, Henning A, Coughlin C, Greenberg M. Radiation-induced effects in multiprogrammable pacemakers and implantable defibrillators. *Pacing Clin Electrophysiol* 1991;14:2143–2153.
18. Zaremba T, Jakobsen AR, Thøgersen AM, Riahi S, Kjærgaard B. Effects of high-dose radiotherapy on implantable cardioverter defibrillators: an in vivo porcine study. *Pacing Clin Electrophysiol* 2013;36:1558–1563.
19. Zaremba T, Jakobsen AR, Søgaard M, Thøgersen AM, Johansen MB, Madsen LB, Riahi S. Risk of device malfunction in cancer patients with implantable cardiac device undergoing radiotherapy: a population-based cohort study. *Pacing Clin Electrophysiol* 2015;38:343–356.
20. Zaremba T, Jakobsen AR, Thøgersen AM, Oddershede L, Riahi S. The effect of radiotherapy beam energy on modern cardiac devices: an in vitro study. *Europace* 2014;16:612–616.
21. Brambatti M, Mathew R, Strang B, Dean J, Goyal A, Hayward JE, Long L, DeMeis P, Smoke M, Connolly SJ, Morillo CA, Amit G, Capucci A, Healey JS. Management of patients with implantable cardioverter-defibrillators and pacemakers who require radiation therapy. *Heart Rhythm* 2015;12:2148–2154.
22. Naseri A, Mesbahi A. A review on photoneutrons characteristics in radiation therapy with high-energy photon beams. *Rep Pract Oncol Radiother* 2010;15:138–144.
23. Grant JD, Jensen GL, Tang C, Pollard JM, Kry SF, Krishnan S, Dougherty AH, Gomez DR, Rozner MA. Radiotherapy-induced malfunction in contemporary cardiovascular implantable electronic devices: clinical incidence and predictors. *JAMA Oncol* 2015;1:624–632.
24. Hurkmans CW, Knegjens JL, Oei BS, Maas AJJ, Uiterwaal GJ, Borden AJ van der, Ploegmakers MMJ, Erven L van, Dutch Society of Radiotherapy and Oncology (NVRO). Management of radiation oncology patients with a pacemaker or ICD: a new comprehensive practical guideline in The Netherlands. Dutch Society of Radiotherapy and Oncology (NVRO). *Radiat Oncol* 2012;7:198.
25. Salerno F, Gomellini S, Caruso C, Barbara R, Musio D, Coppi T, Cardinale M, Tombolini V, Paula U de. Management of radiation therapy patients with cardiac defibrillator or pacemaker. *Radiol Med* 2016;121:515–520.
26. Soejima T, Yoden E, NIshimura Y, Ono S, Yoshida A, Fukuda H, Fukuhara N, Sasaki R, Tsujino K, Norihisa Y. Radiation therapy in patients with implanted cardiac pacemakers and implantable cardioverter defibrillators: a prospective survey in Japan. *J Radiat Res* 2011;52:516–521.
27. Bravo-Jaimes K, Samala V, Fernandez G, Moravan MJ, Dhakal S, Shah AH, Messing S, Singh K, Aktas MK. CIED malfunction in patients receiving radiation is a rare event that could be detected by remote monitoring. *J Cardiovasc Electrophysiol* 2018;29:1268–1275.